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Sedentary behaviour, physical activity, cardiorespiratory fitness and cardiometabolic risk in psychosis: The PsychiActive project

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ABSTRACT

This study aimed to explore the possible independent associations of sedentary behaviour (SB), physical activity (PA), and cardiorespiratory fitness (CRF) with clustered (CCRS) and individual cardiometabolic risk (waist circumference [waist], systolic/diastolic blood pressure, triglycerides, high-density lipoprotein-cholesterol, and fasting blood glucose) in patients with psychosis. In 43 outpatients with psychosis (mean age \pm SD: 42.3 \pm 8.5 years, 86% men), SB and light, moderate-to-vigorous, and total PA were measured with the SenseWear Pro3 Armband, and CRF with the 6-minute walking test. Multiple linear regression models adjusted for multiple confounders were applied. High SB, low PA and low CRF levels were associated with an unfavourable cardiometabolic risk profile (increased presence of metabolic syndrome and number of cardiometabolic abnormalities, as well as worse values and elevated presence of abnormalities for all individual cardiometabolic risk factors). SB was associated with CCRS, number of cardiometabolic abnormalities, waist, and fasting blood glucose (all $p < 0.05$). After adjusting for PA and CRF, waist and fasting blood glucose remained significant. Light PA was associated with waist, moderate-to-vigorous PA with CCRS, and total PA with CCRS and waist (all $p < 0.05$). These results became non-significant after adjusting for SB and CRF. CRF was associated with CCRS, waist, and systolic blood pressure (all $p < 0.05$). The associations with CCRS and waist remained significant after adjusting for SB and PA. Together, these results suggest the importance of considering SB and CRF, regardless PA, in the prevention and treatment of cardiometabolic disorders among patients with psychosis.

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1. Introduction

Patients with psychosis, including schizophrenia and bipolar disorders (World Health Organization, 1992), have a greatly reduced life expectancy, up to 15 years, compared to the general population (Lawrence et al., 2013), with cardiometabolic disease being the main contributor (Correll et al., 2017). The increased prevalence of metabolic syndrome and cardiometabolic abnormalities is also evident (Vancampfort et al., 2015b), and has become a major health challenge. Of concern, a recent study (Bruins et al., 2017) revealed that cardiometabolic risk factors remain seriously undertreated in people with psychosis and, therefore, better prevention and treatment of metabolic disorders are imperative for reducing the overwhelming risk of premature mortality.

In general population, there is an established-evidence base indicating that, independently, less sedentary behaviour (SB) and greater physical activity (PA) decrease cardiometabolic risk (Biswas et al.,

2015). Two meta-analyses (Stubbs et al., 2016a; Stubbs et al., 2016b) highlighted that patients with psychosis engage in more SB and in less PA than the general population. To date, some studies (e.g., Nyboe et al., 2015; Stubbs et al., 2015; Vancampfort et al., 2015a) have suggested associations of SB and PA with cardiometabolic risk in patients with psychosis. While helpful, almost all of these studies have relied upon self-report measures, which introduce bias (Soundy et al., 2014), and only one study examined the independent associations of SB and PA with cardiometabolic risk (Stubbs et al., 2017). In this regard, more research, as well as the preferential use of objective measures, is necessary to improve our understanding of the independent effects of these two exposures on cardiometabolic health in this population.

There is also a firmly established-base indicating that a low cardiorespiratory fitness (CRF) level is a strong independent predictor of all-cause and cardiovascular mortality (Harber et al., 2017), with two recent studies (Knaeps et al., 2016a; Knaeps et al., 2016b) finding that CRF mediates the association of SB and PA with clustered-cardiometabolic risk and its individual-components. Patients with psychosis have significantly lower CRF compared with controls (Vancampfort et al., 2017), and the independent associations of SB, PA, and CRF with clustered-cardiometabolic risk and individual-cardiometabolic risk factors remain unexplored.

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The aim of this study was to explore the possible independent associations of SB, PA, and CRF with clustered-cardiometabolic risk and individual-cardiometabolic risk factors in patients with psychosis (schizophrenia and bipolar disorders).

2. Methods

2.1. Participants and setting

Adults with a diagnosis of psychotic illness including schizophrenia and bipolar disorders according to ICD-10 criteria and stabilized on antipsychotic medication was recruited from 11 different outpatient mental healthcare settings in southern Spain. Patients were excluded if they had clinical instability, co-morbid substance abuse, or evidence of uncontrolled cardiovascular, neuromuscular and endocrine disorders. Participants received a full-fasting laboratory screening and anthropometric measurement, performed a walk test, wore a multisensor armband, and completed questionnaires about sociodemographic characteristics and symptomatology. Patient's medical records were also registered. The study procedure was approved by the Universidad Pablo de Olavide Ethics Committee. All patients gave their informed written consent prior to enrolling in the study and after receiving information about the aims and protocol. There was no compensation for participation.

