Andersen, E., Holmen, T. L., Egeland, J., Martinsen, E. W., Bigseth, T. T., Gry, B. ... Engh, J. A. (2018). Physical activity pattern and cardiorespiratory fitness in individuals with schizophrenia compared with a population-based sample. *Schizophrenia Research.*

Title page

Physical activity pattern and cardiorespiratory fitness in individuals with schizophrenia compared with a population-based sample

Eivind Andersen[1], Tom Langerud Holmen[2], Jens Egeland[2,3], Egil Wilhelm Martinsen[4,5], Therese Torgersen Bigseth[2], Gry Bang-Kittilsen[2], Sigmund Alfred Anderssen[6], Bjørge Herman Hansen[6] and John Abel Engh[2]

[1]Faculty of Humanities, Sports and Educational Science, University College of Southeast Norway, Horten, Norway [2]Division of Mental Health and Addiction, Vestfold Hospital Trust, Tønsberg, Norway, [3]Department of Psychology, University of Oslo, Oslo, Norway, [4]Clinic Mental Health and Addiction, Oslo University Hospital, Oslo, Norway, [5]Institute of Clinical Medicine, University of Oslo, Oslo, Norway, [6]Department of Sports Medicine, Norwegian School of Sports Sciences, Oslo, Norway

Running title: PA pattern and CRF in schizophrenia

Corresponding author:

Eivind Andersen

Tlf: +4790059514

E-mail: Eivind.andersen@usn.no

University College of Southeast Norway, PO box 235, 3603 Kongsberg

Abstract

Objective: Thorough description of objectively assessed physical activity (PA) and sedentary time in people with schizophrenia is lacking, and previous studies comparing PA and cardiorespiratory fitness levels with healthy controls are limited by their small sample size and/or poor methodology.

Method: PA, sedentary behavior, and cardiorespiratory fitness level were assessed in 67 adults diagnosed with schizophrenia (EPHAPS study) and compared with a population-based sample of 2809 adults (NPASS study).

Results: Fifty-five percent of the participants with schizophrenia had the unhealthy combination of not meeting the PA recommendations *and* sitting more than 7.5 h per day compared to 32% in the population-based sample. The PA level was especially low on weekday afternoons and evenings and throughout most of the day on weekends. The peak oxygen uptake for EPHAPS women was on average 23% lower than that for NPASS women, while EPHAPS men achieved on average 34% lower oxygen uptake on the exercise test compared with NPASS men.

Conclusion: People with schizophrenia are significantly less physically active, more sedentary, and have a poorer cardiorespiratory fitness level compared with the general population. Tailor-made PA interventions for people with schizophrenia should target their PA and sedentary behavior on afternoons and weekends especially.

Key words: Schizophrenia, physical activity, sedentary time, cardiorespiratory fitness

1. Introduction

People with schizophrenia have mortality rates 2–3 times higher than the general population, equating to a mortality gap of 10–20 years (Saha et al., 2007). This heightened mortality risk can be partly explained by the high prevalence of noncommunicable diseases such as cardiovascular diseases (CVD) (Capasso et al., 2008) and type 2 diabetes (T2D) (Vancampfort et al., 2016). The reasons for this increased risk of CVD and T2D among patients with schizophrenia are likely to be a complex interplay between many factors, such as genetic disposition (Andreassen et al., 2013), adverse effects of antipsychotic medication (Mitchell et al., 2013; Wu et al., 2015), and health inequalities (De Hert et al., 2011; Mitchell et al., 2009). Moreover, an observed low physical activity (PA) level (Stubbs et al., 2016), high amount of time spent in sedentary behavior (defined as any waking behavior characterized by an energy expenditure ≤ 1.5 metabolic equivalents, while in a sitting, reclining, or lying posture (Tremblay et al., 2017)) (Janney et al., 2013), and low cardiorespiratory fitness (CRF) level (Vancampfort et al., 2015) have been recognized as potentially crucial factors (Mitchell et al., 2009; Ratliff et al., 2012; Vancampfort et al., 2013).

Although some studies have reported on PA level (Soundy et al., 2013) and time spent sedentary (Janney et al., 2013) with the use of accelerometers in people with schizophrenia, the full potential of the device to describe PA and sedentary patterns in detail has not been explored. Important aspects of accelerometer PA and sedentary data, such as weekend vs. weekday and time of day (hour-by-hour) have not yet been described in persons with schizophrenia. By including these data we can obtain more comprehensive PA and sedentary profiles that highlight critical opportunities for intervention. Furthermore, comparison of the data with a population-based sample ensures that epoch lengths (sample time), nonwear definitions, and cutoff points for intensity are harmonized, providing a solid basis to investigate how physically active and sedentary patients with schizophrenia really are, and in what way (if any) their PA and sedentary profiles differ from the general population. The few studies that have compared PA (Soundy et al., 2013; Stubbs et al., 2016) and CRF (Kimhy et al., 2014; Ostermann et al., 2013; Ozbulut et al., 2013; Strassnig et al., 2011; Vancampfort et al., 2015) levels with healthy controls are, except for one Dutch study (Scheewe et al., 2012), limited by their small sample size and/or poor measurement methods, and none have compared their results to a national representative sample. In short, a more detailed picture of the PA and sedentary patterns in this vulnerable population would assist clinicians and others in how best to help patients with schizophrenia become more physically active and less sedentary, and thereby reduce the burden of noncommunicable diseases and presumably improve quality of life.

Thus, the aim of this study was to provide a detailed description of the PA pattern, sedentary behavior, and cardiorespiratory fitness level in a sample of outpatients with schizophrenia and to compare these with a population-based sample.

2. Material and methods

2.1 Design

This study is based on baseline data from the Effects of Physical Activity in Psychosis study (EPHAPS) (ClinicalTrials.gov, registration number NCT02205684) and the Norwegian Physical Activity Surveillance Survey (NPASS). Both studies were approved by the Regional Ethics Committee for Medical Research (EPHAPS; 2014/372, NPASS; S-08046b). The methods used in EPHAPS and NPASS have been described in detail elsewhere (Edvardsen et al., 2013; Engh et al., 2015; Hansen et al., 2012). Briefly, the EPHAPS study was designed as a randomized controlled, parallel group, observer-blinded clinical trial with the aim of investigating the effects of an supervised aerobic high-intensity, interval-training program, performed twice a week for 12 weeks, on maximal oxygen uptake (VO_{2max}), cognitive function, psychiatric symptom load, well-being, and CVD risk factors in outpatients with schizophrenia. The NPASS study is a surveillance system, involving 10 regional test centers throughout Norway, which aims to monitor and track the PA activity level and sedentary behavior among the Norwegian adult population. In 2008–2009, a national representative sample was invited to wear an accelerometer for 7 days and to complete a questionnaire. In addition, a subsample of NPASS participants was invited to perform a VO_{2max} test.

