

Early View

Original article

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Mechanisms associated with increased physical activity in patients undergoing self-management behaviour modification in the randomised PHYSACTO[®] trial

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Take-home message (limit 256 characters):

Self-management improves motivation & confidence to engage in physical activity in

COPD patients in PHYSACTO[®]

Plain language summary

COPD symptoms can worsen over years. As a consequence, physical activity also decreases, which can make the patient's condition worse. Self-management programmes to assist patients in changing their behaviours can help them gain the skills needed to better manage their disease. In this study, we wanted to see if such a programme could improve activity levels. We also wanted to see what factors might help this improvement.

We looked at patients who received the medicine tiotropium or combination of medicines tiotropium/olodaterol or placebo (no active medicine), with or without exercise training. All of these patients received behaviour training. After 12 weeks, physical activity increased for all groups of patients, as shown by an increase in the number of steps taken per week. The study showed for the first time that the increase in physical activity was due to the self-management programme but also specifically in the capacity of this programme to improve patient motivation, confidence and readiness to change.

The results suggest that a well-designed self-management behaviour programme can lead to improvements in physical activity, irrespective of other treatments.

Abstract

Introduction: In this analysis of the PHYSACTO[®] study, we assessed the efficacy of a self-management behaviour modification (SMBM) programme to improve physical activity (PA) levels, and the extent to which effects were mediated by readiness to change, motivation and confidence.

Methods: PHYSACTO[®] was a randomised, partially double-blind, parallel-group, 12-week trial to evaluate the effects of treatment on exercise capacity and PA. COPD patients received placebo, tiotropium 5 µg or tiotropium/olodaterol 5/5 µg, with or without exercise training, all with an SMBM intervention (the Living Well with COPD programme). Changes were assessed in readiness to change (Stage of Change Visual Analogue Scale [VAS]), motivation (Treatment Self-Regulation Questionnaire [TSRQ]), and confidence (Perceived Competence Scale [PCS]) to engage in PA.

Results: PA was increased in all patients with complete PA data at Week 12 (n=262; +6038 steps/week, p<0.001). Significant increases were observed in patients' readiness to change (VAS 0.7 [0.6-0.8]), autonomous regulation (TRSQ 0.2 [0.1-0.3]) and confidence (PCS 0.5 [0.3-0.6]) (all p<0.01). Of note, 23% of the total effect of SMBM on steps/week was found to be mediated by increases in readiness to change, 5% by TSRQ autonomous regulation and 12% by PCS.

Conclusion: Our study demonstrated that an SMBM programme delivered to COPD patients increased PA, mediated by an improvement of three key hypothesised mechanisms of change: readiness to change, autonomous motivation and confidence. For the first time, this study shows that an SMBM programme can be successful in changing the mechanisms of change targeted by the intervention.

Word count: 246/250 words

Introduction

Patients with chronic obstructive pulmonary disease (COPD) progressively decrease physical activity (PA) over time [1]. Patients who decrease their PA levels are at increased mortality risk and show more rapid disease progression than those who maintain or increase PA levels [1, 2]. Reductions in PA are associated with an increased rate of exacerbations requiring hospitalisation and worse health status [1, 3] These findings have led to further interest in the best way to deliver interventions to increase participation in PA in patients with COPD.

There is limited and inconsistent evidence on the effects of bronchodilators and pulmonary rehabilitation on getting patients to engage in more PA [4]. Pulmonary rehabilitation programmes have reported small average improvements in PA, with slightly larger changes observed after longer-lasting programmes [5]. It has been argued that, to be successful, interventions targeting PA – which is a behavioural target – should aim to increase readiness and levels of motivation and confidence to engage in PA [6]. Behaviour change counselling programmes, which typically aim to increase readiness, motivation (desire) and confidence (perceived ability) to engage in PA through the use of established behavioural and motivation strategies [7], have generally demonstrated larger and more consistent improvements in PA than rehabilitation programmes with exercise training as the primary focus [6, 8-10]. However, one important limitation of these studies is the failure to assess the extent to which the behavioural intervention was successful in changing the hypothesised mechanisms of change – i.e., readiness, motivation and confidence [11]. Interventions are generally judged to be efficacious if they change the target behaviour; but without measuring if the intervention “worked” as expected (i.e., the same way we would measure blood pressure reductions before concluding that an anti-hypertensive drug was

able to reduce hypertension), we have no idea *why* the intervention worked, making it impossible to attribute the behaviour change to intervention.

A group of experts has proposed a conceptual definition of COPD self-management behaviour modification (SMBM) intervention as “structured but personalised and often multicomponent, with goals of motivating, engaging and supporting the patients to positively adapt their health behaviour(s) and develop skills to better manage their disease” [12]. While many SMBM programmes will target increasing readiness, motivation and confidence, these factors are not always the focus of treatment, and even when they are, they are rarely (if ever) assessed.

We present a study embedded into the PHYSACTO[®] trial that was specifically designed to enhance patient readiness, motivation and confidence to engage in PA through the use of established behavioural and motivation strategies [7]. The trial included an SMBM intervention (based on the “Living Well with COPD” [LWWCOPD] programme [www.livingwellwithcopd.com]) delivered using a motivational counselling approach [13], that targeted motivation and confidence for patients with COPD to become more physically active. The aim of the present study was to assess the impact of the SMBM intervention (which was offered to all PHYSACTO[®] treatment arms) on hypothesised mediating variables: increases in readiness to change, motivation, and confidence to engage in PA.

Methods

PHYSACTO[®] trial design

The PHYSACTO[®] trial was a randomised, partially double-blinded, placebo-controlled, parallel-group trial (NCT02085161). The study design has been described elsewhere [14], but briefly, patients with COPD aged 40–75 years with forced expiratory volume in 1

second (FEV_1) $\geq 30\%$ and $< 80\%$ predicted, FEV_1 /forced vital capacity (FVC) $< 70\%$ and a smoking history of > 10 years were included. Patients were randomised to four groups: placebo, tiotropium 5 μg (Tio), tiotropium/olodaterol 5/5 μg (Tio/Olo), and Tio/Olo + exercise training (ExT) (Figure 1). All groups received 12 weeks of an SMBM intervention based on the LWWCOPD programme, which was delivered using a motivational counselling approach. The treated set comprised 303 patients. A double-blind design was used for the groups receiving placebo + SMBM, Tio + SMBM and Tio/Olo + SMBM. It was not possible to implement blinding in the group that received Tio/Olo + SMBM + ExT, and the complementary intervention of placebo + ExT was not feasible, as it was not in accordance with recommendations at the time of trial conduct [14].

The primary endpoint of the trial was endurance time during an endurance shuttle walk test to symptom limitation after 8 weeks; primary and secondary results are published elsewhere [15]. The secondary endpoint was patients' PA measured using a triaxial accelerometer (Dynaport. McRoberts BV, The Hague, Netherlands) including walking intensity, walking time, and number of steps.

