Journal of Psychosomatic Research 183 (2024) 111830

Contents lists available at ScienceDirect

Journal of Psychosomatic Research

journal homepage: www.elsevier.com/locate/jpsychores

Online acceptance and commitment therapy (iACT) for adults with persistent physical symptoms – 3-month follow-up study of a randomized controlled trial

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ARTICLE INFO

Keywords:
Persistent physical symptoms
Chronic fatigue syndrome
Indoor environments
Acceptance and commitment therapy
Treatment as usual
Internet-based

ABSTRACT

Objective: Persistent physical symptoms (PPS) represent a major health problem affecting daily functioning. This RCT aimed to examine whether a guided Internet-based treatment based on acceptance and commitment therapy (ACT) provided additional benefits compared to Treatment as Usual (TAU) in reducing somatic complaints and psychological distress in adults with PPS.

Methods: A total of 103 adults with PPS related to indoor environments, chronic fatigue or both conditions were assigned to receive either either a 14-week intervention (video-based case conceptualization + Internet-based ACT) combined with TAU (iACT + TAU; $n = 50$) or TAU alone ($n = 53$). Somatic symptoms, depression, anxiety, insomnia, and psychological flexibility were assessed from pre-intervention to a 3-month follow-up. Additionally, the association between changes in psychological flexibility from pre- to post-intervention and changes in symptoms from pre to 3-month follow-up was explored. Analyses were conducted using a multigroup method with full information maximum likelihood estimator.

Results: The results revealed a significant interaction effect, indicating reductions in somatic symptoms and symptoms of depression and anxiety with moderate to large between-group effects ($d = 0.71–1.09$). No significant interaction effect was observed in insomnia and measures of psychological flexibility.

Conclusion: Internet-based ACT, when combined with Treatment as Usual, demonstrated efficacy for individuals with PPS associated with indoor environments and chronic fatigue. These findings are pertinent for primary healthcare providers, suggesting that the current treatment model could serve as a low-threshold first-line treatment option.

The clinical trial registration number: NCT04532827

1. Introduction

Persistent physical symptoms (PPS) present a significant health challenge due to their association with frequent healthcare usage, high costs and a prevalence ranging between 10% and 49% among patients in primary care [1,2]. PPS are characterized by the presence of physical symptoms lasting at least three months without identifiable organic or toxicological causes, and leading to functional impairments [3,4]. They are associated with significant distress, disability, long-term work disability, sickness absence [5,6], and symptoms of depression and anxiety [7,8]. PPS encompass a wide range of symptoms with varying severity [9], including chronic fatigue and symptomatology associated with indoor environments which can significantly reduce quality of life and cause disability [10–13]. Chronic fatigue manifests as persistent fatigue lasting six months or more, unrelieved by rest [14] and accompanied by post-exertional malaise, neurocognitive problems, and unrefreshing sleep [15]. PPS associated with indoor environments have some similar features and specific characteristics. It refers to non-specific symptoms across multiple organ systems, such as upper-respiratory symptoms, headaches, and fatigue, that purportedly

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https://doi.org/10.1016/j.jpsychores.2024.111830
Received 17 March 2024; Received in revised form 9 June 2024; Accepted 10 June 2024
Available online 13 June 2024

attributed to very low or non-existent exposure in indoor environments. Previously known as Sick building syndrome [16], this increased reactivity is now referred to as building-related environmental intolerance, mainly explained by nocebo mechanisms [4,17]. Chronic reactivity to perceived indoor triggers prompts individuals to avoid these environments.

Despite the high burden of PPS, effective interventions are scarce. Cognitive Behavior Therapy (CBT) has shown moderate effectiveness in reducing symptom severity and improving functioning among PPS patients [18–21]. However, these treatments can be costly and inaccessible [22]. Self-help interventions may offer promise for individuals with less severe chronic symptoms, significantly reducing symptom severity and improving quality of life [23]. Guided Internet-based treatments, effective compared to waiting-list or usual care and equivalent to traditional interventions [24–27], provide a viable alternative. In addition, the recent COVID-19 pandemic has highlighted the importance of alternative delivery options for psychological treatments [28]. As only a small number of individuals with PPS seek help due to the stigma and unfavorable attitudes towards psychological treatments [22,29–31], Internet-based treatment could possibly offer these populations a more acceptable means to seek help. Indeed, there is growing evidence showing that Internet-based CBT (iCBT) interventions has shown efficacy in in reducing somatic symptoms in adults with PPS [25,32–37].

Acceptance and commitment therapy (ACT), a cognitive behavioral approach, integrates acceptance and mindfulness, and behavior change strategies to promote *psychological flexibility* (PF) [39] which is considered a trainable set of coping skills for managing distress and enhancing functioning [40]. Research suggests that ACT is particularly well suited for chronic health conditions, as persistent symptoms are seen as a result of experiential avoidance and subsequent psychological inflexibility (PI), such as efforts to suppress or eliminate unwanted thoughts, emotions, or bodily sensations [41,42]. Avoidance may display in many different ways: as overuse of the healthcare system to reduce worry about the disease, substance use, or poor self-management behaviors [41]. ACT facilitates PI by helping the individual to stay more in the present moment, noticing and taking distance from difficult thoughts such as catastrophizing or ruminating, and, instead, teaches acceptance skills and value-based living as an alternative. Meta-analytic findings have demonstrated promising effects of ACT and iACT for long-term health conditions [41,43] and chronic pain [43–45], suggesting that ACT is comparable to inactive controls and available active treatments. Preliminary evidence suggests that ACT may be an acceptable, and effective treatment for chronic fatigue [42,46–48]. However, to our knowledge, studies investigating Internet-based ACT for PPS associated with indoor environments and chronic fatigue are lacking.