2.2 Study sample

In the EPHAPS study, 84 participants were recruited from August 2014 through September 2016 from catchment area-based and publicly funded outpatient psychiatric clinics in Vestfold County, Norway. A subgroup of patients was referred from primary health care to the outpatient clinics for specific participation in the project. Patients who fulfilled the Diagnostic and Statistical Manual of Mental Disorders (5th ed.; DSM-5; American Psychiatric Association) (AmericanPsychiatricAssociation, 2013) criteria for schizophrenia spectrum disorder (schizophrenia, schizoaffective disorder, and schizophreniform disorder), were aged 18–67 years old, and who understood and spoke a Scandinavian language were eligible for the study. Patients who were pregnant, experienced chest pain during the cardiorespiratory exercise test, had unstable angina pectoris, recent myocardial infarction, uncontrollable cardiac arrhythmias, severe hypertension (>180/110 mmHg), comorbid diagnosis of mild mental retardation, and/or other medical conditions incompatible with participation in the main study were excluded. Initial information about the EPHAPS study was given to eligible patients by clinical staff in the outpatient clinic or in primary health services. Contingent on understanding the nature of the research and a willingness to participate, written consent was obtained. All participants were asked to wear an accelerometer for four consecutive days and conduct a maximal exercise test. Sixty-seven participants (80 %) wore the accelerometer for two days or more and were included in the current study.

In the NPASS study, a representative sample of 11,515 adults aged 20–85 years old from the areas surrounding each test center was drawn from the Norwegian population register and invited by mail to join the study. There were no inclusion or exclusion criteria apart from age. Written informed consent was obtained from 3867 individuals (34 %). To ensure comparability with the EPHAPS study, all individuals above 67 years of age and with an accelerometer wear time of less than two days were excluded from the NPASS material, giving a total sample of 2809 participants in the current study. Furthermore, from the initial sample of 3867 individuals, a subsample of predominately Caucasians (N = 1930) was randomly selected and invited to participate in the maximal exercise test. Finally, 904 men and women undertook the examination, where 794 individuals successfully completed the test and were within the age criteria of the present study.

2.3 Measurements

Assessment of PA. In both samples, free-living PA was assessed using the ActiGraph GT3X+ and GT1M accelerometers (ActiGraph, LLC, Pensacola, FL, USA) vertical axis collection mode. The participants were instructed to wear the accelerometer over the left hip while awake, except during water-based activities (e.g., showering, swimming), for four consecutive days (EPHAPS) or seven days (NPASS). The epoch length (sample interval) was set to 10 s. All data were reintegrated into 60 s epochs and further processed and analyzed using a specialized accelerometer analytical software (Kinesoft, version 3.3.80, Saskatchewan, Canada). In the analysis of accelerometer data, consecutive strings of epochs with a count value of zero lasting at least 60 minutes (with two exceptions) were treated as non wear and thus removed from the data array (Cooper et al., 2015). Analyses were restricted to participants who wore the accelerometer for a minimum of 10 h per day (Wolff-Hughes et al., 2014) on at least two days (including one weekday and one weekend day). To identify different intensities of PA, count thresholds corresponding to the energy cost of the given intensity were applied to the data set. Sedentary time was defined as all activity < 100 counts per minute (CPM), a threshold that corresponds with sitting, reclining, or lying down (Matthews et al., 2008). Light intensity PA was defined as 100–2019 CPM, moderate as 2020–5998 CPM, and vigorous as CPM ≥ 5999 (Troiano, 2005). The numbers of minutes per day at different intensities were based on summing the time where the activity count met the criteria for that intensity. All MVPA that occurred in bouts of 10 min (with allowance for interruptions of 1–2 min) during the registration period were divided by the number of valid days to examine whether PA recommendations were met. This definition allows participants to have longer bouts of activity on certain days and to be less active on other days and still meet the recommendations. We also calculated whether the participants reached 150 min of MVPA per week without the 10 min bout criterion. Furthermore, participants were classified according to whether they accumulated more than 7.5 h and 10 h of sedentary time per day (Loyen et al., 2017).

Assessment of maximal oxygen uptake. Cardiorespiratory fitness or peak VO_2, defined as the highest measured oxygen uptake, was assessed through a maximum exercise test on a treadmill. For various reasons some individuals may fail to reach a true VO_{2max}, and for the sake of conservative reporting, we therefore use the term VO_{2peak}. Both EPHAPS and NPASS participants used a modified Balke protocol (Balke and Ware, 1959), where speed was held constant at 5 km/h and the inclination angle was increased by one degree every minute until exhaustion. Gas exchanges were continuously sampled in a mixing chamber every 30 s by breathing into a Hans Rudolph two-way breathing valve (2700 series, Hans Rudolph Inc, Kansas City, KS, USA). In the EPHAPS study, the breathing valve was connected to a Jaeger Oxycon Pro (Erich Jaeger GmbH, Hoechberg, Germany) used to analyze the oxygen and carbon content. In the NPASS study, three types of gas analyzers were used: Oxycon Pro (Erich Jaeger GmbH; n 5 2), Vmax SensorMedics (CareFusion Corporation; n 5 6), and the Moxus Modular V o 2 system (AEI Technologies, Inc; n 5 1). A correction factor was calculated for each gas analyzer to ensure reliable and comparable data between the test laboratories. The analyzer was volume- and gas-calibrated before each test. Maximal heart rate and respiratory exchange ratio (RER) were measured immediately after completion of the exercise test. The test result was included in the current study if the RER was ≥ 1.00.

Other measures. Weight was measured without shoes in light clothing by a SECA electronic scale (SECA model 767, Germany) to the nearest 0.5 kg. Height was measured without shoes with a transportable stadiometer (Harpenden; Holtain, Crymych, Wales) and set to the nearest 0.5 cm. Weight and height were self-reported in the NPASS study. Overweight and obesity were defined as a BMI of 25–29 and ≥ 30, respectively (2000). Data on education, employment, and marital status were obtained through a self-complete questionnaire.

2.4 Statistical analysis

All statistical analyses were performed using SPSS (Statistical Package for the Social Sciences for Windows, version 24, IBM, Inc., Chicago, IL, USA). Descriptive data are presented as proportion, mean, and standard deviation (SD) with 95% confidence intervals (CIs) where appropriate. Within- and between-differences of interval data were evaluated by *t* tests (independent *t* tests and paired *t* tests). Differences between groups were assessed using a univariate general linear model. Accelerometer wear time, sex, age, bodyweight and RER were considered potential confounders and included in the relevant analysis. Differences between the proportions of individuals meeting PA recommendations, education level, employment and marital status were assessed using chi-squared tests. All tests were based on two-sided probability.

