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Changes in physical and psychiatric health after a multidisciplinary lifestyle enhancing treatment for inpatients with severe mental illness: The MULTI study I

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ABSTRACT

Patients hospitalized with severe mental illness (SMI) often have an unhealthy lifestyle. Changing their sedentary behavior and deficiency in physical activity is challenging and effective interventions are lacking. We evaluated changes in sedentary behavior, physical activity, metabolic health and psychotic symptoms after 18 months of Multidisciplinary Lifestyle enhancing Treatment for Inpatients with SMI (MULTI) compared to treatment as usual (TAU) and explored mediation by change in total activity. We measured sedentary behavior and physical activity using accelerometry (ActiGraph GT3X+), reflected in total activity counts. Data on metabolic health and psychotic symptoms were retrieved from routine screening data within our cohort of inpatients with SMI. Of 65 patients receiving MULTI versus 43 receiving TAU, data were analyzed using linear and logistic multilevel regression, adjusting for baseline values of outcome and differences between groups. Compared to TAU, in which no improvements were observed, we found significantly ($p < 0.05$) improved total activity (B = 0.5 standardized total activity counts per hour), moderate-to-vigorous physical activity (B = 1.8%), weight (B = −4.2 kg), abdominal girth (B = −3.5 cm), systolic blood pressure (B = −8.0 mmHg) and HDL cholesterol (B = 0.1 mmol/l). No changes in psychotic symptoms were observed. Changes in total activity did not mediate metabolic improvements, suggesting that multiple components of MULTI contribute to these improvements. In contrast to previously unsuccessful attempts to change lifestyle behavior in inpatients with SMI in the longer term, MULTI showed to be a feasible treatment to sustainably improve PA and metabolic health.

1. Introduction

It is well known that the physical condition of patients with Severe Mental Illness (SMI) is a cause for concern in the daily practice of mental healthcare. Compared to the general population, the mortality rate of these patients is two- to three times higher and their life expectancy is 10–20 years less, mainly due to cardiovascular disease (Laursen et al., 2013; Lawrence et al., 2013; Walker et al., 2015). Metabolic syndrome (MetS), which clusters risk factors of cardiovascular health problems and type 2 diabetes, is highly prevalent in patients with SMI (Stubbs et al., 2015; Vancampfort et al., 2015a) and – despite several guidelines – still seriously undertreated (Bruins et al., 2017; Swaby et al., 2017). Sedentary behavior (SB), defined as any waking behavior in a sitting or reclining posture costing ≤1.5 times the basal metabolic rate (Sedentary Behaviour Research Network, 2012), has been found to be independently associated with developing the abovementioned health problems and increased mortality (Biswas et al., 2015; Brocklebank et al., 2015). Physical activity (PA) is an important intervenable factor in reducing these risks (Cabassa et al., 2010). Recent systematic reviews and meta-analyses showed that patients with SMI are very sedentary and are deficient in PA (Stubbs et al., 2016b; Vancampfort et al., 2017a). Previous research in this area has focused mainly on outpatients or short-term inpatients and in many cases on self-reports, which may underestimate SB (Firth et al., 2017). However, recent objective measurements have also confirmed these findings in long-term hospitalized patients (Kruisdijk et al., 2017; Stubbs et al., 2017). Especially for these inpatients, whose metabolic health and

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physical fitness are generally worse compared to patients with a shorter duration of illness (Mitchell et al., 2013; Vancampfort et al., 2013), it is important to increase PA. Recent systematic reviews and meta-analyses have shown that increased PA is associated with lower metabolic risk and weight in both inpatients and outpatients with SMI (Dauwan et al., 2016; Naslund et al., 2017; Rosenbaum et al., 2014; Vera-Garcia et al., 2015) as well with beneficial changes in psychotic symptoms (Dauwan et al., 2016; Rosenbaum et al., 2014). The improvement in both physical and psychiatric health is very relevant for long-term hospitalized patients with SMI, especially considering their often poor physical health status and severe psychiatric health problems.

However, currently there is no clear answer on how we can sustainably increase the PA levels of inpatients with SMI. Studies to improve the lifestyle of inpatients with SMI, especially over the longer term, are lacking (Levitt et al., 2017; Stanton and Happell, 2014; Vancampfort et al., 2015b) and behavioral change is very challenging in this inpatient population. Previous research has indicated that only verbally motivating patients and facilitating them to improve self-efficacy, may be insufficient to sustainably increase the level of activity (Deenik et al., 2017). Additionally, studies focusing on factors in lifestyle interventions for effectively increasing PA indicate that such interventions should include multiple components (e.g. diet and psycho-education in addition to increasing PA), personalization/tailoring, qualified professionals, a duration of at least four months of active intervention (Bonfioli et al., 2012; Vancampfort et al., 2017b; Ward et al., 2015) and, above all, a culture change driven at management level (Long et al., 2016; Vancampfort et al., 2015b; Ward et al., 2015). However, previous intervention studies on lifestyle improvements in patients with SMI often failed to employ multiple components and their methodological quality was highly variable (Chalfoun et al., 2016; Stanton and Happell, 2014; Ward et al., 2015).

