



Metabolic syndrome among older adults with schizophrenia spectrum disorder: Prevalence and associated factors in a multicenter study



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ABSTRACT

Metabolic syndrome and its associated morbidity and mortality have been well documented in adults with schizophrenia. However, data is lacking for their geriatric counterparts. We sought to investigate the frequency of screening and the prevalence of metabolic syndrome in older adults with schizophrenia, as well as its possible correlates, using the Cohort of individuals with schizophrenia Aged 55 years or more study ($n = 353$). We found that 42.2% ($n = 149$) of our sample was screened for metabolic syndrome. Almost half of those ($n = 77$; 51.7%) screened positive according to ATPIII criteria. Hypertension and abdominal obesity were the two most prevalent metabolic abnormalities. Screening was positively associated with male gender and urbanicity, and metabolic syndrome diagnosis was positively associated with cardiovascular disorders and consultation with a general practitioner (all $p < 0.05$). However, there were no significant associations of metabolic syndrome with socio-demographic or clinical characteristics, psychotropic medications, other medical conditions and other indicators of mental health care utilization. Our findings support that the prevalence of metabolic syndrome among older adults with schizophrenia spectrum disorder is high and screening is crucial mainly in those patients with hypertension and/or abdominal obesity. Factors at play might be different than those in the younger population.

1. Introduction

One in three schizophrenia patients suffers from a co-morbid metabolic syndrome (Mitchell et al., 2013). Rates of metabolic syndrome are increased in these individuals, to the point of being comparable to that of the general population when 10–15 years older (Bobes et al., 2007). In addition to the hypothesized common genetic basis for schizophrenia and metabolic disturbances, environmental factors are established contributors of metabolic syndrome (Gough and O'Donovan,

2005; Saha et al., 2007). Dietary habits, sedentary lifestyle and smoking increase the risk of metabolic syndrome and may have an additive effect on the antipsychotics' adverse effects (Correll et al., 2015; Matta et al., 2019; Mitchell et al., 2013; Scigliano and Ronchetti, 2013). The latter were found to negatively alter lipid and glucose profiles, even independently of their adverse influence on weight (Bak et al., 2014; Correll et al., 2015).

The difference in life expectancy between individuals suffering from schizophrenia and the general population can be up to two decades

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(Crump et al., 2013; Tiihonen et al., 2009). This high mortality rate may be due in large part to cardiovascular diseases (CVD) (Crump et al., 2013), including coronary heart disease, stroke and heart failure (Arango et al., 2008; Goff et al., 2005). Schizophrenia patients are also less likely to seek medical care (Cradock-O'Leary et al., 2002) and more likely to face delays before accessing general medical services (Mojtabai et al., 2014), which is associated with poorer health status, under-diagnosis and increased mortality (Crump et al., 2013; Hoertel et al., 2014; Mojtabai et al., 2014). Even when medical care is sought, poor compliance to cardiovascular medications affects more than a third of schizophrenia patients (Dolder et al., 2003; Owen-Smith et al., 2016), and behavioral interventions such as exercising may be hindered by negative symptoms. The “Cardiovascular, Lipid and Metabolic Outcomes Research in Schizophrenia Study” (CLAMORS) has provided alarming estimates of CVD risk and mortality, which in turn were found associated with the presence of metabolic syndrome (Arango et al., 2008). This is in line with well-established findings in the general population linking cardiovascular mortality and metabolic syndrome, with a relative risk ranging from 1.23 to 1.60 (Ford, 2005; Galassi et al., 2006; Gami et al., 2007; Ju et al., 2017). Additionally, metabolic syndrome represents a substantial burden to the healthcare system (Nichols and Moler, 2011).

Most available studies on metabolic syndrome in schizophrenia include young and middle-aged patients and typically exclude older persons. However, the high mortality of individuals with schizophrenia prevails in later life (Cohen et al., 2015) and may be due mainly to high rates of CVD. In fact, metabolic syndrome is associated with a relative risk of CVD mortality of 1.24 in the elderly (Ju et al., 2017). Furthermore, longitudinal studies conducted in the geriatric population have linked metabolic syndrome with increased likelihood of decline in global cognitive function and visual working memory, as well as with 7 years incident disability (Carriere et al., 2014; Raffaitin et al., 2011). The latter finding entails social restriction, limitation in mobility and alteration in instrumental activities of daily living, independently of the presence of dementia and cardiovascular diseases (Carriere et al., 2014).

To our knowledge, only one study to date has evaluated the prevalence of metabolic syndrome in geriatric patients with severe mental illness (Konz et al., 2014). Among 48 schizophrenia older patients and 52 bipolar older patients, there was no significant difference in the prevalence of metabolic syndrome in comparison to the age-matched general population in the full sample and in the subsamples of older participants with bipolar disorder and schizophrenia (Konz et al., 2014). However, this finding may be related to insufficient statistical power or reflect merely a survival bias or may emanate from a plateau effect beyond a certain age. In addition, no study to our knowledge has examined if the prevalence of metabolic syndrome among older adults with schizophrenia spectrum disorder varies across socio-demographic characteristics and clinical correlates. Therefore, research using a larger multicenter sample of older adults with schizophrenia spectrum disorder may help provide a more precise estimation of the prevalence of metabolic syndrome in this population and a better understanding of its related clinical characteristics. This knowledge may help improve early recognition and treatment of metabolic syndrome in this vulnerable population.

