



## The impact of clinical and social factors on the physical health of people with severe mental illness: Results from an Italian multicentre study

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### ABSTRACT

Our manuscript aims to: 1) assess physical health in a sample of patients with severe mental disorders; and 2) identify the psychopathological and psychosocial characteristics associated with an increased likelihood of having a poor physical health. The study, funded by the Italian Ministry of Education, has been carried out in psychiatric outpatient units of six Italian University sites. All recruited patients have been assessed through standardized assessment instruments. Moreover, anthropometric parameters have been obtained at recruitment and a blood samples have been collected to assess cardiometabolic parameters.

Four-hundred and two patients with a primary diagnosis of bipolar disorder (43.3%), schizophrenia or other psychotic disorder (29.9%), or major depression (26.9%) were recruited. Internalized stigma, psychosocial functioning, quality of life, psychiatric hospitalizations, depressive/anxiety and manic symptoms and cognition were those domains more strongly associated with poor metabolic parameters, including high body mass index, HOMA and Framingham indexes and waist circumference. There were no statistically significant differences among the three diagnostic groups.

Our findings highlight the importance of perceived stigma and quality of life on patients' physical health. This should be taken into account when developing plans for reducing the mortality rate in patients with severe mental disorders.

### 1. Introduction

People with severe mental illness (SMI) have a higher incidence of physical disorders and a higher mortality rate, with a life expectancy reduced by 10 to 20 years compared to the general population (Plana-Ripoll et al., 2020; World Health Organization, 2018; Thornicroft, 2011). Only a minority of premature deaths is attributable to unnatural

causes, such as suicide, homicide, or accidents (De Rosa et al., 2017). In fact, premature deaths in patients with SMI are mainly due to the co-occurrence of physical diseases (Hoang et al., 2013), such as cardiovascular (van Os et al., 2019) and metabolic ones (Global Burden of Diseases, 2016).

The association between physical and mental disorders is due to a complex interplay of factors, which are attributable to the patients

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themselves, to the illness, and to psychotropic medications. Patients with SMI receive fewer physical health check-ups and screenings compared to patients without SMI, and are less likely to receive a timely diagnosis of any physical illness, including cardiovascular diseases and cancer (Lawrence et al., 2003). The premature mortality in patients with SMI is also influenced by the adoption of unhealthy lifestyle behaviours, such as low physical activity, high rates of tobacco use and poor diet (Vancampfort et al., 2019; Firth et al., 2019). As far as illness-related factors are concerned, these include several psychopathological domains, such as cognitive impairment, depressive and negative symptoms, and some psychosocial factors, including social isolation and self-stigma, which hamper patients' help-seeking for physical illnesses (Kimhy et al., 2014; Mucheru et al., 2020). Finally, the risk of developing physical illnesses is increased by several psychotropic medications, including second-generation antipsychotics, mood stabilizers and tricyclic antidepressants (Schneider et al., 2020; Solmi et al., 2020; Taipale et al., 2020).

The presence of physical health problems in patients with SMI has traditionally been explored according to their main psychiatric diagnosis, while only a minority of studies assessed the relationship between psychopathological dimensions and poor physical health, in order to clinically characterize those patients with SMI with a higher risk to develop physical diseases, independently from diagnostic categories. In fact, it has recently been proposed that poor physical health may not be related to a specific diagnostic category (i.e., schizophrenia or major depression) but it could be associated with specific clusters of symptoms (i.e., having depressed mood vs. cognitive deficits) (Mansell, 2019). Moreover, physical health in patients with SMI may also be influenced by their overall levels of functioning and insight, the quality of their social network and the presence of adaptive coping strategies (World Health Organization, 2018; Firth et al., 2020), which are transdiagnostic and are impaired in most patients with SMI.

This paper, based on the LIFESTYLE randomized controlled study (Sampogna et al., 2018), aims to: 1) assess physical health in a sample of patients with severe mental disorders; and 2) identify which psychopathological and psychosocial characteristics increase the likelihood of poor physical health.

## 2. Materials and methods

The LIFESTYLE trial is a multicentre randomized controlled trial with blinded outcome assessments. The project was carried out at six Italian university sites (Universities of Campania "L. Vanvitelli", Bari, Genova, L'Aquila, Pisa and Roma Tor Vergata) and funded by the Italian Ministry of Education, Universities and Research.

Patients attending the outpatient units of participating centres were consecutively recruited from September 2017 to May 2018. Inclusion criteria were the following: 1) a diagnosis of schizophrenia or other psychotic disorder, bipolar disorder or depressive disorder, according to the DSM-5 criteria; 2) age between 18 and 65 years; 3) body mass index (BMI)  $\geq 25$ ; 4) ability to provide written informed consent. Exclusion criteria were: 1) inability to perform moderate physical activity (i.e., walking at least 150 min per week, or 75 min of vigorous exercise twice a week, according to the guidelines of the Italian Ministry of Health); 2) pregnancy or breast feeding; 3) severe cognitive impairment or intellectual disability; 4) a worsening of their clinical status or hospital admission in the previous 3 months.

After the baseline assessments, recruited patients were randomly assigned to receive an experimental psychosocial intervention to improve their physical health and promote lifestyle behaviours or to a control group. The full study protocol has been described in detail previously (Sampogna et al., 2018).

This study was conducted in accordance with globally accepted standards of good practice, in agreement with the Declaration of Helsinki and with local regulations. A formal ethical approval for conducting the trial was obtained by the Coordinating Center's Ethics

Committee, which approved the whole study protocol on January 2017 (approval number: prot. 64). All recruited patients gave written informed consent to participate in the study.