3. Results

The participants wore the monitor for an average (± standard deviation (SD)) of 3.3 ± 0.8 days (EPHAPS) and 6.4 ± 0.9 days (NPASS). The mean wearing time was 12.9 ± 1.4 $h \cdot day^{-1}$ and 14.8 ± 1.1 $h \cdot day^{-1}$ for the EPHAPS and NPASS participants, respectively.

Table 1 displays the relevant demographic information for both groups. The EPHAPS population of patients with schizophrenia was significantly younger, heavier, less educated, and far fewer were employed and married. Except for one patient, all patients were using antipsychotic medication. Sixty-one percent were on atypical antipsychotic medication, and 4.5% were using typical antipsychotic medication. Polypharmacy was applied to 33% of the patients. Additional regular anxiolytic and/or antidepressant or mood stabilizing medication was received by 24 and 11 participants, respectively.

PLEASE INSERT TABLE 1 ABOUT HERE

The EPHAPS participants spent a significantly longer part of the day sedentary (69% ± 11 vs. 61% ± 9; 7.4 mean diff, 95% CI = 10 to 5) and less time in light intensity PA (28% ± 10 vs. 34% ± 8; –6.3 mean diff, 95% CI = –9 to –4) and MVPA (3.0% ± 2.5 vs. 4.0% ± 2.6; 1.0 mean diff, 95% CI = –1.7 to 0.5) compared with the NPASS population. The EPHAPS participants were significantly less physically active and more sedentary on both weekdays (Table 2A) and weekends (Table 2B) compared with the NPASS participants. Furthermore, while the NPASS participants increased the amount of MVPA slightly from weekdays to weekends (1.1 min; 95% CI = 0.3 to 2.1), and reduced the amount of sedentary time (57 min; 95% CI = 53 to 61), the EPHAPS participants reduced the amount of MVPA (-6.6 min; 95% CI = 1.4 to 13) and were just as sedentary on weekends as on weekdays.

PLEASE INSERT TABLE 2 ABOUT HERE

Figure 1 shows the prevalence of participants meeting different PA and sedentary recommendations. Approximately two-thirds of the EPHAPS participants did not achieve the PA recommendation, based on total time in MVPA (≥ 21.5 min per day), and almost nobody accumulated ≥ 10,000 steps per day. According to the official criteria (WHO, 2010), which state that MVPA must be in ≥ 10 min bouts, only 18% would be classified as sufficiently physically active. Furthermore, many EPHAPS participants were sedentary for longer than recommended and more than half of this population had the unhealthy combination of sitting too much and not engaging in enough MVPA. Only 13% were classified as low sedentary (≤ 7.5 h per day) *and* high PA (≥ 21.5 min of MVPA per day). Compared with the NPASS population, the prevalence of EPHAPS participants who did not meet the PA recommendations was higher, but somewhat lower for sedentary time. The differences between the groups were especially notable when looking at accumulation of MVPA (25%, 95% CI = 23–26), steps (23%, 95% CI = 21–24) and the combination of MVPA and sitting time (23%, 95% CI = 19–24).

PLEASE INSERT FIGURE 1 ABOUT HERE

In the EPHAPS group compared with NPASS participants, the PA level was significantly lower ($P \leq 0.05$) in the afternoons (17:00–20:00) and evenings (22:00–24:00) during weekdays, and throughout most of the day during weekends (09:00–17:00) (Figure 2). Furthermore, while EPHAPS participants reduced their PA level on weekends, the NPASS population increased their PA level significantly on weekends compared with weekdays.

PLEASE INSERT FIGURE 2 ABOUT HERE

Tables 3A and 3B show the average peak oxygen uptake for women and men, respectively, for the two cohorts. The EPHAPS participants who performed the maximal exercise test were significantly younger, heavier, had a lower level of MVPA, and achieved lower RER and maximal HR at the end of the test compared with the NPASS group. Adjusted for body weight, age, and RER, the peak oxygen uptake for EPHAPS women was on average 23% lower than that for NPASS women, while EPHAPS men achieved on average 34% lower oxygen uptake on the exercise test compared with NPASS men.

PLEASE INSERT TABLE 3 ABOUT HERE

4. Discussion

The patients with schizophrenia performed less MVPA and spent more time sedentary compared with the NPASS population-based sample, on both weekdays and at weekends. Interestingly, while the NPASS participants were more active and less sedentary on weekends compared with weekdays, no such increment was found for the EPHAPS group. The PA level of EPHAPS participants was especially low in the afternoons and evenings during weekdays and throughout most of the day on weekends compared with the NPASS group. Finally, although the EPHAPS population was ~10 years younger than the NPASS group, they had a much lower peak oxygen uptake.

Findings of a lower level of MVPA and more sedentary time in patients with schizophrenia compared with healthy controls fits well with two meta-analyses (Soundy et al., 2013; Stubbs et al., 2016), although it should be noted that only two studies using accelerometers were included in these analyses, and both had small sample sizes. Contrary to these studies, we found that the patients with schizophrenia also were engaged in less light intensity PA than controls. Our findings of a significant difference in maximal oxygen uptake between people with schizophrenia and healthy controls is in accordance with the few other high quality studies with adequate number of participants investigating this (Scheewe et al., 2012; Strassnig et al., 2011). The reason for this observed low fitness level is not known, but probably the low PA level and/or high amount of sedentary time (Vancampfort et al., 2017) contributes substantially. The impaired fitness level has been shown previously to be present already before their first-episode psychosis (Vancampfort et al., 2015).

By splitting the accelerometer variables into weekdays and weekends, and furthermore hour-by-hour, the data provide some interesting insights regarding PA patterns. First, it is clear that the difference in PA and sedentary time between the patients and the population-based sample is most pronounced at times when people are normally off duty. While the EPHAPS participants markedly reduced their PA level on weekday afternoons, the NPASS participants increased their PA level slightly. Furthermore, on weekends, the NPASS population significantly increased their PA level, while the EPHAPS participants were at their most inactive. At these times, the PA level of the EPHAPS group was just half that of the NPASS sample. At all other times, the PA levels and sedentary time were not markedly different between the two groups. These findings are interesting, and activity data in this detail has not previously been published.

