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ORIGINAL ARTICLE

# Assessment of cardiovascular risk in an Italian psychiatric outpatient sample: A chart review of patients treated with second-generation antipsychotics

***Elena Severi, Maria Ferrara, Enrico Tedeschini, Francesca Vacca, Francesco Mungai, Rocco Amendolara, Flavia Baccari and Fabrizio Starace***

*Department of Mental Health and Drug Abuse, Azienda Unità Sanitaria Locale Modena, Modena, Italy*

**ABSTRACT:** *Despite the call by the scientific community for a systematic monitoring of physical health in people with psychiatric illnesses, national and international audits have reported poor quality of cardiovascular risk assessments and management in this vulnerable population. Available evidence indicates that in people affected by mental illness, life expectancy is reduced by 10–20 years, mainly due to cardiovascular accidents and metabolic syndrome (MetS)-related diseases. The primary aim of the present study was to evaluate the accuracy of cardiovascular risk monitoring in an outpatient sample of patients taking second-generation antipsychotics. The sample consisted of 200 patients consecutively recruited from two community mental health centres. A clinical chart review was performed on the following laboratory tests: total cholesterol, high- and low-density lipoprotein, serum triglycerides, fasting blood glucose, γ-glutamyl transpeptidase. Blood pressure and waist circumference were measured. A complete cardiovascular risk assessment was available only in 60 patients out of 200 (33.3%). The only variable associated with laboratory tests for MetS was receiving three or more psychotropic medications, which increased fourfold the probability of metabolic screening. In the subsample of patients with full screening, the prevalence of MetS was 33.3%. Our findings suggest that mental health professionals working in community mental health services should incorporate a more systematic assessment of physical health in their practice, and intervene proactively to reduce the significant cardiovascular burden carried by people with several mental illness.*

**KEY WORDS:** *antipsychotics, cardiovascular risk, metabolic syndrome, physical health.*

## INTRODUCTION

Physical illness is acknowledged as the leading cause of death in people with psychiatric illnesses (Liu *et al.* 2017; Parks *et al.* 2006; Vreeland 2007). Cardiovascular mortality among young adults (25–44 years) with psychosis is seven times higher compared to the general population; young adults die up to 25 years earlier (Leucht *et al.* 2007). Furthermore, the mortality rate has been reported to be worse in Western countries (Saha *et al.* 2007). Several factors, such as genetic risk, unhealthy lifestyle, and psychopharmacological treatment have been associated with psychiatric illness and recognized as main etiopathogenic determinants. However, mortality rates related to medical conditions are mostly preventable with a reduction of cardiovascular risk factors, such as obesity, hyperglycaemia, hypertension, dyslipidaemia, smoking, and poor physical activity.

**Correspondence:** Francesco Mungai, Department of Mental Health and Drug Abuse, AUSL Modena, Viale Muratori 201 Modena 41124, Italy. Email: f.mungai@ausl.mo.it
Elena Severi, MD.
Maria Ferrara, MD.
Enrico Tedeschini, MD.
Francesca Vacca, MD.
Francesco Mungai, MD.
Rocco Amendolara, MD.
Flavia Baccari, MD.
Fabrizio Starace, MD, MPh.
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Poor-quality medical care seems to explain the excess of cardiovascular mortality in patients with mental illnesses (Druss *et al.* 2001).

During the past 20 years, the use of second-generation antipsychotics (SGA) has steadily increased due to their better tolerability profile, but the observation of the increased incidence of metabolic abnormalities (e.g. hyperglycaemia, weight gain, and hyperlipidaemia) and metabolic syndrome (MetS; Alberti 2006; Levesque & Lamarche 2008) has tempered initial enthusiasm (Cuerda *et al*. 2014; De Hert *et al*. 2011, 2012; Reist *et al.* 2007; Stahl *et al.* 2009). It has been estimated that, in drug-naïve patients with schizophrenia, the prevalence of MetS varies from 3% to 26%, while it is 69% in medicated patients (Malhotra *et al.* 2013; Pallava *et al.* 2012; Sahoo *et al.* 2007). The highest association of MetS with a particular SGA was observed in cross-sectional studies with clozapine and olanzapine (Grover *et al.* 2012; Brunero *et al.* 2009). Similarly, longitudinal studies have reported that clozapine and olanzapine significantly increase the risk of MetS compared to other SGA (Malhotra *et al.* 2013).