### 2.1. Measures

All patients were assessed at baseline and after 2, 4, 6, 12 and 24 months. The data collected at T0 are used for the analyses of this paper.

The patients' physical health was assessed using the following instruments: a) the Cumulative Illness Rating Scale (CIRS) (Linn et al., 1968), a 14-item questionnaire exploring the presence and severity of physical comorbidities; b) an anthropometric schedule with information on weight, height, BMI, waist circumference, blood pressure, resting heart rate, high-density lipoprotein (HDL), low-density lipoprotein (LDL) and overall levels of cholesterol, blood glucose, triglycerides, blood insulin; c) the homeostasis model assessment of insulin resistance (HOMA-IR), calculated as follows: fasting insulin (mg/dL)  $\times$  fasting glucose (mmol/L)/405; d) the Framingham 10-year risk score (FRS) for the evaluation of cardiovascular risk.

The patients' psychiatric symptoms and psychosocial functioning were assessed by: a) the Structured Clinical Interview for DSM-5, a semi-structured interview guide for DSM-5 diagnoses. (American Psychiatric association (APA), 2013)) the Brief Psychiatric Rating Scale (BPRS), a semi-structured 18-items interview on psychopathological status. Each item is rated on a Likert scale ranging from 0 to 7. Items are grouped in four subscales: positive symptoms (range 0–28), negative symptoms (range 0–28), depressive-anxiety symptoms (0–28), and manic-hostility symptoms (range 0–21) (Lukoff et al., 1986); c) the Personal and Social Performance Scale (PSP) (Morosini et al., 2000), a 100-point single-item rating scale, subdivided into 10 equal intervals. The ratings are based on the assessment of patient's functioning in four main areas (socially useful activities, personal and social relationships, self-care, disturbing and aggressive behaviours). Higher PSP total score indicate a better functioning; d) the 17-item Manchester Short Assessment of Quality of Life (MANSA), a 17-item questionnaire assessing quality of life focusing on satisfaction with life as a whole and with life domains (Pribe et al., 1999). Each item is rated on a 7-point Likert scale from 1 (could not be worse) to 7 (could not be better); e) the Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) Consensus Cognitive Battery (MCCB), brief version, including the MATRICS Consensus Trail Making Test—part A, Brief Assessment of Cognition in Schizophrenia: Symbol Coding and Category Fluency-Animal Naming (Kern et al., 2008) the Internalized Stigma of Mental Illness (ISMI), a 29-item questionnaire for evaluating the experience of stigma and internalized self-rejection. Each item is rated on a 4-level Likert scale, where higher scores indicate greater levels of internalized stigma (Ritsher et al., 2003); f) The Morisky Medication Adherence Scale (MMAS), a 4-items questionnaire on adherence to pharmacological treatments, with a total score ranging from 0 to 4. A Higher total score indicates a better adherence to pharmacological treatments (Morisky et al., 1986); g) the Pattern of Care Schedule (PCS), is a 40-item questionnaire on pharmacological and non-pharmacological treatments as well as on health care treatments received by the patient (Fiorillo et al., 2015).

The inter-rater reliability of participating researchers has been tested through Cohen's kappa coefficient (29), which was satisfactory for both the PSP (k value=0.918) and the BPRS (k value ranging from 0.835 to 0.972). A 100% agreement rate was found for the SCID-5 diagnoses.

### 2.2. Statistical analyses

Descriptive statistics were calculated for socio-demographic, clinical and metabolic variables. Data are presented as means and standard deviations (SD) or frequencies and percentages (%), as appropriate. The Kolmogorov-Smirnov test was used to check the normality of distribution of the sample.

Differences in the three diagnostic categories (i.e., schizophrenia and other psychotic disorders, major depression, and bipolar disorder) with respect to cardio-metabolic parameters were assessed with the ANOVA test with Bonferroni correction. Linear regression analyses were performed using cardio-metabolic and anthropometric variables as dependent variables (i.e., waist circumference, CIRS severity and comorbidity indexes, FRS total point, HOMA index and BMI). Independent variables were Number of hospitalizations, MANSA total score, ISMI total score, PSP total score, B-MCCB symbol coding; B-MCCB Trial making test A, BPRS depressive/anxiety subscale, BPRS positive symptoms subscale; BPRS manic symptoms subscale; BPRS negative symptoms subscale; MMAS negative symptoms subscale. All regression models were adjusted for age, gender, diagnosis, pharmacological treatments, duration of illness and educational level. Pharmacological treatments and psychiatric diagnoses were included in the regression models as dummy variables (i.e., mood stabilizers, tricyclic antidepressants, new-generation antidepressants, first- and second-generation antipsychotics, depressive disorder, bipolar disorders, psychosis).

Statistical analyses were performed with the Statistical Package for Social Sciences version 21. The level of statistical significance was set at  $p < .05$ .