In order to find a way to address this situation and based on previous cross-sectional research (Deenik et al., 2017; Kruisdijk et al., 2017), a Multidisciplinary Lifestyle Enhancing Treatment for Inpatients (MULTI) with SMI was pragmatically implemented within long-term mental healthcare of the psychiatric hospital GGz Centraal in the Netherlands. The purpose of MULTI was overall lifestyle change with a focus on decreasing SB and increasing PA and improving dietary habits. In this first study regarding the evaluation of MULTI, we aimed to evaluate changes in SB/PA, metabolic health and psychotic symptoms after 18 months of MULTI compared to treatment as usual (TAU) and explored whether effects were mediated by change in total activity.

2. Materials and methods

2.1. Study design

This cohort study was conducted at wards for long-term inpatient mental healthcare within a psychiatric hospital of GGz Centraal (The Netherlands). The current study is part of a comprehensive evaluation of MULTI, a new treatment method that was implemented pragmatically in February 2014 at three wards irrespective of any study protocol. To evaluate changes in physical health 18 months after implementation, we used routine screening data which were collected yearly in the context of the treatment and compared it to three wards that continued TAU. For baseline, we used the screening data prior to implementation of MULTI (August–December 2013), supplemented by data from previous cross-sectional research on physical activity (Kruisdijk et al., 2017), collected in the same period. Data from screening 18 months after implementation (August–December 2015) was used as follow-up, supplemented by a repeated physical activity measurement. The study protocol was approved by Medical Ethical Committee of the Isala Academy (case 14.0678). All subjects gave written informed consent in accordance with the Declaration of Helsinki.

2.2. Study population

The cohort consisted of patients with SMI who were hospitalized for at least one year. Patients were included if baseline accelerometer data were available and excluded if they (1) moved or were discharged from the hospital, (2) were deceased or (3) received another intervention related to lifestyle within 18 months after the start of MULTI. Patients who were included for follow-up, were excluded from further analysis if they refused repeated accelerometer measurement, had insufficient accelerometer data (see 2.5.1) or if we had no or hardly any baseline or follow-up data on them, defined as at least two out of the three screening measurements (somatic, blood test and psychotic symptoms) missing.

2.3. Randomization and blinding

Due to the observational nature of this study, whereby MULTI was already implemented pragmatically at three wards before the start of this study, no randomization took place. Therefore, we analyzed potential differences between groups at baseline and corrected for these differences in analyses if significant. Screening data were collected by research assistants, who –although not actively informed about the treatment condition– were not blinded due to visible differences regarding daily program.

2.4. Treatment

We evaluated MULTI 18 months after its implementation. The purpose of this treatment method was overall lifestyle change with a focus on decreasing SB and increasing PA, and improving dietary habits. The treatment was based on improving daily structure, by starting each day with getting up on time, having three joint meals per day and an active day program consisting of sports-related activities (e.g. walking, running, yoga, biking, indoor team sports), work-related activities (e.g. gardening and working in services within the hospital such as a copy shop or lunchroom), psycho-education (e.g. about side effects, dietary habits) and daily living skills training (e.g. making a grocery list, shopping, cooking). In addition, existing policies were reviewed critically – such as limiting the use of personal transport within walking distance around the hospital area for every patient. Based on heterogeneity in illness severity and different capabilities and interests, the content and intensity of the day to day program was tailored to the particular ward and individual patients in order to intend sustainable change. Although the actual frequency, intensity, kind of activities and format (e.g. group or alone) could therefore vary per patient, it was expected that all patients were doing any of the possible activities in the morning and afternoon, instead of lying in bed or sitting at the ward. A final essential element concerned the participation of the nurses in the day to day program, which contributed to the culture change and support of patients. MULTI was based on a 'change from within-principle', using current resources and staff, including supervision by psychiatrists, activity coordinators, nurse practitioners, a dietician and nurses. Adherence to and compliance with treatment was registered by the nurses in the electronic patient records and discussed in weekly multidisciplinary consultation. If needed, it was agreed that specific action would be taken to physically activate the particular patient, using motivational counselling by their mentor (one of the nurses) or psychiatrist.

Patients who received TAU continued their treatment, which mainly consisted of pharmacological treatment and a less structured day program, excluding any supported lifestyle interventions or adjustments.

2.5. Measurements

2.5.1. Sedentary behavior and physical activity

The ActiGraph GT3X+ (*ActiGraph*, Pensacola, Florida, VS) was used to measure SB and PA. The specific procedures and settings were similar

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to the baseline-measurement and are described elsewhere (Kruisdijk et al., 2017). Accelerometers were worn on the right hip with an elastic strap between two belt loops. Patients without belt loops, used a pouch pinned on the right hip. Wear time of ≥6 h/day for ≥3 days was used as the criterion for sufficient measurement. To compare individual data, the same timeframe was used for each dataset: 09.00 am till 10.00 pm. Data were analyzed using the ActiLife 6.8.0 software and converted into average total activity counts per hour (TAC/h) as a continuous and detailed outcome variable, where more counts indicate a higher level of activity. For regression analysis, TAC/h was standardized to facilitate interpretation by subtracting individual values by the mean and divide it by its standard deviation. Therefore, B can be interpreted as Cohen's *d*. To differentiate activity intensities, percentage of valid wear time in SB (<150 cpm), light intensity physical activity (LPA; 151–3207 cpm) and moderate to vigorous physical activity (MVPA; ≥3208 cpm) were reported (Santos-Lozano et al., 2013). For patients >65 years old, the MVPA-threshold was fixed at ≥2751 cpm. The GT3X + has a high inter- and intra-instrumental reliability and validity (Gatti et al., 2015; Jarrett et al., 2015; McMinn et al., 2013).