Despite the case made by the scientific community for more systematic monitoring of physical health in people with psychiatric illnesses (Cohn & Sernyak 2006; Holt *et al.* 2004; Lambert & Chapman 2004; Maj 2009), international audits have documented that the quality of assessment and management of cardiovascular risk in this vulnerable population remain suboptimal (Rosenbaum *et al.* 2014; Smith *et al*. 2013).

In Italy, community mental health centres (CMHC) offer universalistic and multidisciplinary mental health care, representing the ideal setting to assess and monitor cardiovascular risk; however, due to the lack of systematic studies, little is known about the frequency and accuracy of physical health assessment in patients under the care of CMHC. Moreover, to date, no structured and consistent guidance has been provided by health authorities on how to monitor physical health in mental health services users.

The main aim of the present study was to explore the frequency of the assessment of cardiovascular risk factors in a mental health community sample treated with SGA, addressing clinical variables associated with the adequate monitoring of physical health.

## METHODS

### Study design

A cross-sectional analysis of physical health assessment was carried out in a sample of 200 adult patients in treatment with SGA. Participants were consecutively recruited at two CMHC in the province of Modena (northern Italy), between 1 July and 30 September 2014. Inclusion criteria were: age ≥18 years, current psychopharmacological treatment with at least one SGA, under the care of the CMHC and receiving regular psychiatric evaluation, supervised psychopharmacological treatment, or attending rehabilitation activities. Patients who had access to the CMHC for psychiatric emergencies or were unable to provide consent were not included in the sample. A trained nurse gathered information regarding current pharmacological treatment by means of a data-collection form. In addition, the sample underwent a full physical examination. Additional data on the patients' physical health were collected from clinical notes.

The research received formal approval by the Internal Review Board of the Local Health Care Agency of Modena on June 2014 (no. 45309/14). Written, informed consent was obtained from all study participants before enrolment.

### Data collection

Data regarding medical history, pharmacological treatment, and laboratory tests were gathered by means of a data collection form for the following: (i) psychiatric diagnoses; (ii) SGA treatment; (iii) physical examination and medical history; (iv) laboratory tests; and (v) MetS.

*Psychiatric diagnoses*

Psychiatric diagnoses, codified according to the International Classification of Diseases, 9th Revision, Clinical Modification, were confirmed by fully trained psychiatrists. For the purpose of the present study, the diagnoses were categorized and grouped as follow: psychosis, neurosis, personality disorders, oligophrenia, and psychosis due to medical condition, and substance use/abuse.

*SGA treatment*

Patients recruited were undergoing treatment with one or more of the following SGA: aripiprazole, clozapine, olanzapine, paliperidone, quetiapine, and risperidone. Data on concurrent psychopharmacological treatment (e.g. antidepressant, anxiolytic, or antiepileptic medications) were recorded from the clinical notes.

*Physical examination and medical history*

Physical examinations were performed by a trained nurse and included the following: systolic blood

pressure and diastolic blood pressure, assessed using automated mercury sphygmomanometers in seated patients. Patients' waist circumference, height, and weight were measured and recorded. General medical history and data on lifestyle, such as, smoking and physical exercise habits, were also investigated, Physical exercise were rated as 'less than optimal' when below 150 min $week^{-1}$, or 30 min per day, according to World Health Organization (2010) guidelines. A diagnosis of diabetes mellitus was made according to the expert committee on the Classification of Diabetes Mellitus criteria (2003) (Genuth *et al.* 2003).