### 3. Results

#### 3.1. Socio-demographic and clinical characteristics

Four hundred and two patients with a primary diagnosis of bipolar disorder (43.3%), schizophrenia or other psychotic disorder (29.9%), or

**Table 1**  
Socio-demographic and Clinical Characteristics of the sample (N = 402).

Gender, female,% (N)	57 (227)
Age, M (sd)	45.8 (11.8)
Living situation,% (N)	71.4 (287)
Alone	28.6 (115)
Married	
Years of education, M (SD)	11.69 (2.9)
Employed, yes,% (N)	35.7 (143)
Diagnosis,% (N)	
Bipolar disorder	43.3 (174)
Schizophrenia and other psychotic disorders	29.6 (120)
Major depression	27.1 (108)
Years in charge to the mental health service, M (SD)	5.9 (6.9)
Duration of illness, M (SD)	15.6 (11.3)
Number of hospitalization, M (SD)	2.8 (5.1)
Suicide attempts, M (SD)	1.8 (1.6)
BPRS, positive symptoms subscale, M (SD)	5.4 (2.1)
BPRS, negative symptoms subscale, M (SD)	7.7 (3.1)
BPRS, depressive/anxiety symptoms subscale, M (SD)	8.8 (3.1)
BPRS, manic/hostility symptoms subscale, M (SD)	4.7 (1.9)
MANSA, total score, M (SD)	4.1 (1.0)
ISMI, alienation subscale, M (SD)	2.3 (0.6)
ISMI, stereotype endorsement subscale, M (SD)	2.0 (0.5)
ISMI, perceived discrimination subscale, M (SD)	2.1 (0.6)
ISMI, social withdrawal subscale, M (SD)	2.1 (0.6)
ISMI, stigma resistance subscale, M (SD)	2.4 (0.4)
ISMI, total score, M (SD)	10.9 (2.1)
MMAS, total score, M (SD)	1.06 (1.1)
B-MCCB, symbol coding, M (SD)	36.9 (50.3)
B-MCCB, animal naming, M (SD)	20.3 (49.3)
B-MCCB trial making test A, M (SD)	69.1 (127.9)
PSP, total score, M (SD)	65.5 (15.1)
Typical antipsychotics, yes% (N)	22.5 (90)
Atypical antipsychotics, yes% (N)	59 (236)
Antidepressants, yes% (N)	51.5 (205)
Benzodiazepine, yes% (N)	47.1 (189)
Mood stabilizers, yes%(N)	65.8 (264)

MANSA: Manchester Short Assessment of Quality of Life; ISMI: Internalized Stigma of Mental Illness scale, MMAS: Morisky Medication Adherence Scale; B-MCCB: Brief MATRICS Consensus Cognitive Battery; PSPS: Personal and Social Performance Scale; BPRS: Brief Psychiatric Rating Scale.

major depression (26.9%) were recruited. All socio-demographic and clinical characteristics of recruited patients are reported in Table 1.

The only metabolic differences among the three diagnostic groups were significantly higher levels of systolic and diastolic blood pressure in patients with schizophrenia or other psychotic disorder vs. those with major depression ( $p < .05$ ), and higher heart rates in patients with schizophrenia or other psychotic disorder and bipolar disorder vs. patients with major depression ( $p < .01$  and  $p < .05$ , respectively) (Table 2).

#### 3.2. Multivariate analyses

The multivariate analyses have been performed controlling for age, gender, duration of illness, level of education, diagnosis and pharmacological treatments.

Higher number of hospitalizations ( $B = 0.95$ ;  $p < .000$ ), higher levels of internalized stigma ( $B = 0.30$ ;  $p < .000$ ), higher scores for depressive/anxiety symptoms ( $B = 0.19$ ;  $p < .000$ ), poor quality of life ( $B = -0.34$ ,  $p < .000$ ) and reduced psychosocial functioning ( $B = -0.32$ ;  $p < .05$ ) were associated with higher BMI.

Lower quality of life ( $B = -0.27$ ;  $p < .000$ ), higher levels of internalized stigma ( $0.27$ ;  $p < .000$ ), higher scores for depressive/anxiety ( $B = p < .11$ ;  $< 0.000$ ) and manic symptoms ( $B = 0.05$ ;  $p < .05$ ) and a higher number of psychiatric hospitalizations ( $B = 0.02$ ;  $p < .01$ ) were associated with higher waist circumference. On the other hand, a lower waist circumference was associated with a higher score on the B-MCCB symbol coding ( $B = 0.03$ ;  $p < .000$ ).

Higher levels of self-stigma ( $B = 0.61$ ;  $p < .000$ ), and a reduced

**Table 2**  
Metabolic parameters of the total sample and differences according to the diagnostic groups.

	Total sample	Schizophrenia and other psychotic disorders	Major depression	Bipolar disorder
BMI, kg/m2, M (SD)	32.5 (5.5)	32.4 (5.6)	33.1 (6.6)	32.2 (4.7)
Waist circumference, cm, M (SD)	109.3 (14.2)	106.0 (12.9)	106.8 (13.5)	113.2 (14.8)
Systolic blood pressure, mm Hg, M (SD)	125.6 (13.5)	128.1 (14.0) <sup>a</sup>	123.1 (13.7) <sup>a</sup>	125.2 (12.7)
Diastolic blood pressure, mm Hg, M (SD)	80.7 (9.0)	82.0 (8.6) <sup>a</sup>	79.0 (9.0) <sup>a</sup>	80.9 (9.2)
Heart rate, bpm, M (SD)	77.2 (12.2)	79.2 (13.0) <sup>a,b</sup>	74.0 (11.5) <sup>a,b</sup>	77.9 (11.7)
Blood glucose, mg/dL, M (SD)	95.5 (28.0)	92.8 (20.6)	99.4 (34.0)	95.0 (28.3)
Total cholesterol, mg/dL, M (SD)	189.9 (42.5)	184.6 (40.3)	194.8 (47.3)	190.5 (40.7)
LDL cholesterol, mg/dL, M (SD)	121.6 (58.6)	115.7 (33.3)	120.3 (37.2)	126.4 (79.0)
HDL cholesterol, mg/dL, M (SD)	48.5 (51.7)	42.8 (13.4)	47.7 (13.9)	53.0 (76.9)
Serum triglycerides, mg/dL, M (SD)	163.4 (98.0)	167.5 (92.2)	145.8 (80.1)	171.4 (110.5)
Framingham Risk Score, total score, M (SD)	9.8 (4.5)	9.6 (4.9)	10.2 (4.0)	9.8 (4.6)
HOMA index, M (SD)	4.9 (11.6)	4.4 (4.2)	5.8 (9.1)	4.8 (15.7)
CIRS, severity index, M (SD)	0.3 (0.3)	0.2 (0.3)	0.4 (0.4)	0.3 (0.3)
CIRS, comorbidity index, M (SD)	0.3 (1.4)	0.4 (2.0)	0.45 (1.6)	0.1 (0.5)

BMI: Body Mass Index; CIRS: Cumulative Illness Rating Scale; HOMA: Homeostatic Model Assessment of Insulin Resistance; bpm: beats per minute.