Positive and negative symptoms represent profound challenges to social and general functioning for patients with schizophrenia (AmericanPsychiatricAssociation, 2013; Green et al., 2004). Cognitive impairments may interfere with the planning and executing of various activities, and the structuring of life in general. Low education level, a high unemployment rate and a high proportion of the participants living alone, reflect the challenges with daily functioning faced by this patient group. Positive and negative psychotic symptoms, general feelings of mental unwellness and adverse effects of antipsychotic medication have all been identified as specific barriers to PA for individuals with schizophrenia (Rastad et al., 2014; Vancampfort et al., 2012a; Vancampfort et al., 2012b). Other highly prevalent factors within this patient population, such as noncommunicable diseases (e.g, CVD and T2D) (Vancampfort et al., 2012b), obesity (McLeod et al., 2009), low CRF level (Vancampfort et al., 2015) and drug and alcohol abuse (Ringen et al., 2008), may create further barriers to PA and thus incite sedentary behavior (O'Donoghue et al., 2016; Vancampfort et al., 2013; Vancampfort et al., 2012b). Moreover, the disorder-related difficulties with social functioning and activity engagement represent major obstacles to active leisure time, particularly in the absence of social support. Many have limited personal networks to engage with during evenings and weekends, and outpatient psychiatric treatment and community-based psychosocial and activity services are often offered during weekday business hours only. We do not know the reason for the passivity of the patients with schizophrenia outside working hours, but one hypothesis is that their activity is to a larger degree connected to organized activities like going to work, being at work or in training or treatment. Activity on evenings and weekends is probably more self-driven and self-initiated, and many individuals with schizophrenia have difficulties with initiative and self-regulation. Discrepancies in PA level between the two groups are also likely to arise from the fact that it is commonplace for the general population in Norway to exercise and go hiking in their leisure time. For the majority this is also a social event. Many people with severe mental disorders are lonely (Badcock et al., 2015) and may have fewer people around them, and hence go out with or to exercise with.

In our sample of patients with schizophrenia, only 18% achieved the PA recommendations. Overall, they took on average 5000 steps per day, 70% of the day was spent completely sedentary, half of the population combined too little MVPA with too much sedentary time, and the CRF level was comparable with the age group of 70–85 years in the general population (Edvardsen et al., 2013). Although these results are alarming, they are not new to the scientific community. Several studies have reported a very low PA level and high sedentary time among people with schizophrenia (Janney et al., 2015; Soundy et al., 2013; Stubbs et al., 2016), although somewhat higher MVPA levels were reported in a meta-analysis by Stubbs et al. (2016) (Stubbs et al., 2016) than in the current study. The low level of MVPA, the high sedentary time, and the low CRF level might be important explanations for the high prevalence of CVD in this population. Although the evidence is scarce regarding the impact of PA on cardiometabolic variables in schizophrenia, there should be sufficient evidence to recommend that schizophrenia patients follow the PA recommendation for the general public, but with specific adaptations based on disease- and treatment-related limitations (Vancampfort et al., 2012a). According to our results, more than 80 % need to increase their MVPA level to reduce the risk of developing, or further worsening, CVD. Moreover, sedentary time, independent of MVPA, is an underappreciated contributing cause to at least 35 unhealthy conditions, including the majority of the 10 leading causes of death in the USA (Booth et al., 2017). There is no precise cutoff value for what constitutes "too much sitting" and national guidelines are vague, typically stating that one should "reduce sitting time." The cutoff point of 7.5 h per day adopted in the current study was based on a meta-analysis suggesting that all-cause mortality risk increases between 7 h and 8 h of sedentary time per day (Chau et al., 2013). Because this meta-analysis was based on self-reported data, which tend to be underreported, we selected an additional cutoff point of 10 h (Loyen et al., 2017). Most of the EPHAPS participants registered > 7.5 h of sedentary time per day, but only one-fifth had levels > 10 h. However, since most of our time is spent sedentary, this variable will be greatly affected by accelerometer wear time. When adjusting for wear time in our analysis, the average sedentary time was almost 10 h, which would mean that around half of the group is sitting so much that it likely affects length of life (Chau et al., 2013). Blair et al. (2009) noted that low CRF was a stronger predictor of mortality than any other risk factors (i.e., smoking, fat accumulation) (Blair, 2009). Furthermore, in people with schizophrenia, a low CRF level has been associated with negative symptoms (Vancampfort et al., 2015), cognitive impairment (Holmen et al., 2017), increased BMI (Vancampfort et al., 2015), and impaired daily functioning (Kimhy et al., 2014). The very low CRF levels reported in this study would therefore most likely not only increase the risk of developing lifestyle diseases, but also affect both disease-specific symptoms and the ability to move around without strain and discomfort.

The main strength of the current study is the rigorous measurement methods used for both PA (accelerometry) and cardiorespiratory fitness (indirect calorimetry). By exploiting the potential of the accelerometer device, we were able to examine PA patterns and sedentary behavior in depth. Thereby, our study presents important and new results about these two behaviors in persons with schizophrenia. Another major strength is the relatively large sample size in both cohorts.

However, we also acknowledge some limitations, the major one being whether the samples are representative of larger cohorts. The individuals who volunteered to participate in EPHAPS had to be willing to undergo high-intensity interval training for 12 weeks, and patients with medical conditions that were incompatible with exercise were excluded. This may have led to a biased sample of patients who were more interested in PA and had healthier behavior; this might lead to an overestimation of both PA and CRF. The same issues are probably also valid for the NPASS population. The NPASS study had low participation rate and dropout analysis showed that responses varied according to sociodemographic variables (Hansen et al., 2012). Other limitations in the current study concern the measurement of PA and CRF. First, the accelerometer was attached to the hip, which underestimates upper body movement such as carrying heavy loads and lifting weights, but also cycling and swimming. However, the device is very sensitive to ambulatory activities such as walking (and running), which was by far the most commonly reported activity in both cohorts (data not shown). Second, we included participants with two days of accelerometer recordings, which is less than the 3-5 days that has been recommended ((Trost et al., 2005)). However, we decided to include these participants (N = 10) because there were no differences in PA level between the participants wearing the monitor for two days and those wearing the monitor for three days or more. Third, the use of several test laboratories may have increased the possibility of different measurement accuracies, although all laboratories used the same exercise protocol and calibration procedures, and all technicians were rigorously trained in test procedures and were experienced with maximal exercise testing.

In summary, patients with schizophrenia were significantly less physically active, more sedentary, and had a poorer cardiorespiratory fitness level compared with the cohort from the general population. Tailor-made PA interventions for people with schizophrenia should target their PA and sedentary behavior during the afternoons and weekends especially. The many extra barriers to PA that people with schizophrenia face, should be taken into consideration when developing and implementing much needed interventions aimed at this vulnerable population. There is also a need for well-designed exercise intervention studies, to address how these persons can be helped into a more active lifestyle.

