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The association between quality of life and psychological flexibility, depressive, anxiety or insomnia symptoms in patients with persistent indoor environment-related symptoms or chronic fatigue

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Abstract

Background Persistent physical symptoms (PPS) can significantly impair health-related quality of life (HRQoL) and are often accompanied by psychiatric comorbidity. Psychological flexibility (PF), characterized by the ability to adapt functionally and congruently to diverse situations based on personal values, may play a crucial role in determining HRQoL. This study aims to examine the associations between symptoms of depression, anxiety or insomnia or PF and HRQoL among individuals with PPS associated with (i) the indoor environment (IE), (ii) chronic fatigue, or (iii) both.

Methods We utilized the baseline data ($n = 103$) from a randomized controlled trial focused on improving the HRQoL of individuals (mean age 46.1, SD 7.8, 86% women) experiencing PPS associated with IE or chronic fatigue. Self-report questionnaires were administered to evaluate symptoms of depression, anxiety, insomnia, and dimensions of PF, including acceptance, cognitive fusion, and thought suppression. The primary outcome was HRQoL, assessed using a 15D questionnaire. The association between symptoms, PF dimensions, and HRQoL was examined using Pearson's correlation and ANCOVA.

Results Symptoms of depression, anxiety, and insomnia were negatively associated with HRQoL ($p < .001$) across all participants. Among individuals with PPS associated with IE, higher PF was significantly associated with higher HRQoL. No association was found between PF and HRQoL in those with chronic fatigue-associated PPS or both conditions.

Conclusions PF associated with positive outcomes in HRQoL in individuals with PPS associated with the indoor environment, but not in those with chronic fatigue. Further research on the differences between these groups is warranted to enhance treatment targeting.

Trial registration Clinicaltrials.gov NCT04532827 (registered 26.08.2020).

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Keywords Indoor environment, Quality of life, Chronic fatigue, Psychological flexibility, Depression, Persistent physical symptoms

Background

Persistent physical symptoms (PPS) refer to a unifying concept of prolonged symptoms and syndromes such as PPS associated with environmental factors or chronic fatigue. PPS lead to poor quality of life, substantial functional impairments, work disability, or daily life limitations [1–3]. These symptoms are often multiple, non-specific and exhibit in various organ systems, and may include dizziness, headaches, fatigue, and cognitive difficulties, such as concentration problems [1, 4]. PPS pose a challenge to the healthcare system, as PPS often correspond poorly to underlying disease. This leads to repeated but inconclusive clinical examinations and a lack of effective treatments, contributing to patient uncertainty and feelings of dismissal [5, 6]. Exploring the processes that perpetuate PPS and their impact on health-related quality of life (HRQoL), an individual's perceived physical, mental, and social well-being related to their health conditions and ability to function, could improve outcomes by enabling targeted treatments to those processes.

PPS associated with environmental factors such as indoor air manifest as reactions and symptoms at pollutant levels far below the toxicologically established exposure levels. These symptoms, i.e. respiratory tract, mucosal, skin and general symptoms often continue despite environmental repairs [7–11]. Chronic fatigue-associated PPS involve a marked reduction in activity levels, post-exertional malaise, and persistent symptoms like pain or cognitive difficulties [12, 13]. While these conditions share similarities in symptom profiles and duration, it's essential to note that not all individuals with PPS fit into one diagnostic category [4]. Thus, it is crucial to understand the factors that perpetuate symptoms.

Individuals with PPS share mutual bodily reactivity and behavioral patterns in symptom control and management. Approaches include avoiding triggers (e.g., events, environments) linked to symptom manifestation, attributing somatic causes to symptoms, and focusing on signs of symptoms and catastrophic thoughts [1, 4, 14, 15, 16]. Such behavioural patterns impact well-being and social connectedness, potentially conflicting with long-term goals for wellbeing. This creates a detrimental cycle where rigid pursuits hinder acceptance of the prolonged condition, restricting daily lives [17]. Consequently, avoidant strategies, meant to control distress, may inadvertently worsen functional impairments by reducing adaptability to different situations [18].

Recent emphasis has highlighted the significance of biopsychosocial processes in comprehending the perpetuation of prolonged symptoms [1, 19]. Psychological flexibility, consisting of adaptive, trainable behaviors facilitated by its subprocesses (acceptance, cognitive defusion, present-moment awareness, self-as-context, values, and committed action) [18, 20], has emerged as a crucial process of well-being in groups with persistent physical symptoms (PPS). Psychological flexibility is suggested to improve functioning despite unwanted sensations, thoughts or emotions [18, 20]. Its´ protective role has been recognised for example among adults suffering from somatic symptom and related disorders [21, 22], persistent symptoms associated with COVID-19 [23] or chronic pain [24] for which the recently updated definition includes the influence of psychosocial factors on subjective pain experience [25]. Although there is mixed evidence regarding the role of psychological flexibility in enhancing the quality of life for those with chronic fatigue-associated PPS [26, 27], involvement in PPS related to environmental factors remains largely unexplored.