To address this gap in the literature, we examined the characteristics of a large multicentric sample of adults with schizophrenia spectrum disorder. Our aims were threefold: (i) to examine the frequency of screening of metabolic syndrome criteria in real clinical settings, (ii) to determine the prevalence of metabolic syndrome in the group of participants who underwent this screening, and (iii) to examine potential associations of metabolic syndrome with socio-demographic characteristics, clinical characteristics of schizophrenia, psychiatric and other medical co-morbidities, psychotropic medications, mental health care utilization, quality of life and overall functioning.

We hypothesized that schizophrenia spectrum disorder patients are

under-screened for the presence of metabolic syndrome components. We also hypothesized that the prevalence of metabolic syndrome in this population is high and is related to clinical severity of the disorder.

2. Methods

2.1. Sample

Cross-sectional data were drawn from the CSA study, a cohort of 353 inpatients (34.1%, mean duration of hospitalization = 134.7 days (SD = 133.0)) or outpatients (65.9%), aged 55 to 86 years with schizophrenia spectrum disorder, which included people with an International Classification of Diseases, Tenth edition (ICD-10) diagnosis of schizophrenia (82.4%) or schizoaffective disorder (17.6%) (Hoertel et al., 2019; Schuster et al., 2019). Participants were recruited between February 2010 and June 2013 from 63 French state hospital psychiatric departments, each of them covering one mutually independent catchment area (Raucher-Chéné et al., 2015). We decided to include patients aged of at least 55 years of age because the life expectancy of patients with schizophrenia is reduced by 15 to 25 years and given their presumed accelerated aging (Wildgust et al., 2010). In France, state hospitalization services are organized into “sectors”. Each psychiatric sector is in charge of the mental health of a mutually independent catchment area comprising a mean population of 54,000 inhabitants aged over 20 years, with a total of 839 sectors for adults across France (Verdoux, 2007). Each sector disposes of psychiatric beds in one French state hospital, which could be either a general or a psychiatric hospital, and provides outpatient psychiatric treatment in Community Mental Health Centers (CMHCs), free of charge. French patients can also freely consult a private psychiatrist and choose to be hospitalized in another private or public hospital offering inpatient psychiatric care. Compulsory hospitalizations, however, have to take place in the French state hospital of the sector, apart from certain exceptions. The primary aims of this organization were to ensure that any subject living in France has easy access to a mental health service, and to promote the development of prevention and community care by an identified team (Verdoux, 2007). Details about the organization of the French mental health care system can be found elsewhere (Verdoux, 2007). Exclusion criteria included having limited French proficiency, not being affiliated to the social security system, meeting ICD-10 criteria for any pervasive developmental disorder or major neurocognitive disorder, and having any neurological disorder affecting the central nervous system or any serious, life threatening medical or surgical condition that requires immediate treatment. Each participant was interviewed face-to-face by his/her treating psychiatrist, who collected all clinical data. The research protocol, including informed consent procedures, was conducted in accordance with the Declaration of Helsinki ethical guidelines, and received full ethical review and approval from the local research ethics committee, the Advisory Committee on Information Processing in Material Research in the Field of Health and the National Board on Computerized Information and Freedoms.

2.2. Assessment of schizophrenia spectrum disorder

Diagnoses of schizophrenia and schizoaffective disorder were established face-to-face by the treating psychiatrist following the ICD-10 criteria. Age at first psychotic symptoms was retrospectively investigated and the duration of the disorder was estimated.

2.3. Assessment of metabolic syndrome

Investigators were asked whether the participant had a measure of blood pressure and waist circumference and a blood test in the past year and had to detail all results. All these data were extracted from the patient's electronic health record.

Metabolic syndrome diagnosis was assessed during the year preceding the interview following the revised criteria of the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATPIII) (Eckel et al., 2005; Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults, 2001; Grundy et al., 2005). This diagnosis requires three or more alterations of the following five domains: abdominal obesity, triglycerides, HDL cholesterol, blood pressure and fasting glucose. ATPIII cut-off values to define these alterations are as follows: waist circumference >102 cm for men and >88 cm for women, triglycerides \geq 150 mg/dl or specific treatment for this lipid abnormality, HDL cholesterol <40 mg/dl for men and <50 mg/dl for women or specific treatment for this lipid abnormality, blood pressure \geq 130/ \geq 85 mm Hg or treatment of previously diagnosed hypertension, and fasting glucose \geq 100 mg/dl or previously diagnosed type 2 diabetes. Following this definition, participants with alterations in at least three domains were defined as having a metabolic syndrome even if the measure of 1 or 2 criteria was missing. Similarly, individuals with no alteration in at least three domains were considered as not having a metabolic syndrome, even if the measure of 1 or 2 criteria was missing. Finally, individuals for whom the measure of at least 3 domains was missing were considered as not having been evaluated for the presence of metabolic syndrome.