Intervention: SMBM based on LWWCOPD

The SMBM intervention, delivered after randomisation, was based on the LWWCOPD programme and focused on improving patient engagement in exercise and PA using a combination of education on benefits of PA, goal setting, action planning, self-monitoring and problem-solving. We cannot exclude that patients at participating sites may have been aware of the LWWCOPD programme, although collecting this information was not part of standard practice. Site case managers were specifically trained to use client-centred

motivational communication (MC) techniques for the study [7] to increase patients' readiness, autonomous motivation and confidence to engage in PA.

The methodological considerations when integrating behaviour-change interventions into a multicentre study are described in detail in a previous manuscript; a summary can be found in Supplementary File 1 [13]. Finally, robust quality control procedures included self-assessments conducted by case managers, audiotaping individual and group sessions, and independently assessing the fidelity of intervention delivered by the site case manager. The assessments verified whether 1) intervention content was delivered per protocol; 2) interventionists delivered the intervention using an MC style (i.e., using guiding counselling style and open questions to increase readiness and build motivation/confidence; expressing empathy using reflective listening; and asking for feedback after giving information); and 3) the intervention was personalised according to the patient's personal PA goals (see assessment tools in Supplementary File 2).

Measures and outcomes

The SMBM focused on increasing a specific behaviour: daily PA, measured using step count and walking time via a triaxial accelerometer. Patients wore the monitor every day during waking hours 1 week prior to the Week 0 (baseline), Week 9 and Week 12 visits. The St. George's Respiratory Questionnaire (SGRQ) was conducted at Weeks 9 and 12 as a measure of health status.

Mediating variables

To assess readiness to change, we administered a Stage of Change for PA Visual Analogue Scale (VAS) representing the five stages of change (see readiness to change tool in Supplementary File 3); patients were asked to choose the image that best reflects their

current level of PA (ranging from 1, not currently engaging in PA, to 5, has been engaging in regular PA for some time) [16].

Other mediating ‘process of change’ variables were assessed using validated questionnaires: the Treatment Self-Regulation Questionnaire (TSRQ) and Perceived Competence Scale (PCS). The TSRQ measures motivational style and includes three subscales (autonomous regulation, controlled regulation and amotivation, i.e. the state of lacking any motivation) and 15 questions on a 7-point scale from “not at all true” to “very true” [17]. Scores range from 1 to 7, with higher scores indicating the more dominant motivational style, with higher autonomous motivation being the strongest predictor of lasting behavioural change and decreases in controlled motivation also being a positive behaviour change indicator (amotivation was not examined in this study as it was not a target of the intervention). The PCS assesses perceived confidence in one’s ability to engage in a particular behaviour and includes four questions on a 7-point scale from “not at all true” to “very true” [18]. Total scores range from 4 to 28, with higher scores indicating greater patient confidence in their ability to engage in regular PA.

Statistical analyses

We tested the effect of the SMBM intervention on PA (steps/week) and the mediator effect of readiness, motivation, and confidence, on the change in PA after receiving the SMBM intervention using a multiple mixed-effect random model, adjusting for age, sex, body mass index, smoking, FEV₁ % predicted, treatment group and baseline endurance time. The mediator model was tested using the procedures described by Baron and Kenny (1986) [19]. According to the authors, three regression equations are tested to determine mediation: Model 1 regress the dependent variable on the independent variable to confirm

that the independent variable is a significant predictor of the dependent variable: $Y = i_1 + cX + \varepsilon_1$, significant; Model 2 regress the mediator on the independent variable to confirm that the independent variable is a significant predictor of the mediator: $M = i_3 + \alpha X + \varepsilon_3$, significant; Model 3 regress the dependent variable on both the mediator and independent variable to confirm that the mediator is a significant predictor of the dependent variable, and the previously significant independent variable in Model #1 is now greatly reduced: $Y = i_2 + c'X + \beta M + \varepsilon_2$. Mediation is established if the first and the second equations are shown to be significant. In addition, two criteria must be met in the third equation: 1) the mediator (M) must significantly predict the outcome variable (Y) and 2) the direct relationship between the X and the Y must reduce to zero (or be reduced in absolute size but different from zero) in the third equation in order to establish full mediation or partial mediation. In our mediator models, multiple mixed-effect random models were used to increase power [20], adjusted for baseline age, sex, body mass index, smoking pack-years, FEV₁ % predicted, treatment groups, and baseline endurance time. Adjustments were made based on a priori selected covariates that are expected to influence outcomes [21], rather than on observed differences at baseline. In light of no established clinical cut-offs, we used an arbitrary metric such as the 10% rule to define partial mediation effect of mediators between SMBM intervention and PA in magnitude of the ratio of mediated effect (indirect effect) to total effect.

Results

In total, 303 patients with COPD were enrolled, with a mean age of 64.8 years. Two hundred and sixty-two (85%) patients had complete PA data at Week 12 (full analysis set [FAS]). Mean FEV₁ % predicted normal was 48.4 ± 13.4 and baseline steps/week was

37684.5 \pm 19996.9 (Table 1). There were no significant differences in baseline characteristics between treatment groups. Furthermore, there were no significant differences between patients who did and did not complete the follow-up visits (Supplementary Table 1).

Changes in PA and mediating variables

Table 2 shows changes in PA and mediating variables for the FAS (n=262) at 12 weeks as compared to baseline, and changes as a function of treatment group. There were significant increases in PA for the FAS over the 12-week follow-up period (+6038 steps/week, $p < 0.001$) and for all treatment groups except for Tio + SMBM (at 12 weeks: Tio/Olo + SMBM + ExT [+5028 steps; $p = 0.006$]; Tio/Olo + SMBM [+11142 steps, $p < 0.001$]; Tio + SMBM [+1905 steps; $p = 0.28$]; placebo + SMBM [+5923 steps; $p = 0.023$]). The differences between groups were not statistically significant ($p = 0.099$). Walking duration also increased significantly in the FAS and all treatment groups, except in the Tio + SMBM group, where the increase did not reach statistical significance.

Scores on the Stage of Change VAS significantly increased in all intervention groups at Week 12 as compared with baseline. The differences between groups were not statistically significant. TSRQ autonomous regulation (motivation) increased significantly in the FAS and in the Tio + SMBM intervention group compared with the other groups at Week 12 as compared with baseline; there were no statistically significant increases in TSRQ controlled regulation. PCS scores (confidence) increased significantly in the FAS, as well as in all intervention groups at Week 12 as compared with baseline. The differences between groups were not statistically significant.