Individuals with environmental factors or chronic fatigue associated PPS frequently report comorbid symptoms of depression, anxiety or insomnia [2, 28]. Mood and anxiety symptoms are more prevalent among individuals with PPS, particularly those with chronic fatigue, compared to those without PPS [2, 29]. Poorer quality of life and increased functional impairments are noted in individuals with multiple comorbidities [2, 30, 31, 32]. Previous research has shown that there is a relationship between avoidant coping strategies, attempting to control or suppress thoughts and feelings reflecting psychological inflexibility, and poorer psychological health in adults with PPS [33]. Conversely, targeting these behavioral patterns has become a promising strategy for improving psychological health [34, 35]. Given the established importance of psychological flexibility for physical and mental health, it is reasonable to assume that it also influences the quality of life in PPS associated with environmental factors or chronic fatigue. However, few studies have specifically examined the role of psychological flexibility in these conditions.

In this study, we first aimed to investigate the associations between symptoms of depression, anxiety, or insomnia and health-related quality of life (HRQoL) among working-age adults with persistent physical symptoms (PPS) associated with (i) environmental factors, (ii) chronic fatigue, or (iii) both. In addition, we aimed to respond to the lack of research on the role of psychological flexibility in these prolonged conditions. Thus, secondly, we examined the association between HRQoL

and psychological flexibility and psychological inflexibility (i.e. thought suppression or cognitive fusion), in these individuals. Thirdly, we assessed whether HRQoL differs between the study groups, and if the symptoms or psychological flexibility are associated with the differences. Our hypotheses posited negative associations between psychiatric symptoms and positive associations between psychological flexibility and HRQoL.

Methods

Study population

The study population consists of participants recruited for a randomized controlled trial (Clinicaltrials.gov NCT04532827, registered 26.08.2020) carried out in Finland by the Finnish Institute of Occupational Health (FIOH), University of Helsinki, University of Jyväskylä between 8/2020 and 5/2022. Please see the full study protocol with a detailed description of the recruitment procedure and inclusion criteria published elsewhere [36].

Inclusion criteria

Table 1. shows the summary of inclusion criteria (see [9, 12, 37]). Participants enrolled at FIOH were interviewed using structured, clinical video-based interviews regarding the inclusion and exclusion criteria.

Table 1 Summary of inclusion and exclusion criteria of the study [36]

Criteria	Description
Inclusion	
Demographics	Employed or studying Finnish-speaking individuals aged 18 to 65 years, all genders
Symptomatology A) Indoor air-related symptoms [9, 37] or	A) Indoor air-related symptoms: Self-reported symptoms attributed to indoor (non-industrial) environments including multiorgan recurrent symptoms that occur in more than one indoor environment or despite environmental improvements
B) Chronic fatigue [12]	B) Chronic fatigue: Self-reported post-exertional malaise and/or post-exertional fatigue with unrefreshing sleep or sleep disturbances, pain, neurological, cognitive and other multiorgan symptoms.
Duration and severity of the condition	≥ six months; onset of symptoms with substantial functional restrictions in daily life less than 3 years before the study.
Informed consent	Given.
Exclusion	
Work situation	Not actively participating in the study or work life (retired or unemployed) and no return-to-work plan
Medical reasons	Some serious and/or acute medical condition that explains the symptoms, severe psychiatric disorders or developmental disorder
Psychotherapy	Psychotherapy (current)
Other	Patient refusal

Inclusion criteria were assessed in a video-based clinical interview conducted by medical doctors ($n = 5$) specializing in occupational medicine. A modified version of the semi-structured Research Interview for Functional Somatic Disorders (RIFD) [38] identified comprehensive symptom clusters or disorders. These included cardiopulmonary, gastrointestinal, musculoskeletal, neurological, general, and other symptoms; fatigue; environmental intolerance; health anxiety; depression; anxiety, and other mental disorders. The interviewer assessed symptom existence, severity, impairment, and potential medical conditions contributing to the individual's symptoms and functional impairment. Pre-interview questionnaire data served as the interview baseline. Participants needing medical care or further examination were referred to healthcare professionals and excluded from the study.

Outcomes

Before the inclusion interview, participants completed a structured pre-interview questionnaire on health status, with clinical interviews validating health information. Here we report the participants´ clinical characteristics.

The primary outcome, health-related quality of life (HRQoL), was measured using the 15D questionnaire [39]. This utility-based, generic and standardized measure assesses physical, mental, and social well-being on 15 questions regarding mobility, vision, hearing, breathing, sleeping, eating, speech, excretion, usual activities, mental function, discomfort and symptoms, depression, distress, vitality, and sexual activity. Responses, rated on a 1–5 scale, indicate the functional impairment in the 15 categories (1 = no problems, 5 = severe problems). The 15D yields an overall score ranging from 1 (full health) to 0 (dead). The reliability and the validity of the measurement have been adequate in Finnish population-based studies and comparison to similar instruments [39–42]. Scale reliability in this study was good (Cronbach´s $\alpha = 0.72$).