2.4. Socio-demographic and clinical characteristics

2.4.1. Socio-demographic characteristics

Socio-demographic characteristics included gender, age, education, marital status, parenthood and urbanicity (defined as living in an area comprising more than 1000 inhabitants per km²). The age of the participants was categorized into one of three groups: 55–64 years; 65–74 years and 75–86 years.

2.4.2. Assessment of the severity of the disorder and psychiatric comorbidity

Severity of the disorder and psychiatric comorbidity was measured using the Brief Psychiatric Rating Scale (BPRS) and the Clinical Global Impression (CGI) scale. The Brief Psychiatric Rating Scale (BPRS) (Overall, Gorham, 1962), a well-validated 18-item scale (Leucht et al., 2005), was used to measure general psychiatric symptoms, including affective, positive and negative symptoms. Each symptom is rated from 1 (absence) to 7 (severe). In our study, internal consistency reliability of the BPRS scale was good, with Cronbach's alpha = 0.85. The CGI scale is a 7-point scale with a range of responses from 1 (amongst the less severely ill patients) to 7 (amongst the most severely ill patients) (Guy, 1976). This scale asks the clinicians to rate the patient from their past experience with other patients with the same diagnosis. Depression was measured using the Center of Epidemiologic Studies Depression scale (CES-D) (Radloff, 1977). This 20-item questionnaire has been designed for use in community studies (Airagnes et al., 2016; Matta et al., 2018; Radloff, 1977; Shafer, 2006; Vulser et al., 2018) and has been validated in adult samples with psychiatric disorders (Furukawa et al., 1997; Herniman et al., 2017; Shafer, 2006; Zich et al., 1990). Based on the validation of the French version of the CES-D (Morin et al., 2011), a global score of \geq 19 was used as primary indicator of depression. In our study, internal consistency reliability of the CES-D scale was acceptable, with Cronbach's alpha = 0.72.

Current smoking status was recorded. At-risk alcohol consumption was evaluated using the CAGE questionnaire (Ewing, 1984; Kitchens, 1994). All participants were also asked whether they ever attempted suicide and whether they attempted suicide during the year preceding the interview.

2.4.3. Psychotropic medications

For each participant, all psychotropic medications prescribed at the time of the interview, in particular antipsychotics, antidepressants and benzodiazepines were recorded. We converted all antipsychotic doses to chlorpromazine equivalents, using published equivalencies for oral

conventional (American Psychiatric Association, 1997) and atypical (Woods, 2003) antipsychotics.

2.4.4. Mental health care utilization

The lifetime and past-year number of hospitalizations in a psychiatric department was recorded at the time of the interview.

2.4.5. Medical conditions

The number of comorbid non-psychiatric medical conditions (e.g., cardiovascular disorder, cancer) was recorded for all participants at the time of the interview. Investigators were asked whether the participant consulted a general practitioner, had an electrocardiogram or was hospitalized in a non-psychiatric medical department in the past year.

2.4.6. Overall functioning, cognitive functioning and institutionalization

The Global Assessment of Functioning (GAF) scale (Endicott et al., 1976) was used for evaluating the overall social, occupational, and psychological functioning of participants. Scale scores range from 0 to 100 with higher scores signifying better functioning. Prior studies support the reliability and convergent validity of the GAF scale scores in populations with psychiatric disorders (Jones et al., 1995). The Mini-Mental Status Examination (MMSE) (Folstein et al., 1975) was used for evaluating cognitive impairment. In our study, internal consistency reliability of the GAF and MMSE scores was good (Cronbach's alpha = 0.87 and 0.93, respectively).

Long-term institutionalization was also assessed. In this study, long-term institutionalization was defined as living in a dwelling that offers some form of formal supervision, including nursing homes, homes for the aged, hospital stays longer than 3 months, chronic care beds, and psychiatric institutions (Hébert et al., 2001). Temporary admission for convalescence or rehabilitation was not considered as institutionalization.

2.4.7. Quality of life

We used the Quality of Life Scale (QLS) (Heinrichs et al., 1984), an instrument widely used to assess quality of life in clinical studies of schizophrenia (Lehman, 1996). The QLS has 21 items rated on a 7-point scale from 0 to 6 with descriptive anchors; higher scores reflect higher quality of life (Heinrichs et al., 1984). In our study, internal consistency reliability of the QLS was excellent (Cronbach's alpha = 0.91).