<sup>a</sup>  $p < 0.05$ .

<sup>b</sup>  $p < 0.001$ ;

<sup>c</sup>  $p < 0.05$ .

number of psychiatric hospitalizations ( $B = -0.27$ ;  $p < .05$ ) were associated with higher HOMA index. Moreover, a higher Framingham Risk Score (FRS) was associated with higher levels of internalized stigma ( $B = 0.16$ ;  $p < .05$ ) and higher B-MCCB trail making test mean scores ( $B = 0.05$ ;  $p < .05$ ), while the FRS was reduced in patients with a better quality of life ( $B = -0.27$ ;  $p < .000$ ) and with higher B-MCCB symbol coding mean scores ( $B = 0.04$ ;  $p < .05$ ).

Patients with a reduced quality of life ( $B = -0.43$ ;  $p < .000$ ), reduced psychosocial functioning ( $B = -0.25$ ;  $p < .000$ ), and a higher score on the BPRS manic symptoms subscale ( $B = 0.85$ ;  $p < .000$ ) were more likely to present higher means at CIRS severity index.

Finally, higher levels of the CIRS comorbidity score were associated with a reduced quality of life ( $B = -0.73$ ;  $p < .000$ ), reduced social functioning ( $B = -1.01$ ;  $p < .000$ ), poor adherence to pharmacological treatments ( $B = -0.09$ ;  $p < .05$ ), higher levels of internalized stigma ( $B = 0.43$ ;  $p < .01$ ) and a higher score on the BPRS manic symptoms subscale ( $B = 0.58$ ;  $p < .05$ ). The multivariable models are reported in Table 3.

#### 4. Discussion

The present study provides additional insight into the complex relationship between the mental and physical health of patients with severe mental disorders. In particular, we found that several domains of patients' mental health, including internalized stigma, psychosocial functioning, quality of life, psychiatric hospitalizations and depressive/anxiety and manic symptoms were strongly associated to poor metabolic parameters.

The most important finding of our study is the fact that internalized stigma, which is the subjective perception of devaluation, marginalization, secrecy, shame, and withdrawal (Boyd et al., 2014), correlates with basically all the physical health dimensions analysed. It has been reported that SMI patients perceive stigmatizing attitudes in their health care providers, and thus are reluctant to seek medical help (Thorncroft, 2011). Moreover, internalized stigma causes social withdrawal which, in turn, may lead to reduced check-up visits for physical health (Mazzi et al., 2018), with a consequent increase of incidence of cardiovascular diseases (Valtorta et al., 2018) and excess mortality (Holt-Lunstad et al.,

2015; Thorncroft et al., 2019). Finally, the physical health of patients with severe mental illness is very often neglected by health care providers due to negative stereotypes and diagnostic overshadowing (Correll et al., 2020; Hassan et al., 2020; Magliano et al., 2004).

A poor quality of life is the other most important factor significantly associated with poor physical health, being associated with BMI, waist circumference, CIRS comorbidity and severity indexes and cardiovascular risk score. These findings are in line with the available literature (Bressington et al., 2016), which reports a significant association between BMI, waist circumference and quality of life of people with SMI. Obesity is also associated with a significant worsening of patients' quality of life, independently from the diagnosis of any mental disorder (Paniganti et al., 2020). Moreover, studies have showed that even moderate reductions in BMI levels are associated with a significant improvement in patients' quality of life (Jahromi et al., 2020). Of course, the relationship between BMI and quality of life may be bidirectional, meaning that poor physical health may influence quality of life, and therefore only longitudinal studies can help to better understand the directionality of this relationship.

Poor psychosocial functioning was associated in our sample to BMI, CIRS severity and comorbidity indexes. The association between social functioning and physical health has only been explored in a few studies, reporting that patients with reduced social functioning have a greater risk of developing physical illnesses due to poor skills in help seeking and in taking care of themselves (Harvey et al., 2019), and to low levels of physical and daily activities (Falkai et al., 2019).

Patients with a higher number of psychiatric hospitalizations were more likely to have a greater BMI and waist circumference. This result is of particular relevance, since psychiatric hospitalizations are considered a proxy of global severity and of higher economic health costs (Sprah et al., 2017; Knapp et al., 2020). Available evidence shows that the risk of psychiatric hospitalization of patients with bipolar disorder and schizophrenia or other psychotic disorder is higher if they have co-occurring physical disorders (Sprah et al., 2017; Knapp et al., 2020; Leucht et al., 2007; Chwastiak et al., 2014), and it may be that the presence of physical illnesses could contribute to the "revolving door" phenomenon in mental health (Sprah et al., 2017). However, the