2.2. SB and PA

SB and PA were obtained with a SenseWear Pro3 Armband (BodyMedia Inc., Pittsburgh, PA, USA), a device to accurately estimate energy expenditure (Johannsen et al., 2010). Patients were required to wear the SenseWear on their left arm triceps muscle for nine consecutive days, 24 h/day, except when showering or swimming. The first and last days were excluded from the analysis to minimize the Hawthorne effect (i.e., "a general scientific fact that the process of observation alters the phenomenon being observed") (Corder et al., 2008). Seven days of recordings with a minimum of 1368 min of registration per day was necessary to be included in the analysis. Energy expenditure was estimated using data recorded from multiple sensors and using specific-algorithms developed by the manufacturer (SenseWear Professional software, version 8.1). Time spent in SB ($1.0 < \text{MET} \leq 1.5$) and PA intensities (light, $1.5 < \text{MET} \leq 3.0$; moderate-to-vigorous, $>3.0 \text{ MET}$; and total $>1.5 \text{ MET}$) was derived using the measured MET values during waking hours.

2.3. CRF

CRF was assessed using the 6-minute walking test according to Rikli and Jones (1999) in an indoor course with a flat, firm surface and with minimal external stimuli. Patients were instructed to walk as far as possible during a 6-minute period around a 45.7-meter rectangular course delimited by cones, without running or jogging. Resting was allowed if necessary, but walking was to be resumed as soon as possible. Standardized-encouragements were used at recommended intervals (Rikli and Jones, 1999). The same trained instructor explained the protocol, gave a demonstration prior to the start, supervised the test and recorded the total distance walked to the nearest 0.1 m for each patient. The 6-minute walking test has been shown to be a reliable and valid method to assess CRF in patients with psychosis (Gomes et al., 2016).

2.4. Cardiometabolic risk

The cardiometabolic risk factors were collected by trained-staff in the morning after an overnight fast including waist circumference (waist), systolic/diastolic blood pressure, triglycerides, high-density lipoprotein-cholesterol, and fasting blood glucose. Waist was measured to the nearest 0.1 cm using a measuring tape (Harpenden

Anthropometric Tape; Holtain, Dyfed, UK) placed at the midpoint between the last rib and the iliac crest. Blood pressure was measured in a seated position after 10-minute rest period with an electronic monitor (Omron Healthcare Europe BV, Hoofddorp, The Netherlands) placed on the left arm wrist. The mean of the two measures was used for analysis. If the two measures differed by $>1\%$ for waist, $>20 \text{ mm Hg}$ for systolic and $>10 \text{ mm Hg}$ for diastolic blood pressure, a third measure was taken, and the median of the three was used for analysis (Ward and Anderson, 1998). The presence of metabolic syndrome and cardiometabolic abnormalities was assessed using the International Diabetes Federation criteria (Alberti et al., 2006). Additionally, a clustered-cardiometabolic risk score (CCRS) was constructed. The standardized-normalized indexes ($z\text{-score} = [\text{value} - \text{mean}] / \text{standard deviation}$) for blood pressure ($[\text{systolic} + \text{diastolic blood pressure}] / 2$), triglycerides, fasting blood glucose, waist, and the inverse of high-density lipoprotein cholesterol were summarized and divided by the number of variables included ($x = 5$) to generate the CCRS. Scores above zero represent higher cardiometabolic risk.

2.5. Severity of psychiatric symptoms

Severity of psychiatric symptoms during the previous week was assessed using the Brief Symptoms Inventory-18 (Derogatis, 2001), which has been recommended in patients with mental illness (Prinz et al., 2013). Scores range 0–72, with higher scores indicating a higher severity.

2.6. Demographic, illness-related, and medication data

Marital, educational, occupational and smoking status were self-reported. Weight and height were measured with to the nearest 0.1 kg and 0.1 cm using a scale (TANITA BC-420; Tanita, Tokyo, Japan) and stadiometer, respectively, and body mass index was calculated. Age, diagnosis, illness duration, and medication were retrieved from the patients' medical records, and antipsychotic medication was converted into daily equivalent dosages of chlorpromazine (Gardner et al., 2010).

2.7. Statistical analysis

Due to the skewed distributions, the analyses included the logarithmically transformed data of moderate-to-vigorous PA, triglycerides, and illness duration, as well as the reciprocally transformed data of fasting blood glucose and the square root-transformed data of chlorpromazine and severity of psychiatric symptoms. Differences in SB, PA, and CRF between metabolic syndrome presence were tested using Student's *t*-test. Patients were divided into groups according to high or low levels of SB, PA (light, moderate-to-vigorous and total), and CRF using the median splits, while Student's *t*, Chi-square, and Fisher exact tests were applied to establish differences. Pearson correlation coefficients were calculated between SB, PA, CRF, and cardiometabolic risk. Multiple linear regression analyses were performed with the cardiometabolic risk outcomes as dependent variables and SB, PA, and CRF as the independent variables. Model-1 was adjusted for gender, age, smoking, education, severity of psychiatric symptoms, illness duration, and chlorpromazine dose. Waist was added in Model-2. Additionally, SB, PA, and CRF, as applicable, were added in the fully adjusted models. Only patients with a complete dataset were included in the regression analysis. Residuals were tested for homoscedasticity, linearity and independence. Other than when light and total PA were simultaneously used as independent variables, the variance inflation factor never exceeded five, indicating that multi-collinearity was not a concern (Montgomery et al., 2012). The data were analysed using SPSS Statistics for Windows, Version 22.0 (Armonk, NY: IBM Corp), with statistical significance set at $p\text{-value} < 0.05$. Statistical comparisons between the two psychiatric

groups were not carried out because the small sample size for bipolar disorders ($n = 11$) data could have led to type II statistical errors.