2.5. Statistical analyses

Percentages and means (\pm standard deviation (SD)) were estimated to provide descriptive information on socio-demographic and clinical characteristics, psychiatric and other medical co-morbidity, quality of life and overall functioning, psychotropic medications and mental health care utilization in older adults with schizophrenia spectrum disorder between those who had been screened for metabolic syndrome versus those who did not, and between those with and without metabolic syndrome. Between-group differences regarding individual factors were tested using *t*-tests or unequal variance *t*-tests (if the null hypothesis of equality of variances was rejected by the *F*-test) for continuous variables, or chi-square tests for categorical variables. Next, we performed multivariable logistic regression analyses focused on the effects of physical health features and monitoring, severity of disorder and psychiatric co-morbidity, cognitive and social functioning and mental health care utilization on the dependent variables “metabolic syndrome” and “screening for metabolic syndrome”, while adjusting for potential confounders defined *a priori* (i.e., age, sex, duration of the schizophrenia spectrum disorder, current smoking status and at-risk drinking). To reduce the risk of type I error due to multiple testing, these multivariable logistic regression analyses were only performed when the crude associations (estimated using *t*-tests or unequal variance *t*-tests or chi-square tests as described above) were significant. For all regression models, we examined potential collinearity problem by

performing collinearity diagnostics produced by linear regressions with the option tolerance and variance inflation factor. Because our tests were generally exploratory in this understudied population, statistical significance was evaluated using a two-sided design with alpha risk set *a priori* at 0.05. Statistical analyses were performed using PASW Statistics 18 software (IBM Corp., Armonk, NY, USA, released 2009).

2.6. Missing data

The mean percentage of missing data was 1.5%. Missing data were imputed using Markov chain Monte Carlo (MCMC) methods (Schafer, 1997). All significant results remained unchanged in sensitivity analyses excluding respondents with missing data.

2.7. Supplementary analyses

To examine the robustness of our findings on correlates of metabolic syndrome among older adults with schizophrenia spectrum disorder, we conducted the same analyses in the full sample while imputing data for metabolic criteria, including participants for whom the measure of at least 3 criteria for metabolic syndrome was missing. We also performed a multivariable logistic regression model examining simultaneously the effects of all variables with a bivariate association at p -value < 0.20 on the risk of metabolic syndrome.

3. Results

3.1. Screening for metabolic syndrome

We found that metabolic syndrome had been searched for in 42.2% ($n = 149$) of older adults with schizophrenia spectrum disorder. The screening was significantly more likely to be performed in men, in those living in an area comprising less than 1000 inhabitants per km², and in patients who had at least one blood test in the past-year (eTables 1–4). Other socio-demographic characteristics, clinical characteristics, psychotropic medications and medical conditions, psychiatric co-morbidity, history of suicide attempt, institutionalization and mental health care utilization did not significantly contribute to the likelihood of the screening of metabolic syndrome.

3.2. Prevalence of metabolic syndrome

Among the 149 older adults with schizophrenia spectrum disorder for whom the presence of metabolic syndrome was examined, 51.7% ($n = 77$) fulfilled the NCEP-ATPIII criteria for metabolic syndrome. Particularly, the prevalence of metabolic syndrome was 42.9% and 63.6% at 55–60 years, 48.1% and 51.4% at 61–70 years, and 50.0% and 66.7% >70 years of age, respectively, among men and women. Prevalence rates of metabolic syndrome components among those with and without metabolic syndrome are given in Table 1. Hypertension and abdominal obesity were the two most prevalent metabolic abnormalities in the group of participants with metabolic syndrome.

3.3. Correlates of metabolic syndrome

There were no significant associations of metabolic syndrome with any socio-demographic characteristics (Table 2) nor with the duration of the disorder. Most notably, its prevalence did not differ by gender or by age. There was no significant difference between patients with metabolic syndrome and those without regarding the number of antipsychotics prescribed, their type (typical vs atypical) or their dosage (Table 3). The presence of metabolic syndrome was positively associated with cardiovascular disorders (Table 4). In spite of its association with CVD, no association was found with the monitoring of cardiac status by electrocardiogram, or with past-year hospitalization in a non-psychiatric department. However, we found a significant association

Table 1

Frequency of metabolic syndrome criteria in older participants with schizophrenia spectrum disorder with and without metabolic syndrome ($N = 353$).

	Metabolic syndrome ^a ($n = 77$; 21.8%)	No metabolic syndrome ($n = 72$; 20.4%)	No screening for metabolic syndrome ($n = 204$; 57.8%)
	n (%)	n (%)	n (%)
Abdominal obesity			
Yes	62 (80.5)	28 (38.9)	100 (48.5)
No	12 (15.6)	40 (55.6)	68 (33.3)
Missing data	3 (3.9)	4 (5.6)	37 (18.1)
Triglycerides abnormality			
Yes	40 (51.9)	2 (2.8)	2 (1.0)
No	26 (33.8)	63 (87.5)	14 (6.9)
Missing data	11 (14.3)	7 (9.7)	188 (92.2)
Fasting glucose abnormality			
Yes	41 (53.2)	10 (13.9)	14 (6.9)
No	31 (40.3)	55 (76.4)	36 (17.6)
Missing data	5 (6.5)	7 (9.7)	154 (75.5)
HDL cholesterol abnormality			
Yes	44 (57.1)	6 (8.3)	6 (2.9)
No	20 (26.0)	55 (76.4)	7 (3.4)
Missing data	13 (16.9)	11 (15.3)	191 (93.6)
Hypertension			
Yes	73 (94.8)	31 (43.1)	139 (68.1)
No	4 (5.2)	40 (55.6)	54 (26.5)
Missing data	0 (0.0)	1 (1.4)	11 (5.4)