Mediating variable effect on PA

Figure 2 shows the partial mediation effect of the mediating variables: a) readiness to change (VAS), b) autonomous and controlled regulations (TSRQ) and c) confidence (PCS) (see also Table 2 and Supplementary Figures 1 and 2) on the increase in PA expressed in steps/week after SMBM intervention. After SMBM intervention, PA was significantly increased by 563.64 steps/week (estimate from multiple mixed-effect random model), of which the mediating effect (indirect effect) of the mediators was 128 for stage of change (after accounting for stage of change, the regression coefficient of SMBM in predicting steps/week dropped from 563.64 to 435.61, and the ratio of mediated effect to total effect is 23%, suggesting a partial mediation effect of stage of change between SMBM and step/week), 29 for TSRQ autonomous regulation (accounting for 5% of the total effect) and 70 for PCS (accounting for 12% of the total effect).

Discussion

The study results show that COPD patients who participated in an SMBM intervention (based on the LWWCOPD programme: www.livingwellwithcopd.com) that was specifically designed to enhance patient readiness, motivation and confidence to engage in PA demonstrated significant increases in PA that were mediated by improving three key hypothesised mechanisms of change: readiness to change, autonomous motivation and perceived confidence. To our knowledge, this is the first study to link an SMBM intervention focusing on increasing PA to specific mechanisms of change among COPD patients. Importantly, this study demonstrated that PA was directly increased by the SMBM programme and indirectly increased by mediators that were specifically targeted by the SMBM intervention, e.g., readiness to change, autonomous (intrinsic) motivation but not

controlled (extrinsic) motivation and confidence. Of note, the intervention was not designed to change controlled motivation, so results indicating no significant change show our intervention was specific enough to only increase the variables targeted by the intervention.

To be effective, therapies need to be prescribed to the patients who would benefit most, and patients must also adopt a certain pattern of behaviour, e.g. they must be adherent. However, there are many challenges; for example, patients are not always ready or motivated to adopt a particular behaviour even when there appear to be obvious benefits. This may be related to psycho-cognitive factors such as anxiety and depression or even socio-cultural status and educational level [22, 23]. There is also a complex interaction between the healthcare professional's communication and the patient. Too often, healthcare professionals encourage patients to adopt a particular behaviour (e.g. trying a new therapy or increasing their PA) by giving encouraging information and advice that tends to work in only a minority of patients [24, 25]. Furthermore, communication style is a critical clinical skill that may not get the attention it deserves, because when providers communicate poorly, they can inadvertently increase patient resistance to advice by seeming to "tell patients what to do" [25, 26].

In the proposed conceptual definition of a COPD self-management intervention, the recent consensus of international experts has clearly emphasised the need for a process that ensures that an intervention is properly constructed and implemented. This requires interaction between patients and healthcare professionals acting as health coaches, with a focus on 1) identifying the patient's needs, beliefs and enhancing autonomous motivations; 2) eliciting personalised goals; 3) formulating appropriate strategies to achieve these goals; and 4) evaluating and readjusting strategies [12]. It is also proposed that behaviour change techniques should be used to elicit patient motivation, confidence and competence. MC

[27] is often used as an evidence-based communication style designed to strengthen a person's autonomous motivation and commitment to change [28]. MC involves establishing a collaborative partnership, evoking motivation/desire to change, strengthening confidence to change and respecting the patient's autonomy. It is designed to evoke what is already present (i.e. motivation, confidence), rather than manufacture needs or impose an agenda. To our knowledge, this is the first study to operationalise and measure these concepts in a randomised clinical trial among COPD patients using robust quality control procedures, including audiotapes of sessions assessing whether the site case manager delivered the intervention as intended (fidelity). The PHYSACTO[®] study supports the feasibility of employing these methods and provides a framework for promoting PA in COPD patients. This was possible through the development and implementation of new assessment tools, making it possible to verify if all the educational topics were covered properly, whether an MC delivery style (open questions, reflective listening, etc.) was used, and the extent to which the intervention was personalised (patient-centred) [29]. The implementation of a quality assurance programme and the precise methodology we used to assess fidelity of the delivery of the SMBM programme by the case managers was described in detail previously [13]. Our results show that interventionist fidelity was judged to be 'satisfactory to highly satisfactory' for 79% of 153 audited education sessions. This suggests that our SMBM programme was indeed delivered as intended, and supports the importance of assessing intervention fidelity in behavioural intervention trials [30].

The results of the present study are consistent with those of previous studies in other chronic disease populations. For example, MC-based approaches have been shown to increase confidence and readiness to change to discontinue health risk behaviours among patients with cardiovascular disease and diabetes, as well as in smokers [30]. Moreover, the

present results are also consistent with those of a study examining the effects of MC on asthma medication adherence, which revealed a medium to large effect size for improved asthma-related self-efficacy (confidence) from baseline to 12 months (intent-to-treat, $d=0.43$; per-protocol analysis, $d=0.53$) [31]. The present study thus adds to the existing literature demonstrating the ability of MC-based SMBM programmes to successfully influence these behavioural mediators of change.

The results of this study need to be interpreted in light of some methodological limitations. First, all of the treatment groups received the SMBM programme, so we cannot compare patients who participated in the programme and those who did not. While it is possible that changes in motivation and confidence were due to other aspects of the trial interventions (e.g., bronchodilators, exercise training), this is highly unlikely for two reasons: 1) unlike the SMBM programme, medication and exercise training do not specifically target improving motivation and confidence to engage in PA, and there is no reason to believe these would improve spontaneously as a result of these interventions; and 2) our findings indicate that motivation and confidence increased significantly across all treatment groups, with no observed between-group differences, suggesting that these variables were responding to the SMBM programme, which was the only treatment received by all patients. Another limitation is the small sample size of the study groups; this does not provide enough precision to analyse the indirect effect of mediators within treatment group. In a previous analysis of the PHYSACTO cohort, patients with improved PA and exercise capacity after SMBM also had lower anxiety and depression scores [22]. Given this potential association between psycho-cognitive factors (i.e. anxiety and depression) and PA levels, it is possible that patient differences at baseline could have affected the outcomes of our study. Patients' socio-cultural status at baseline could also

have affected outcomes. However, given the sample size and the multi-site and multi-country nature of the study (8 countries speaking 11 languages), factoring socio-cultural status into the analysis would have been complex. Finally, there was no long-term follow-up to determine the impact of the programme beyond the end of the trial, which would be important to include in future studies.