2.5.2. Metabolic health

Data on metabolic health – weight, abdominal girth, blood pressure, fasting glucose, triglycerides and total and HDL-cholesterol – were screened routinely by trained nurses in the context of prevention and treatment of somatic complications associated with the use of antipsychotics (Cahn et al., 2008). Weight was measured to the nearest 0.1 kg without clothes on. Abdominal girth was measured to the nearest 0.1 cm, under the clothes at the level of the umbiculus (with the patient standing). We used the harmonized definition to determine whether patients had MetS, which requires the presence of any three of the following: increased waist circumference (men: ≥94 cm, women: ≥80 cm), low HDL cholesterol (men: <1 mmol/l, women: <1.3 mmol/l), hypertriglyceridemia(≥1.7 mmol/l), elevated blood pressure (systolic ≥130 mmHg and/or diastolic ≥85 mmHg), elevated fasting glucose (≥5.6 mmol/l) or any drug treatment regarding those last four (Alberti et al., 2009).

2.5.3. Psychotic symptoms

Psychotic symptoms were screened routinely parallel to the somatic screening using the Dutch version of the Positive and Negative Syndrome Scale Remission tool (PANSS-r) within a semi-structured interview. It includes eight core symptoms of the diagnosis schizophrenia (two general psychopathology items and three items of both positive and negative symptoms), scored from 1 (absent) to 7 (extreme) (Kay et al., 1987; van Os et al., 2006a). Separate item scores were used for analysis. The instrument was validated for clinical research within health services (Linden et al., 2007; van Os et al., 2006b) and can be used in both outpatients and inpatients (Linden et al., 2007). Unfortunately, the item 'unusual thought content' was not measured at baseline and was therefore excluded for the current analyses.

2.6. Statistical analysis

Data analyses were performed using SPSS 22.0 and MLwiN 2.22 and interpreted at two-tailed significance level of $p < 0.05$. Potential differences in patient and disease characteristics between patients receiving MULTI and TAU were analyzed using *t*-tests and chi-square statistics. Patients for whom a change score for one measurement was missing were excluded from analysis for this particular variable ($n = 1$ for abdominal girth, $n = 1$ for blood pressure, $n = 2$ for blood levels and $n = 12$ for PANSS-r). Continuous variables were examined for normality and homogeneity by comparing means with medians and analyzing frequency histograms and normality plots. Linearity was determined by analyzing scatterplots and plots of residual versus predicted values. If variables were not distributed linearly towards the dependent variables, they were added as tertiles in the analysis, with the first tertile as reference category.

We used linear multilevel regression to evaluate the treatment effects. Possible clustering of data within wards was taken into account, using a two-level structure with the wards as the first level and the participants as the second. The treatment variable was regressed on the change scores of the different outcome variables and adjusted for the baseline value to prevent potential regression to the mean (crude, model 1). We added patient and disease characteristics, which significantly differed between patients receiving MULTI and TAU as covariates in models 2 and 3, respectively. To evaluate recovery of MetS (yes/no, meaning that a patient no longer meets these criteria) we performed logistic multilevel regression, using the same covariates. Additionally, to gain more insight into the contribution of different elements of MULTI in the total outcome effect, final significant models were analyzed in SPSS using the PROCESS tool (Hayes, 2012) to calculate the mediating effect of changes in TAC/h on the association between the treatment condition and the particular outcome. Therefore, we used the product of the coefficient method (Fig. 1) in which associations were calculated using linear regression models. The mediation effect is the product of the a- and b-coefficient (ab, not shown within models) and was considered significant if the bias-corrected and accelerated (BCa) bootstrapped confidence intervals did not include zero.

3. Results

Of the eligible patients, 108 were included for analyses and 15 dropped out (Fig. 2). Table 1 shows the baseline characteristics of patients receiving MULTI and TAU. On average, patients receiving MULTI were younger ($t = 3.22$, $p = 0.002$), had a higher baseline illness severity ($t = -3.18$, $p = 0.002$) and were more frequently diagnosed with schizophrenia or other psychotic disorders ($X^2 = 18.41$, $p < 0.001$) compared to patients receiving TAU.

3.1. Sedentary behavior and physical activity

Table 1 shows that TAC/h increased with 3918 counts per hour (13.5%) in the patients receiving MULTI and decreased with 330 counts per hour (−1.4%) in TAU. The final adjusted model (Table 2) confirms this observation, showing a significant effect on TAC/h in patients receiving MULTI, compared to TAU (B = 0.46 standardized TAC/h, $p = 0.02$). This effect was mainly reflected in a non-significant decrease of SB (B = −2.15%, $p = 0.07$) and a significant increase in MVPA (B = 1.78%, $p = 0.03$).