**Table 3**  
Regression analyses.

	Waist Circumference (cm)	CIRS severity index	CIRS comorbidity index	FRS total point	HOMA index	BMI
	B (95% CI)	B (95% CI)	B (95% CI)	B (95% CI)	B (95% CI)	B (95% CI)
Number of hospitalizations	.02 (0.12 to 0.80)**	–	–	–	–0.27 (–0.60 to 0.02)*	.95 (0.13 to 0.39)****
MANSA, total score	–0.27 (–8.49 to 5.60)***	–0.43 (–8.45 to –2.77)***	–0.76 (–0.31 to –0.17)****	–0.27 (–0.94 to 0.44)****	–	–0.34 (–3.22 to –2.08)****
ISMI, total score	.27 (2.00 to 3.32)****	–	.43 (–0.09 to 0.02)**	.16 (–0.27 to 0.034)*	.61 (0.38 to 1.04)****	.30 (0.64 to 1.11)****
PSP, total score	–	–0.25 (–0.06 to 0.20)****	–1.01 (–0.02 to –0.01)****	–	–	–0.32 (–3.64 to –0.65)**
B-MCCB symbol coding	–0.03 (–0.71 to 0.00)****	–	–	–0.041 (–0.013 to 0.00)*	–	–
B-MCCB trial making test A	–	–	–	.05 (0.00 to 0.01)*	–	–
BPRS, depressive/anxiety symptoms subscale	.11 (0.73 to 1.99)****	–	–	–	–	.19 (0.48 to 0.88)****
BPRS, positive symptoms subscale	–	–	–	–	–	–
BPRS, manic symptoms subscale	.049 (0.10 to 2.04)*	.85 (5.99 to 11.47)****	.58 (0.10 to 0.21)*	–	–	–
BPRS, negative symptoms subscale	–	–	0.34 (0.020–0.09)***	–	–	–
MMAS, total score	–	–	–0.09 (–0.16 to 0.01)*	–0.04 (–0.51 to 0.00)	–	–

CIRS: Cumulative Illness Rating Scale; HOMA: Homeostatic Model Assessment of Insulin Resistance; MANSA: Manchester Short Assessment of Quality of Life; ISMI: Internalized Stigma of Mental Illness scale, MMAS: Morinsky Medication Adherence Scale; B-MCCB: Brief MATRICS Consensus Cognitive Battery; PSP: Personal and Social Performance; BPRS: Brief Psychiatric Rating Scale. All regression analyses have been adjusted for age, gender, diagnosis, pharmacological treatments, duration of illness and years of education.

\* $p < .05$ ; \*\* $p < .01$ ; \*\*\* $p < .001$ ; \*\*\*\* $p < .0001$ .

relationship between physical health and psychiatric hospitalizations should be further investigated, and studies should focus particularly on the identification of which health domains are most frequently associated with multiple admissions to psychiatric wards.

As far as psychiatric symptoms are concerned, we found that the symptoms most strongly associated with poor physical health were the depressive/anxiety and manic ones. Anxiety patients frequently adopt unhealthy lifestyle behaviours (Allgulander, 2016), which can influence their physical health. The presence of depressive symptoms is frequently associated with a worse physical health, since these patients may be less motivated to attend physical health consultations (Adams et al., 2006; Maj et al., 2020) and show poor adherence to pharmacological treatments both for physical and mental illnesses. Furthermore, patients with depressive symptoms also have unhealthy lifestyle behaviours, including low physical activity and poor diet (Jacob et al., 2020; Fiorillo et al., 2019).

It is noteworthy that we did not find any clinically relevant difference in physical health between patients with major depression, schizophrenia or other psychotic disorder and bipolar disorder. This finding may be explained by the fact that physical health in patients with SMI is not influenced by any specific psychiatric diagnostic category but by certain psychopathological dimensions, supporting the importance of a transdiagnostic approach to mental health care (Reininghaus et al., 2019; Fusar-Poli et al., 2019; McGorry and Nelson, 2019; Mansell, 2019).

Lastly, in our sample, poor cognitive performance was associated with increased waist circumference and cardiovascular risk score. The relationship between cognitive performance and physical health of people with SMI has been mainly investigated in patients with schizophrenia, and the relationship between cognitive impairment and metabolic diseases has been documented (Foguet-Boreu et al., 2020). In particular, patients with schizophrenia with higher BMI have a worse performance on recall, verbal and working memory (Foguet-Boreu et al., 2020; Green et al., 2019). However, only a few studies have assessed the impact of cognitive performance on the physical health of patients with affective disorders. Foguet-Boreu et al. (2020) reported a significantly higher risk for cardiovascular diseases in a sample of SMI patients with cognitive impairment compared to patients without this impairment. It is possible that cognitive deficits impair patients' ability to understand their need for health check-ups and healthy lifestyle behaviours. Moreover, patients with reduced cognitive and social functioning may be less motivated to participate and to be actively involved in interventions for the promotion of physical health (Bar Deucher et al., 2016). Contrary to what we expected, the impact of cognitive deficits on physical health was evident not only on patients with schizophrenia, but also on patients with major depression and in those with bipolar disorder. Therefore, the presence of cognitive deficits should be explored in all patients with SMI, since they can influence the long-term outcome. A transdiagnostic approach would be advisable in order to deepen our knowledge about the relationship between physical health and cognitive performance in people with SMI.

The present study has some limitations, such as the recruitment of patients with a BMI  $\geq 25$ , which may reduce the generalizability of our findings, and the cross-sectional design of the study, with patients being assessed only once, so that it was not possible to explore the direction of the causality between physical and mental health domains. Another possible limitation of the study is that we did not assess the longitudinal exposure to medications, which could contribute to increase BMI and worsen metabolic parameters of patients.

In conclusion, the results of our study provide additional support to the notion that poor physical health is influenced more by certain clinical and psychosocial factors, such as internalized stigma, quality of life, and psychosocial and cognitive functioning, rather than by specific psychiatric diagnoses. In order to reduce the mortality rate in patients with SMI, supportive interventions should include the improvement of patients' cognitive and social functioning and quality of life, as well as

addressing and overcoming patients' self-stigma and discrimination.