Despite some limitations, this study also has a number of notable strengths. First, the results provide a novel and important contribution to the empirical evidence supporting that readiness, motivation and confidence are important factors in behaviour change. Second, the strengths of this study included an SMBM programme that was based on an established behavioural intervention for COPD patients (LWWCOPD delivered using an MC approach), standardised training with ongoing supervision and feedback of the site case managers with fidelity assessments (i.e., self-assessments of performance and expert assessments of audiotaped individual and group sessions), and the use of a quality assurance programme. Interventionist fidelity was judged to be ‘satisfactory to highly satisfactory’ for nearly 80% of case managers delivering the SMBM programme, increasing our ability to attribute treatment effects to our interventions (data not published). Third, our primary behavioural outcome measure (PA) was assessed objectively at multiple time points using an accelerometer, which increases the validity and reliability of the measure. Finally, PHYSACTO[®] was an international trial conducted in 11 countries in 8 different languages. Despite its complexity, this study demonstrates the feasibility of implementing an SMBM programme in diverse populations and cultures, attesting to the generalisability of the findings.

Conclusion

The PHYSACTO[®] study shows that a carefully designed and implemented SMBM intervention to increase patients' readiness, motivation and confidence to engage in PA is associated with significant improvements in PA behaviour, irrespective of other treatments (bronchodilators, exercise training). This study supports the need to use behavioural strategies to change behaviour, and the importance of measuring hypothesised mechanisms of behaviour change for attributing efficacy to the intervention. The effectiveness of the SMBM intervention may vary depending on the population targeted. There is likely to be a range of different support needed for patients at different stages in their disease, in different social circumstances and with different skill levels. However, the PHYSACTO[®] study provides a framework for effectively promoting PA in COPD patients and sets a precedent that this can be achieved in the context of an international, multisite randomised clinical trial.

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Disclosures

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Data sharing statement

Data are available from the corresponding author upon reasonable request.

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Table 1. Baseline characteristics of full analysis set (n=262) at Week 12 and according to treatment arm

| Variables | Total N=262 | Tio/Olo 5 µg/5 µg + SMBM + ExT N=65 | Tio/Olo 5 µg/5 µg + SMBM N=69 | Tio 5 µg + SMBM N=64 | Placebo + SMBM N=64 | Overall p value |
|--------------------------------------|------------------------|--|--|---------------------------------|--------------------------------|----------------------------|
| Age, years | 65.0 ± 6.3 | 65.0 ± 6.2 | 64.9 ± 7.1 | 65.6 ± 6.1 | 64.8 ± 6.0 | 0.85 |
| Sex, male gender, n (%) | 174 (66.4) | 39 (60.0) | 42 (60.9) | 48 (75.0) | 45 (70.3) | 0.195 |
| Current smokers, n (%) | 96 (36.6) | 24 (36.9) | 26 (37.7) | 21 (32.8) | 25 (39.1) | 0.896 |
| mMRC | 1.3 ± 0.9 | 1.3 ± 0.9 | 1.3 ± 0.9 | 1.3 ± 0.8 | 1.5 ± 0.8 | 0.626 |
| SGRQ activity | 55.7 ± 19.5 | 56.0 ± 20.0 | 55.6 ± 21.3 | 54.7 ± 19.4 | 56.4 ± 17.6 | 0.954 |
| FEV ₁ , % predicted | 48.4 ± 13.4 | 48.4 ± 13.2 | 49.5 ± 13.0 | 48.6 ± 14.2 | 47.0 ± 13.3 | 0.688 |
| FEV ₁ /FVC, % | 46.8 ± 10.6 | 45.7 ± 9.6 | 48.6 ± 12.2 | 46.5 ± 9.9 | 46.4 ± 10.6 | 0.662 |
| Steps per week | 37684.5 ± 19996.9 | 38141.6 ± 19210.1 | 38253.9 ± 21242.9 | 36651.3 ± 19455.1 | 36602.3 ± 20307.7 | 0.837 |
| Walking duration per week, in min | 464.1 ± 226.1 | 466.2 ± 216.3 | 477.4 ± 243.6 | 457.1 ± 217.7 | 456.4 ± 229.6 | 0.943 |
| TSRQ autonomous regulation | 5.9 ± 1.1 | 6.1 ± 0.9 | 6.1 ± 1.1 | 5.7 ± 1.4 | 5.7 ± 1.1 | 0.200 |
| TSRQ controlled regulation | 3.0 ± 1.3 | 3.0 ± 1.3 | 3.0 ± 1.2 | 2.9 ± 1.2 | 3.1 ± 1.4 | 0.962 |
| PCS score | 5.4 ± 1.4 | 5.6 ± 1.1 | 5.6 ± 1.2 | 5.1 ± 1.5 | 5.1 ± 1.5 | 0.152 |
| Stage of change scale | 3.5 ± 1.1 | 3.6 ± 1.0 | 3.5 ± 1.1 | 3.4 ± 1.2 | 3.3 ± 1.1 | 0.421 |

| Variables | Total N=262 | Tio/Olo 5 µg/5 µg + SMBM + ExT N=65 | Tio/Olo 5 µg/5 µg + SMBM N=69 | Tio 5 µg + SMBM N=64 | Placebo + SMBM N=64 | Overall p value |
|---------------------------------------|------------------------|--|--|---------------------------------|--------------------------------|----------------------------|
| Stage of change scale (1–5), n (%) | | | | | | 0.162 |
| 1 | 8 (3.1) | 0 (0.0) | 3 (4.4) | 2 (3.1) | 3 (4.7) | |
| 2 | 47 (17.9) | 9 (13.9) | 9 (13.0) | 18 (28.1) | 11 (17.2) | |
| 3 | 78 (30.0) | 21 (32.3) | 21 (30.4) | 13 (20.3) | 23 (35.9) | |
| 4 | 75 (28.6) | 19 (29.2) | 25 (36.2) | 14 (21.9) | 17 (26.6) | |
| 5 | 54 (20.6) | 16 (24.6) | 11 (15.9) | 17 (26.6) | 10 (15.6) | |

Data are presented as mean \pm SD unless otherwise specified.

Abbreviations: ExT, exercise training; FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity; mMRC, modified Medical Research Council; PCS, Perceived Competence Scale; SD, standard deviation; SGRQ, St. George's Respiratory Questionnaire; SMBM, self-management behaviour modification; Tio, tiotropium; Tio/Olo, tiotropium/olodaterol; TSRQ, Treatment Self-Regulation Questionnaire.