3. Results

Forty-three patients with psychosis were included in the analysis, and characteristics are summarized in Table 1. Within the sample, 28 patients (65.2%) met the criteria for metabolic syndrome. Those with metabolic syndrome were significantly more sedentary, less physically active (for all PA variables), and had lower CRF than those without metabolic syndrome (all $p < 0.05$; data not shown). As presented in Table 2, the high SB, low PA (all variables) and CRF groups exhibited a higher presence of metabolic syndrome and number of cardiometabolic abnormalities than their counterparts, yet not reaching statistical significance except when comparing light PA levels (both $p < 0.05$). Furthermore, worse values and a higher presence of abnormalities for all individual-cardiometabolic risk factors were found in the high SB and low light

PA, moderate-to-vigorous PA, and CRF groups compared with their counterparts; however, significance was only indicated in diastolic blood pressure between SB levels and in waist and triglycerides between light PA levels (all $p < 0.05$). The low total PA group had a significantly higher waist than the high total PA group ($p = 0.025$). Additionally, a heightened CCRS was found in the high SB, and low PA (all variables) and CRF groups, albeit significant only when comparing light and total PA levels (both $p < 0.05$; data not shown).

Correlations between SB, PA, CRF, and cardiometabolic risk are presented in Table 3. SB had a significant negative correlation with all PA variables and CRF (all $p < 0.05$). Furthermore, moderate-to-vigorous and total PA had a significant moderate positive correlation with CRF (both $p < 0.05$). The CCRS and the number of cardiometabolic abnormalities were positively associated with SB and negatively associated with light PA, total PA, and CRF (all $p < 0.05$). In general, significant correlations with individual-cardiometabolic risk factors were fair to moderate, ranging from 0.30 to 0.57, expressed in absolute terms (Table 3).

Due to missing data, a subsample of 38 patients (32 men and 11 with bipolar disorders) with no changes in the correlation coefficients of the significant correlates (all $p < 0.05$; data not shown) was included in the multiple regression analysis (Table 4). SB was associated with the CCRS ($\beta = 0.28$, $p = 0.049$), the number of cardiometabolic abnormalities ($\beta = 0.33$, $p = 0.023$), waist ($\beta = 0.45$, $p = 0.001$), and fasting blood glucose ($\beta = 0.38$, $p = 0.023$) (Model-1). The associations with the CCRS and the number of cardiometabolic abnormalities became non-significant after adjustment for the combined PA and CRF. A significant association for waist remained after adjusting for moderate-to-vigorous PA and CRF. Furthermore, the association with fasting blood glucose remained significant after adjusting for all PA variables, in separate fully adjusted models, and for CRF. Light PA was associated with waist ($\beta = 0.40$, $p = 0.005$) (Model-1). The association attenuated to non-significance after adjusting for SB, moderate-to-vigorous PA, and CRF. Moderate-to-vigorous PA was associated with the CCRS ($\beta = -0.30$, $p = 0.043$) (Model-1). The association moved beyond the threshold of significance after adjusting for SB, PA (light and total PA, in separate fully adjusted models), and CRF. Total PA was associated with the CCRS ($\beta = -0.32$, $p = 0.024$) and waist ($\beta = -0.38$, $p = 0.008$) (Model-1). These results became non-significant after adjust for SB, moderate-to-vigorous PA, and CRF. CRF was significantly associated with the CCRS ($\beta = -0.42$, $p = 0.026$) (Model 2), waist ($\beta = -0.55$, $p = 0.001$), and systolic blood pressure ($\beta = -0.45$, $p = 0.028$) (Model-1). The associations with the CCRS and waist remained after adjusting for SB and all PA variables (in separate fully adjusted models) (Table 4).

4. Discussion

This is one of the few studies (Ekblom et al., 2015; Greer et al., 2015; Knaeps et al., 2016a; Knaeps et al., 2016b; Shuval et al., 2014; van der Velde et al., 2015) to evaluate the independent associations of SB, PA, and CRF with cardiometabolic risk, and the first to focus on patients with psychosis. The main result suggests that although high levels of SB and low levels of PA and CRF are associated with a higher clustered-cardiometabolic risk, only CRF remains significantly related independent of multiple confounders (including SB and PA). Additionally, when examining independently the single cardiometabolic risk factors, CRF and SB are associated with waist and SB with fasting blood glucose, and all of these associations are independent of the other potential exposures. Taken together, these results suggest the importance of considering CRF and SB, regardless of PA, in the prevention and treatment of metabolic disorders among patients with psychosis.

Our results showed the independent association between CRF and clustered-cardiometabolic risk consistent with aforementioned similar studies (Ekblom et al., 2015; Greer et al., 2015; Knaeps et al., 2016a; Knaeps et al., 2016b; Shuval et al., 2014; van der Velde et al., 2015), including three (Ekblom et al., 2015; Knaeps et al., 2016b; van der Velde

Table 1
Patients' characteristics ($n = 43$).