This randomized controlled trial (RCT) aimed to investigate whether a therapist-guided iACT treatment + TAU was superior to TAU alone in alleviating somatic symptoms, depression, and anxiety, and improving sleep and psychological flexibility skills in individuals with PPS related to indoor environments, chronic fatigue, or both. We expected based on earlier studies that adding iACT to TAU would show larger changes compared to TAU alone. Additionally, we aimed to explore whether the changes in psychological flexibility skills during treatment (from pre- to post-measurement) were associated with changes in symptoms over time (from pre to 3-month follow-up). We expected higher correlations between process measures and symptom measures in the iACT + TAU group compared to TAU alone.

2. Methods

2.1. Study design

This study was designed as an RCT with two parallel groups and carried out in Finland by the Finnish Institute of Occupational Health (FIOH) in collaboration with the University of Jyväskylä, the HUS University of Helsinki and the Helsinki University Hospital 2020–2023. The trial was registered under the number NCT04532827. Ethical approval was obtained from the Ethics Committee of the HUS Helsinki University Hospital (HUS 915/2020).

2.2. Procedure and participants

The study details were outlined in a study protocol [49]. Briefly, individuals reporting PPS related to indoor environments or chronic fatigue were recruited through occupational health services and various other recruitment channels via print and social media between August 2020 and June 2022. A total of 351 candidates expressed interest in the study, out of which 192 provided informed consent and participated in eligibility assessment and a clinical video-based, structured interview (45–60-min) delivered via the doxy.me videoconference application, conducted by an occupational health physician at the FIOH [49]. Eligible participants were required to: 1) have PPS associated with indoor environments [50], or chronic fatigue [51], 2) be aged between 18 and 65, 3) be actively working or studying, and 4) sign an informed consent form. Based on the doctor's interview, 86 individuals did not meet the inclusion criteria and three participants withdrew from the study (Fig. 1). Reasons included absence from work ($n = 6$), ongoing psychotherapy ($n = 9$) or both ($n = 1$), failure to meet symptom criteria ($n = 15$), excessively long-lasting symptoms ($n = 11$) with insufficient investigation or poor control ($n = 8$), insufficient investigation of symptoms ($n = 23$), or poor symptom control ($n = 13$). Among these individuals, the doctor recommended 39 seek medical attention for further examinations related to illness, suspected illness, or untreated symptoms/disease. Thus, the final sample comprised 103 participants randomly allocated to either receive Internet-delivered ACT with therapist guidance (iACT + TAU; $n = 50$) or Treatment as Usual alone (TAU; $n = 53$). Participants were allocated equally to the iACT + TAU and the TAU groups (allocation ratio 1:1) using block randomization so that the number of participants with either indoor air-related symptomatology or with chronic fatigue was balanced in these two groups. Online questionnaires were administered at baseline (pre), 14 weeks (post), and 3 months after the post-measurement (3-month follow-up). Based on the clinical interview administrated by the medical doctor using the Research Interview for Functional Somatic Disorders [52] (Table 1), participants were categorized into three PPS categories 1) PPS indoor environments ($n = 27$), 2) Chronic fatigue (CF; $n = 56$) or 3) Both ($n = 20$). The study flow is depicted in Fig. 1.

2.3. iACT + Treatment as usual

Participants assigned to iACT + TAU ($n = 50$) were provided with two video meetings (2 × 45–60 min) with a psychologist using the doxy.me videoconference application to develop an individual, functional case conceptualization in graphical form [53,54]. These sessions were delivered by two clinical psychologists. The first session involved a psychosocial interview [55] to understand the individual's symptomatology and life situation. Between sessions, a graphical case conceptualization was constructed [56]. In the second session, the graphical case conceptualization was presented and discussed, and individual goals were set based on it.

Subsequently, participants were offered a 10-week (10 module) web-based program to work through consecutive modules at one-week intervals. The program included psychoeducation, short texts, pictures, and 18 audio-based exercises and metaphors aligned with ACT principles. Additionally, audio-based progressive relaxation exercises were assigned as homework (Table 2). eCoaches, health care professionals (psychologists, psychotherapists, social workers), trained in web-based interventions conducted a brief registration phone call and monitored participants' progress throughout the program, providing weekly feedback in writing via the platform's messaging system. Participants were able to contact their assigned eCoach via the messaging system at any