^a Metabolic syndrome was defined following ATPIII criteria as described in the Methods. Individuals with an alteration in at least three of the 5 domains were considered as having metabolic syndrome; individuals with no alteration in at least three of these domains were considered as not having metabolic syndrome; individuals for whom the measure of at least three domains was missing were considered as not having been evaluated for the presence of metabolic syndrome.

between metabolic syndrome and consultation with a general practitioner but not with the mean number of visits. No correlation was found between metabolic syndrome and smoking, alcohol consumption or other physical conditions. Finally, the severity of the schizophrenia spectrum disorder, psychiatric co-morbidities and suicidal history, cognitive and social functioning, institutionalization and mental health care utilization were not related to the presence of metabolic syndrome in our sample (Table 5). In all multivariable logistic regressions, the variance inflation factor and tolerance values of each predictor variable were respectively lower than 2.5 and higher than 0.2, supporting that multicollinearity was not a concern (Midi et al., 2010) (eTable 10).

3.4. Supplementary analyses

Among the 204 individuals for whom less than 3 ATPIII criteria were screened, the mean percentage of missing data was 32.3%. Analyses conducted in the full sample of older adults with schizophrenia spectrum disorder using imputed data indicated very similar results, suggesting the robustness of our findings (eTables 5–9). In those analyses, the prevalence of metabolic syndrome was 43.6%.

When examining simultaneously the effects of all variables with a bivariate association at p -value < 0.20 on the risk of metabolic syndrome, we found that the presence of metabolic syndrome was positively associated with cardiovascular disorders and consultation with a general practitioner both in the sample excluding participants for whom less than 3 ATPIII criteria were screened and in the full sample using imputed data, and with current antipsychotic dosage only in the full sample using imputed data (eTables 11 and 12).

4. Discussion

To our knowledge, this is the largest study reporting on the screening for metabolic syndrome, its prevalence and its clinical correlates in older adults with schizophrenia spectrum disorder. We found

Table 2
Sociodemographic characteristics associated with metabolic syndrome in older participants with schizophrenia spectrum disorder ($N = 149$).

	Metabolic syndrome ($n = 77$; 51.7%)	No metabolic syndrome ($n = 72$; 48.3%)		
<i>Sociodemographic characteristics</i>	<i>n (%)</i>	<i>n (%)</i>	χ^2 test (df)	<i>p</i> -value
Sex			1.31 (1)	0.253
Men	41 (53.2)	45 (62.5)		
Women	36 (46.8)	29 (37.5)		
Education			1.60 (2)	0.449
Less than high school	52 (67.1)	45 (62.5)		
High school	10 (13.2)	15 (20.8)		
College or higher	15 (19.7)	12 (16.7)		
Marital status			5.23 (3)	0.156
Married or as if married	19 (24.7)	8 (11.1)		
Divorced or separated	15 (19.5)	14 (19.4)		
Widowed	6 (7.8)	5 (6.9)		
Never married	37 (48.1)	45 (62.5)		
Parenthood	36 (46.8)	25 (34.7)	2.23 (1)	0.136
Urbanicity ^a	59 (76.3)	46 (63.9)	2.73 (1)	0.098
Age			0.19 (2)	0.910
55–64	36 (46.8)	32 (44.4)		
65–74	33 (42.9)	31 (43.1)		
75–86	8 (10.4)	9 (12.5)		
	Mean (SD)	Mean (SD)	$t^{\#}$	<i>p</i> -value
Duration of disorder	38.3 (10.8)	35.6 (12.2)	1.14	0.256

^a Urbanicity was defined as living in an area comprising more than 1000 inhabitants per km².

Continuous variables are presented as their mean values and standard deviation (SD). Categorical variables are presented as percentages.

[#] t -test or unequal variance t -test (df = 147).

that less than half ($n = 149$; 42.2%) of older adults with schizophrenia spectrum disorder were evaluated for metabolic syndrome in clinical settings. Among those for whom the presence of metabolic syndrome was examined, more than half of them ($n = 77$; 51.7%) screened positive. Following the imputation of missing data, this proportion was estimated to be 43.6%.

We found that 42.2% of older adults with schizophrenia spectrum disorder were screened for metabolic syndrome. This proportion is greater than previous estimates ranging from 11% to 34% in the United Kingdom (Barnes et al., 2015), possibly due to the greater accessibility to mental health care for people with schizophrenia in France, in large part because it is organized into sectors and because of the lower medical costs. However, this rate of screening still denotes a critical gap between available guidelines and current practice. In fact, a systematic review and evaluation of monitoring guidelines proposed a protocol whereby each component of the metabolic syndrome is screened for, at least annually (De Hert et al., 2011). Another study concluded that the adherence to these guidelines would potentially allow to detect a substantial number of previously unrecognized metabolic abnormalities in almost half of older patients with severe mental illness (Konz et al., 2014). Both the psychiatrist and the general practitioner should put

into practice these screening guidelines. In real world settings, it is possible that the psychiatrist's preoccupation with psychiatric symptoms and the general practitioner lower knowledge of psychotropics' monitoring parameters may hinder the effective implementation of these recommendations.