Variables	Values
Age (years)	42.3 \pm 8.5
Body mass index (kg/m ²)	30.5 \pm 5.5
SB (h/day, % of waking time)	8.8 \pm 2.1 (59)
LPA (h/day, % of waking time)	4.3 \pm 1.6 (28)
MVPA (h/day, % of waking time)	1.9 \pm 1.2 (13)
TPA (h/day, % of waking time)	6.2 \pm 2.3 (41)
CRF (m)	598.7 \pm 94.6
Mets ^a	28 (65.1)
No. of meeting Mets ^a	2.8 \pm 1.7
Waist (cm)	105.6 \pm 16.5
IDF criteria	36 (83.7)
SBP (mm Hg)	126.3 \pm 17.8
IDF criteria	21 (48.8)
DBP (mm Hg)	82.4 \pm 11.0
IDF criteria	20 (46.5)
TG (mg/dL)	210.5 \pm 177.0
IDF criteria	25 (58.1)
HDL-C (mg/dL)	44.4 \pm 11.8
IDF criteria	21 (48.8)
FBG (mg/dL)	106.9 \pm 38.8
IDF criteria	20 (46.5)
Severity of psychiatric symptoms (0–72) ^{b, c}	14.7 \pm 11.6
Illness duration (years) ^b	16.2 \pm 9.3
Chlorpromazine equivalent dose (mg/day) ^b	643.7 \pm 576.2
Smoking status (current smoker)	25 (58.1)
Gender (women)	6 (14.0)
Race (Caucasian)	43 (100)
Diagnoses	
Schizophrenia spectrum disorders	32 (74.4)
Bipolar disorders	11 (25.6)
Marital status	
Married	6 (14.0)
Unmarried	32 (74.4)
Separated/divorced	5 (11.6)
Educational status ^b	
Unfinished secondary school	20 (47.6)
Finished secondary school	22 (52.4)
Occupational status ^b	
Working	13 (31.0)
Unemployed	10 (23.8)
Retired	19 (45.2)

Note: Values are in mean \pm SD or n (%). SB, LPA, MVPA, and TPA are for an average day. CRF: cardiorespiratory fitness; DBP: diastolic blood pressure; FBG: fasting blood glucose; HDL-C: high-density lipoprotein cholesterol; IDF: International Diabetes Federation; LPA: light physical activity; Mets: metabolic syndrome; MVPA: moderate-to-vigorous physical activity; SB: sedentary behaviour; SBP: systolic blood pressure; TG: triglycerides; TPA: total physical activity; Waist: waist circumference.

^a According to the International Diabetes Federation criteria.

^b Missing data. Reasons: Incomplete patient medical record data for illness duration and chlorpromazine equivalent dose ($n = 1$ and 3, respectively); incomplete questionnaire data for severity of psychiatric symptoms, educational and occupational status (all $n = 1$).

^c Severity of psychiatric symptoms was assessed using the Brief Symptom Inventory-18; with higher scores indicating high severity of psychiatric symptoms.

Table 2
Comparison of cardiometabolic characteristics between levels of ST, PA, and CRF among outpatients with psychosis (n = 43).

	SB (cut-off: 8.8 h/day)		LPA (cut-off: 4.7 h/day)		MVPA (cut-off: 1.7 h/day)		TPA (cut-off: 6.3 h/day)		CRF (cut-off: 607.2 m)	
	High (n = 21)	Low (n = 22)	Low (n = 21)	High (n = 22)	Low (n = 21)	High (n = 22)	Low (n = 21)	High (n = 22)	Low (n = 21)	High (n = 22)
Mets ^a	16 (76.2)	12 (54.5)	17 (81.0)	11 (50.0)	15 (71.4)	13 (59.1)	16 (76.2)	12 (54.5)	16 (76.2)	12 (54.5)
No. of meeting Mets ^a	3.3 ± 1.7	2.4 ± 1.7	3.4 ± 1.4	2.3 ± 1.8	3.2 ± 1.7	2.5 ± 1.7	3.1 ± 1.7	2.5 ± 1.8	3.2 ± 1.7	2.5 ± 1.7
Waist (cm)	110.3 ± 18.0	101.2 ± 14.0	113.2 ± 12.6	98.4 ± 16.8	106.4 ± 17.6	104.8 ± 15.8	111.3 ± 15.2	100.1 ± 16.2	109.4 ± 18.5	102.0 ± 13.8
IDF-criteria	19 (90.5)	17 (77.3)	21 (100.0)	15 (68.2)	19 (90.5)	17 (77.3)	20 (95.2)	16 (72.7)	19 (90.5)	17 (77.3)
SBP (mm Hg)	130.3 ± 18.0	122.5 ± 17.2	127.9 ± 17.7	124.8 ± 18.2	127.7 ± 19.5	125.0 ± 16.4	131.3 ± 17.7	121.5 ± 16.9	131.2 ± 17.6	121.6 ± 17.1
IDF-criteria	12 (57.1)	9 (40.9)	11 (52.4)	10 (45.5)	12 (57.1)	9 (40.9)	13 (61.9)	8 (36.4)	13 (61.9)	8 (36.4)
DBP (mm Hg)	85.8 ± 11.6	79.1 ± 9.6	83.7 ± 11.9	81.2 ± 10.3	83.8 ± 12.3	81.1 ± 9.7	85.7 ± 11.0	79.2 ± 10.3	85.2 ± 11.5	79.7 ± 10.1
IDF-criteria	13 (61.9)	7 (31.8)	9 (42.9)	11 (50.0)	12 (57.1)	8 (36.4)	11 (52.4)	9 (40.9)	11 (52.4)	9 (40.9)
TG (mg/dL)	231.3 ± 196.6	190.6 ± 158.1	215.4 ± 102.9	205.7 ± 228.6	233.5 ± 198.5	188.5 ± 155.3	208.7 ± 101.3	212.2 ± 230.0	209.7 ± 144.7	211.3 ± 206.7
IDF-criteria	15 (71.4)	10 (45.5)	16 (76.2)	9 (40.9)	15 (71.4)	10 (45.5)	15 (71.4)	10 (45.5)	15 (71.4)	10 (45.5)
HDL-C (mg/dL)	43.0 ± 12.8	45.7 ± 11.0	41.3 ± 9.9	47.3 ± 13.0	44.2 ± 13.7	44.6 ± 10.1	42.4 ± 12.1	46.3 ± 11.6	43.7 ± 11.7	45.1 ± 12.2
IDF-criteria	10 (47.6)	11 (50.0)	11 (52.4)	10 (45.5)	11 (52.4)	10 (45.5)	11 (52.4)	10 (45.5)	11 (52.4)	10 (45.5)
FBG (mg/dL)	117.0 ± 51.2	97.2 ± 17.8	110.7 ± 52.7	103.2 ± 38.1	113.9 ± 51.7	100.2 ± 19.4	106.7 ± 40.8	107.0 ± 37.9	112.4 ± 41.9	101.5 ± 35.9
IDF-criteria	12 (57.1)	8 (36.4)	11 (52.4)	9 (40.9)	11 (52.4)	9 (40.9)	9 (42.9)	11 (50.0)	11 (52.4)	9 (40.9)