*Laboratory tests*

Patients' clinical notes were examined in detail to verify the presence/absence of laboratory tests. Blood tests considered for the study were full blood count (FBC), total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein, serum triglycerides, and fasting blood glucose (FBG). Laboratory tests dating from before 6 months were not included in the analysis.

*MetS*

Metabolic syndrome was diagnosed according to the Adult Treatment Panel National Cholesterol Education Program-ATP (Adult Treatment Panel) III criteria (National Cholesterol Education Program, 2002), which require the concurrent presence of three or more of the following: (i) serum triglycerides ≥150 mg $dL^{-1}$ or in treatment for dyslipidaemia; (ii) HDL-cholesterol <40 mg $dL^{-1}$ in males or <50 mg $dL^{-1}$ in females; (iii) blood pressure ≥130/85 mmHg or in treatment for hypertension; (iv) FBG ≥110 mg $dL^{-1}$ or in treatment with oral antidiabetics, or previously-diagnosed diabetes mellitus; and (v) waist circumference ≥102 cm in men or ≥88 cm in women.

## Statistical analysis

Descriptive statistics were performed to outline the demographic and clinical variables, and pharmacological treatment of the sample.

Univariate analysis was separately carried out on the above variables between patients with and without laboratory tests available in the medical records.

Furthermore, a stepwise logistic regression analysis was performed to assess the variables associated with the likelihood of being screened for MetS. Categories including less than five cases (e.g. paliperidone, amisulpride, and substance use/abuse) were excluded from the analysis. Categories with the highest frequency (e.g. male sex, psychosis, quetiapine) were used as reference, with the exception of number of medication prescribed. In this case, the reference category was represented by patients prescribed one psychotropic medication, assuming that cumulative cardiovascular risk increases with the number of prescribed medications.

Finally, the presence of MetS and the distribution of cardiovascular risk factors among the subsample with available laboratory tests was calculated. Analysis was performed using SAS Enterprise guide version 5.1 (SAS Institute Inc., Cary, NC, USA).

## RESULTS

Demographic and clinical features of the sample are summarized in Table 1. Males represented 57.5% of the sample, with a mean age of 48.7 years (±13.2). A diagnosis of affective and non-affective psychosis accounted for 58.5% of patients. Quetiapine and olanzapine were the most frequently-prescribed SGA as primary treatment; 23.5% of participants were in treatment with a single SGA, while the rest were on more than one medication (e.g. antidepressants, anxiolytics, mood stabilizers) (Fig. 1).

Evidence of laboratory tests was documented in 60 patients (33.3%) in the sample (Table 2).

The multivariate analysis showed that taking three or more medications increased fourfold (odds ratio: 3.69, 95% confidence interval: 1.49–9.17) the probability of undergoing metabolic screening (Table 3).

Metabolic syndrome was diagnosed in 33.3% of patients with available laboratory tests (Fig. 2); 90% showed three or more cardiovascular risk factors, while the presence of two and one cardiovascular risk factors were present in 8.3% and 1.7%, respectively (Fig. 3).

However, no statistical significance was found in the comparison of patients with and without laboratory screening with respect to diagnosis, sex, age and prescribed SGA, with the only exception of olanzapine and the number of psychotropic drugs prescribed (i.e. one and three or more medications prescribed).

## DISCUSSION

To the best of our knowledge, the present study is the first to explore the frequency of cardiovascular risk assessment and address the factors associated with physical health monitoring among a sample of Italian CMHC users. Our findings indicate that only a minority of the sample affected by psychiatric illnesses (33.3%) had metabolic screening in their clinical notes.