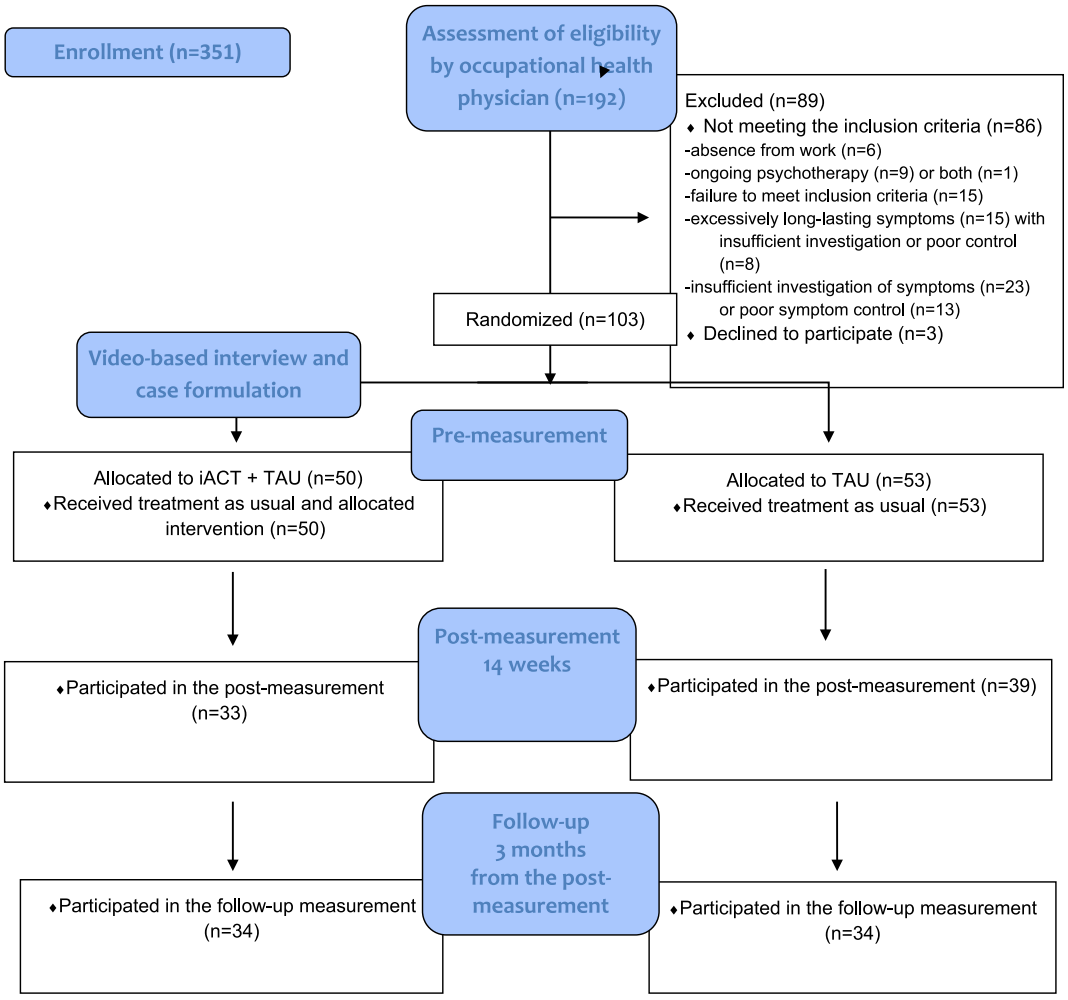

Fig. 1. Participant flow.

time, and the eCoach replied within a week. Thus, beyond the messaging system and the initial introductory phone call, the therapists had no contact with their assigned client. The duration of time that participant spent on each weekly session was approximately one hour. Automatic reminders were sent if a participant had not been active. At the program's conclusion, eCoaches summarized each participant's progress.

2.4. Treatment as usual

TAU comprised routine care received by participants seeking treatment for their symptoms across various healthcare levels, including primary care. Both the iACT + TAU and TAU participants received customary care, which could vary based on individual needs and regional guidelines. Participants were provided with an information leaflet detailing the conditions and the biopsychosocial perpetuating mechanisms of PPS.

2.5. Outcome measures

The primary outcome measure was health-related quality of life. These results will be reported in a forthcoming study.

2.6. Symptom measures

Somatic symptoms were measured by the Patient Health Questionnaire (PHQ-15) [57], a 15-item scale rated on a three-point Likert scale of 1 (not at all) to 3 (bothered a lot), with higher scores reflecting more somatic symptoms. The total score ranges from 0 to 30 and scores of $\geq$5, $\geq$10, $\geq$15 represent mild, moderate, and severe levels of somatization. Cronbach alpha in this study was acceptable, $\alpha = 0.69$.

To account for parallel mental disorders in individuals with PSS, *depressive symptoms* were assessed using by the Patient Health Questionnaire (PHQ-9) [58]. PHQ-9 is a 9-item measure using a scale of 0 (not at all) to 3 (nearly every day), with the total score ranging from 0 to 27. A total score of <4 indicates no or minimal levels of depressive symptoms, 5 to 9 mild, 10 to 14 moderate, 15 to 19 moderately severe, and over 20 severe depression. In this study, the scale demonstrated good reliability ($\alpha = 0.81$). *Anxiety* was assessed using the 7-item Generalized Anxiety Disorder (GAD-7) questionnaire [59]. The respondent is asked to rate on a scale from 0 (not at all) to 3 (nearly every day), how often he/she has experienced anxiety symptoms during the past two weeks (minimum 0, maximum 21). Scores below 5 indicate minimum levels of anxiety, 5 to 9 points mild, 10 to 14 points moderate, and scores beyond 15 high levels of anxiety. In this study, Cronbach alpha was very good ($\alpha = 0.87$). *Insomnia* was assessed with the Insomnia Severity Index (ISI) [60], measuring the severity of insomnia symptoms, distress, and daytime impairment. The seven items are rated on a five-point scale ranging from 0 to 4. The total score ranges from 0 to 28, where 0–7 indicate no clinically significant insomnia, 8–14 subthreshold insomnia, 15–21 moderate severe, and 22–28 severe clinical insomnia. In this study, the ISI demonstrated very good reliability ($\alpha = 0.87$).