Notes: The sample was divided into low and high levels of SB, LPA, MVPA, TPA, and CRF using the median splits. Analyses were conducted with TG logarithmically transformed and FBG reciprocally transformed to obtain a normal distribution, yet crude values are presented in the table for easier interpretation. Values are in mean ± SD or n (%). SB, LPA, MVPA, and TPA are for an average day.

CRF: cardiorespiratory fitness; DBP: diastolic blood pressure; FBG: fasting blood glucose; HDL-C: high-density lipoprotein cholesterol; IDF: International Diabetes Federation; LPA: light physical activity; Mets: metabolic syndrome; MVPA: moderate-to-vigorous physical activity; SB: sedentary behaviour; SBP: systolic blood pressure; TG: triglycerides; TPA: total physical activity; Waist: waist circumference.

Boldface indicates statistical significance (p-value < 0.05).

^a According to the International Diabetes Federation-criteria.

et al., 2015) that objectively measured SB and PA and two (Knaeps et al., 2016a; Knaeps et al., 2016b) that used a clustering of individual-cardiometabolic risk factors in the same individual that might reflect cardiometabolic risk even better than single independent risk factors, as well as the number of cardiometabolic abnormalities and metabolic syndrome (Wijndaele et al., 2006). Our results in patients with psychosis indicated that, together with the lack of association of SB and PA, CRF is the most important exposure for cardiometabolic risk, concurring with the findings of the two studies that used the CCRS (Knaeps et al., 2016a; Knaeps et al., 2016b). An explanation may be because CRF reflects both participation in sedentary and physical activities and the state of physiological systems, thereby providing more information about health status. Moreover, each 5-mL·kg⁻¹·min⁻¹ decrement in peak oxygen uptake (the criterion measure of CRF) corresponds to 56% higher prevalence of cardiovascular risk factors (Aspenes et al., 2011), being a deficient CRF one of the main cardiovascular mortality risk factors (Harber et al., 2017). These findings are of clinical interest, and, consistent with strongly supported evidence (Ross et al., 2016),

highlight that CRF must be considered as a vital sign in clinical practice and in public health.

No study has accounted for SB, PA, and CRF simultaneously in patients with psychosis, and consequently, our results can be compared only with studies including two of the three exposures. Consistent findings in patients with psychosis reported that only CRF, and not PA, was significantly correlated with clustered-cardiometabolic risk (metabolic syndrome) (Nyboe et al., 2015). In another study (Stubbs et al., 2015), it was found that SB, and not PA, was associated with high-sensitivity C-reactive protein level, an inflammatory-marker associated with metabolic syndrome (Kazemi-Bajestani et al., 2017). Although similar findings, the two aforementioned studies (Nyboe et al., 2015; Stubbs et al., 2015) were based on self-reported measures of SB and PA, and consequently, direct comparisons with our results may not be valid. Therefore, in addition to examining the relationship of SB, PA and CRF together for predicting clustered-cardiometabolic risk, our work contributes to the knowledge by objectively measuring behaviour.

Table 3
Pearson correlation coefficients (r) for the association between SB, PA, CRF, and cardiometabolic risk among outpatients with psychosis (n = 43).