**TABLE 1:** *Demographic and clinical characteristics of 200 patients with serious mental illness taking second-generation antipsychotics (SGA)*

| | Total sample ($n$ = 200) |
|---|---|
| Demographics | |
| Age, years (SD) | 48.7 (±13.2) |
| Sex, male | 115 (57.5%) |
| Psychiatric diagnosis[†] | |
| Psychosis | 117 (58.5%) |
| Neurosis | 29 (14.5%) |
| Personality disorder | 43 (21.5%) |
| Oligophrenia and psychosis due to medical condition | 7 (3.5%) |
| Substance use/abuse | 2 (1.0%) |
| Missing | 2 (1.0%) |
| SGA | |
| Quetiapine | 58 (29.0%) |
| Olanzapine | 47 (23.5%) |
| Clozapine | 36 (18.0%) |
| Aripiprazole | 28 (14.0%) |
| Risperidone | 27 (13.5%) |
| Paliperidone | 3 (1.5%) |
| Amisulpride | 1 (0.5%) |

[†]Psychosis included International Classification of Diseases, 9th Revision, Clinical Modification (ICD9-CM): 295.*-296.*-297.*-298.*-299.*; neurosis included ICD9-CM 300.*-302.*-306.*-307.*-308.*-309.*-310.*-311.*-312.*-313.*-314.*-315.*-316.*; personality disorders included ICD9-CM 301.*; oligophrenia and psychosis due to medical condition included ICD9-CM 290.*-291.*-292.*-293.*-294.*-317.*-318.*-319.*; substance use/abuse included ICD9-CM 303.*-304.*-305.*. SD, standard deviation.

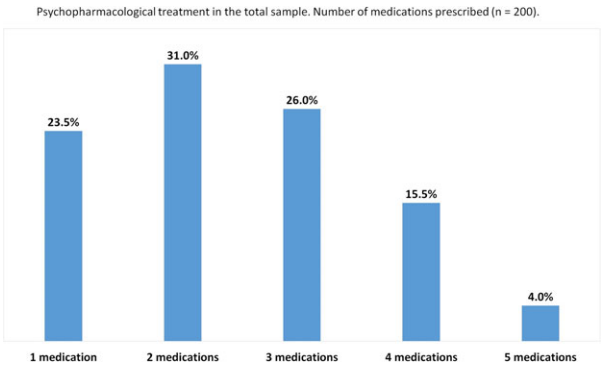


**FIG. 1:** *Psychopharmacological treatment in the total sample. Number of medications prescribed* (n = *200). [Colour figure can be viewed at wileyonlinelibrary.com]*

Moreover, the only clinical variable associated with screening was being prescribed three or more psychotropic medications.

Different scenarios could be hypothesized at the heart of the insufficient level of screening found. First,

**TABLE 2:** *Comparison of demographic and clinical characteristics of patients with and without metabolic screening*

| | With metabolic screening ($n$ = 60) | Without metabolic screening ($n$ = 140) | $P$-value |
|---|---|---|---|
| Demographics | | | |
| Age, years (SD) | 50.5 (±11.2) | 47.9 (±14.0) | 0.2145 |
| Sex, male | 31 (51.7%) | 84 (60.0%) | 0.2746 |
| Psychiatric diagnosis[†] | | | |
| Psychosis | 36 (60.0%) | 81 (57.9%) | 0.7781 |
| Neurosis | 8 (13.3%) | 21 (15.0%) | 0.7590 |
| Personality disorder | 15 (25.0%) | 28 (20.0%) | 0.4303 |
| Oligophrenia and psychosis due to medical condition | 1 (1.7%) | 6 (4.3%) | 0.3557 |
| Substance use/abuse | 0 (0.0%) | 2 (1.4%) | 0.3521 |
| Missing | 0 (0.0%) | 2 (1.4%) | 0.3521 |
| SGA use | | | |
| Quetiapine | 23 (38.3%) | 35 (25.0%) | 0.0569 |
| Olanzapine | 8 (13.3%) | 39 (27.9%) | 0.0264 |
| Clozapine | 10 (18.7%) | 26 (18.6%) | 0.7480 |
| Aripiprazole | 7 (11.7%) | 21 (15.0%) | 0.5336 |
| Risperidone | 10 (16.7%) | 17 (12.1%) | 0.3909 |
| Paliperidone | 1 (1.7%) | 2 (1.4%) | 0.8990 |
| Amisulpride | 1 (1.7%) | 0 (0.0%) | 0.1257 |
| No. medications | | | |
| 1 | 7 (11.7%) | 40 (28.6%) | 0.0079 |
| 2 | 16 (26.7%) | 46 (32.9%) | 0.3339 |
| ≥3 | 37 (61.6%) | 53 (37.9%) | 0.0016 |