Table 2. Changes in PA and mediating variables for the full analysis set (n=262) and by treatment groups at 12 weeks as compared with baseline

| | Total (n=262) | | Tio/Olo 5 µg/5 µg + SMBM + ExT (n=65) | | Tio/Olo 5 µg/5 µg + SMBM (n=69) | | Tio 5 µg + SMBM (n=64) | | Placebo + SMBM (n=64) | | Overall p value ^b |
|----------------------------|---------------------------|----------------------|---------------------------------------|----------------------|---------------------------------|----------------------|----------------------------|----------------------|----------------------------|----------------------|------------------------------|
| Changes in Variables | Change after 12 weeks | p value ^a | Change after 12 weeks | p value ^a | Change after 12 weeks | p value ^a | Change after 12 weeks | p value ^a | Change after 12 weeks | p value ^a | The 4 groups comparison |
| PA variables | | | | | | | | | | | |
| Steps per week | 6038.2 (3674.3-8401.4) | <0.001* | 5028.1 (608.3-9447.9) | 0.006* | 11141.9 (6487.6-15796.2) | <0.001* | 1904.7 (-1619.8-5429.9) | 0.284 | 5923.4 (-266.0-12112.1) | 0.023* | 0.099 |
| Walking duration, in min | 61.6 (36.4-86.8) | <0.001* | 53.2 (4.2-101.5) | 0.007* | 110.6 (62.3-159.6) | <0.001* | 23.1 (-17.5-64.4) | 0.262 | 58.1 (-7.7-123.9) | 0.047* | 0.188 |
| Behaviour | | | | | | | | | | | |
| TSRQ autonomous regulation | 0.2 (0.1-0.3) | 0.002* | 0.0 (-0.2-0.2) | 0.516 | 0.2 (-0.0-0.4) | 0.105 | 0.3 (0.0-0.6) | 0.027* | 0.2 (-0.0-0.4) | 0.086 | 0.424 |
| TSRQ controlled regulation | 0.1 (-0.0-0.3) | 0.165 | 0.0 (-0.3-0.3) | 1.000 | 0.1 (-0.2-0.4) | 0.721 | 0.2 (-0.1-0.5) | 0.166 | 0.1 (-0.2-0.4) | 0.423 | 0.698 |
| PCS score | 0.5 (0.3-0.6) | <0.001* | 0.4 (0.1-0.7) | 0.003* | 0.5 (0.2-0.7) | <0.001* | 0.6 (0.3-0.9) | <0.001* | 0.5 (0.2-0.9) | <0.001* | 0.953 |
| Stage of change scale | 0.7 (0.6-0.8) | <0.001* | 0.6 (0.4-0.9) | <0.001* | 0.8 (0.5-1.0) | <0.001* | 0.7 (0.4-1.0) | <0.001* | 0.8 (0.5-1.0) | <0.001* | 0.767 |

Data are presented as mean (95% CI)

a. P values were obtained by performing paired t-test or Wilcoxon signed rank test;

b. P values were obtained by performing Anova or Kruskal–Wallis Test.

Abbreviations: ExT, exercise training; PA, physical activity; PCS, Perceived Competence Scale; SMBM, self-management behaviour modification; Tio, tiotropium; Tio/Olo, tiotropium/olodaterol; TSRQ, Treatment Self-Regulation Questionnaire.

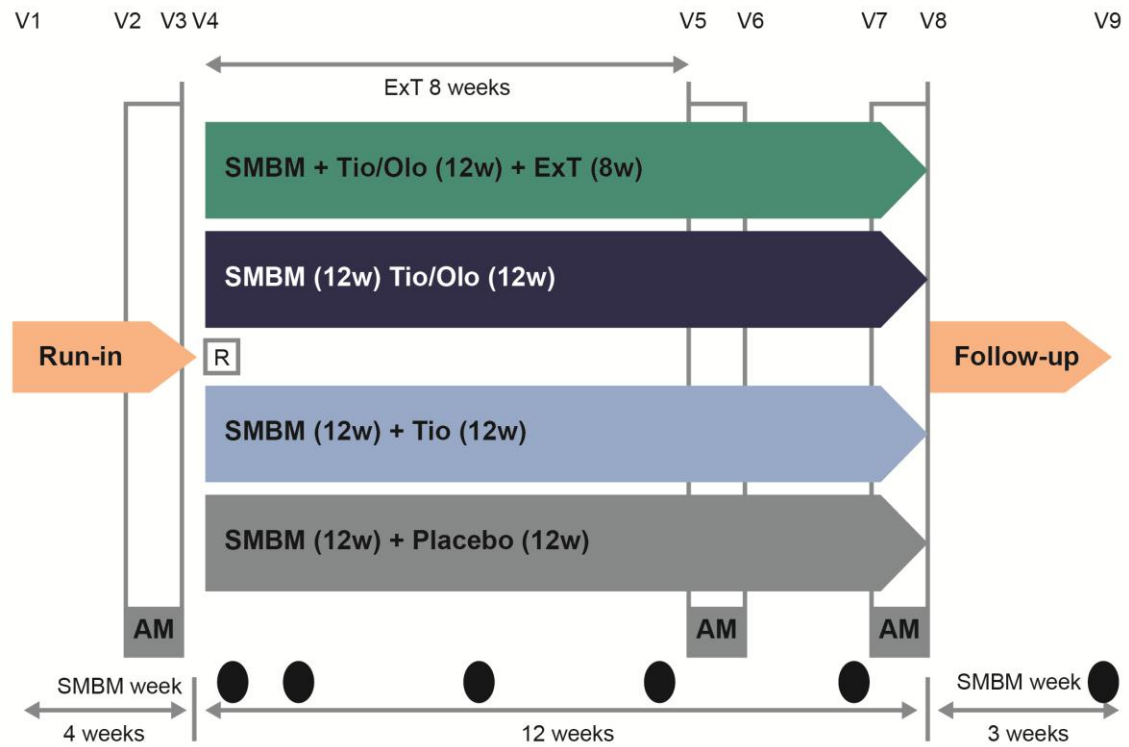
Figure legends

Figure 1. Design of the PHYSACTO[®] trial: 12-week, randomised, partially double-blind, placebo-controlled, parallel-group trial (NCT02085161) in patients with chronic obstructive pulmonary disease.

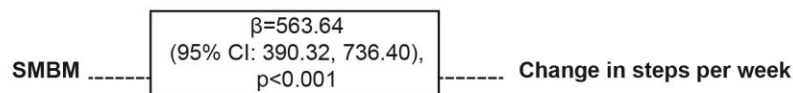
Abbreviations: AM, activity monitoring, 1 week; ExT, exercise training 3 times per week; R, run-in; SMBM, self-management behavioural modification at Weeks 1, 2, 5, 8, 11 and 15; Tio/Olo, tiotropium/olodaterol; Tio, tiotropium; w, weeks; V, visit.

Figure 2. Mediator model: stage of change, TSRQ and PCS as mediators of SMBM to change in steps/week.