	SB		LPA		MVPA		TPA		CRF	
	r	p-Value	r	p-Value	r	p-Value	r	p-Value	r	p-Value
CCRS	0.43	0.004	-0.45	0.002	-0.27	0.084	-0.39	0.009	-0.45	0.003
No. of meeting Mets ^a	0.38	0.012	-0.41	0.006	-0.23	0.130	-0.40	0.004	-0.35	0.021
Waist	0.51	0.001	-0.57	<0.001	-0.25	0.111	-0.47	<0.001	-0.34	0.025
SBP	0.34	0.026	-0.25	0.101	-0.17	0.280	-0.24	0.060	-0.38	0.012
DBP	0.34	0.026	-0.28	0.066	-0.08	0.618	-0.24	0.061	-0.25	0.099
TG	-0.18	0.258	0.24	0.123	0.17	0.277	0.25	0.051	0.17	0.270
HDL-C	0.20	0.203	-0.20	0.188	-0.21	0.182	-0.30	0.025	-0.26	0.088
FBG	0.39	0.010	-0.10	0.522	0.06	0.722	-0.24	0.120	-0.07	0.677
SB	1.00	-	-0.60	<0.001	-0.55	<0.001	-0.67	<0.001	-0.37	0.014
LPA	-0.60	<0.001	1.00	-	0.45	0.003	0.88	<0.001	0.24	0.126
MVPA	-0.55	<0.001	0.45	0.003	1.00	-	0.78	<0.001	0.53	<0.001
TPA	-0.67	<0.001	0.88	<0.001	0.78	<0.001	1.00	-	0.47	0.001
CRF	-0.37	0.014	0.24	0.126	0.53	<0.001	0.47	<0.001	1.00	-

Notes: Analyses were conducted with MVPA and TG logarithmically transformed, and FBG reciprocally transformed, to obtain a normal distribution.

CCRS: clustered-cardiometabolic risk score; CRF: cardiorespiratory fitness; DBP: diastolic blood pressure; FBG: fasting blood glucose; HDL-C: high-density lipoprotein; LPA: light physical activity; Mets: metabolic syndrome; MVPA: moderate-to-vigorous physical activity; SB: sedentary behaviour; SBP: systolic blood pressure; TG: triglycerides; TPA: total physical activity; Waist: waist circumference.

Boldface indicates statistical significance (p-value < 0.05).

^a According to the International Diabetes Federation-criteria (cita).

Table 4
Standardized regression coefficients (β) of SB, PA, and CRF for cardiometabolic risk among patients with psychosis ($n = 38$).