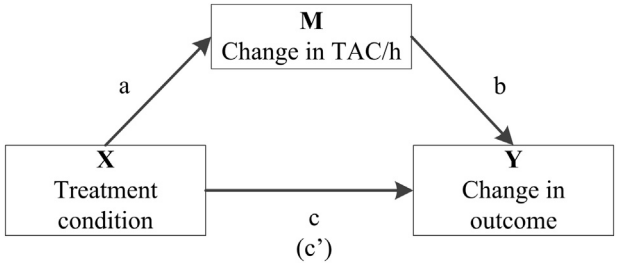

Fig. 1. Model summarizing how the role of change in average total activity counts per hour (TAC/h) as potential mediator (M) in the association between treatment condition (X) and significant change in measures for metabolic health or psychotic symptoms (Y) is quantified in mediation analysis. It includes the associations between treatment condition and TAC/h (a), TAC/h and the particular outcome variable (b) and treatment condition on the particular outcome variable (c). Mediation is only possible if (a) and (b) are significant. The coefficient between the latter two, controlling for change in TAC/h, is in parentheses (c').

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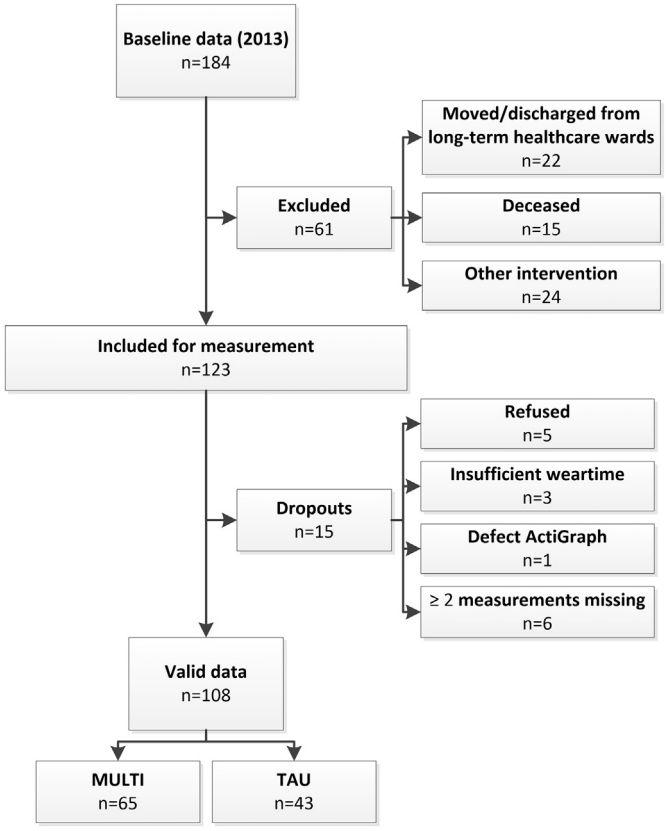

Fig. 2. Flowchart of the study population. MULTI, Multidisciplinary Lifestyle-enhancing Treatment for Inpatients with severe mental illness; TAU, Treatment As Usual. Baseline data reported in Kruisdijk et al. (2017).

3.2. Metabolic health

We observed several significant changes in metabolic health after adjustment for age, diagnosis and baseline illness severity. When compared to TAU, we observed significantly greater changes in weight (B = −4.18 kg, $p = 0.04$), abdominal girth (B = −3.48 cm, $p = 0.04$), systolic blood pressure (B = −8.03 mmHg, $p = 0.02$) and HDL cholesterol (B = 0.10 mmol/l, $p = 0.03$) in the group receiving MULTI. Weight loss in patients receiving MULTI corresponded to an average of 4.2% reduction in the initial weight. Regarding change in MetS status, too few patients recovered from MetS as a whole to make a valid corrected analysis (Vittinghoff and McCulloch, 2007). Therefore, we analyzed recovery of at least one MetS criterion, which was the case in 24 (36.9%) patients receiving MULTI and in 10 (23.3%) patients receiving TAU, compared to no change and deterioration. Corrected for criteria met at baseline, age, diagnosis and baseline illness severity, analysis showed a non-significant effect in favor of MULTI (OR = 2.06, $p = 0.22$).

3.3. Psychotic symptoms

As shown in Table 1, we observed a decrease in negative symptoms in patients receiving MULTI, indicated by blunted affect (M = −1.34, SD = 2.43), passive/apathetic social withdrawal (M = −0.61, SD = 2.28) and lack of spontaneity and flow of conversation (M = −0.49, SD = 2.18). These symptoms increased in TAU. Although coefficients in the regression models confirm these directions, effects were not significant.

3.4. Mediation by change in average total activity counts

With regard to the mediation analysis (Fig. 3), except for systolic blood pressure, none of the mediation models showed statistically significant standardized regression coefficients between treatment condition and change in TAC/h (a). All models showed non-significant coefficients between change in TAC/h and the specific outcome measure (b). In line with these findings, mediation analyses showed that change in TAC/h did not mediate the effect of MULTI on weight (ab = −0.38; 95% BCa CI: −2.24–0.17), abdominal girth (ab = −0.51; 95% BCa CI: −2.01–0.06), systolic blood pressure (ab = 0.74; 95% BCa CI: −0.49–3.56) and HDL cholesterol (ab = −0.001; 95% BCa CI: −0.03–0.01).