Acknowledgments

The authors would like to give thanks to all participants from EPHAPS and NPASS. The authors also thanks Ole-Jakob Bredrup, Helge Bjune, Jan-Freddy Hovland, Bjørn-Einar Oscarsen, Camilla Lahn-Johannessen and Ellen Gurine Færvik for conducting the measurements. EPHAPS received funding from Vestfold Hospital Trust, Norwegian Extra Foundation for Health and Rehabilitation through EXTRA funds, Norwegian Research network in Severe Mental Illness (NORSMI), NORMENT/KG Jebsen Centre for Psychosis Research, Torgeir Lindvik's Trust, and Civitan International. NPASS received funding from the Norwegian Directorate of Health.

References

2000. Obesity: preventing and managing the global epidemic. Report of a WHO consultation. World Health Organ Tech Rep Ser 894, i-xii, 1-253.
AmericanPsychiatricAssociation, 2013. Diagnostic and statistical manual of mental disorders (DSM-5®). American Psychiatric Pub.
Andreassen, O.A., Djurovic, S., Thompson, W.K., Schork, A.J., Kendler, K.S., O'Donovan, M.C., Rujescu, D., Werge, T., van de Bunt, M., Morris, A.P., McCarthy, M.I., International Consortium for Blood Pressure, G., Diabetes Genetics, R., Meta-analysis, C., Psychiatric Genomics Consortium Schizophrenia Working, G., Roddey, J.C., McEvoy, L.K., Desikan, R.S., Dale, A.M., 2013. Improved detection of common variants associated with schizophrenia by leveraging pleiotropy with cardiovascular-disease risk factors. Am J Hum Genet 92(2), 197-209.
Badcock, J.C., Shah, S., Mackinnon, A., Stain, H.J., Galletly, C., Jablensky, A., Morgan, V.A., 2015. Loneliness in psychotic disorders and its association with cognitive function and symptom profile. Schizophr Res 169(1-3), 268-273.
Balke, B., Ware, R.W., 1959. An experimental study of physical fitness of Air Force personnel. U S Armed Forces Med J 10(6), 675-688.
Blair, S.N., 2009. Physical inactivity: the biggest public health problem of the 21st century. Br J Sports Med 43(1), 1-2.
Booth, F.W., Roberts, C.K., Thyfault, J.P., Ruegsegger, G.N., Toedebusch, R.G., 2017. Role of Inactivity in Chronic Diseases: Evolutionary Insight and Pathophysiological Mechanisms. Physiol Rev 97(4), 1351-1402.
Capasso, R.M., Lineberry, T.W., Bostwick, J.M., Decker, P.A., St Sauver, J., 2008. Mortality in schizophrenia and schizoaffective disorder: an Olmsted County, Minnesota cohort: 1950-2005. Schizophr Res 98(1-3), 287-294.
Chau, J.Y., Grunseit, A.C., Chey, T., Stamatakis, E., Brown, W.J., Matthews, C.E., Bauman, A.E., van der Ploeg, H.P., 2013. Daily sitting time and all-cause mortality: a meta-analysis. PLoS One 8(11), e80000.
Cooper, A.R., Goodman, A., Page, A.S., Sherar, L.B., Esliger, D.W., van Sluijs, E.M., Andersen, L.B., Anderssen, S., Cardon, G., Davey, R., Froberg, K., Hallal, P., Janz, K.F., Kordas, K., Kreimler, S., Pate, R.R., Puder, J.J., Reilly, J.J., Salmon, J., Sardinha, L.B., Timperio, A., Ekelund, U., 2015. Objectively measured physical activity and sedentary time in youth: the International children's accelerometry database (ICAD). Int J Behav Nutr Phys Act 12, 113.
De Hert, M., Cohen, D., Bobes, J., Cetkovich-Bakmas, M., Leucht, S., Ndetei, D.M., Newcomer, J.W., Uwakwe, R., Asai, I., Moller, H.J., Gautam, S., Detraux, J., Correll, C.U., 2011. Physical illness in patients with severe mental disorders. II. Barriers to care, monitoring and treatment guidelines, plus recommendations at the system and individual level. World Psychiatry 10(2), 138-151.
Edvardsen, E., Hansen, B.H., Holme, I.M., Dyrstad, S.M., Anderssen, S.A., 2013. Reference values for cardiorespiratory response and fitness on the treadmill in a 20- to 85-year-old population. Chest 144(1), 241-248.
Engh, J.A., Andersen, E., Holmen, T.L., Martinsen, E.W., Mordal, J., Morken, G., Egeland, J., 2015. Effects of high-intensity aerobic exercise on psychotic symptoms and neurocognition in outpatients with schizophrenia: study protocol for a randomized controlled trial. Trials 16, 557.
Green, M.F., Kern, R.S., Heaton, R.K., 2004. Longitudinal studies of cognition and functional outcome in schizophrenia: implications for MATRICS. Schizophr Res 72(1), 41-51.
Hansen, B.H., Kolle, E., Dyrstad, S.M., Holme, I., Anderssen, S.A., 2012. Accelerometer-determined physical activity in adults and older people. Med Sci Sports Exerc 44(2), 266-272.
Holmen, T.L., Egeland, J., Andersen, E., Bigseth, T.T., Engh, J.A., 2017. The association between cardio-respiratory fitness and cognition in schizophrenia. Schizophr Res.