		CCRS		No. of meeting MetS ^a		Waist (cm)		SBP (mm Hg)		DBP (mm Hg)		TG (mg/dL)		HDL-C (mg/dL)		FBG (mg/dL)	
		β	p-Value	β	p-Value	β	p-Value	β	p-Value	β	p-Value	β	p-Value	β	p-Value	β	p-Value
SB	M1	0.28	0.049	0.33	0.023	0.45	0.001	0.26	0.128	0.29	0.090	0.20	0.198	-0.16	0.297	0.38	0.023
	M2							0.01	0.967	-0.01	0.945	0.24	0.202	-0.09	0.642	0.44	0.032
	M2 + LPA	0.34	0.042	0.29	0.108	0.34	0.038	0.01	0.960	-0.01	0.979	0.30	0.159	-0.11	0.595	0.59	0.010
	M2 + MVPA	0.22	0.104	0.35	0.072	0.48	0.007	0.01	0.953	0.06	0.805	0.16	0.495	0.05	0.824	0.77	0.002
	M2 + TPA	0.30	0.099	0.31	0.128	0.38	0.040	0.04	0.864	0.01	0.966	0.20	0.397	-0.02	0.921	0.71	0.005
	M2 + CRF	0.19	0.124	0.28	0.086	0.31	0.026	-0.04	0.848	-0.02	0.895	0.21	0.278	-0.04	0.845	0.43	0.045
	M2 + LPA + CRF	0.22	0.179	0.26	0.189	0.22	0.161	-0.03	0.888	-0.02	0.936	0.28	0.212	-0.07	0.757	0.58	0.015
	M2 + MVPA + CRF	0.19	0.147	0.32	0.107	0.40	0.016	0.02	0.938	0.06	0.801	0.16	0.498	0.05	0.836	0.77	0.002
	M2 + TPA + CRF	0.24	0.166	0.29	0.164	0.32	0.069	0.04	0.880	0.01	0.971	0.20	0.409	-0.02	0.935	0.71	0.005
LPA	M1	-0.26	0.063	-0.24	0.109	-0.40	0.005	-0.22	0.197	-0.25	0.150	-0.03	0.836	0.09	0.585	-0.03	0.851
	M2							0.00	0.994	0.02	0.922	0.00	0.983	-0.01	0.977	0.05	0.797
	M2 + SB	-0.05	0.758	-0.06	0.745	-0.19	0.230	0.01	0.976	0.01	0.942	0.13	0.517	-0.06	0.784	0.32	0.134
	M2 + MVPA	-0.15	0.381	-0.18	0.316	-0.36	0.035	0.00	0.998	-0.03	0.886	0.14	0.498	-0.13	0.513	0.02	0.933
	M2 + CRF	-0.12	0.356	-0.18	0.268	-0.27	0.045	0.03	0.888	0.02	0.895	0.02	0.920	-0.03	0.849	0.07	0.722
	M2 + SB + MVPA + CRF	-0.03	0.867	-0.07	0.718	0.25	0.163	-0.02	0.940	-0.03	0.897	0.18	0.420	-0.12	0.590	0.17	0.423
MVPA	M1	-0.30	0.043	-0.21	0.178	-0.29	0.061	-0.16	0.379	-0.13	0.497	-0.21	0.200	0.23	0.161	0.01	0.954
	M2							0.00	0.991	0.07	0.657	-0.21	0.229	0.18	0.287	0.07	0.713
	M2 + LPA	-0.21	0.242	-0.10	0.599	-0.07	0.689	0.00	0.994	0.09	0.654	-0.28	0.174	0.20	0.442	0.06	0.792
	M2 + SB	-0.25	0.093	0.03	0.873	0.05	0.776	0.01	0.965	0.11	0.620	-0.12	0.588	0.21	0.334	0.51	0.023
	M2 + TPA	-0.08	0.762	0.01	0.980	0.12	0.644	-0.06	0.845	0.14	0.615	-0.21	0.491	0.25	0.217	0.15	0.669
	M2 + CRF	-0.10	0.536	-0.12	0.529	-0.06	0.717	0.09	0.654	0.11	0.549	-0.18	0.362	0.12	0.518	0.16	0.468
	M2 + SB + LPA + CRF	0.07	0.722	0.10	0.660	0.25	0.163	0.10	0.690	0.16	0.534	-0.15	0.550	0.31	0.239	0.54	0.033
	M2 + SB + TPA + CRF	0.07	0.761	0.12	0.677	0.30	0.197	0.02	0.943	0.19	0.550	-0.12	0.704	0.26	0.403	0.48	0.122
	M2 + SB + MVPA + CRF	-0.09	0.700	-0.06	0.821	-0.18	0.436	0.11	0.724	-0.06	0.839	0.06	0.860	-0.12	0.715	0.19	0.534
TPA	M1	-0.32	0.024	-0.25	0.097	-0.38	0.008	-0.19	0.277	-0.23	0.197	-0.17	0.290	0.17	0.268	-0.05	0.784
	M2							0.03	0.872	0.03	0.863	-0.18	0.329	0.11	0.524	0.03	0.898
	M2 + SB	-0.10	0.586	-0.03	0.888	-0.11	0.545	0.05	0.819	0.04	0.872	-0.06	0.791	0.10	0.660	0.44	0.057
	M2 + MVPA	-0.26	0.295	-0.26	0.342	-0.48	0.061	0.08	0.802	-0.09	0.761	-0.01	0.980	-0.11	0.720	-0.09	0.788
	M2 + CRF	-0.13	0.389	-0.17	0.332	-0.19	0.214	0.11	0.576	0.05	0.775	-0.13	0.609	0.04	0.823	0.09	0.671
	M2 + SB + MVPA + CRF	-0.09	0.700	-0.06	0.821	-0.18	0.436	0.11	0.724	-0.06	0.839	0.06	0.860	-0.12	0.715	0.19	0.534
CRF	M1	-0.42	0.026	-0.29	0.118	-0.55	0.001	-0.45	0.028	-0.40	0.058	-0.18	0.350	0.30	0.113	-0.22	0.296
	M2							-0.21	0.359	-0.05	0.807	-0.20	0.393	0.25	0.265	-0.18	0.492
	M2 + SB	-0.46	0.005	-0.12	0.553	-0.37	0.034	-0.22	0.357	-0.06	0.791	-0.13	0.575	0.24	0.311	-0.05	0.850
	M2 + LPA	-0.45	0.010	-0.21	0.293	-0.43	0.011	-0.21	0.362	-0.06	0.798	-0.20	0.399	0.26	0.267	-0.19	0.472
	M2 + MVPA	-0.45	0.018	-0.22	0.317	-0.52	0.009	-0.26	0.314	-0.12	0.634	-0.10	0.708	0.18	0.470	-0.27	0.355
	M2 + TPA	-0.42	0.026	-0.17	0.423	-0.43	0.026	-0.26	0.294	-0.08	0.740	-0.13	0.609	0.23	0.355	-0.23	0.431
	M2 + SB + LPA	-0.37	0.039	-0.11	0.583	-0.35	0.045	-0.22	0.366	-0.06	0.793	-0.14	0.565	0.24	0.315	-0.06	0.808
	M2 + SB + MVPA	-0.42	0.026	-0.14	0.505	-0.42	0.021	-0.26	0.323	-0.12	0.637	-0.10	0.701	0.18	0.481	-0.29	0.250
	M2 + SB + TPA	-0.38	0.043	-0.12	0.570	-0.37	0.046	-0.26	0.305	-0.08	0.745	-0.13	0.622	0.23	0.365	-0.21	0.400

Notes: M1 is adjusted for gender, age, smoking, education, severity of psychiatric symptoms, illness duration, and chlorpromazine dose. M2 is adjusted for all covariates in M1 and adjusted for waist circumference (except when CCRS, No. of meeting MetS and Waist were the outcomes). Analyses were conducted with MVPA and TG logarithmically-transformed, and FBG reciprocally-transformed, to obtain a normal distribution.

CCRS: clustered-cardiometabolic risk score; CRF: cardiorespiratory fitness; DBP: diastolic blood pressure; FBG: fasting blood glucose; HDL-C: high-density lipoprotein cholesterol; LPA: light physical activity; M: model; MetS: metabolic syndrome; MVPA: moderate-to-vigorous physical activity; SB: sedentary behaviour; SBP: systolic blood pressure; TG: triglycerides; TPA: total physical activity, Waist: waist circumference.

Boldface indicates statistical significance (p -value < 0.05).

^a According to the International Diabetes Federation-criteria.