Structured self-report questionnaires assessed secondary measures, i.e. symptoms of depression, anxiety, and insomnia, as well as psychological flexibility. The Patient Health Questionnaire-9 [43], General Anxiety Disorder-7 [44] and the Insomnia Severity Index [45] were used, applying clinical cut-off scores to determine symptom severity (for depressive symptoms PHQ-9 < 5 were considered as none/few symptoms, 5 ≤ mild ≤ 9, 10 ≤ moderate ≤ 14 and 15 ≤ were considered as severe symptoms; for anxiety GAD-7 < 5 none/few symptoms, 5 ≤ mild ≤ 9, 10 ≤ moderate ≤ 15 and 16 ≤ severe symptoms; for insomnia ISI ≤ 7 none/few symptoms, 8 ≤ mild ≤ 14, 15 ≤ moderate ≤ 21 and 22 ≤ severe symptoms). These measurements have demonstrated good psychometric properties and usability in the Finnish population [46–49] with good internal consistency in this study (Cronbach´s α for

PHQ-9 was α = 0.81, for GAD-7 α = 0.79 and for ISI α = 0.85).

Psychological flexibility was evaluated using the Comprehensive Assessment of Acceptance and Commitment Therapy processes (CompACT) [50], while thought suppression and cognitive fusion reflecting psychological inflexibility were measured by the White Bear Suppression Inventory (WBSI) [51] and Cognitive Fusion Questionnaire (CFQ) [52].

The CompACT is a 23-item scale, where an individual rates items of psychological flexibility on a seven-point Likert scale ranging from 0 (strongly disagree) to 6 (strongly agree). The scale assesses three sub-processes of psychological flexibility, but only the total scale was used in this study. The total score ranges between 0 and 138, with higher scores indicating greater psychological flexibility. The scale has shown excellent internal consistency in previous studies based on Finnish university student population [53, 54] and in this study, the scale showed good internal consistency (Cronbach´s α = 0.89).

The WBSI, a 15-item questionnaire, measures thought suppression, the process of psychological inflexibility. Chronic thought suppression is related to obsessive thinking and negative affect associated with depression and anxiety. The WBSI is rated on a 5-point scale from strongly disagree (1) to strongly agree (5). Total scores range from 15 to 75 with higher scores indicating a greater tendency to suppress thoughts, i.e., a negative outcome. Studies show that the WBSI is a reliable and valid instrument also in Finnish samples [36, 55, 56, 57]. In this study, the scale showed excellent reliability (Cronbach´s = 0.93).

Cognitive fusion, a facet of psychological inflexibility, was assessed by CFQ-7 [52]. It gauges the inability to distance oneself from thoughts, reflecting behavior that is overly regulated by cognition and one's relationship with thoughts and beliefs. The CFQ-7 comprises seven items rated on a Likert scale (1 = never true; 7 = always true). Total scores range from 7 to 49 and higher scores indicate higher levels of cognitive fusion with thoughts, i.e., a negative outcome. The CFQ has demonstrated excellent internal consistency and good test-retest reliability in previous Finnish study [52, 54]. In this sample, the scale demonstrated high internal consistency (Cronbach´s alpha = 0.94).

Statistical methods

First, frequencies, means and standard deviations regarding the demographics and clinical data are presented. Demographic data was gathered from the pre-interview questionnaire and clinical data was combined from the questionnaire and clinical interview. Then, the differences in the distributions of the participants with different symptom groups and clinical characteristics were evaluated using $\chi 2$ tests. Pearson's r was used to measure the correlations between psychiatric symptoms, psychological flexibility and HRQoL in the whole sample and separately for different core symptom groups. Effect sizes were interpreted according to Cohen's $r \geq .10$ small, $r \geq .30$ moderate and $r \geq .50$ high strength [58]. The associations between psychological flexibility and HRQoL are presented on scatter plots, and the regression lines were fitted for different symptom groups. R^2 estimates are given to express the amount of variation in the data that processes of psychological flexibility explain the total variation of HRQoL. Differences in HRQoL between groups based on inclusion criteria (PPS associated with IE, chronic fatigue or both) were tested by analysis of covariance. Analyses were adjusted for age and gender and in different analyses for psychiatric symptoms (measured with PHQ, GAD-7, ISI) and processes of psychological flexibility (measured with CompACT, CFQ, WBSI). The level of significance was set at $p < .05$. As women constituted 86% of the sample, we conducted the analyses for women only and for both genders. In addition, as COVID-19 infection has been linked with chronic fatigue-related PPS [59], we conducted sensitivity analyses by excluding those with COVID-19 self-reports. Regarding strategies for missing data handling, the dependent and independent outcomes do not include item-level missing or error values due to coding because of the computerized forced protocol for the questionnaires. We used version 27.0 of IBM-SPSS for Windows (SPSS Illinois, Chicago, Illinois, USA) for the statistical analyses.

Results

Table 2 displays demographic data for the study population. Participants had a mean age of 46.1 years (SD 7.8), with 86% being women. Demographic and most clinical factors did not differ among groups with PPS associated with IE, chronic fatigue, or both (Table 2). For further details, Supplemental Table 1 provides demographics, and Supplemental Table 2 summarizes diagnosed diseases from clinical interviews. Notably, the group with PPS associated with chronic fatigue had more individuals linking symptom onset to COVID-19 infection ($p < .001$) and reported higher symptoms of depression ($p = .024$).