[†]Psychosis included International Classification of Diseases, 9th Revision, Clinical Modification (ICD9-CM): 295.*-296.*-297.*-298.*-299.*; neurosis included ICD9-CM 300.*-302.*-306.*-307.*-308.*-309.*-310.*-311.*-312.*-313.*-314.*-315.*-316.*; personality disorders included ICD9-CM 301.*; oligophrenia and psychosis due to medical condition included ICD9-CM 290.*-291.*-292.*-293.*-294.*-317.*-318.*-319.*; substance use/abuse included ICD9-CM 303.*-304.*-305.*. SD, standard deviation.

**TABLE 3:** *Logistic regression model for patients with and without metabolic screening*

| | Odds ratio (95% confidence interval) | $P$-value |
|---|---|---|
| No. medications | | |
| 1 | 1.00 (1.00) | – |
| 2 | 1.84 (0.68–5.01) | 0.2300 |
| ≥3 | 3.69 (1.48–9.17) | 0.0049 |

the assessment of metabolic parameters is not systematized in CMHC practice, as opposed to acute psychiatric care units (e.g. hospital wards), where comprehensive laboratory tests, including urinalysis for illicit drugs, pregnancy tests, and electrocardiograph, are mandatory and routinely requested. It cannot be excluded that blood tests, which were indeed

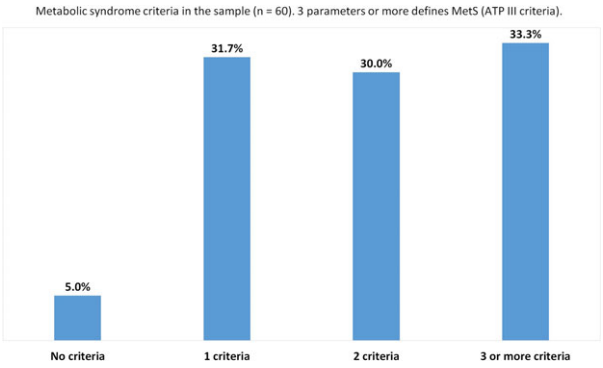


**FIG. 2:** *Metabolic syndrome criteria in the sample* (n = 60). *3 *parameters or more defines MetS (ATP III criteria). [Colour figure can be viewed at wileyonlinelibrary.com]*

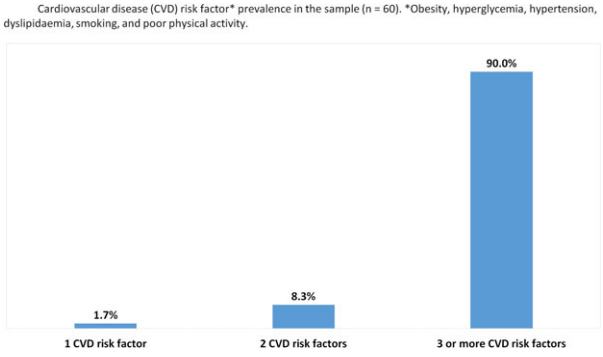


**FIG. 3:** *Cardiovascular disease (CVD) risk factor* prevalence in the sample* (n = 60). **Obesity, hyperglycemia, hypertension, dyslipidaemia, smoking, and poor physical activity. [Colour figure can be viewed at wileyonlinelibrary.com]*

requested, might fail to be registered into clinical notes due to the pressure that mental health professionals often work under. In addition, poor communication between CMHC and general practitioners, and uncertainty regarding responsibilities for undertaking physical health in people with psychiatric illnesses, might also play a role. Finally, we cannot rule out that, despite psychiatrists being well aware of the significant risk of physical health of their patients, mental health problems are given priority, while metabolic assessment remains largely overlooked (Piccinelli *et al.* 2002).