4. Discussion

MULTI showed to be an effective treatment resulting in sustainable and significant improvements in PA and metabolic health in inpatients with SMI. In addition –although it was not a specific research question– this study showed no substantial change within the treatment as usual group.

Overall, we observed a 13.5% increase in total activity, showing a significant treatment effect. Although modest, the non-significant decrease in SB and the significant 1.8% increase of MVPA compared to TAU correspond to recommendations to replace SB by PA in patients with SMI (Stubbs et al., 2016a; Stubbs et al., 2016b). To our knowledge, no intervention studies have been conducted in a comparable population presenting follow-up data on objectively measured activity counts. Improvements in PA, however, correspond to findings in small exercise-focused outpatient studies (Pearsall et al., 2014) and outpatients with psychotic and bipolar disorder after receiving group PA and education on diet (Masa-Font et al., 2015). Taking the substantial effects on metabolic health into account, it seems that these relatively small changes in SB and PA after 18 months of MULTI could be of value as part of such an integrated lifestyle approach.

Given the fact that the MetS is still highly prevalent and undertreated in patients with SMI (Bruins et al., 2017; Stubbs et al., 2015; Swaby et al., 2017; Vancampfort et al., 2015a), the finding that patients receiving MULTI had two times higher odds to recover from at least one MetS criterion compared to TAU is clinically relevant. Changes in individual MetS criteria included significant improvements in weight, abdominal girth and systolic blood pressure and HDL cholesterol. The 4.2% reduction of the initial weight in patients receiving MULTI approaches the clinically significant marker of 5% weight loss, associated with reduced cardiovascular risk among overweight and obese individuals (Brown et al., 2016). A meta-analytic review of previous intervention studies in adults with a serious mental illness reported a much smaller weight loss of 2% (Olker et al., 2016). This disparity may be explained by the different setting – primarily outpatients – and less comprehensive add-on interventions, as about half of them focused on education instead of an integrated supported approach. Although our findings correspond with small to medium effects after PA and nutrition interventions on anthropometric measures in patients with SMI (Rosenbaum et al., 2014; Teasdale et al., 2017), they are inconsistent with a recent study which included Dutch inpatients with SMI – a population quite similar to ours – as they found no effect on waist circumference and metabolic health after 12 months (Looijmans et al., 2017). This difference could be explained by the use of another intervention design, in which lifestyle coaches from outside the organization were used instead of an integrated 'change from within' approach. A systematic review of studies on blood pressure, triglycerides, fasting glucose and cholesterol reported inconsistent findings (Firth et al., 2015), which may be explained by the high heterogeneity of interventions and methodological quality (e.g. small sample sizes) of the included studies.

We observed no significant improvements in psychotic symptoms, which is inconsistent with recent reviews and meta-analysis that reported significant improvements as a result of increased PA (Dauwan et al., 2016; Firth et al., 2015; Rosenbaum et al., 2014; Vera-Garcia et al., 2015) in patients with SMI. However, the majority of their

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Table 1
Baseline characteristics and baseline and follow-up measurements of participants on sedentary behavior and physical activity, metabolic health and psychotic symptoms ($N = 108$).

Outcome (scale)	MULTI ($n = 65$)				TAU ($n = 43$)			
	Baseline		Follow-up		Baseline		Follow-up	
Baseline participant characteristics								
Sex, *n* (%) male	43	(66.2)			23	(53.5)		
Age, years	**52.2**	(**8.9**)			**58.6**	(**12.1**)		
Diagnosis, *n* (%)								
Schizophrenia and other psychotic disorders	**61**	(**93.8**)			**26**	(**60.5**)		
Other disorders	**4**[a]	(**6.2**)			**17**[b]	(**39.5**)		
Illness severity, CGI-S scale 1–7	**5.0**	(**1.2**)			**4.2**	(**1.1**)		
Years of hospitalization	14.4	(10.9)			14.2	(13.1)		
Sedentary behavior & physical activity								
Wear time during measurement (hours)	55.9	(7.8)	53.6	(9.1)	55.1	(10.6)	52.8	(10.4)
Average total activity counts per hour	29,102	(12,371)	33,020	(14,453)	23,994	(14,571)	23,664	(13,151)
Intensity during wear time								
% Sedentary behavior	82.0	(5.9)	80.0	(6.4)	83.1	(9.1)	83.0	(9.2)
% Light physical activity	10.9	(4.3)	12.0	(5.0)	11.4	(7.4)	11.7	(7.6)
% Moderate-to-vigorous physical activity	7.1	(3.8)	8.0	(4.4)	5.4	(3.6)	5.4	(3.4)
Metabolic health								
Weight (kg)	92.2	(20.1)	87.7	(18.0)	79.8	(18.2)	81.8	(18.2)
Abdominal girth (cm)[c]	111.1	(16.5)	107.3	(14.2)	103.1	(12.9)	104.3	(14.1)
Systolic blood pressure (mmHg)[c]	124.7	(17.4)	120.8	(13.5)	130.1	(18.8)	135.0	(19.5)
Diastolic blood pressure (mmHg)[c]	81.7	(11.0)	79.8	(9.6)	81.3	(8.7)	79.7	(11.0)
Triglycerides (mmol/l)[d]	2.1	(1.1)	1.8	(1.0)	1.6	(0.9)	1.9	(1.0)
Cholesterol total (mmol/l)[d]	4.8	(1.0)	4.6	(1.1)	4.9	(1.1)	4.9	(1.2)
Cholesterol HDL (mmol/l)[d]	1.0	(0.3)	1.1	(0.3)	1.2	(0.3)	1.2	(0.3)
Fasting glucose (mmol/l)[d]	6.7	(2.9)	5.9	(1.2)	6.2	(2.0)	6.0	(1.4)
Metabolic syndrome, *n* (%)[e]	50	(77.0)	43	(66.2)	25	(58.1)	28	(65.1)
Psychotic symptoms (1–7)[f]								
Delusions	3.4	(2.5)	3.6	(1.9)	2.0	(2.1)	2.5	(1.8)
Conceptual disorganization	2.7	(2.3)	2.5	(1.9)	2.6	(2.2)	2.2	(1.5)
Hallucinatory behavior	2.7	(2.4)	3.2	(1.9)	1.9	(2.2)	2.4	(1.7)
Blunted affect	3.0	(2.3)	1.7	(1.2)	1.8	(1.7)	2.1	(1.6)
Passive/apathetic social withdrawal	2.9	(2.2)	2.3	(1.7)	1.8	(1.8)	2.2	(1.7)
Lack of spontaneity and flow of conversation	2.5	(2.2)	2.0	(1.5)	1.9	(1.9)	2.2	(1.7)
Mannerisms/posturing	2.2	(2.0)	1.2	(0.6)	1.3	(1.5)	1.0	(0.2)