Table 1
Inclusion and exclusion criteria.

Criteria	Description
Inclusion criteria	
Age	Age 18 to 65 years
Language	Fluent Finnish
Duration of symptoms	Onset of symptoms with disability of 3 years maximum before the study
Symptomatology A) Indoor air-related symptoms (Lacour et al., 2005, IPCS/WHO, 1996) or	A) Indoor air-related symptoms a) Self-reported symptoms attributed to indoor (non-industrial) environments including: i) symptoms in at least two different organ systems e.g. respiratory, digestive or nervous system. b) Symptoms recurring i) in more than one indoor environment or ii) despite environmental improvements (e.g. work arrangements and/or workplace reparations)
B) Chronic fatigue(Jason et al., 2010)	B) Chronic fatigue a) Post-exertional malaise and/or post-exertional fatigue b) Unrefreshing sleep or disturbance of sleep quantity or rhythm disturbance c) Pain, often widespread d) Two or more neurological or cognitive symptoms e) At least two symptoms from the following categories i) Autonomic manifestations, ii) Neuroendocrine manifestations or iii) Immune manifestations
Duration and severity of condition	Minimum of six months; Symptoms are not lifelong and result in substantial functional restrictions in daily life.
Exclusion criteria	
Work situation	Long sick leave (≥3 months) without return-to-work plan, not actively participating in study or work life (retired or unemployed)
Medical reasons	a) Some serious and/or acute medical disease or illness that explains the symptoms i) Somatic disease that explains the symptoms (e.g. uncontrolled asthma, hypothyroidism, sleep apnoea) ii) Psychiatric disorder (bipolar disorder, psychotic disorders, alcohol and/or drug dependency or abuse, eating disorders, and/or severe mood disorders) b) Developmental disorders
Psychotherapy	Psychotherapy (current)
Other	Patient refusal

2.7. Psychological inflexibility and flexibility measures

Psychological inflexibility was measured by the Acceptance and Action Questionnaire (AAQ-II) **[61]** that assesses experiential avoidance with seven questions on a scale of 1 (never true) to 7 (always true). The total score ranges from 7 to 49, whereby a higher score indicates a higher level of psychological inflexibility (a negative outcome). In this study, the scale demonstrated excellent reliability (α = 0.92). *Psychological flexibility subskills* were measured with the Comprehensive Assessment of ACT processes (CompACT) **[62]**, a 23-item questionnaire that in addition to the total score includes the subscales openness to experience (CompACT-OE), behavioral awareness (CompACT-BA), and valued action (CompACT-VA). The items are answered on a 7-point Likert scale ranging from 0 (strongly disagree) to 6 (strongly agree), with higher scores representing greater levels of psychological flexibility. In this study, the CompACT demonstrated good reliability: α = 0.83 for OE, α = 0.89 for BA, and α = 0.81 for VA. *Cognitive fusion*, i.e., not being able to distance oneself from thoughts, was measured by the Cognitive Fusion Questionnaire (CFQ-7) **[63]** consisting of seven items rated on a scale from 1 (never true) to 7 (always true). Higher scores indicate higher

Table 2
Contents of the iACT program.

Online module	Theme	Examples of exercises and home assignments
1. Module	**Introduction and bodily symptoms.** Brief introduction to program including practical information. Information on central nervous system functioning.	"Ready for change" questionnaire, progressive relaxation [a] ***Home assignment***: Progressive relaxation exercise begins [a]
2. Module	**Stress system.** Getting information about stress system and identifying the factors and actions have an impact on wellbeing.	'Tug-of-war' metaphor, 'Mindful breathing' exercise ***Home assignment***: progressive relaxation exercise continues[a], 'Mindful breathing' exercise, taking action to increase wellbeing
3. Module	**Learning how our thoughts, emotions, bodily sensations, and behaviors influence each other.** Increasing understanding of language as a double-edged sword and defusing the content of thoughts.	'Leaves in a stream' exercise, mind mapping factors that influence on one's wellbeing, 'Activating event – thoughts and beliefs – consequences'exercise ***Home assignment:*** 'Activating event – thoughts and beliefs – consequences'exercise, Progressive relaxation exercise: short relaxation[a]
4. Module	**Automatic thoughts.** Identifying automatic thoughts and coping with automatic thoughts. Increasing understanding of language and defusing the content of thoughts.	*'Cognitive distortions exercise* ***Home assignment***: Continue with 'Activating event – thoughts and beliefs – consequences'exercise, Progressive relaxation exercise: short relaxation[a]
5. Module	**Experiential avoidance and worrying** Finding alternative actions for experiential avoidance and worrying.	'Warm donuts' exercise, Chain analysis of core beliefs ***Home assignment***: 'Worry time' exercise, Progressive relaxation exercise: short relaxation[a], 'Mindful breathing' exercise
6. Module	**Emotions and the body.** Gaining more understanding about emotions and learning about observing and describing emotions.	'The observer' exercise', 'The sky and the weather' metaphor ***Home assignment***: 'contacting the present moment' exercise, breathing exercise, additional relaxation exercise
7. Module	**Thoughts and emotions as a guide.** Increasing defusion skills. Self-as-context is also discussed.	'Navigator' metaphor, 'Leaves in a stream' exercise, cognitive defusion methods ***Home assignment***: Mindful walk, 'Gentle hand' exercise
8. Module	**Self-perception and self-compassion.** Promoting self-perception and self-compassion by assessing literal rules and their consequences and interpersonal relationships.	'Gentle hand' exercise and reflection task on important relationships, 'My 80th birthday' exercise ***Home assignment:*** Mindful walk, 'Gentle hand' exercise
9. Module	**Values and compassion**. Clarifying values, and practising acceptance-based strategies in relation to inner experiences.	Reflection task on values, 'Beach ball' metaphor, exercise on acceptance, exercises on self-compassion and compassion towards others ***Home assignment***: exercise on acceptance, 'Gentle hand' exercise
10. Module	**Summary.** Reviewing important content from each module with reflection on progress. Making an individual plan for how to continue practising.	Review of progress work sheet, 'My plan' worksheet