Our results indicated that CRF and SB are both related to waist, independent from each other and from PA, suggesting that CRF and SB are two independent predictors of waist. Consistent findings in patients with psychosis have revealed significant associations between CRF and waist accounting for self-reported PA (Nyboe et al., 2015; Vancampfort et al., 2015a). However, our results were inconsistent with the findings of the only study in patients with psychosis that explored the SB-waist association adjusting for PA (Stubbs et al., 2017). This discrepancy may be because the authors of that study (Stubbs et al., 2017) used accelerometers to obtain an objective indirect estimations of SB and PA through the absence of whole-body movement and the number of steps, respectively, which could introduce bias for both exposures. Considering SB as the absence of whole-body movement is an important conceptual error (Sedentary Behaviour Research, 2012), and the number of steps only provides a value of total ambulatory PA, thereby excluding a range of free-living physical activities aside from walking and or running, such as gardening or washing, which have shown beneficial effects on cardiovascular health (van den Berg et al., 2010). Accordingly, the use of sensor combining physiological measures with movement and position sensing to identify SB and PA may be a more appropriate way to obtain accurate results.

Again, inconsistent with the aforementioned study (Stubbs et al., 2017), our results showed that the relationship between SB and fasting blood glucose remained significant when adjusting for PA. Discrepancies between studies can be explained, in addition to the different instruments of assessment of SB and PA used, because we assessed PA at different intensities and controlled for waist, a predisposing factor for the development of type 2 diabetes mellitus (Freemantle et al., 2008), showing that the SB-fasting blood glucose association did not vary. Additionally, our findings remained significant even when CRF was included with the rest of the confounders, suggesting that SB seems to be an important and independent risk factor for fasting blood glucose in patients with psychosis. However, further research combining SB, PA, and CRF interactions with cardiometabolic outcomes in patients with psychosis is needed before any firm conclusions can be made.

The major strength of the study is the objective measurement of SB and PA using strict inclusion criteria. All patients wore the SenseWear for seven consecutive days with at least 1368 min/day, and the Hawthorne effect (explained in brief in the method section) was minimized. Another strength is the use of the time spent in different intensities of PA which extends the knowledge on the independent association of SB, PA, and CRF with cardiometabolic risk and informs, in greater detail,

on intervention strategies for treating metabolic disorders among patients with psychosis focused on the development of a more active life-style that enhance/maintain CRF. Finally, the adjustment for covariates that could influence the relationships between SB, PA, and CRF with cardiometabolic risk can also be considered a strength. Multiple linear regression analyses were adjusted for obesity in addition to other covariates such as gender, age, smoking, education, symptom severity, illness duration, and antipsychotic medication, previously controlled in psychiatric patients studies (i.e., Stubbs et al., 2017). This approach was only applied in two (Shuval et al., 2014; van der Velde et al., 2015) of the six studies (Ekblom et al., 2015; Greer et al., 2015; Knaeps et al., 2016a; Knaeps et al., 2016b; Shuval et al., 2014; van der Velde et al., 2015) that evaluated the independent associations of SB, PA, and CRF with cardiometabolic risk.

Some limitations should be noted. The small sample size of outpatients, predominantly men diagnosed with schizophrenia, may limit the generalization to other groups. Future research should use large and homogeneous sample, and compare between different clinical settings, genders, and psychiatric disorders. Another limitation is that the current study was cross-sectional in design. Longitudinal studies are needed to identify any casual relationships. Although the absence of control group can be considered a study limitation, we compared our data against all published studies that have examined the independent associations of SB, PA, and CRF with cardiometabolic risk, each of which is based on observations from hundreds of healthy individuals. Nevertheless, further studies including control group are required to confirm or refute our findings. The SenseWear cannot differentiate body positions, and consequently, standing may be considered as SB. However, it may solve limitations presented by accelerometers and inclinometers through heat production measurements and placement on the upper arm. Additionally, the SenseWear underestimates energy expenditure at higher PA intensities (Drenowatz and Eisenmann, 2011). However, because we used time engaged in moderate-to-vigorous PA, it is unlikely that this affected our results. Moreover, because the objective measurement did not inform about the type of SB and PA, future studies should combine objective with self-report measurements. In patients with severe mental illness, the Sedentary Behaviour and the International Physical Activity questionnaires seem appropriate for quantifying time engaged in different SBs (Bueno-Antequera et al., 2017) and PAs (Faulkner et al., 2006), respectively. The assessment of CRF using an indirect measurement and a submaximal test could be considered as another limitation. However, the test used in this study has been found to be a reliable and valid method in patients with psychosis (Gomes et al., 2016). The CCRS has several advantages for evaluating cardiometabolic risk (Wijndaele et al., 2006), is sample-specific and is based on the assumption that each component is weighted equally in predicting cardiometabolic risk. Finally, dietary information was not considered as a covariate, and the data on symptomatology was self-reported.

In conclusion, low CRF was found to be a predictor of high clustered-cardiometabolic risk independent of multiple confounders, including SB and PA, in patients with psychosis. This study further found associations of SB, PA, and CRF with individual-cardiometabolic risk factors. Therefore, in addition to developing interventions to reduce SB and increase PA, interventions of randomized controlled trials of physical exercise in patients with psychosis are needed to determine whether reduced CRF and increased cardiometabolic risk can be improved.

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Contributors

JB and DM designed the study and wrote the protocol. All authors were responsible for the acquisition of the data. JB and DM performed the statistical analyses and JB wrote the manuscript. All authors provided critical review of the manuscript and approved the final version.

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