Janney, C.A., Ganguli, R., Richardson, C.R., Holleman, R.G., Tang, G., Cauley, J.A., Kriska, A.M., 2013. Sedentary behavior and psychiatric symptoms in overweight and obese adults with schizophrenia and schizoaffective disorders (WAIST Study). Schizophr Res 145(1-3), 63-68.
Janney, C.A., Ganguli, R., Tang, G., Cauley, J.A., Holleman, R.G., Richardson, C.R., Kriska, A.M., 2015. Physical activity and sedentary behavior measured objectively and subjectively in overweight and obese adults with schizophrenia or schizoaffective disorders. J Clin Psychiatry 76(10), e1277-1284.
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(3), 784-791.
Loyen, A., Clarke-Cornwell, A.M., Anderssen, S.A., Hagstromer, M., Sardinha, L.B., Sundquist, K., Ekelund, U., Steene-Johannessen, J., Baptista, F., Hansen, B.H., Wijndaele, K., Brage, S., Lakerveld, J., Brug, J., van der Ploeg, H.P., 2017. Sedentary Time and Physical Activity Surveillance Through Accelerometer Pooling in Four European Countries. Sports Med 47(7), 1421-1435.
Matthews, C.E., Chen, K.Y., Freedson, P.S., Buchowski, M.S., Beech, B.M., Pate, R.R., Troiano, R.P., 2008. Amount of time spent in sedentary behaviors in the United States, 2003-2004. Am J Epidemiol 167(7), 875-881.
McLeod, H.J., Jaques, S., Deane, F.P., 2009. Base rates of physical activity in Australians with schizophrenia. Psychiatr Rehabil J 32(4), 269-275.
Mitchell, A.J., Malone, D., Doebbeling, C.C., 2009. Quality of medical care for people with and without comorbid mental illness and substance misuse: systematic review of comparative studies. Br J Psychiatry 194(6), 491-499.
Mitchell, A.J., Vancampfort, D., Sweers, K., van Winkel, R., Yu, W., De Hert, M., 2013. Prevalence of metabolic syndrome and metabolic abnormalities in schizophrenia and related disorders--a systematic review and meta-analysis. Schizophr Bull 39(2), 306-318.
O'Donoghue, G., Perchoux, C., Mensah, K., Lakerveld, J., van der Ploeg, H., Bernaards, C., Chastin, S.F., Simon, C., O'Gorman, D., Nazare, J.A., Consortium, D., 2016. A systematic review of correlates of sedentary behaviour in adults aged 18-65 years: a socio-ecological approach. BMC Public Health 16, 163.
Ostermann, S., Herbsleb, M., Schulz, S., Donath, L., Berger, S., Eisentrager, D., Siebert, T., Muller, H.J., Puta, C., Voss, A., Gabriel, H.W., Koch, K., Bar, K.J., 2013. Exercise reveals the interrelation of physical fitness, inflammatory response, psychopathology, and autonomic function in patients with schizophrenia. Schizophr Bull 39(5), 1139-1149.
Ozbulut, O., Genc, A., Bagcioglu, E., Coskun, K.S., Acar, T., Alkoc, O.A., Karabacak, H., Sener, U., Ucok, K., 2013. Evaluation of physical fitness parameters in patients with schizophrenia. Psychiatry Res 210(3), 806-811.
Rastad, C., Martin, C., Asenlof, P., 2014. Barriers, benefits, and strategies for physical activity in patients with schizophrenia. Phys Ther 94(10), 1467-1479.
Ratliff, J.C., Palmese, L.B., Reutenauer, E.L., Liskov, E., Grilo, C.M., Tek, C., 2012. The effect of dietary and physical activity pattern on metabolic profile in individuals with schizophrenia: a cross-sectional study. Compr Psychiatry 53(7), 1028-1033.
Ringen, P.A., Melle, I., Birkenaes, A.B., Engh, J.A., Faerden, A., Vaskinn, A., Friis, S., Opjordsmoen, S., Andreassen, O.A., 2008. The level of illicit drug use is related to symptoms and premorbid functioning in severe mental illness. Acta Psychiatr Scand 118(4), 297-304.
Saha, S., Chant, D., McGrath, J., 2007. A systematic review of mortality in schizophrenia: is the differential mortality gap worsening over time? Arch Gen Psychiatry 64(10), 1123-1131.
Scheewe, T.W., Takken, T., Kahn, R.S., Cahn, W., Backx, F.J., 2012. Effects of exercise therapy on cardiorespiratory fitness in patients with schizophrenia. Med Sci Sports Exerc 44(10), 1834-1842.

Soundy, A., Wampers, W., Probst, M., De Hert, M., Stubbs, B., vancampfort, D., 2013. Physical activity and sedentary behaviour in outpatients with schizophrenia: A systematic review and meta-analysis. International Journal of Therapy and Rehabilitation 20(12), 588-596.
Strassnig, M., Brar, J.S., Ganguli, R., 2011. Low cardiorespiratory fitness and physical functional capacity in obese patients with schizophrenia. Schizophr Res 126(1-3), 103-109.
Stubbs, B., Firth, J., Berry, A., Schuch, F.B., Rosenbaum, S., Gaughran, F., Veronesse, N., Williams, J., Craig, T., Yung, A.R., Vancampfort, D., 2016. How much physical activity do people with schizophrenia engage in? A systematic review, comparative meta-analysis and meta-regression. Schizophr Res 176(2-3), 431-440.
Tremblay, M.S., Aubert, S., Barnes, J.D., Saunders, T.J., Carson, V., Latimer-Cheung, A.E., Chastin, S.F.M., Altenburg, T.M., Chinapaw, M.J.M., Participants, S.T.C.P., 2017. Sedentary Behavior Research Network (SBRN) - Terminology Consensus Project process and outcome. Int J Behav Nutr Phys Act 14(1), 75.
Troiano, R.P., 2005. A timely meeting: objective measurement of physical activity. Med Sci Sports Exerc 37(11 Suppl), S487-489.
Trost, S.G., McIver, K.L., Pate, R.R., 2005. Conducting accelerometer-based activity assessments in field-based research. Med Sci Sports Exerc 37(11 Suppl), S531-543.
Vancampfort, D., Correll, C.U., Galling, B., Probst, M., De Hert, M., Ward, P.B., Rosenbaum, S., Gaughran, F., Lally, J., Stubbs, B., 2016. Diabetes mellitus in people with schizophrenia, bipolar disorder and major depressive disorder: a systematic review and large scale meta-analysis. World Psychiatry 15(2), 166-174.
Vancampfort, D., De Hert, M., Myin-Germeys, I., van Winkel, R., Firth, J., Van Damme, T., Probst, M., 2017. Lower cardiorespiratory fitness is associated with more time spent sedentary in first episode psychosis: A pilot study. Psychiatry Res 253, 13-17.
Vancampfort, D., De Hert, M., Skjerven, L.H., Gyllensten, A.L., Parker, A., Mulders, N., Nyboe, L., Spencer, F., Probst, M., 2012a. International Organization of Physical Therapy in Mental Health consensus on physical activity within multidisciplinary rehabilitation programmes for minimising cardio-metabolic risk in patients with schizophrenia. Disabil Rehabil 34(1), 1-12.
Vancampfort, D., De Hert, M., Sweers, K., De Herdt, A., Detraux, J., Probst, M., 2013. Diabetes, physical activity participation and exercise capacity in patients with schizophrenia. Psychiatry Clin Neurosci 67(6), 451-456.
Vancampfort, D., Knapen, J., Probst, M., Scheewe, T., Remans, S., De Hert, M., 2012b. A systematic review of correlates of physical activity in patients with schizophrenia. Acta Psychiatr Scand 125(5), 352-362.
Vancampfort, D., Rosenbaum, S., Probst, M., Soundy, A., Mitchell, A.J., De Hert, M., Stubbs, B., 2015. Promotion of cardiorespiratory fitness in schizophrenia: a clinical overview and meta-analysis. Acta Psychiatr Scand 132(2), 131-143.
WHO, 2010. Global Recommendations on Physical Activity for Health, Geneva.
Wolff-Hughes, D.L., Bassett, D.R., Fitzhugh, E.C., 2014. Population-referenced percentiles for waist-worn accelerometer-derived total activity counts in U.S. youth: 2003 - 2006 NHANES. PLoS One 9(12), e115915.
Wu, S.I., Kao, K.L., Chen, S.C., Juang, J.J., Lin, C.J., Fang, C.K., Wu, C.S., Dewey, M., Prince, M.J., Stewart, R., 2015. Antipsychotic exposure prior to acute myocardial infarction in patients with serious mental illness. Acta Psychiatr Scand 131(3), 213-222.