[a] Following the procedure presented in applied relaxation training (Öst, 1987).

levels of cognitive fusion, i.e., a negative outcome. In this sample, the scale demonstrated high reliability (α = 0.96).

2.8. Statistical analyses

Statistical analyses were conducted using Mplus, version 8.8 [64], and SPSS, version 26 [65]. The baseline differences between demographic measures of the three groups were explored using the linear modelling analyses (similar to ANOVA) and chi-square tests. Differences in initial levels at pre-intervention were analyzed using SPSS, while changes from pre- to post-, and to follow-up were analyzed using multigroup methods with full information maximum likelihood estimator (MLR estimator in Mplus). This estimation method accounts for values missing at random (MAR) and includes all available data and is robust against nonnormality. Hierarchical Linear Modelling (HLM) accounts for values missing at random (MAR) and includes all randomized participants in the analyses. The interaction effects are indicated in the form of Wald-test values *(W)* and *p*-values. Thus, Intention-to-treat analyses were performed to investigate the effect of the iACT + TAU intervention in comparison to the control group (TAU alone). The corrected between-group effect sizes (ES), Cohen's *d* value, were calculated at post/follow-up as follows: The between-group effect sizes for both the pre- and post/follow-up intervention measurements were calculated by dividing the mean difference between the intervention groups (i.e., iACT + TAU and TAU) by the mean standard deviation at pre-measurement of the two conditions correcting the possible differences between the groups at the pre-intervention measurement. The within-group ES from pre to post/follow-up was calculated by dividing the mean change from the pre- to post/follow-up-intervention measurement times by the mean standard deviation (SD). An effect size of $d = 0.20$ was considered small, $d = 0.50$ moderate, and $d = 0.80$ large [66]. Further, we investigated whether the changes in psychological flexibility during the intervention (pre to post) were associated with changes in symptoms from pre to follow-up. We considered $r = 0.10$–0.29 as a small correlation, a moderate within $r = 0.30$–0.49, and a high within $r = 0.50$–1 [66].

3. Results

3.1. Participants

The majority of all participants were female ($n = 89$; 86%) with an average age of 46.1 (*SD* 7.81) years old (range 30–63 years). >80% were employed ($n = 88$; 85%), and close to 60% were highly educated ($n = 59$; 57%). About 41% ($n = 42$) exhibited moderate somatic symptoms (PHQ-15 score ≥ 10). Over 81% reported co-morbid, at least mild depressive symptoms ($n = 62$), and approximately 43% ($n = 44$) reported at least mild symptoms of anxiety (Table 3). At pre-measurement, the two groups did not statistically differ in any demographic variables or outcome variables (Table 3). Among the three intervention subgroups, differences were observed only in marital status ($\chi^2 = 15.306$ df $= 6$, $p = 0.018$), with the chronic fatigue group having more divorced participants. In the iACT + TAU group, 33 participants (66%) and in the TAU group 39 participants (74%) completed the post-intervention assessment (14 weeks from the pre-measurement) and 34 participants participated in the 3-month follow-up (3 months from the post-measurement) in both groups (68% and 64%, respectively).

3.2. Changes in symptoms from pre to three-month follow-up

Significant interaction effects (group by time) were observed in somatic symptoms and symptoms of depression and anxiety, indicating that symptoms decreased more in the iACT + TAU group compared to TAU alone. Especially, symptoms of depression and anxiety increased significantly from pre to follow-up in the TAU group, while there was a significant decrease in the iACT + TAU condition (Table 4). Between group effect sizes at post-intervention were very small (PHQ-9, $d = 0.09$), small (PHQ-15, $d = 0.34$) and moderate (GAD-7, $d = 0.53$). At 3-month follow-up, between-group effect sizes were moderate (PHQ-9, $d = 0.71$ [CI = 0.21;1.19]; PHQ-15, $d = 0.75$, [CI = 0.35;1.14]) and large (GAD-7, $d = 1.09$ [CI = 0.57;1.58]). Within-group changes are presented in Table 4. No significant interaction effect was observed in insomnia and process measures (AAQ-II, CFQ, CompACT). However, based on the within *p*-values and effect sizes, the iACT + TAU group showed a tendency towards larger within-group changes in insomnia, psychological inflexibility (AAQ-II), cognitive defusion (CFQ), and openness to experiences (i.e., acceptance, CompACT subscale).

Table 3
Demographics and baseline symptom severity of the participants (n = 103) in Treatment as Usual (TAU), iACT + TAU, and in the three PPS categories.