Notes: Mean (SD) unless noted otherwise. Significant differences in characteristics between groups are shown in bold.
MULTI: Multidisciplinary Lifestyle-enhancing Treatment for Inpatients with severe mental illness; TAU: Treatment As Usual; CGI-S: Clinical Global Impression – Severity scale.
[a] Mood disorders ($n = 2$), a pervasive disorder not otherwise specified ($n = 1$) and an anxiety disorder ($n = 1$).
[b] Mood disorders ($n = 8$), personality disorders ($n = 3$), alcohol-related disorders ($n = 3$), somatoform disorders ($n = 2$) and a pervasive disorder not otherwise specified ($n = 1$).
[c] Missing baseline value ($n = 1$).
[d] Missing baseline value ($n = 1$) and missing follow-up because patient refused blood tests ($n = 1$).
[e] According to consensus criteria (Alberti et al., 2009).
[f] Missing baseline value ($n = 11$) and missing follow-up because patient was discharged before measurement ($n = 1$).

included studies concerned outpatients, who may be more likely to achieve reduction of symptom severity compared to inpatients with a higher and prolonged illness severity. Our findings did correspond to a previous study evaluating high aerobic intensity training in inpatients with schizophrenia and a recent RCT in residential and clinical teams treating patients with SMI with a combined diet- and exercise lifestyle intervention, both finding no effects on PANSS (Heggelund et al., 2011; Stiekema et al., 2018). Mediation by change in total activity was absent, indicating that the improvements we found were not just because of increased physical activity. It suggests that improvements are a result of a combination of components of MULTI. We speculate that the organizational culture change is the main factor, with multiple components complementing PA, including a focus on dietary habits, psychoeducation, personal tailoring, support by peers and qualified participating staff. This corresponds to results of recent studies, which advocated the use of such elements (Long et al., 2016; Roberts and Bailey, 2011; Teasdale et al., 2017; Vancampfort et al., 2017b; Ward et al., 2015).

Some limitations of our study should be discussed. Firstly, because we evaluated a treatment that was already implemented, we were not able to randomize the wards. By using multilevel regression correcting for differences between MULTI and TAU, we aimed to minimize bias and obtain robust results. Secondly, our analyses were largely dependent on the number of patients and available data within the cohort. As a result, our analysis on the recovery of the MetS was affected by the limited group size and should be interpreted with caution (Vittinghoff and McCulloch, 2007). Thirdly, we had a relatively large amount of missings of baseline PANSS-r scores. However, it is likely that these scores were missing due the greater difficulty of obtaining measurements from patients with severe illness. Consequently, we could presume that this understated rather than overstated the impact of the intervention. Fourthly, no international consensus exists on how to set up and process accelerometer data and on the heterogeneity of chosen thresholds, which can hinder comparisons between studies, especially percentages of SB, light PA and MVPA. By using average total activity counts, which was suggested to reach a better standard for comparability (Bassett et al., 2015), we took initial steps to improve comparability of accelerometer data. Lastly, as MULTI was based on prolonged hospital stay, such an approach may be less feasible for other healthcare settings. However, previously mentioned important elements of the treatment that are supported by literature such as multidisciplinary cooperation, combining multiple components (e.g. instead of PA and diet separately) and support of peers and qualified staff should be possible to implement in other settings, such as sheltered housing or outpatient facilities, as well.