## Author statement

Data published in this paper are available at the corresponding author upon request.

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## Declaration of Competing Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

## References

- Adams, K.F., Schatzkin, A., Harris, T.B., Kipnis, V., Mouw, T., Ballard-Barbash, R., Hollenbeck, A., Leitzmann, M.F. 2006. Overweight, obesity, and mortality in a large prospective cohort of persons 50 to 71 years old. *N. Engl. J. Med.* 355, 763–78.
- Allgulander, C. 2016. Anxiety as a risk factor in cardiovascular disease. *Curr. Opin. Psychiatry.* 29, 13–7.
- Boyd, J.E., Adler, E.P., Otilingam, P.G., Peters, T. 2014. Internalized Stigma of Mental Illness (ISMI) scale: a multinational review. *Compr. Psychiatry.* 55, 221–31.
- Bressington, D., Mui, J., Tse, M.L., Gray, R., Cheung, E.F., Chien, W.T. 2016. Cardiometabolic health, prescribed antipsychotics and health-related quality of life in people with schizophrenia-spectrum disorders: a cross-sectional study. *BMC Psychiatry.* 16, 411.
- Bär Deucher A., Hengartner M.P., Kawohl W., Konrad J., Puschner B., Clarke E., Slade M., Del Vecchio V., Sampogna G., Égerházi A., Süveges Á., Krogsgaard Bording M., Munk-Jørgensen P., Rössler W.; CEDAR study group. 2016. Participation in medical decision-making across Europe: an international longitudinal multicenter study. *Eur. Psychiatry.* 35:39–46.
- Chwastiak, L.A., Davydow, D.S., McKibbin, C.L., Schur, E., Burley, M., McDonell, M.G., Roll, J., Daratha, K.B. 2014. The effect of serious mental illness on the risk of rehospitalization among patients with diabetes. *Psychosomatics.* 55, 134–43.
- Correll, C.U., Sikich, L., Reeves, G., Johnson, J., Keeton, C., Spanos, M., Kapoor, S., Bussell, K., Miller, L., Chandrasekhar, T., Sheridan, E.M., Pirmohamed, S., Reinblatt, S.P., Alderman, C., Scheer, A., Borner, I., Betha, T.C., Edwards, S., Hamer, R.M., Riddle, M.A. 2020. Metformin add-on vs. antipsychotic switch vs. continued antipsychotic treatment plus healthy lifestyle education in overweight or obese youth with severe mental illness: results from the IMPACT trial. *World Psychiatry.* 19:69–80.
- De Rosa, C., Sampogna, G., Luciano, M., Del Vecchio, V., Pocaï, B., Borriello, G., Giallonardo, V., Savorani, M., Pinna, F., Pompili, M., Fiorillo, A. 2017. Improving physical health of patients with severe mental disorders: a critical review of lifestyle psychosocial interventions. *Expert Rev. Neurother.* 17, 667–81.
- Falkai, P., Schmitt, A. 2019. The need to develop personalized interventions to improve cognition in schizophrenia. *World Psychiatry.* 18, 170.
- Fiorillo, A., Del Vecchio, V., Luciano, M., Sampogna, G., De Rosa, C., Malangone, C., Volpe, U., Bardicchia, F., Ciampini, G., Crocamo, C., Iapichino, S., Lampis, D., Moroni, A., Orlandi, E., Piselli, M., Pompili, E., Veltro, F., Carrà, G., Maj, M. 2015. Efficacy of psychoeducational family intervention for bipolar I disorder: a controlled, multicentric, real-world study. *J. Affect. Disord.* 172, 291–9.
- Fiorillo, A., Luciano, M., Pompili, M., Sartorius, N. 2019. Editorial: reducing the mortality gap in people with severe mental disorders: the role of lifestyle psychosocial interventions. *Front. Psychiatry.* 10, 434.
- Firth, J., Solmi, M., Wootton, R.E., Vancampfort, D., Schuch, F.B., Hoare, E., Gilbody, S., Torous, J., Teasdale, S.B., Jackson, S.E., Smith, L., Eaton, M., Jacka, F.N., Veronese, N., Marx, W., Ashdown-Franks, G., Siskind, D., Sarris, J., Rosenbaum, S., Carvalho, A.F., Stubbs, B. 2020. A meta-review of "lifestyle psychiatry": the role of exercise, smoking, diet and sleep in the prevention and treatment of mental disorders. *World Psychiatry.* 19, 360–80.
- Firth, J., Teasdale, S.B., Allott, K., Siskind, D., Marx, W., Cotter, J., Veronese, N., Schuch, F., Smith, L., Solmi, M., Carvalho, A.F., Vancampfort, D., Berk, M., Stubbs, B., Sarris, J. 2019. The efficacy and safety of nutrient supplements in the treatment of mental disorders: a meta-review of meta-analyses of randomized controlled trials. *World Psychiatry.* 18, 308–24.
- Foguet-Boreu, Q., Guàrdia Sancho, A., Santos Lopez, J.M., Roura Poch, P., Palmarola Ginesta, J., Puig-Ribera, A.M., Muñoz Prados, J. 2020. Association between cognitive impairment and cardiovascular burden in patients with severe mental disorder. *Cogn. Neuropsychiatry.* 25, 1–3.