Bivariate correlations on variables (Table 3) indicate large negative associations between depression symptoms and HRQoL and a moderate correlation between symptoms of anxiety or insomnia and HRQoL (all $p < .001$). Separate analysis in different groups of PPS revealed a large negative correlation between depressive, anxiety and insomnia symptoms and HRQoL among those with PPS associated with IE ($p < .001$). Symptoms of depression had large ($p < .001$) and insomnia symptoms moderate ($p < .01$) negative correlation with HRQoL

Table 2 Demographic and clinical data of the study participants

		All					
		n	%	M	Sd	Min	Max
Gender	Woman	89	86.4				
	Man	14	13.6				
Age		103		46.1	7.8	30.0	63.0
Marital status	Unmarried	17	16.5				
	Married or cohabit	70	68.0				
	Divorced	16	15.5				
Education	Low	1	1.0				
	Middle	43	41.7				
	High	59	57.3				
Occupational status	Higher non-manual	12	11.7				
	Lower non-manual	48	46.6				
	Manual	43	41.7				
Working, years sum		103		23.4	9.9	5.0	45.0
Self-reported health	Extremely good	0	0.0				
	Good	23	22.3				
	Mid	42	40.8				
	Poor	36	35.0				
	Extremely poor	2	1.9				
Number of self-reported chronic diseases per participant	None	3	2.9				
	Physical disease	95	92.2	3.5	2.5	0	17
	Mental disorder	57	55.3	0.7	0.8	0	3
	Functional disorder	73	75.7	1.1	1.0	0	4
	All	100	97.1	5.4	3.3	0	24
PHQ-9	None	41	39.8				
	Mild	40	38.8				
	Moderate	16	15.5				
	Severe	6	6.0				
GAD-7	None	59	57.3				
	Mild	39	37.9				
	Moderate	4	3.9				
	Severe	1	1.0				
ISI-7	None	36	35.0				
	Mild	49	47.6				
	Moderate	15	14.6				
	Severe	3	2.9				
Covid-19		22	21.4				
Sick leave, days during the preceding 6 months		92*	98	18.5	36.8	0.0	180.0
Physician visits, during the preceding 6 months		103		4.9	5.5	0.0	50.0

* 11 cases missing due to coding error

M = Mean; Sd = Standard deviation

Number of self-reported chronic diseases per participant = The number and percentage columns indicate the number of participants with at least one disease or disorder

GAD-7 = General Anxiety Disorder-7, GAD-7 < 5 no symptoms, 5 ≤ mild ≤ 9, 10 ≤ moderate ≤ 15 and 16 ≤ severe symptoms; ISI = Insomnia Severity Index, ISI < 7 no symptoms, 8 ≤ mild ≤ 14, 15 ≤ moderate ≤ 21 and 22 ≤ severe symptoms; PHQ-9 = Patient Health Questionnaire-9, PHQ-9 < 5 no symptoms, 5 ≤ mild ≤ 9, 10 ≤ moderate ≤ 14 and 15 ≤ severe symptoms

Covid-19 = Participants reported that Covid-19 was associated with their PPS onset

among those with chronic fatigue-associated PPS. Only symptoms of depression had a large negative correlation among those with both conditions ($p < .01$) (Table 3).

Figures 1, 2 and 3. show scatter plots for the association between factors of psychological flexibility and HRQoL. Among the group of IE-related PPS, psychological flexibility (as measured by CompACT) was significantly (** $p < .01$) associated with HRQoL whereas among those with chronic fatigue-associated PPS or both conditions, we observed small and non-significant or nearly no association between psychological flexibility and HRQoL. Among those with IE-associated PPS, psychological

Table 3 Means (SD) and Pearson´s correlations (95% CI) between health-related quality of life and independent variables

	M	SD	PHQ-9	95% CI	GAD-7	95% CI	ISI	95% CI
All (*n* = 103)								
HRQoL (15D)	0.80	0.08	−0.62***	[-0.73, −0.48]	−0.38***	[-0.54, −0.21]	−0.47***	[-0.61, −0.31]
Symptoms of depression (PHQ-9)	6.49	4.38						
Symptoms of anxiety (GAD-7)	4.22	3.12						
Symptoms of insomnia (ISI)	9.79	5.17						
IE (*n* = 27)								
HRQoL (15D)	0.84	0.08	−0.72***	[-0.86, −0.46]	−0.60***	[-0.80, −0.28]	−0.63***	[-0.82, −0.33]
Symptoms of depression (PHQ-9)	3.74	3.37						
Symptoms of anxiety (GAD-7)	3.30	2.78						
Symptoms of insomnia (ISI)	7.44	4.38						
Chronic fatigue (*n* = 56)								
HRQoL (15D)	0.78	0.07	−0.53***	[-0.69, −0.30]	−0.29*	[-0.51, −0.03]	−0.41**	[-0.61, −0.17]
Symptoms of depression (PHQ-9)	8.32	4.37						
Symptoms of anxiety (GAD-7)	4.91	3.46						
Symptoms of insomnia (ISI)	11.14	4.96						
Both (*n* = 20)								
HRQoL (15D)	0.79	0.09	−0.65**	[-0.85, −0.29]	-0.20	[-0.59, 27]	-0.23	[-0.61, 0.24]
Symptoms of depression (PHQ-9)	5.05	3.02						
Symptoms of anxiety (GAD-7)	3.55	1.99						
Symptoms of insomnia (ISI)	9.15	5.71						