Compared to previous research, our study has several advantages. Firstly, because of the observational design and a treatment developed within the current clinical practice and resources of inpatient mental healthcare, our data support the generalizability of our findings and the feasibility of MULTI, which is very relevant for clinical practice (Naslund et al., 2017). Secondly, we used a follow-up period of 18 months in this study, compared to the majority of previous studies which followed patients for ≤6 months (Chalfoun et al., 2016; Naslund

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Table 2
Linear multilevel regression estimating treatment effects between MULTI and treatment as usual on sedentary behavior and physical activity, metabolic health and psychotic symptoms ($N = 108$).

Outcome (scale)	Model 1			Model 2			Model 3		
	B	(95% CI)	p	B	(95% CI)	p	B	(95% CI)	p
Sedentary behavior & physical activity									
Average total activity counts per hour[a]	**0.37**	(**0.04–0.69**)	**0.03**	**0.34**	(**0.01–0.68**)	**0.05**	**0.46**	(**0.08–0.84**)	**0.02**
% Sedentary behavior	**−2.32**	(**−4.38 to −0.26**)	**0.03**	−1.82	(−3.93–0.27)	0.09	−2.15	(−4.48–0.18)	0.07
% Light physical activity	0.95	(−0.40–2.30)	0.17	0.70	(−0.73–2.12)	0.33	0.62	(−0.96–2.19)	0.44
% Moderate-to-vigorous physical activity	1.34	(−0.01–2.69)	0.05	1.33	(−0.6–2.72)	0.06	**1.78**	(**0.22–3.34**)	**0.03**
Metabolic health									
Weight (kg)	**−4.39**	(**−7.86 to −0.93**)	**0.01**	**−5.24**	(**−8.75 to −1.73**)	**0.004**	**−4.18**	(**−8.13 to −0.23**)	**0.04**
Abdominal girth (cm)[b]	**−3.27**	(**−6.25 to −0.28**)	**0.03**	**−3.20**	(**−6.33 to −0.07**)	**0.04**	**−3.48**	(**−6.88 to −0.08**)	**0.04**
Systolic blood pressure (mmHg)[b]	**−12.10**	(**−17.68 to −6.52**)	**<0.001**	**−10.38**	(**−16.12 to −4.64**)	**0.001**	**−8.03**	(**−14.55 to −1.52**)	**0.02**
Diastolic blood pressure (mmHg)[b]	−0.05	(−3.42–3.33)	0.98	−0.20	(−3.76–3.36)	0.91	−0.05	(−4.04–3.93)	0.98
Triglycerides (mmol/l)[c]	**−0.37**	(**−0.67 to −0.07**)	**0.02**	**−0.39**	(**−0.71 to −0.07**)	**0.02**	−0.25	(−0.61–0.11)	0.16
Cholesterol total (mmol/l)[c]	−0.20	(−0.53–0.14)	0.25	−0.15	(−0.51–0.20)	0.40	−0.04	(−0.43–0.35)	0.85
Cholesterol HDL (mmol/l)[c]	0.06	(−0.02–0.14)	0.15	0.06	(−0.02–0.14)	0.11	**0.10**	(**0.01–0.19**)	**0.03**
Fasting glucose (mmol/l)[c,d]	−0.65	(−1.35–0.02)	0.06	−0.50	(−1.23–0.13)	0.14	−0.55	(−1.37–0.18)	0.14
Psychotic symptoms (1–7)[e]									
Delusions	0.53	(−0.22–1.27)	0.16	**0.83**	(**0.07–1.59**)	**0.03**	0.36	(−0.37–1.08)	0.33
Conceptual disorganization	0.47	(−0.21–1.15)	0.17	0.56	(−0.16–1.27)	0.12	0.10	(−0.67–0.86)	0.80
Hallucinatory behavior	0.48	(−0.25–1.22)	0.19	0.63	(−0.14–1.41)	0.11	0.34	(−0.44–1.13)	0.37
Blunted affect	−0.54	(−1.10–0.03)	0.06	−0.35	(−0.93–0.23)	0.23	−0.45	(−1.02–0.13)	0.13
Passive/apathetic social withdrawal	−0.25	(−0.93–0.44)	0.48	−0.11	(−0.83–0.62)	0.76	−0.18	(−0.94–0.58)	0.64
Lack of spontaneity and flow of conversation	−0.52	(−1.16–0.11)	0.17	−0.40	(−1.08–0.28)	0.24	−0.45	(−1.15–0.25)	0.21
Mannerisms/posturing[d]	0.13	(−0.10–0.35)	0.26	0.12	(−0.11–0.36)	0.31	0.02	(−0.14–0.18)	0.77

Notes: Significant results shown in bold. MULTI: Multidisciplinary Lifestyle-enhancing Treatment for Inpatients with severe mental illness.
Model 1: crude model, corrected for baseline measurement.
Model 2: adjusted model, corrected for baseline measurement and age.
Model 3: adjusted model, corrected for baseline measurement, age, diagnosis (schizophrenia and other psychotic disorders, yes/no) and illness severity at baseline.
[a] Standardized to facilitate interpretation; individual values were subtracted by the mean total activity counts per hour and divided by its SD. B can be interpreted as Cohen's *d*.
[b] Missing change score because of missing baseline value ($n = 1$).
[c] Missing change score because of missing baseline value ($n = 1$) and missing follow-up because patient refused blood tests ($n = 1$).
[d] Bootstrapped (1000 samples) because of left skewed distribution.
[e] Missing change score because of missing baseline value ($n = 11$) and missing follow-up because patient was discharged before measurement ($n = 1$).