Among the patients with available metabolic screening, the prevalence of MetS was 33.3%, which is higher than the 22.3% and 17% prevalence reported in two large cohort Italian studies on the general population (Casula *et al.* 2009; Miccoli *et al.* 2005), and higher than 27.5% prevalence reported among psychiatric inpatients (Santini *et al.* 2016). However, as we included in the analysis only patients with available screening, we cannot exclude that the high prevalence of MetS observed is related to selection bias (i.e. cardiovascular risk monitoring was performed among patients for whom metabolic risk was already known).

The study presents other limitations that are worth acknowledging: the small size of the sample and the lack of a control group might have led to an underestimation of cardiovascular risk assessment. The limited number of patients with cardiovascular risk assessment and the high prevalence of MetS might not be representative of Italian service users in treatment with SGA. Yet a systematic revision of clinical notes focussing on SGA and MetS could be easily replicated in other CMHC, both retrospectively (with larger and more representative samples), as well as prospectively.

Finally, the cross-sectional nature of the present study does not allow us to draw definitive conclusions between the use of SGA and the onset of MetS. We cannot exclude that a pre-existing MetS or the presence of metabolic risk factors influenced the clinicians towards the prescription of SGA with a more favourable metabolic profile.

However, despite these limitations, the present study highlights a fundamental issue: as the majority of screened patients ($n$ = 34) showed at least two modifiable cardiovascular risk factors (e.g. tobacco smoking and inadequate physical activity), it would be worthwhile to consider that the implementation of healthy living interventions, such as smoking cessation programs, dietary consultations, and physical exercise groups, should become a standard practice of CMHC. Robust evidence suggests that even minor changes in lifestyle have a positive impact on patients affected by psychiatric illnesses (Vampfort *et al.* 2013; Werneke *et al.* 2013; Wu *et al.* 2008). In addition, physical activity has been reported to reduce symptoms of schizophrenia and improve anthropometric measures, aerobic capacity, and quality of life among people with psychiatric illnesses (Rosenbaum *et al.* 2014). Therefore, education modules outlining the role of exercise for the treatment of psychiatric illnesses are highly desirable.

The disparities suffered by mental health service users in accessing physical care, which too often leads to premature mortality, has been legitimately defined as a 'scandal' and a form of structural discrimination (Thornicroft 2011). Mental health professionals in general and community psychiatric nurses in particular can play a strategic role to respond to the physical health needs of their patients in a holistic approach, and have the duty of care of monitoring and intervening

proactively, in collaboration with general practitioners, to reduce the cardiovascular burden of psychiatric illness.

## Relevance to clinical practice

Psychiatric nurses account for the largest proportion of the mental health workforce and provide regular face-to-face therapeutic contact with service users (Happel *et al.* 2011). Therefore, their practice should encompass the systematic assessment of metabolic parameters. Positive outcomes have been documented just with the introduction of a screening checklist for MetS in clinical practice (O'Callaghan *et al.* 2011).

If CMHS represent the optimal setting to implement these changes, community mental health nurses can provide the leadership needed to improve mental health research and practice to reduce inequalities in physical care among people with mental illness (Happell *et al.* 2016). Mental health nurses are also critical in reorganizing health-care services to better support people with mental illness in recovery and well-being. The potential gains from these changes are invaluable, as improving physical health is associated with better quality of life and reduced mortality.

Alleviating the burden of long-term physical illnesses in people with psychiatric illnesses should be one of the primary goals of community psychiatry, especially for young service users prescribed antipsychotic medication for the first time (Crabb *et al*. 2009; Curtis *et al.* 2012).

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