*** $p < .001$

** $p < .01$

* $p < .05$

M = Mean; SD = Standard Deviation; 95% CI = 95% Confidence interval

IE = symptoms related to the indoor environment; Both = symptoms related to the indoor environment and chronic fatigue

HRQoL (15D) = 15D Health-related Quality of Life questionnaire; GAD-7 = General Anxiety Disorder-7; ISI = Insomnia Severity Index; PHQ-9 = Patient Health Questionnaire-9

flexibility had a high, statistically significant positive correlation ($r = .61$) with good HRQoL and explained 37% ($R^2 = 0.37$) of the HRQoL variation (Fig. 1.). In contrast, it had a small and non-significant positive correlation with a weak explanatory power among those with PPS related to chronic fatigue ($r = .22$) and those with both conditions ($r = .24$, $R^2 = 0.05$ for chronic fatigue and $R^2 = 0.06$ for both) (Fig. 1.) suggesting limited real-world importance. On the contrary, the tendency to cognitive fusion (measured with CFQ) (Fig. 2.) and thought suppression (measured with WBSI) (Fig. 3.) had high, statistically significant, negative correlations with HRQoL and explained 41% ($R^2 = 0.41$) and 36% ($R^2 = 0.36$) of the HRQoL among those with PPS associated with IE (** $p < .01$). The correlations were non-significant and small or negligible with very small explanatory power between these factors and HRQoL among those with PPS related to chronic fatigue (r = -.22 for cognitive fusion and r = -.24 for thought suppression, respectively) and with both conditions (r = -.07 for cognitive fusion and r = -.01 for thought suppression, respectively) which indicates limited or no relationship with no real-world importance between these factors.

According to the analysis of covariance (ANCOVA), the HRQoL differed significantly between study groups: those with PPS associated with IE had better HRQoL than those with PPS associated with chronic fatigue or both conditions (Table 3). ANCOVA further examined the differences between PPS groups by adjusting for the symptoms of depression, anxiety or insomnia and factors of psychological (in)flexibility in separate analyses (Table 4.). The differences in the level of HRQoL between the PPS groups diminished after adjusting for the symptoms of anxiety and psychological processes as covariates. They disappeared when the symptoms of depression and insomnia were adjusted as covariates. Significant effects of symptoms of depression, anxiety, and insomnia on HRQoL were observed. Further, also processes of psychological inflexibility, cognitive fusion (assessed with CFQ) and thought suppression (assessed with WBSI) had significant effects on HRQoL in ANCOVA. Also, psychological flexibility (assessed by CompACT) had a significant effect on HRQoL in ANCOVA.

The results for female participants only yielded similar results as results for the whole sample (data not shown).