et al., 2017; Stanton and Happell, 2014; Vancampfort et al., 2015b). Another strength is the use of accelerometers instead of self-reports to measure SB and PA (Soundy et al., 2014; Stubbs et al., 2016b), which greatly improved the reliability of the data, especially in this population. Furthermore, in the multilevel analysis, we corrected for possible clustering within wards (e.g. patients or the way staff works within a ward might differ between wards, influencing results), regression to the mean (e.g. overweight patients are more likely to lose weight) and differences between MULTI and TAU, as randomization was not possible. Finally, by analyzing possible mediation by total activity, we took a first step to gain more insight into the contribution of different elements of MULTI to the observed improvements.

Before this intervention can be widely implemented in inpatient mental healthcare, replication of MULTI including the measurements at other sites is needed. Nevertheless, the findings provide important implications for clinical practice. Previous interventions involving

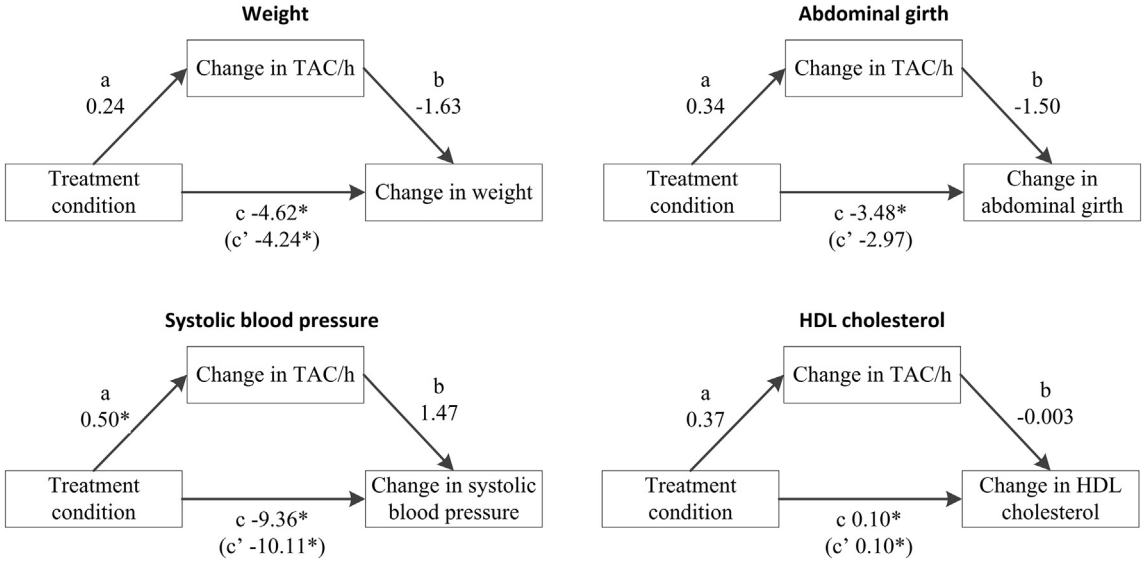

Fig. 3. Regression coefficients for significant changes on weight, abdominal girth, systolic blood pressure and HDL cholesterol, analyzed for mediation by change in average total activity counts per hour (TAC/h). The association between treatment condition and specific outcome, controlling for change in TAC/h, is in parentheses. Models were corrected for baseline measurement, age, diagnosis (schizophrenia/other psychotic disorders, yes/no) and illness severity at baseline. $^{*}p < 0.05$.

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inpatients with SMI failed to achieve desired improvements (Levitt et al., 2017; Looijmans et al., 2017) and often lack an integrated approach and culture change. After maintaining such promising results over the longer term, with a treatment developed within the current clinical practice and resources of inpatient mental healthcare, our study suggests that a sustainable solution towards a healthier lifestyle is already at our fingertips. This could have an even bigger impact if transferred into standard care, where MULTI could be an essential part of a treatment strategy to interrupt the deterioration of physical health usually seen within this population and to improve PA and metabolic health in the longer term. Although this is a hopeful message, an integrated multi-component treatment requires a culture change driven by multidisciplinary cooperation and staff participation, supported at management level. Future implementation-evaluation identifying barriers and facilitators towards implementation are therefore critical for clinical practice. Additionally, since especially SMI starts at early age (Kessler et al., 2007) and somatic comorbidities are associated with more frequent rehospitalization (Filipcic et al., 2017), an integrated and culture changing approach can provide lifelong improvements and prevent major health issues that are currently seen these days in patients with a long history of SMI.

In summary, this 18 months follow-up study shows that an integrated multi-component and multidisciplinary lifestyle enhancing treatment can improve PA and metabolic health substantially compared to treatment as usual. We urge long-term follow-up studies on multi-component lifestyle enhancing interventions to improve the disproportional metabolic health problems in SMI patients.

Conflict of interest

None to declare.

Contributors

JD and DT designed the study and collected the data. JD, DT and FR contributed to the data analysis. All authors contributed to the data interpretation. JD developed the first draft of the article. All authors contributed to critical revisions of the article and gave final approval for the version to be submitted.

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