We also observed that hypertension and abdominal obesity, two parameters easily measurable in an office setting, were the two most prevalent metabolic abnormalities in participants with metabolic syndrome. Since metabolic syndrome is associated with greater risk for cardiovascular mortality and morbidity, its systematic screening among older adults with schizophrenia spectrum disorder, especially those with hypertension and/or abdominal obesity, may lead to a better detection and treatment of those ailments in this vulnerable population.

Our findings support that the prevalence of metabolic syndrome among older adults with schizophrenia spectrum disorder is high and may affect most of them (51.7%). However, the absence of a control group in our study prevented us from determining whether this rate is similar or significantly higher than that of the general population, as the only available study that investigated the prevalence of metabolic syndrome specifically among older patients with schizophrenia reported similar rates as in healthy peers (Konz et al., 2014). We found

Table 3
Psychotropic medications associated with metabolic syndrome in older participants with schizophrenia spectrum disorder ($N = 149$).

	Metabolic syndrome ($n = 77$; 51.7%)	No metabolic syndrome ($n = 72$; 48.3%)		
<i>Psychotropic medications</i>	<i>n (%)</i>	<i>n (%)</i>	χ^2 test (df)	<i>p</i> -value
Number of antipsychotics prescribed			0.21 (2)	0.900
0	5 (6.5)	4 (5.6)		
1	55 (71.4)	50 (69.4)		
≥ 2	17 (22.1)	18 (25.0)		
Atypical antipsychotics	45 (58.4)	47 (65.3)	0.74 (1)	0.391
Typical antipsychotics	36 (46.8)	34 (47.2)	0.01 (1)	0.954
Antipsychotic under long-acting injectable (LAI) formulation	24 (31.6)	16 (22.2)	1.64 (1)	0.200
Antidepressants	19 (24.7)	17 (23.6)	0.02 (1)	0.879
Benzodiazepines	21 (27.3)	28 (38.9)	2.28 (1)	0.131
	Mean (SD)	Mean (SD)	$t^{\#}$	<i>p</i> -value
Duration of antipsychotic medication	19.9 (33.2)	16.4 (30.3)	0.66	0.510
Current dosage (chlorpromazine equivalents, mg/day)	408.8 (568.7)	309.2 (344.4)	1.27	0.205

Continuous variables are presented as their mean values and standard deviation (SD). Categorical variables are presented as percentages.

[#] t -test or unequal variance t -test (df = 147).

Table 4

Physical health features and monitoring and physical conditions associated with metabolic syndrome in older participants with schizophrenia spectrum disorder (N = 149).

	Metabolic syndrome (n = 77; 51.7%)	No metabolic syndrome (n = 72; 48.3%)		
	n (%)	n (%)	χ^2 test (df) / p-value	AOR [95% CI] (p-value) ^e
<i>Past-year physical health monitoring</i>				
At least one consultation with a general practitioner	69 (89.6)	55 (76.4)	4.66 (1) / 0.031	2.92 [1.13–7.57] (0.027) ^b
	Mean (SD)	Mean (SD)	t / p-value ^d	
Number of visits with a general practitioner	4.5 (4.2)	4.2 (5.8)	0.33 / 0.741	
	n (%)	n (%)	χ^2 test (df) / p-value	
At least one electrocardiogram	38 (49.4)	40 (55.6)	0.57 (1) / 0.449	
At least one blood test	77 (100.0)	72 (100.0)	na	
Hospitalization in a non-psychiatric department	14 (18.2)	22 (30.6)	3.11 (1) / 0.078	
<i>Physical health features</i>				
Current smokers	22 (28.6)	26 (36.1)	0.97 (1) / 0.325	
At-risk drinking ^a	1 (1.3)	1 (1.4)	na	
<i>Medical conditions</i>				
Cardiovascular disorder	46 (59.7)	26 (36.1)	8.32 (1) / 0.004	3.41 [1.65–7.08] (0.001) ^c
Other physical condition	66 (85.7)	61 (84.7)	0.03 (1) / 0.865	
	Mean (SD)	Mean (SD)	t / p-value ^d	
Number of medical conditions	2.4 (1.7)	2.2 (1.6)	0.92 / 0.362	

p values in bold are statistically significant (p < 0.05).

Abbreviations: SD = standard deviation; na = not applicable.

^a At-risk drinking was defined as having a CAGE test score ≥ 2 .

^b B = 1.07 (SE = 0.49); Hosmer-Lemeshow test p-value = 0.27; Cox & Snell R Square = 0.08.

^c B = 1.23 (SE = 0.37); Hosmer-Lemeshow test p-value = 0.99; Cox & Snell R Square = 0.13.

Continuous variables are presented as their mean values and standard deviation (SD). Categorical variables are presented as percentages.

^d t-test or unequal variance t-test (df = 147).