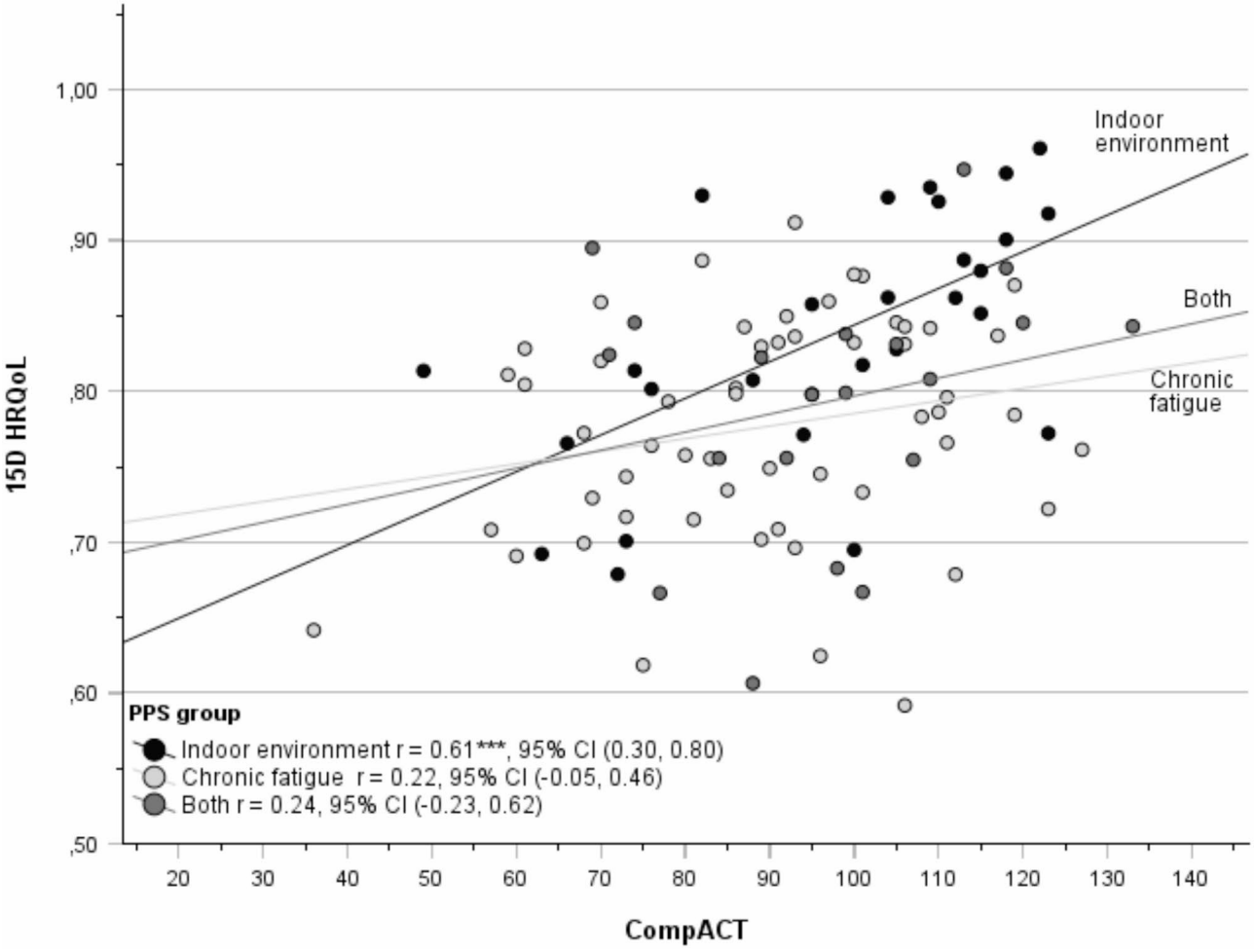

Fig. 1 The association between Psychological flexibility assessed by the Comprehensive assessment of Acceptance and Commitment Therapy (CompACT) and Health-related Quality of Life. 15D HRQoL = Health-related Quality of Life; PPS group = Persistent Physical Symptom group; Indoor environment = PPS associated with indoor environment ($n = 27$); Chronic fatigue = PPS related to chronic fatigue ($n = 56$); Both = PPS related to both conditions ($n = 20$). ***$p < .001$

Furthermore, because nearly 34% of those with PPS related to chronic fatigue reported that their symptom onset was related to COVID-19 -infection, we conducted sensitivity analyses by excluding those with COVID-19 self-reports. Again, except for WBSI, the results were like those with all participants suggesting, that the associations between HRQoL and psychiatric symptoms or psychological processes did not differ by COVID-19-relatedness. However, psychological inflexibility, assessed with WBSI, did not have a significant effect [$F(1,75) = 2.83$, $p = .10$, $\eta_p^2 = 0.04$] on HRQoL in ANCOVA among participants who associated onset of chronic fatigue with Covid-19.

Discussion

In this study, we examined the associations of health-related quality of life (HRQoL) and psychological (in) flexibility or psychiatric symptoms in working-age adults with persistent physical symptoms (PPS) associated with the indoor environment (IE), chronic fatigue, or both. Our results revealed a significant association between depressive symptoms and poor HRQoL among them. However, the associations with anxiety and insomnia symptoms were somewhat weaker. Additionally, there was a notable connection between psychological flexibility and HRQoL but unexpectedly, variations emerged in the associations across the three conditions: We found a relatively strong link in the associations among those individuals with PPS associated with the IE, compared to very small associations with no real-world importance among those with PPS related to chronic fatigue or both conditions. These findings suggest that the impact of psychological flexibility on HRQoL varies based on the specific PPS condition.

Our study found variations in HRQoL among different clinical groups of PPS. Specifically, those with PPS