Baseline characteristics	TAU (n = 53)	iACT + TAU (*n* = 50)	Indoor air (n = 27)	Chronic fatigue (n = 56)	Both (n = 20)
Age *M* (*SD*)	46.3 (*7.57*)	45.9 (*8.12*)	44.9 (*7.3*)	46.5 (*8.4*)	46.9 (*6.9*)
Gender					
Female	47 (88.7%)	42 (84%)	23 (85.2%)	50 (89.3%)	16 (80%)
Male	6 (11.3%)	8 (16%)	4 (14.8%)	6 (10.7%)	4 (20%)
Marital status					
Unmarried	7 (13.2%)	10 (20%)	6 (22.2%)	11 (19.6%)	0%
Married	29 (54.7%)	25 (50%)	17 (63%)	26 (46.4%)	11 (55%
Cohab	8 (15.1%)	8 (16%)	3 (11.1%)	8 (14.3%)	5 (25%)
Divorced	9 (17%)	7 (14%)	1 (3.7%)	11 (19.6%)	4 (20%)
Education*					
Low	0%	1 (2%)	0%	0%	1 (5%)
Middle	24 (45.3%)	19 (38%)	12 (44.4%)	23 (41.1%)	8 (40%)
High	29 (54.7%)	30 (60%)	15 (55.6%)	33 (58.9%)	11 (55%)
Main activity					
Employed	47 (88.7%)	41 (82%)	22 (81.5%)	48 (85.7%)	19 (95%)
Entrepreneur	2 (3.8%)	4 (8%)	4 (14.8%)	1 (1.8%)	1 (5%)
Unemployed	0%	1 (2%)	0%	1 (1.8%)	0%
Student	3 (5.7%)	2 (4%)	0%	5 (8.9%)	0%
*Other***	1 (1.9%)	1 (2%)	1 (3.7%)	1 (1.8%)	0%
Somatic symptoms					
Mild	25 (47.2%)	17 (34%)	11 (40.7%)	21 (37.5%)	10 (50%)
Moderate	20 (37.7%)	22 (44%)	10 (37%)	26 (46.4%)	6 (30%)
Severe	6 (11.3%)	9 (18%)	5 (18.5%)	6 (10.7%)	4 (20%)
Depression					
Mild	19 (35.8%)	21 (42%)	8 (29.6%)	25 (44.6%)	7 (35%)
Moderate	9 (17%)	7 (14%)	2 (7.4%)	12 (21.4%)	2 (10%)
Moderat. severe	3 (5.7%)	2 (4%)	0%	5 (8.9%)	0%
Severe	0%	1 (2%)	0%	1 (1.8%)	0%
Anxiety					
Mild	21 (39.6%)	18 (36%)	8 (29.6%)	26 (46.4%)	5 (25%)
Moderate	2 (3.8%)	2 (4%)	1 (3.7%)	3 (5.4%)	0%
Severe	0%	1 (2%)	0%	1 (1.8%)	0%

Somatic symptoms = The Patient Health Questionnaire (PHQ-15).
Depression = The Patient Health Questionnaire (PHQ-9).
Anxiety = The Generalized Anxiety Disorder (GAD-7).
* Low: 9 years basic education, Middle: Upper secondary education, High: Universities and universities of applied sciences.
** Other = part-time work, on-demand work, work try-out, sick leave.

Table 4
Changes in symptom measures (depression, anxiety, somatic symptoms, and insomnia) and psychological flexibility measures in the iACT (iACT + TAU, n = 50), and the TAU group (n = 53).

	Pre n = 103	Post *n* = 72	Fup *n* = 68	*W*(*df*2) p^1	*W*(*df*2) p^2	Pre-Post	Pre-Fup
	M(*SD*)	M(*SD*)	M(*SD*)			d_w	d_w
Somatic Symptoms				9.47 0.009			
iACT	11.02(*3.53*)	9.75(*3.49*)	9.45(*4.05*)		0.006	−0.37	−0.46
TAU	9.87(*3.25*)	9.74(*3.77*)	10.86(*4.06*)		0.169	−0.04	0.29
Depression				16.81 <0.001			
iACT	6.76(*4.29*)	5.24(*3.62*)	4.72(*3.37*)		0.002	−0.35	−0.47
TAU	6.23(*4.40*)	5.08(*4.62*)	7.28(*4.74*)		0.003	−0.26	0.24
Anxiety				19.20 <0.001			
iACT	4.48(*3.18*)	2.93(*2.34*)	2.93(*2.42*)		<0.001	−0.50	−0.50
TAU	3.98(*3.01*)	4.07(*3.94*)	5.80(*4.46*)		0.004	0.03	0.59
Insomnia				1.95 0.378			
iACT	9.50(*4.51*)	7.59(*4.36*)	7.57(*4.39*)		0.013	−0.37	−0.38
TAU	10.06(*5.67*)	9.28(*6.54*)	9.77(*6.25*)		0.606	−0.15	−0.06
PsychFlex (AAQ-II)				1.94 0.380			
iACT	18.48(*8.46*)	16.32(*7.07*)	16.27(*7.93*)		0.016	−0.27	−0.27
TAU	16.87(*7.68*)	15.68(*8.46*)	16.62(*9.06*)		0.487	−0.15	−0.03
Cognitive Fusion				2.64 0.267			
iACT	18.76(*8.45*)	15.27(*8.16*)	16.20(*8.05*)		0.022	−0.40	−0.29
TAU	17.64(*9.04*)	16.48(*8.99*)	17.07(*9.88*)		0.488	−0.13	−0.07
Openness				1.78 0.411			
iACT	38.14(*10.78*)	42.10(*11.34*)	42.12(*11.82*)		0.006	0.38	0.39
TAU	41.94(*9.86*)	43.91(*11.96*)	43.68(*11.00*)		0.213	0.19	0.17
Awareness				1.04 0.595			
iACT	18.82(*7.45*)	18.24(*7.54*)	18.35(*7.60*)		0.801	−0.08	−0.07
TAU	19.38(*6.72*)	19.04(*7.46*)	18.07(*7.54*)		0.223	−0.05	−0.18
Valued Action				0.64 0.725			
iACT	34.28(*7.56*)	35.72(*7.38*)	35.92(*7.47*)		0.257	0.20	0.23
TAU	34.09(*6.52*)	35.49(*7.06*)	34.55(*9.05*)		0.190	0.20	0.06