^e Adjusted odds ratios were estimated using binary logistic regression with metabolic syndrome as dependent variable and adjusted for age, sex, duration of the schizophrenia spectrum disorder, current smoking status and at-risk drinking.

that the prevalence of metabolic syndrome was 42.9% and 63.6% at 55–60 years, 48.1% and 51.4% at 61–70 years, and 50.0% and 66.7% after 70 years of age, respectively, among men and women. These estimates appear to be higher than those of a study conducted among the French general population indicating that the prevalence of metabolic syndrome may concern 13.6% and 7.6% at 51–60 years, 15.1% and

10.0% at 61–70 years, and 14.1% and 12.0% after 70 years of age, respectively, among men and women (Pannier et al., 2006). In the 3-city study (Raffaitin et al., 2011, 2009), which included a large number of older adults from the general population aged of more than 65 years of age, the prevalence of metabolic syndrome was within the same range, at 15.6%. In our study, the absence of significant differences in

Table 5

Severity of disorder and psychiatric comorbidity, cognitive and social functioning and mental health care utilization associated with metabolic syndrome in older participants with schizophrenia spectrum disorder (N = 149).

	Metabolic syndrome (n = 77; 51.7%)	No metabolic syndrome (n = 72; 48.3%)	
Mean (SD)	Mean (SD)	t / p-value ^d	
<i>Severity of disorder and psychiatric comorbidity</i>			
BPRS total score	44.5 (15.5)	40.9 (14.5)	1.46 / 0.146
CGI total score	4.5 (1.1)	4.4 (1.3)	0.53 / 0.595
QLS total score	49.0 (20.8)	53.2 (19.8)	-1.01 / 0.313
	n (%)	n (%)	χ^2 test (df) / p-value
Depression ^a	29 (37.7)	21 (29.2)	1.20 (1) / 0.272
Lifetime history	19 (24.7)	21 (29.2)	0.38 (1) / 0.536
Past-year history	0 (0.0)	1 (1.4)	na
<i>Cognitive and social functioning</i>			
	Mean (SD)	Mean (SD)	t / p-value ^d
MMSE total score	24.0 (4.7)	23.9 (4.7)	0.14 / 0.887
GAF total score	46.8 (15.9)	46.0 (16.5)	0.27 / 0.786
	n (%)	n (%)	χ^2 test (df) / p-value
Institutionalization	25 (32.5)	27 (37.5)	0.42 (1) / 0.520
<i>Mental health care utilization</i>			
Lifetime number of hospitalizations in a psychiatric department			0.737 (2) / 0.692
0–4	32 (41.6)	34 (47.2)	
5–10	25 (32.5)	19 (26.4)	
> 10	20 (26.0)	19 (26.4)	
Past-year history of hospitalization in a psychiatric department	28 (36.4)	27 (37.5)	0.02 (1) / 0.886

^a Depression was defined as having a global score on the Center for Epidemiologic Studies Depression (CES-D) scale ≥ 19 .

Continuous variables are presented as their mean values and standard deviation (SD). Categorical variables are presented as percentages.

^d t-test or unequal variance t-test (df = 147).

Abbreviations: SD = standard deviation; BPRS = Brief Psychiatric Rating Scale; CGI = Clinical Global Impression; QLS = Quality of Life Scale; MMSE = Mini Mental State Examination; GAF = Global Assessment of functioning; na = not applicable.

prevalence rates by age groups reduces the risk of a survivor bias, where schizophrenia patients who are more vulnerable to the negative effects of metabolic syndrome die earlier. One could argue that the high prevalence rate found in our study is related to unique characteristics of the screened population predisposing it to metabolic syndrome. In other words, participants who were more at risk to develop metabolic syndrome components were screened more often. However, none of the variables associated with the screening process (gender and urbanicity) was related to a positive diagnosis of metabolic syndrome.

Our main analyses did not reveal a significant association between metabolic syndrome and antipsychotics' use. However, we did find that current antipsychotic dosage was positively associated with metabolic syndrome only in the supplementary multivariable analysis of the full sample using imputed data. First- and second-generation antipsychotics use didn't differ between patients with and without metabolic syndrome. These findings contrast with those from studies of younger populations (De Hert et al., 2008; Mitchell et al., 2013) but are in line with a study conducted among geriatric schizophrenia and bipolar patients (Konz et al., 2014). In young patients, antipsychotics may accelerate the disturbance of metabolic pathways in the presence of a genetic predisposition. Since metabolic abnormalities are more common with age (Aguilar et al., 2015), this contrast may no longer be evident in older patients with a plateau effect reached after a certain age, which could also explain the lack of difference in prevalence rates across age groups. Other factors related to aging may become more accountable than antipsychotics for the development of metabolic syndrome, namely a shift to a more sedentary lifestyle. Moreover, it is possible that patients found to have a metabolic syndrome were switched to more weight-neutral antipsychotics to prevent cardiovascular complications. Alternatively, statistical power might have been limited to unmask this association.