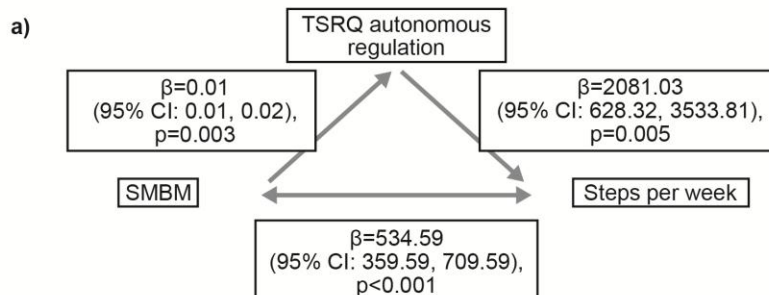
Abbreviations: CI, confidence interval; PCS, Perceived Competence Scale; SMBM, self-management behaviour modification; TSRQ, Treatment Self-Regulation Questionnaire.



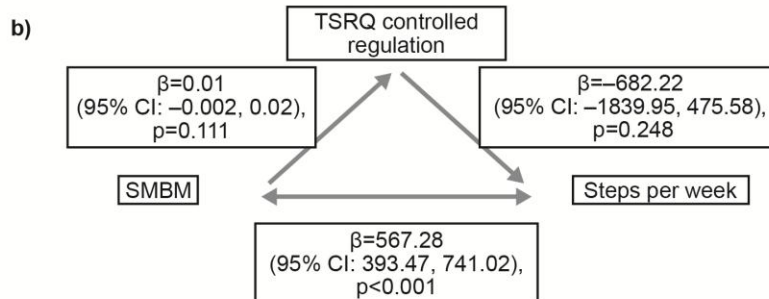
Step 1. Total effect



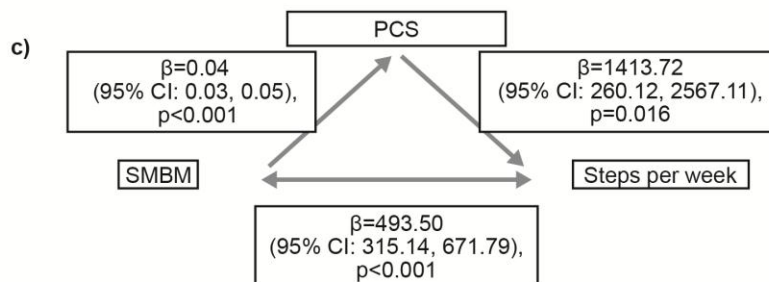
Steps 2 and 3. Direct and indirect effects for TSRQ (a, b), PCS (c), and Stage of change (d)



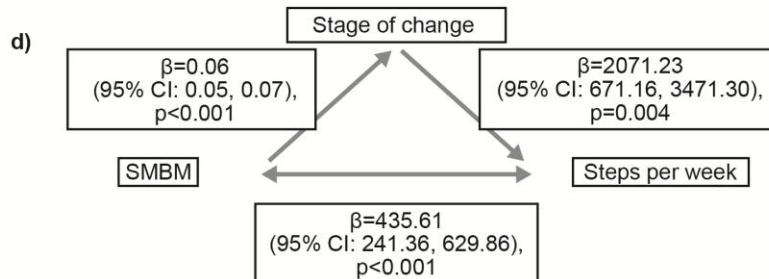
Indirect effect = $563.64 - 534.59 = 29.05$ (reduction=5%)



Indirect effect = $563.64 - 567.28 = -3.64$ (increased=0.6%)



Indirect effect = $563.64 - 493.50 = 70.14$ (reduction=12%)



Indirect effect = $563.64 - 435.61 = 128.03$ (reduction=23%)

SUPPLEMENT

Mechanisms associated with increased physical activity in patients undergoing self-management behaviour modification in the randomised PHYSACTO[®] trial

Jean Bourbeau,¹ Maria Sedenó,¹ Pei Zhi Li,¹ Thierry Troosters,² Alan Hamilton,³ Dorothy De Sousa,³ Francois Maltais,⁴ Damijan Erzen,⁵ Kim L. Lavoie⁶

Supplementary Table 1

Table 1. Baseline characteristics of patients completing/not completing 12 weeks' follow-up

| Variables | Completed N=262 | Not completed N=42 | P value |
|------------------------------------|--------------------|-----------------------|---------|
| Age, years | 65.0 ± 6.3 | 65.2 ± 6.6 | 0.685 |
| Sex, male gender, n (%) | 174 (66.4) | 25 (59.5) | 0.38 |
| Current smokers, n (%) | 96 (36.6) | 17 (40.5) | 0.599 |
| mMRC | 1.3 ± 0.9 | 1.3 ± 0.7 | 0.812 |
| SGRQ activity | 55.7 ± 19.5 | 38.5 ± 14.9 | 0.481 |
| FEV ₁ , % predicted | 48.4 ± 13.4 | 47.6 ± 11.5 | 0.675 |
| FEV ₁ /FVC, % | 46.8 ± 10.6 | 47.2 ± 9.3 | 0.722 |
| Steps per week | 37684.5 ± 19996.9 | 34750 ± 17748.5 | 0.425 |
| Walking duration per week, in min | 464.1 ± 226.1 | 436.8 ± 212.8 | 0.526 |
| TSRQ autonomous regulation | 5.9 ± 1.1 | 5.7 ± 1.3 | 0.741 |
| TSRQ controlled regulation | 3.0 ± 1.3 | 2.8 ± 1.1 | 0.396 |
| PCS score | 5.4 ± 1.4 | 5.3 ± 1.5 | 0.749 |
| Stage of change scale | 3.5 ± 1.1 | 3.5 ± 1.2 | 0.739 |
| Stage of change scale (1–5), n (%) | | | |
| 1 | 8 (3.1) | 3 (8.6) | 0.128 |
| 2 | 47 (17.9) | 4 (11.4) | 0.474 |
| 3 | 78 (30.0) | 10 (28.6) | 0.812 |
| 4 | 75 (28.6) | 9 (25.7) | 0.719 |
| 5 | 54 (20.6) | 9 (25.7) | 0.453 |

Data are presented as mean ± SD unless otherwise specified.

Abbreviations: FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity; mMRC, modified Medical Research Council; PCS, Perceived Competence Scale; SD, standard deviation; SGRQ, St. George's Respiratory Questionnaire; TSRQ, Treatment Self-Regulation Questionnaire.

Supplementary File 1

Summary of the self-management behaviour modification (SMBM) intervention based on the LWWCOPD programme [1]

Among the multiple interrelated components, site case managers had a minimum 2 years' experience in chronic respiratory disease; they received formal training prior to study initiation and were supported throughout the study with educational opportunities and performance feedback.

The training was based on the self-management educational programme “Living Well with COPD™”, adapted for the current study by focusing on improving patient engagement in, and maintenance of, exercise and physical activity. The educational programme started with an individual induction session at the beginning of the intervention period, followed by group sessions at Weeks 2, 5, 8 and 11, with another individual session at follow-up. The sessions were led by the site case managers, who were guiding patients in self-management behaviours that aid in achieving physical activity goals while improving daily COPD management.