p^1 = *interaction effect pre-post-follow-up.*
p^2 = *within group change from pre-post-follow-up.*
Somatic Symptoms = The Patient Health Questionnaire (PHQ-15); Depression = The Patient Health Questionnaire (PHQ-9); Anxiety = The Generalized Anxiety Disorder (GAD-7); Insomnia = The Insomnia Severity Index (ISI);
Psychological Flexibility = The Acceptance and Action Questionnaire (AAQ-II); Cognitive Fusion = The Cognitive Fusion Questionnaire (CFQ-7); Openness = The CompACT subskill Openness to Experiences; Awareness = The CompACT subskill Behavioral Awareness; Valued Action = The CompACT subskill Valued Action.
d_w = within-group effect size.

3.3. Associations between symptoms and psychological flexibility

Additionally, we investigated whether changes in symptoms from pre to 3-month follow-up were associated with changes in process measures (psychological flexibility) during the intervention (pre to post, Table 5). Seven significant associations were found in the iACT + TAU group and two in the TAU alone. Changes in symptoms of depression correlated significantly with changes in cognitive fusion in both the iACT + TAU ($r = 0.59$) and TAU alone ($r = 0.39$). Changes in anxiety correlated significantly with changes in cognitive fusion ($r = 0.62$), openness ($r = -0.37$) and valued actions ($r = -0.42$) in the iACT + TAU. Changes in somatic symptoms correlated significantly with changes in cognitive fusion ($r = 0.48$), openness ($r = -0.38$) and valued actions ($r = -0.41$) in the iACT + TAU. In the TAU group alone, changes in somatic symptoms correlated significantly with changes in cognitive fusion ($r = 0.36$). In two variables the correlation coefficients differed significantly between the iACT + TAU and TAU conditions. The association between cognitive fusion and anxiety ($r = 0.62$ vs 0.14) as well as between valued actions and anxiety ($r = -0.42$ vs -0.05) were significantly higher in the iACT + TAU group compared to TAU (1-sided, $p = 0.006$; $p = 0.030$, respectively).

4. Discussion

The current study aimed to investigate the effectiveness of a guided online Acceptance and Commitment Therapy (iACT) intervention combined with Treatment as Usual (TAU) for individuals with persistent physical symptoms (PPS) associated with indoor environments and chronic fatigue compared to TAU alone. The iACT + TAU group demonstrated larger decreases in somatic symptoms, symptoms of depression, and anxiety compared to TAU alone from pre- to 3-month follow-up measurement. These improvements evidenced medium to large-sized effects. However, the intervention did not significantly impact symptoms of insomnia or participants' psychological flexibility skills.

Second, the findings also indicated that larger decreases in anxiety were associated with larger changes in cognitive fusion and valued action in the iACT + TAU group, whereas these correlations were close to zero in the TAU alone group, accompanied with increases in anxiety. This suggests that cognitive fusion and valued action might play crucial roles in managing anxiety among individuals with persistent symptoms, and these constructs should be investigated more closely in further studies. Furthermore, the change in cognitive fusion was associated with

a larger decrease in somatic and depressive symptoms in both groups and may need further attention in future.

While the observed effects are consistent with a previous meta-analysis investigating the efficacy of online ACT interventions for chronic pain [45], it is notable that the current intervention produced larger effects (moderate to large), particularly in symptom outcomes. Moreover, when examining iCBT for chronic pain and functional somatic syndromes, the meta-analysis of Vugts and colleagues [38] found small effects when Internet-based treatments were compared to passive controls. However, no significant differences in treatment effects were found when compared to active controls at follow-up. In the current study, the positive changes were maintained in the iACT group at 3-month follow-up. Another meta-analysis investigating iCBT for chronic pain found small but significant effects for pain-related and mood variables, with guided interventions showing significantly larger effects (d = 0.33–0.38) than unguided interventions [43]. Indeed, the beneficial effects in symptom outcomes in our study may be associated with professional guidance. First, the intervention comprised of two 45-min video-based meetings with the psychologist and, second, participants received a brief phone call and weekly written feedback from eCoaches. It must be noted, however, that the key components (and support) in the current intervention were provided online: video calls, web-based treatment program and feedback via the platform's messaging system. The importance of professional guidance has been emphasized in earlier research related to health conditions and depression [38,67,68]. Vugts and colleagues [38] found also that efficacy was highest in studies where the program duration was from 7 to 10 weeks and when the study included a higher proportion of female and highly educated participants. These findings corroborate with our study as the program duration was 10 weeks and comprised mainly female and relatively highly educated participants.