Table 1. Demographic and clinical characteristics information for EPHAPS and NPASS participants

Characteristics	EPHAPS Schizophrenia	NPASS Population-based sample
Sample size	67	2809
Sex female (%)	45	46
Age (years)*	37 (13)	45 (12)
Height (cm)	171 (10)	173 (9)
Weight (kg)*	87 (20)	77 (14)
BMI (kg·m^{-2})*	29.4 (5.7)	25.5 (4.0)
Normal weight (%)	17.7	44.5
Overweight (%)	35.5	41.5
Obese (%)	46.8	14.0
Education level (%)*		
Primary school	38	10
High school	34	37
College/University	26	51
Employed at least 50% (%)*	10	84
Married (%)*	7	57
Antipsychotics (DDD)	1.7 (0.90)	
Duration of illness (years)	15 (12)	

Values are mean ± SD if not specified otherwise. EPHAPS, Effects of Physical Activity in Psychosis study; NPASS, Norwegian physical activity surveillance survey; BMI, body mass index; DDD, defined daily doses. *Significant difference between groups ($P \leq 0.01$)

Table 2. Comparison of PA level and sedentary behavior between EPHAPS and NPASS participants matched by sex, age, and accelerometer wear time during weekdays (A) and weekends (B) (mean ± standard deviation)

A. PA data weekdays	EPHAPS Schizophrenia	NPASS Population-based sample	Mean difference ± CI	P-value
Total PA level (CPM)	276 (139)	347 (139)	–60 (–98 to –24)	< 0.01
Light intensity (min·day^{-1})	229 (104)	311 (88)	–25 (–47 to –4.5)	0.018
MVPA (min·day^{-1})	25 (24)	36 (24)	–6.2 (–12 to 0.0)	0.050
Moderate intensity	23 (23)	33 (22)	–4.8 (–10 to 0.7)	0.09
Vigorous intensity	1.0 (3)	2.6 (6)	–1.3 (–2.9 to 0.2)	0.09
Steps per day	5573 (3620)	8495 (3167)	–1619 (–2413 to –824)	< 0.01
Sedentary time (hours·day^{-1})	9.8 (1.5)	9.3 (1.6)	0.5 (0.1 to 0.9)	< 0.01
B. PA data weekends				
Total PA level (CPM)	229 (117)	364 (184)	–97 (–151 to –44)	< 0.01
Light intensity (min·day^{-1})	203 (83)	290 (84)	–44 (–67 to –20)	< 0.01
MVPA (min·day^{-1})	18 (16)	37 (32)	–9.8 (–19 to –0.3)	0.04
Moderate intensity	17 (15)	34 (30)	–9.2 (–18 to –0.4)	0.04
Vigorous intensity	1.2 (4)	2.4 (8)	–0.6 (–3.0 to 1.7)	0.6
Steps per day	4394 (2490)	7944 (3786)	–2092 (–3167 to –1016)	< 0.01
Sedentary time (hours·day^{-1})	9.8 (1.5)	8.5 (1.6)	1.3 (0.9 to 1.8)	< 0.01

EPHAPS, Effects of Physical Activity in Psychosis study; NPASS, Norwegian physical activity surveillance survey; CPM, counts per minute; MVPA, moderate-to-vigorous intensity physical activity; PA, physical activity: CI, confidence interval; Sed, sedentary

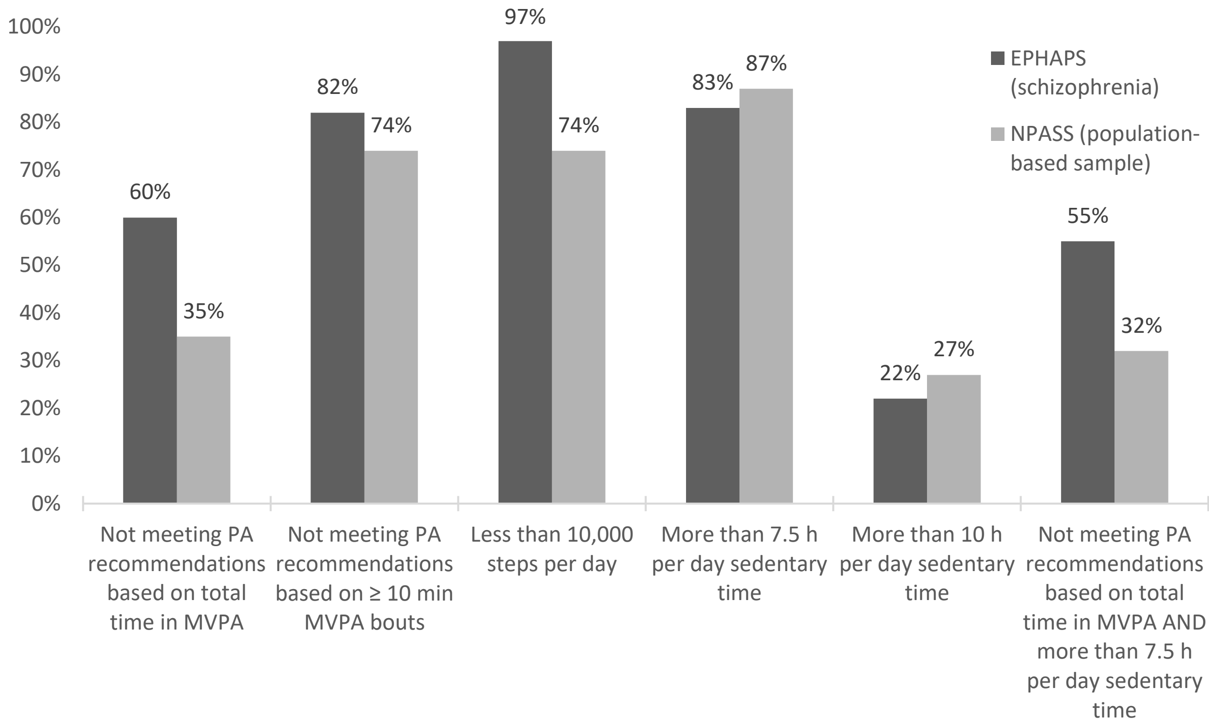

Figure 1. Percentage of participants not meeting different PA and sedentary recommendations.