Patients' comprehension, attitudes and skills were assessed throughout the intervention to determine whether they had met pre-established goals and objectives. Different methods included direct open questioning, problem-solving exercises, simulations (patients demonstrate a proposed technique, such as using an inhaler) and direct observation. A series of questionnaires completed by patients during the course of the intervention assisted the site case manager in assessing the process of change and evaluating individual patient needs and progress, allowing them to make adaptations to the programme as needed over time.

References

1. Bourbeau J, Lavoie KL, Sedeno M, De Sousa D, Erzen D, Hamilton A, Maltais F, Troosters T, Leidy N. Behaviour-change intervention in a multicentre, randomised, placebo-controlled COPD study: methodological considerations and implementation. *BMJ Open* 2016; **6**: e010109.

PATIENT WORKSHEET

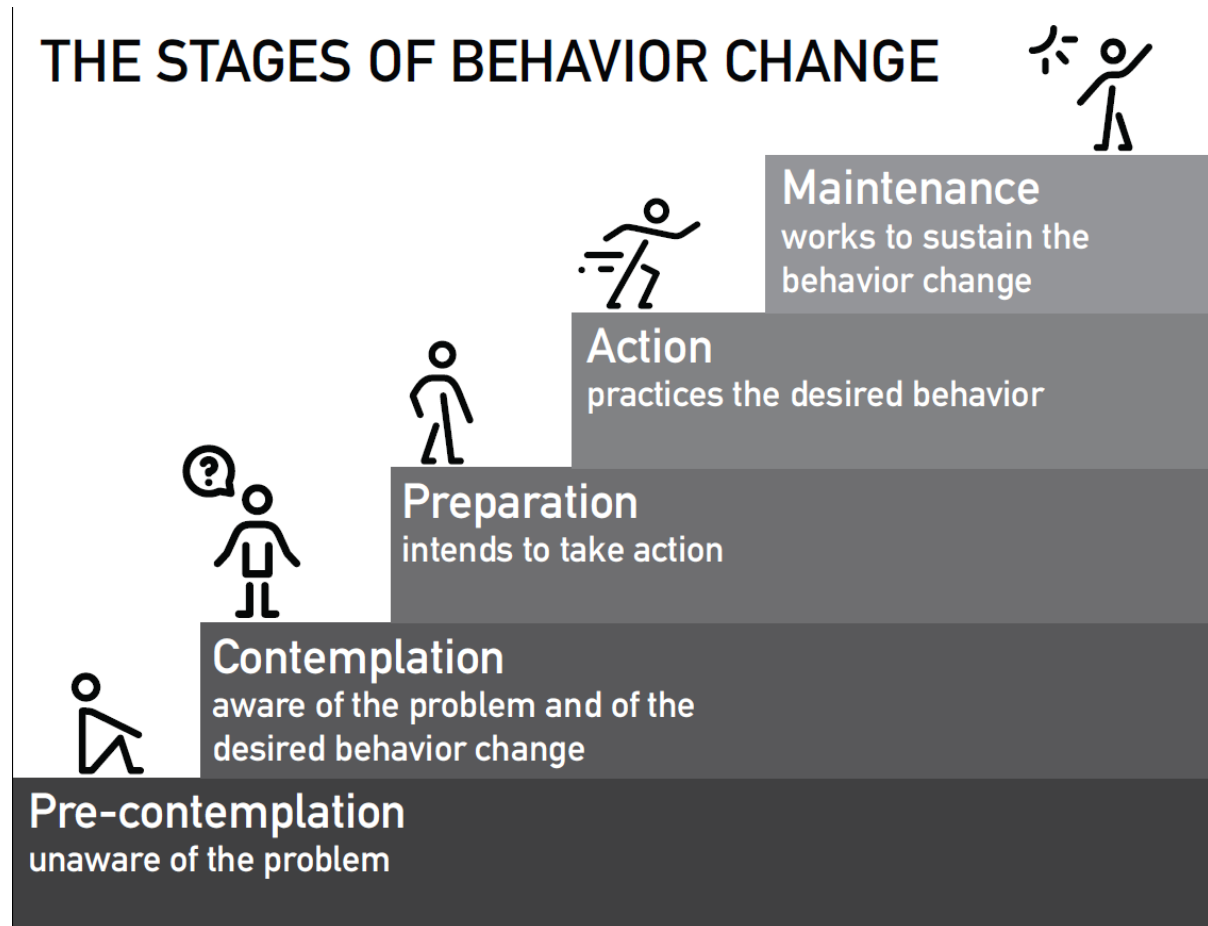
FOLLOW-UP PLAN BY THE EDUCATOR

| | | | |
|---|--|---|--------------------|
| Patient ID: | | Educator: | |
| Initial Assessment | | <input type="checkbox"/> Patient Questionnaires completed | Date: _____ |
| <ul style="list-style-type: none"> What is your ultimate physical activity goal? (<i>e.g. what would you like to be able to do at the end of the program at work, home, leisure</i>) | | | |
| | | | |
| | | | |
| <ul style="list-style-type: none"> What is your goal in terms of average number of steps per day from today until the next session? | | _____ average number of steps per day | |
| <ul style="list-style-type: none"> How much time do you spend per week being physically active? | | _____ minutes per week | |
| Group Session 1 | | <input type="checkbox"/> Patient Questionnaires completed | Date: _____ |
| <ul style="list-style-type: none"> How much time did you spend being physically active over the last week? | | _____ minutes per week | |
| <ul style="list-style-type: none"> What is the average number of steps that you walked per day over the last week? | | _____ average number of steps per day | |
| <ul style="list-style-type: none"> What is your goal in terms of average number of steps per day from today until the next session? | | _____ average number of steps per day | |
| Group Session 2 | | <input type="checkbox"/> Patient Questionnaires completed | Date: _____ |
| <ul style="list-style-type: none"> How much time did you spend being physically active over the last week? | | _____ minutes per week | |
| <ul style="list-style-type: none"> What is the average number of steps that you walked per day over the last week? | | _____ average number of steps per day | |
| <ul style="list-style-type: none"> What is your goal in terms of average number of steps per day from today until the next session? | | _____ average number of steps per day | |
| Group Session 3 | | <input type="checkbox"/> Patient Questionnaires completed | Date: _____ |
| <ul style="list-style-type: none"> How much time did you spend being physically active over the last week? | | _____ minutes per week | |
| <ul style="list-style-type: none"> What is the average number of steps that you walked per day over the last week? | | _____ average number of steps per day | |
| <ul style="list-style-type: none"> What is your goal in terms of average number of steps per day from today until the next session? | | _____ average number of steps per day | |