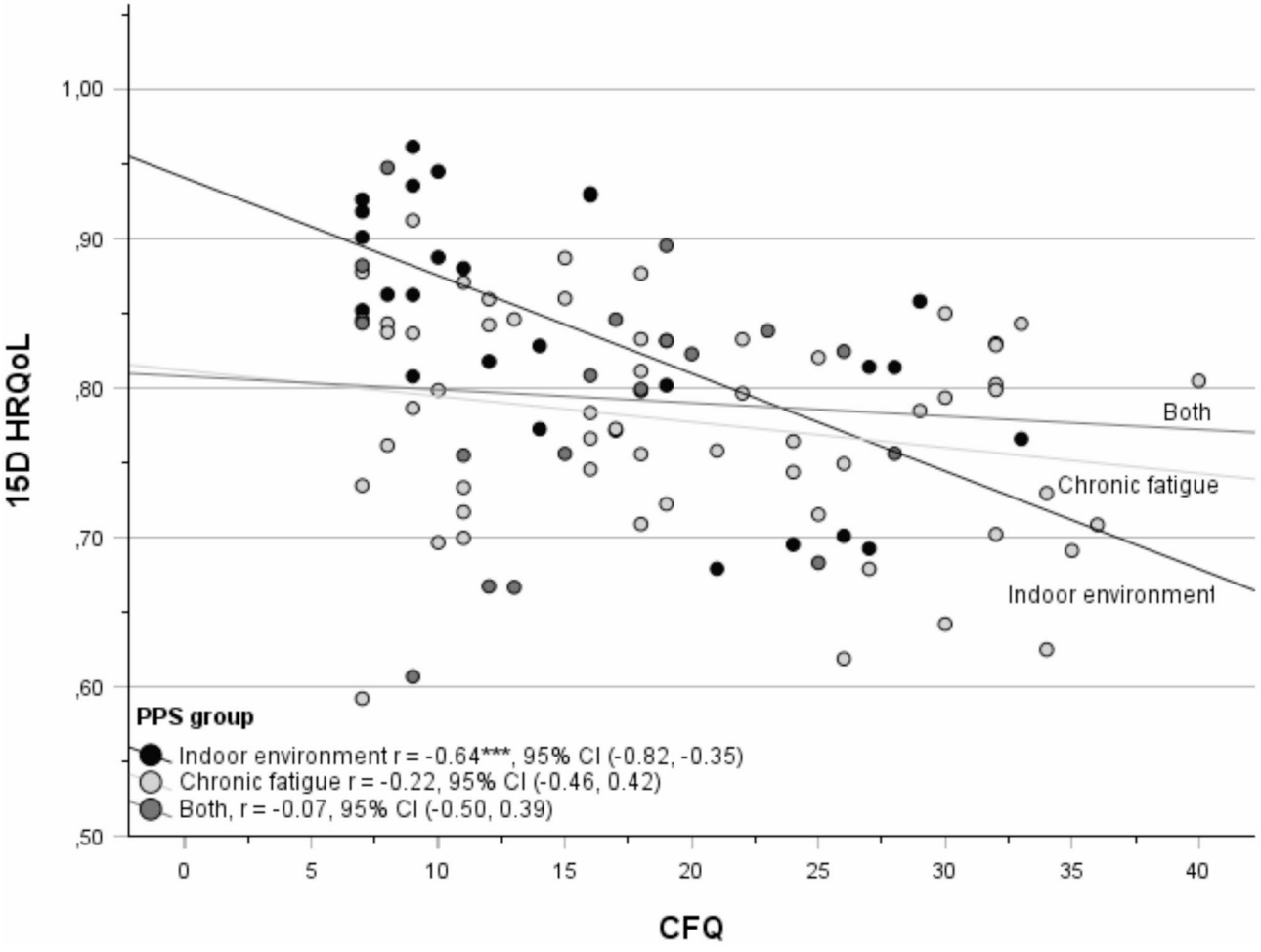

Fig. 2 The association between the process of psychological inflexibility, cognitive fusion, measured by the Cognitive Fusion Questionnaire and Health-related Quality of Life. 15D HRQoL = Health-related Quality of Life; PPS group = Persistent Physical Symptom group; Indoor environment = PPS associated with indoor environment ($n = 27$); Chronic fatigue = PPS related to chronic fatigue ($n = 56$); Both = PPS related to both conditions ($n = 20$). ***$p < .001$

associated with the indoor environment had significantly higher HRQoL compared to those with PPS related to chronic fatigue or both conditions. However, after adjusting for the severity of depression and insomnia, the differences diminished and became statistically insignificant. A similar trend was observed when adjusting for anxiety symptoms, although to a lesser extent. These findings align with previous studies emphasizing the influence of psychiatric symptoms on HRQoL in these populations [2, 30, 32]. They also support earlier findings indicating that symptoms of depression, anxiety, and insomnia are associated with poor HRQoL among adults with PPS [60, 61]. However, the impact of comorbidities on HRQoL was greater in individuals with PPS related to chronic fatigue.

The higher prevalence of depressive symptoms among those with chronic fatigue should be noted. At least three explanations could be linked to such a difference. Firstly, fatigue and sleep-related problems can be symptoms of depression, creating an initial overlap in criteria. Furthermore, it is important to highlight that the same criteria were applied to all participants, ensuring that individuals requiring further examination or with suspicion of untreated medical conditions that could explain the symptoms were equally excluded. Secondly, our findings prompt consideration of whether these PPS groups represent a continuum, with chronic fatigue indicating a more severe condition characterized by a higher burden of comorbidities compared to PPS associated with IE. Thirdly, despite similar underlying mechanisms for PPS, differences in inclusion criteria in our study [9, 12, 37] suggest that PPS related to chronic fatigue may encompass a broader range of symptoms than PPS associated with IE. These distinctions should be considered when designing interventions tailored to the specific symptom profiles within PPS groups.

Our results support the assumption that psychological flexibility, including cognitive defusion and low thought suppression, would positively impact HRQoL, but only to a certain extent. We found a moderate association