- Fusar-Poli, P., Solmi, M., Brondino, N., Davies, C., Chae, C., Politi, P., Borgwardt, S., Lawrie, S.M., Parnas, J., McGuire, P. 2019. Transdiagnostic psychiatry: a systematic review. *World Psychiatry* 18, 192–207.
- Global Burden of Diseases (GBD) 016 DALYs and HALE Collaborators. 2016. Global, regional, and national disability-adjusted life-years (DALYs) for 333 diseases and injuries and healthy life expectancy (HALE) for 195 countries and territories, 1990–2016: a systematic analysis for the Global Burden of Disease Study. *The Lancet*. 390:1260–344.
- Green, M.F., Horan, W.P., Lee, J. 2019. Nonsocial and social cognition in schizophrenia: current evidence and future directions. *World Psychiatry*. 18, 146–161.
- Harvey, P.D., Strassnig, M.T. 2019. Cognition and disability in schizophrenia: cognition-related skills deficits and decision-making challenges add to morbidity. *World Psychiatry*. 18, 165–167.
- Hassan, S., Heinkel, S., Burton, A., Blackburn, R., McCloud, T., Ross, J., Osborn, D., Walters, K. 2020. A qualitative study exploring the barriers and facilitators of implementing a cardiovascular disease risk reducing intervention for people with severe mental illness into primary care contexts across England: the 'PRIMROSE' trial. *BMC Health Serv. Res.* 20, 753.
- Hoang, U., Goldacre, M.J., Stewart, R. 2013. Avoidable mortality in people with schizophrenia or bipolar disorder in England. *Acta Psychiatr. Scand.* 127, 195–201.
- Holt-Lunstad, J., Smith, T.B., Baker, M., Harris, T., Stephenson, D. 2015. Loneliness and social isolation as risk factors for mortality: a meta-analytic review. *Psychol. Sci.* 10, 227–37.
- Jacob, L., Tully, M.A., Barnett, Y., Lopez-Sanchez, G.F., Butler, L., Schuch, F., López-Bueno, R., McDermott, D., Firth, J., Grabovac, I., Yakkundi, A., Armstrong, N., Young, T., Smith, L. 2020. The relationship between physical activity and mental health in a sample of the UK public: a cross-sectional study during the implementation of COVID-19 social distancing measures. *Ment. Health. Phys. Act.* 19, 100345.
- Jahromi, A.S., Rahmani, K. 2020. Relation of health-related quality of life with abnormal weight: a cross-sectional study prior to the weight reduction intervention. *J. Family Med. Prim. Care.* 9, 4662–66.
- Kern, R.S., Nuechterlein, K.H., Green, M.F., Baade, L.E., Fenton, W.S., Gold, J.M. 2008. The MATRICS consensus cognitive battery, part 2: co-norming and standardization. *Am. J. Psychiatry*. 165, 214–20.
- Kimhy, D., Vakhrusheva, J., Bartels, M.N., Armstrong, H.F., Ballon, J.S., Khan, S., Chang, R.W., Hansen, M.C., Ayanruoh, L., Smith, E.E., Sloan, R.P. 2014. Aerobic fitness and body mass index in individuals with schizophrenia: implications for neurocognition and daily functioning. *Psychiatry Res.* 220:784–91.
- Knapp, M., Wong, G. 2020. Economics and mental health: the current scenario. *World Psychiatry*. 19, 3–14.
- Lawrence, D., Holman, C.D.J., Jablensky, A.V., Hobbs, M.S. 2003. Death rate from ischaemic heart disease in Western Australian psychiatric patients 1980–1998. *Br. J. Psychiatry*. 182, 31–6.
- Leucht, S., Burkard, T., Henderson, J., Maj, M., Sartorius, N. 2007. Physical illness and schizophrenia: a review of the literature. *Acta Psychiatr. Scand.* 116, 317–33.
- Linn, B.S., Linn, M.W., Gurel, L. 1968. Cumulative illness rating scale. *J. Am. Geriatr. Soc.* 16, 622–6.
- Lukoff, D., Nuechterlein, K.H., Ventura, J. 1986. Appendix A: manual for expanded Brief Psychiatric Rating Scale (BPRS). *Schizophr. Bull.* 12, 594–602.
- Magliano, L., De, Rosa C., Fiorillo, A., Malangone, C., Guarneri, M., Marasco, C., Maj, M.; Working Group of the Italian National Study. 2004. Beliefs of psychiatric nurses about schizophrenia: a comparison with patients' relatives and psychiatrists. *Int. J. Soc. Psychiatry*, 50:319–30.
- Maj, M., Stein, D.J., Parker, G., Zimmerman, M., Fava, G.A., De Hert, M., Demyttenaere, K., McIntyre, R.S., Widiger, T., Wittchen, H.U. 2020. The clinical characterization of the adult patient with depression aimed at personalization of management. *World Psychiatry*. 19, 269–3.
- Mansell, W. 2019. Transdiagnostic psychiatry goes above and beyond classification. *World Psychiatry*. 18, 360–1.
- Mazzi, F., Baccari, F., Mungai, F., Ciambellini, M., Brescancin, L., Starace, F. 2018. Effectiveness of a social inclusion program in people with non-affective psychosis. *BMC Psychiatry*. 18:179.
- McGorry, P.D., Nelson, B. 2019. Transdiagnostic psychiatry: premature closure on a crucial pathway to clinical utility for psychiatric diagnosis. *World Psychiatry*. 18, 359–60.
- Morisky, D.E., Green, L.W., Levine, D.M. 1986. Concurrent and predictive validity of a self-reported measure of medication adherence. *Med. Care*. 24, 67–74.