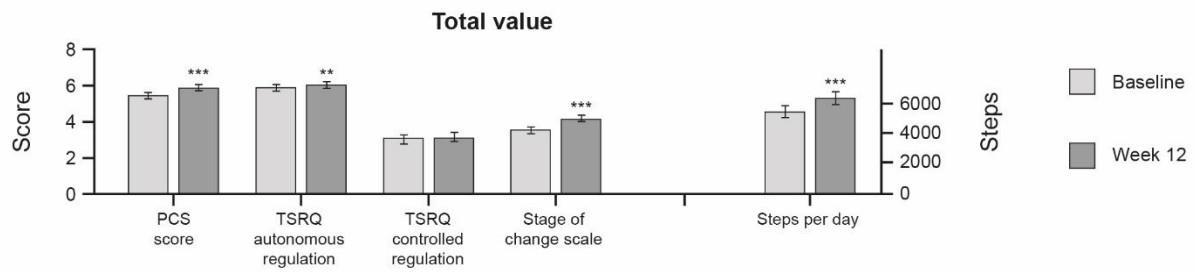
| | | | |
|--|---|---|--------------------|
| Patient ID: | | Educator: | |
| Group Session 4 | | <input type="checkbox"/> Patient Questionnaires completed | Date: _____ |
| • How much time did you spend being physically active over the last week? | | _____ minutes per week | |
| • What is the average number of steps that you walked per day over the last week? | | _____ average number of steps per day | |
| • What is your goal in terms of average number of steps per day from today until the next session? | | _____ average number of steps per day | |
| Follow-up | | <input type="checkbox"/> Patient Questionnaires completed | Date: _____ |
| • How much time did you spend being physically active over the last week? | | _____ minutes per week | |
| • What is the average number of steps that you walked per day over the last week? | | _____ average number of steps per day | |
| • To what degree have you reached your ultimate physical activity goal? | | Not achieved | Partially achieved |
| • If not achieved or only partially, why? | | Achieved fully | |
| • Action plan and recommendations | | | |
| Date | Notes and general comments (e.g. specific follow-ups to be done with patient, homework, contract, etc.) | | |
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Educator signature: _____

Stage of Change Scale

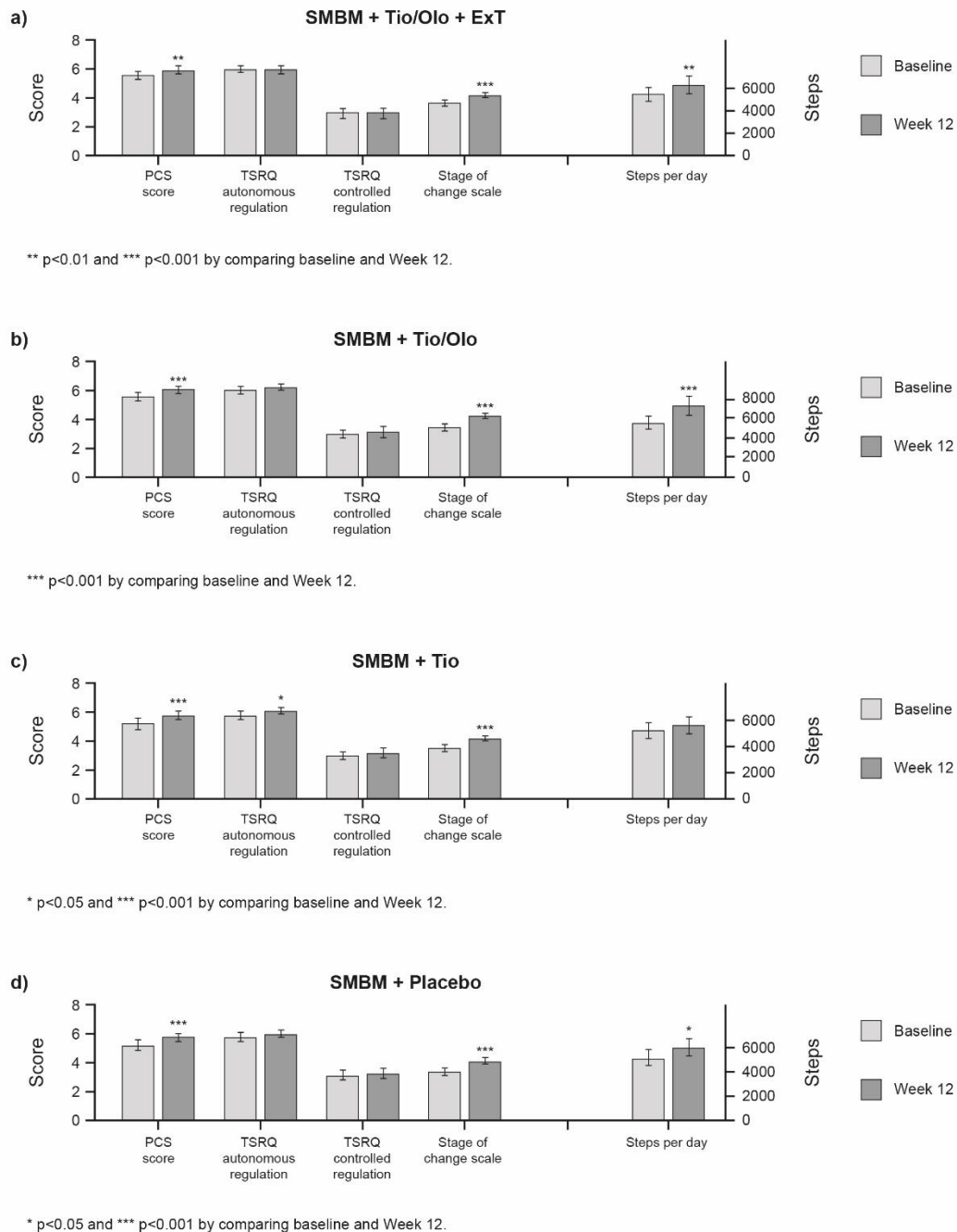


Supplementary Figure 1. Changes over 12 weeks of treatment in Perceived Competence Scale (PCS), Treatment Self-Regulation Questionnaire (TSRQ) autonomous regulation and controlled regulation, stage of change and mean steps/day.



** $p < 0.01$ and *** $p < 0.001$ by comparing baseline and Week 12.

Supplementary Figure 2. Changes over 12 weeks of treatment in Perceived Competence Scale (PCS), Treatment Self-Regulation Questionnaire (TSRQ) autonomous regulation and controlled regulation, stage of change and mean steps per day, per arm group: (a) SMBM + Tio/Olo + ExT, (b) SMBM + Tio/Olo, (c) SMBM + Tio, (d) SMBM + Placebo.



Abbreviations: ExT, exercise training; SMBM, self-management behaviour modification; Tio, tiotropium; Tio/Olo, tiotropium/olodaterol.