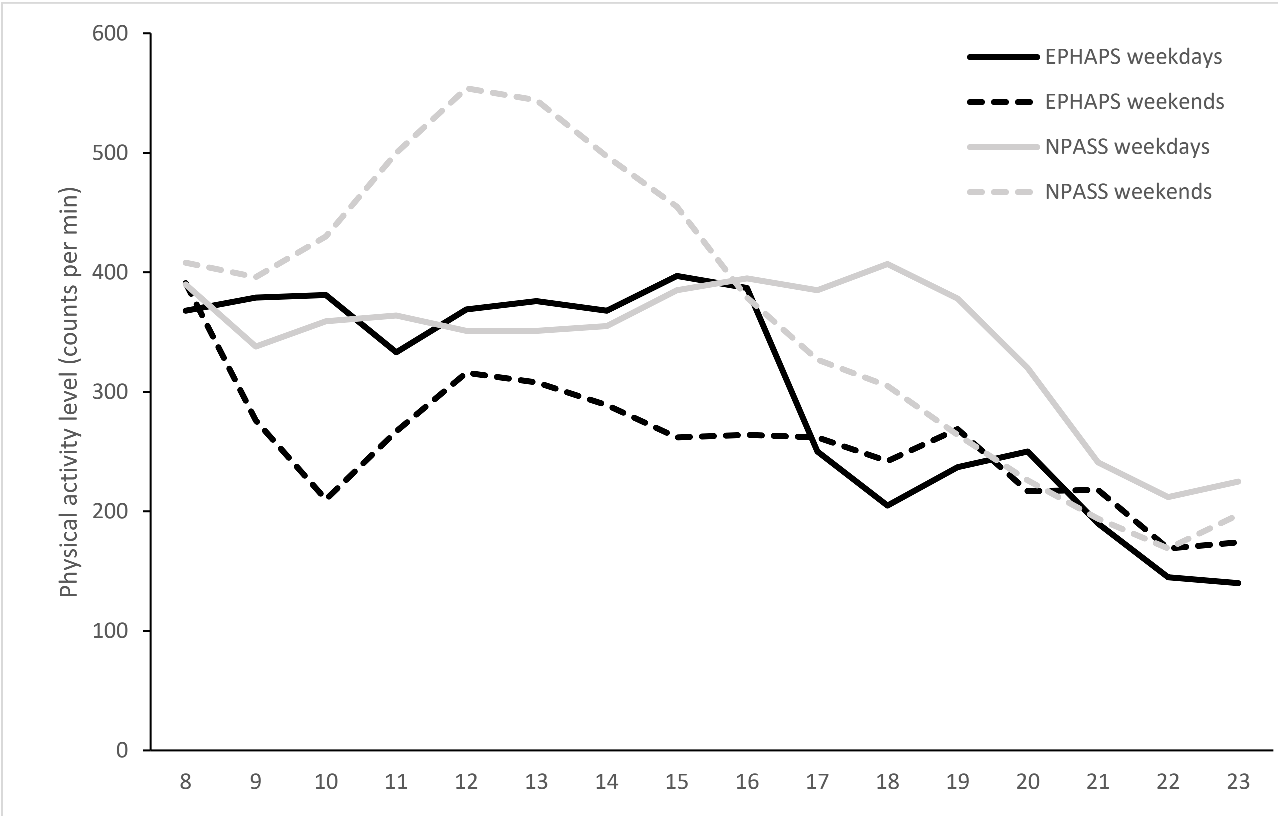

Figure 2. Hour-by-hour PA level for EPHAPS (schizophrenia, black) and NPASS (population-based sample, grey) during weekdays (solid line) and weekends (dashed line)

Table 3. Physiological responses at maximal exercise, BMI, and MVPA level for women (A) and men (B)

A. Response women	EPHAPS Schizophrenia (n = 27)	NPASS Population-based sample (n = 389)	Mean difference ± CI	P-value
Age (years)	38 (14)	46 (12)	–8 (–19 to –5)	< 0.01
VO_{2peak} ($mL \cdot kg^{-1} \cdot min^{-1}$)*	24 (8)	31 (7)	–6.8 (–9 to –4)	< 0.01
VO_{2peak} ($L \cdot min^{-1}$)*	1.8 (0.4)	2.1 (0.5)	–0.3 (–0.5 to –0.1)	< 0.01
RER_{peak} (VCO_{2peak}/VO_{2peak})	1.05 (0.08)	1.17 (0.1)	–0.09 (–0.12 to –0.05)	< 0.01
Heart rate ($beats \cdot min^{-1}$)*	166 (20)	173 (15)	–7 (–11 to –3)	< 0.01
BMI ($kg \cdot m^{-2}$)	29.8 (5.8)	24.7 (4.0)	4.6 (2.2 to 7.0)	< 0.01
Weight (kg)	79.3 (18)	68.7 (11)	10.5 (2.9 to 18)	< 0.01
MVPA ($min \cdot day^{-1}$)	22 (19)	36 (21)	–13 (–21 to –5)	0.01
B. Response men	(n = 40)	(n = 405)		
Age (years)	34.8 (12)	46.8 (12)	–11 (–15 to –7)	< 0.01
VO_2peak ($mL \cdot kg^{-1} \cdot min^{-1}$)*	26 (8)	39.8 (9)	–13 (–16 to -10)	< 0.01
VO_2peak ($L \cdot min^{-1}$)*	2.3 (0.8)	3.3 (0.7)	-0.9 (-1.1 to -0.7)	< 0.01
RER_{peak} (VCO_{2peak}/VO_{2peak})	1.07 (0.07)	1.19 (0.1)	–0.09 (–0.12 to –0.07)	< 0.01
Heart rate ($beats \cdot min^{-1}$)*	164 (19)	175 (18)	–10 (–15 to –6)	< 0.01
BMI ($kg \cdot m^{-2}$)	28.9 (5.6)	26.0 (3.2)	2.7 (0.8 to 4.5)	< 0.01
Weight (kg)	93.0 (21)	84.3 (11)	8.6 (1.6 to 15)	= 0.01
MVPA ($min \cdot day^{-1}$)	21 (15)	39 (24)	–16 (–22 to –10)	< 0.01

Values are mean ± SD. EPHAPS, Effects of Physical Activity in Psychosis study; NPASS, Norwegian physical activity surveillance survey; RER, respiratory exchange ratio; ; BMI, body mass index; MVPA, moderate-to-vigorous intensity physical activity. *Adjusted for age and respiratory exchange ratio (RER)