- Morosini, P.L., Magliano, L., Brambilla, L., Ugolini, S., Pioli, R. 2000. Development, reliability and acceptability of a new version of the DSM-IV Social and Occupational Functioning Assessment Scale (SOFAS) to assess routine social functioning. *Acta Psychiatr. Scand.* 101, 323–9.
- Mucheru, D., Ashby, S., Hanlon, M.C., McEvoy, M., MacDonald-Wicks, L. 2020. Factors to consider during the implementation of nutrition and physical activity trials for people with psychotic illness into an Australian community setting. *BMC Health Serv. Res.* 12, 20:743.
- Plana-Ripoll, O., Musliner, K.L., Dalsgaard, S., Momen, N.C., Weyer, N., Christensen, M. K., Agerbo, E., Iburg, K.M., Laursen, T.M., Mortensen, P.B., Pedersen, C.B., Petersen, L.V., Santomauro, D.F., Vilhjálmsson, B.J., Whiteford, H.A., McGrath, J.J. 2020. Nature and prevalence of combinations of mental disorders and their association with excess mortality in a population-based cohort study. *World Psychiatry*. 19, 339–49.
- Priebe, S., Huxley, P., Knight, S., Evans, S. 1999. Application and results of the Manchester Short Assessment of Quality of Life (MANSA). *Int. J. Soc. Psychiatry*. 45, 7–12.
- Reininghaus, U., Böhnke, J.R., Chavez-Baldini, U., Gibbons, R., Ivleva, E., Clementz, B. A., Pearlson, G.D., Keshavan, M.S., Sweeney, J.A., Tamminga, C.A. 2019. Transdiagnostic dimensions of psychosis in the Bipolar-Schizophrenia Network on Intermediate Phenotypes (B-SNIP). *World Psychiatry*, 18:67–76.
- Ritsher, J., Otilingam, P.G., Grajales, M. 2003. Internalized stigma of mental illness: psychometric properties of a new measure. *Psychiatry Res.* 121, 31–49.
- Sampogna, G., Fiorillo, A., Luciano, M., Del Vecchio, V., Steardo, L. Jr., Pocai, B., Barone, M., Amore, M., Pacitti, F., Dell'Osso, L., Di Lorenzo, G., Maj, M.; LIFESTYLE Working Group. 2018. A randomized controlled trial on the efficacy of a psychosocial behavioral intervention to improve the lifestyle of patients with severe mental disorders: study protocol. *Front. Psychiatry*. 9:235.
- Schneider, M., Pauwels, P., Toto, S., Bleich, S., Grohmann, R., Heinze, M., Greiner, T. 2020. Severe weight gain as an adverse drug reaction of psychotropics: data from the AMSP project between 2001 and 2016. *Eur. Neuropsychopharmacol.* 36, 60–71.
- Solmi, M., Fornaro, M., Ostinelli, E.G., Zangani, C., Croatto, G., Monaco, F., Krinitski, D., Fusar-Poli, P., Correll, C.U. 2020. Safety of 80 antidepressants, antipsychotics, anti-attention-deficit/hyperactivity medications and mood stabilizers in children and adolescents with psychiatric disorders: a large scale systematic meta-review of 78 adverse effects. *World Psychiatry*. 19, 214–32.
- Šprah, L., Dernovšek, M.Z., Wahlbeck, K., Haaramo, P. 2017. Psychiatric readmissions and their association with physical comorbidity: a systematic literature review. *BMC Psychiatry*. 17, 2.
- American Psychiatric Association (APA). Structured Clinical Interview for DSM-5 (SCID-5). American Psychiatric Association publishing, 2013.
- Taipale, H., Tanskanen, A., Mehtälä, J., Vattulainen, P., Correll, C.U., Tiihonen, J. 2020. 20-year follow-up study of physical morbidity and mortality in relationship to antipsychotic treatment in a nationwide cohort of 62,250 patients with schizophrenia (FIN20). *World Psychiatry*, 19, 61–8.
- Thornicroft, G. 2011. Physical health disparities and mental illness: the scandal of premature mortality. *Br. J. Psychiatry*. 199, 441–2.
- Thornicroft, G., Bakolis, I., Evans-Lacko, S., Gronholm, P.C., Henderson, C., Kohrt, B.A., Koschorke, M., Milenova, M., Semrau, M., Votruba, N., Sartorius, N. 2019. Key lessons learned from the INDIGO global network on mental health related stigma and discrimination. *World Psychiatry*. 18, 229–30.
- Valtorta, N.K., Kanaan, M., Gilbody, S., Hanratty, B. 2018. Loneliness, social isolation and risk of cardiovascular disease in the English Longitudinal Study of Ageing. *Eur. J. Prev. Cardiol.* 25, 1387–96.
- van Os, J., Guloksuz, S., Vijn, T.W., Hafkenscheid, A., Delespaul, P. 2019. The evidence-based group-level symptom-reduction model as the organizing principle for mental health care: time for change?. *World Psychiatry*. 18, 88–96.
- Vancampfort, D., Firth, J., Correll, C.U., Solmi, M., Siskind, D., De Hert, M., Carney, R., Koyanagi, A., Carvalho, A.F., Gaughran, F., Stubbs, B. 2019. The impact of pharmacological and non-pharmacological interventions to improve physical health outcomes in people with schizophrenia: a meta-review of meta-analyses of randomized controlled trials. *World Psychiatry*. 18, 53–66.
- World Health Organization (WHO). Management of Physical Health Conditions in Adults with Severe Mental Disorders. WHO Guidelines. 2018. Available at: [https://www.who.int/mental\\_health/evidence/guidelines\\_physical\\_health\\_and\\_severe\\_mental\\_disorders/en/](https://www.who.int/mental_health/evidence/guidelines_physical_health_and_severe_mental_disorders/en/).