The results of the current intervention showed that the intervention had a statistically significant impact on somatic symptoms over a 3-month follow-up period. However, the lack of significant improvement in psychological flexibility skills was unexpected, as ACT primarily aims to enhance psychological flexibility and functioning rather than symptom reduction [69]. Possible reasons for this discrepancy include the general nature of the guidance provided by eCoaches and the focus on promoting adherence rather than assisting clients in applying psychological flexibility skills to their daily life. In general, guidance in Internet-based interventions is often more focused on promoting adherence rather than enhancing the effectiveness [70,71]. The result of no significantly larger improvement in psychological flexibility is congruent with the study of Jacobsen and colleagues [42], where despite improved quality of life and reduced levels of fatigue, no improvement was detected in psychological flexibility in patients with chronic fatigue at post-assessment. According to Jacobsen and colleagues [42], changes in fear-avoidance cognitions and all-or-nothing cognitions may be more important than improvement in psychological flexibility for this PPS-population, leading possibly to improved treatment effects. Additionally, further research is warranted to investigate whether longer treatments are needed to impact psychological flexibility skills among persons with chronic symptoms. Moreover, changes in the symptoms of anxiety were more strongly associated with changes in cognitive fusion (not being able to distance oneself from thoughts) and valued actions (actions based on personal values) in the iACT + TAU compared to TAU alone. Thus, the role of cognitive flexibility and values could be investigated more closely in the future since they may provide a pathway to handle symptoms of anxiety among individuals with persistent symptoms.

5. Limitations

With regard to the results of this study, several limitations have to be considered. First, despite of our efforts to recruit an adequate number of eligible participants, the sample size can be considered relatively small. The small sample size did not allow us to conduct any subgroup analyses and investigate differences between the three PPS groups included in the study, such as PPS associated with indoor environments or chronic fatigue, or individuals reporting both complaints. Second, over 90% of the participants were female which limits the generalizability of the current findings to females with PPS associated with these complaints. Further studies should focus on more diverse and representative samples to implement Internet-based ACT treatments within real-world settings. Third, the attrition rate of 34% must be noted as a further limitation as it can have influenced the results of the study. Fourth, we were not able determine in detail the content of TAU, as despite general treatment guidelines, the content of TAU for individuals with PPS may vary substantially in different health care districts. However, the iACT group was also offered TAU, thus, the results reflect benefits that the iACT could provide to commonly available treatments. Fifth, only self-assessment measures of outcome were applied. Further, we acknowledge that some of the variables registered (ClinicalTrials.gov) as secondary outcomes were not outcomes (e.g., age). Finally, since all participants had access to TAU, potential confounding effects of concurrent treatments have to be taken into consideration.

Despite these limitations, our results suggest that therapist-guided Internet-based ACT combined with usual care could be effective on somatic and mental health symptoms among individuals with PPS associated with indoor environments and chronic fatigue. As this is the first study examining online ACT for these PPS populations, the results need to be interpreted with caution and the intervention needs to be investigated more rigorously in larger trials. Interventions such as the current iACT intervention have the potential to increase access to treatment of PPS as they could offer a low-threshold and scalable treatment option for distress caused by PPS, when face-to-face treatment is unavailable. All the components of the current intervention were conducted remotely which suggests that online-delivered treatments utilizing video calls and a web-based treatment program may produce beneficial outcomes and provide individuals with PPS access to care in rural areas or areas with provider shortages, offering comparable or improved quality of care. As human guidance can be resource-intensive, further research should examine online interventions with less professional support. Earlier findings suggest that ACT interventions for both clinical and non-clinical samples can be successfully delivered by non-mental health professionals, with reductions in psychological distress and in increasing health behaviors [72].

6. Conclusions

Given the high prevalence and the difficulty to treat PPS, it is essential to increase access to interventions that produce beneficial outcomes. The present study provides valuable insights into guided Internet-based treatments that may benefit individuals experiencing persistent symptoms. Our results suggest that Internet-based ACT, when combined with Treatment as Usual, demonstrated efficacy for individuals with PPS associated with indoor environments and chronic fatigue. These findings are pertinent for primary healthcare providers, suggesting that the current treatment model could serve as a low-threshold first-line treatment option.

Funding

This study was funded by the Social Insurance Institution of Finland (75/331/2019) and governmental research funding (TYH2019315).

Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this work the authors used ChatGPT 3.5 in order to spell check and proof-reading assistance. After using this tool, the authors reviewed and edited the content as needed and take full

responsibility for the content of the publication.

CRediT authorship contribution statement

Päivi Lappalainen: Writing – original draft, Methodology, Formal analysis. **Katariina Keinonen:** Writing – review & editing, Conceptualization. **Raimo Lappalainen:** Writing – review & editing, Supervision, Methodology, Conceptualization. **Sanna Selinheimo:** Writing – review & editing, Project administration, Funding acquisition, Conceptualization. **Aki Vuokko:** Writing – review & editing, Funding acquisition, Conceptualization. **Markku Sainio:** Writing – review & editing, Supervision, Conceptualization. **Sanna Liesto:** Writing – review & editing. **Asko Tolvanen:** Software, Methodology, Formal analysis. **Tiina Paunio:** Writing – review & editing, Funding acquisition.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

AV works as a part-time medical consultant at OP Insurance Ltd. and has worked as a part-time medical consultant at The Social Insurance Institution of Finland (Kela, until 30 November 2018), without any conflicts of interest regarding this article. The remaining authors declare that they have no conflict of interest.

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