Although under-screening and under-diagnosis are assumed to be partially related to limited access to healthcare (Crump et al., 2013), our results did not support that assumption since consultation with a general practitioner or hospitalization in a non-psychiatric department or institutionalization did not predict screening. In France, the majority of healthcare costs are covered by the state and it is compulsory to register with one primary doctor or risk high healthcare fees and low reimbursement rates. Hence, in countries with limited healthcare access, where commitment with one general practitioner is not necessary, the discrepancy between the compliant and non-compliant patients might have yielded different results. Furthermore, in our sample, the severity of schizophrenia spectrum disorders, co-morbid depression and functional impairment did not seem to be barriers for undergoing screening, as the screened group did not differ from the rest in terms of these measurements. This finding comes in contrast with previous reports of a positive correlation between depressive symptoms or functional impairment and difficulties accessing healthcare services (Mojtabai et al., 2014), which might result from particularities of the French mental healthcare system organization as previously mentioned.

Our study has several limitations. Firstly, despite our relatively large sample, we cannot rule out that we might have missed some associations due to insufficient statistical power. Second, several metabolic syndrome risk factors (e.g., sedentary lifestyle, dietary habits...) were not assessed in our study (Correll et al., 2015; Matta et al., 2019; Mitchell et al., 2013; Scigliano and Ronchetti, 2013). Third, due to the cross-sectional design, measures of association do not necessarily imply causal association (Le Strat and Hoertel, 2011) and directions of significant associations (e.g. between metabolic syndrome and cardiovascular disorders) could not be determined. Fourth, this study was not designed to be representative of the French general population and the recruiting psychiatric departments were only state hospitals, which can limit the generalizability of our findings. Furthermore, participants were recruited from 63 French state hospital psychiatric departments, each of them covering one mutually independent catchment area with a

mean population of 54,000 inhabitants over 20 years old. Therefore, our sample represents only 7.5% of the total number of sectors in France ($n = 839$). Fifth, because each participant was interviewed by only one psychiatrist and participants were recruited from a large number of centers ($n = 63$) in our study, we were unable to evaluate the reliability and validity of schizophrenia spectrum disorder diagnoses or potential error variance in rating measurements. Sixth, a recall bias in reporting retrospectively the first psychotic period may be at work in this study including older adults with schizophrenia who often present cognitive deficits. Seventh, we defined metabolic syndrome in our study based on the NCEP-ATPIII criteria revised by the American Heart Association and the National Heart Lung and Blood Institute in 2005 (Grundy et al., 2005), and were not able to examine the robustness of our results using other definitions of metabolic syndrome such as that of the WHO (World Health Organization, 1999) because we had no data on microalbuminuria. Future studies using different definitions of metabolic syndrome would be useful to confirm our results. Eighth, our analyses were powered to detect at least a medium effect size but not a small effect size. Post-hoc analyses of statistical power performed using G*Power 3.1.9.2 indicate that when considering $\alpha = 0.05$, a sample size of 149 and a medium effect size of 0.3, we had 95.6% power with χ^2 tests ($df = 1$) and 96.8% with two-sided t -tests, and that when considering $\alpha = 0.05$, a sample size of 149 and a small effect size of 0.1, we had 23.1% power with χ^2 tests ($df = 1$) and 23.0% with two-sided t -tests. Finally, blood pressure was measured only once at the time of the interview and may have led to overestimate its frequency as well as the prevalence of metabolic syndrome. However, the prevalence of hypertension found in our study is consistent with prior estimates. Indeed, Raffaitin et al. found a 98.2% prevalence rate of elevated blood pressure in their cohort of elderly subjects with metabolic syndrome (Raffaitin et al., 2009).

Despite these limitations, this study is the largest study to date that examines metabolic syndrome in geriatric schizophrenia patients in a naturalistic setting. We found that less than half (42.2%) of older adults with schizophrenia were assessed for metabolic syndrome and half of them (51.7%) screened positive. We didn't observe any significant associations with antipsychotic types or other disease-related variables. Taken together, these findings highlight the importance of systematic screening for metabolic syndrome among older adults with schizophrenia spectrum disorder, especially those with hypertension and/or abdominal obesity. Such systematic screening may substantially reduce the high rates of mortality and morbidity linked to cardiovascular diseases in this vulnerable population.

CRedit authorship contribution statement

Sandra Abou Kassm: Visualization, Writing - original draft. **Nicolas Hoertel:** Visualization, Data curation, Formal analysis, Writing - original draft. **Wadih Naja:** Writing - review & editing. **Kibby McMahon:** Writing - review & editing. **Sarah Barrière:** Supervision, Writing - review & editing. **Yvonne Blumenstock:** Supervision, Writing - review & editing. **Christophe Portefaux:** Data curation, Writing - review & editing. **Delphine Raucher-Chéné:** Supervision, Writing - review & editing. **Céline Béra-Potelle:** Supervision, Writing - review & editing. **Christine Cuervo-Lombard:** Supervision, Writing - review & editing. **Christophe Guerin-Langlois:** Writing - review & editing. **Cédric Lemogne:** Writing - review & editing. **Hugo Peyre:** Writing - review & editing. **Arthur Kaladjian:** Writing - review & editing. **Frédéric Limosin:** Visualization, Funding acquisition, Supervision, Writing - review & editing.

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Supplementary materials

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