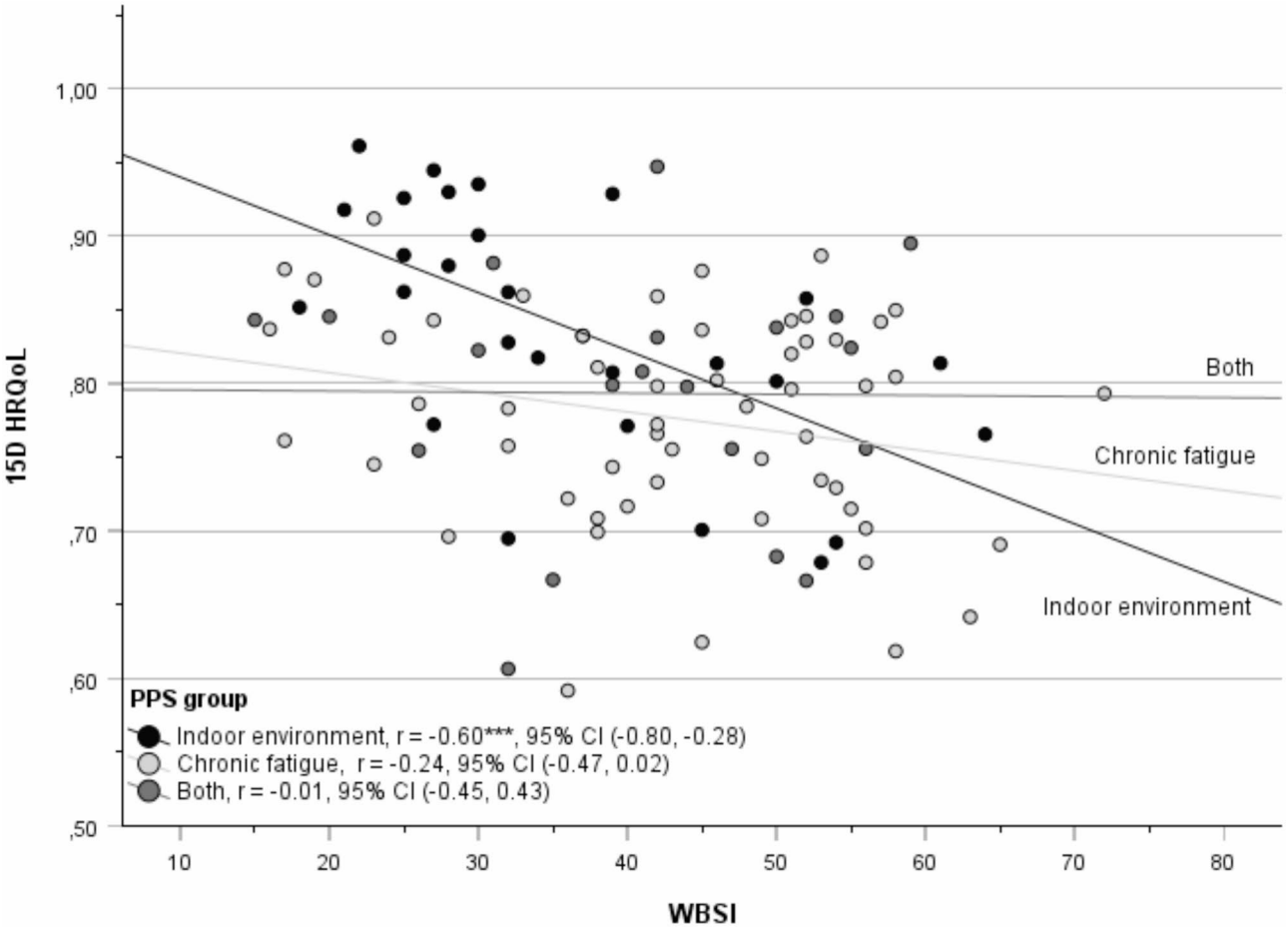

Fig. 3 The association between the process of psychological inflexibility, thought suppression, measured by the White Bear Suppression Inventory (WBSI) and Health-related Quality of Life. 15D HRQoL = Health-related Quality of Life; PPS group = Persistent Physical Symptom group; Indoor environment = PPS associated with indoor environment ($n = 27$); Chronic fatigue = PPS related to chronic fatigue ($n = 56$); Both = PPS related to both conditions ($n = 20$). *** $p < .001$

between high psychological flexibility, i.e. low thought suppression, low cognitive fusion, and high HRQoL among individuals with PPS associated with IE, while no such association was observed in the other two conditions. This finding somewhat contradicts our hypothesis that psychological skills promoting well-being would universally enhance HRQoL in individuals with PPS. Previous research has yielded mixed evidence regarding the association between psychological flexibility and HRQoL in individuals with chronic fatigue. Jacobsen et al. (2017) discovered that enhancing psychological flexibility could enhance the quality of life in individuals with chronic fatigue. However, when fear-avoidance and all-or-nothing cognitions were taken into account, this association disappeared [27]. Similarly, Densham et al. (2016) acknowledged that psychological flexibility and quality of life may represent distinct constructs, implying that enhancing psychological flexibility might not lead to changes in quality of life [26]. Our results align with these findings, demonstrating a weak or negligible association between HRQoL and psychological flexibility in individuals with chronic fatigue compared to those with PPS associated with IE. Therefore, our findings highlight differences between PPS groups, indicating that the role of psychological processes varies across these groups.

Psychological flexibility has been shown to be an important factor in perpetuating health and quality of life among patients with PPS related to chronic pain [24] or somatization [21]. It is also suggested to improve self-management in long-term somatic conditions, potentially enhancing quality of life despite the chronic nature of the condition [62]. Therefore, increasing psychological flexibility could potentially improve the quality of life in such cases. However, our results indicate that interventions solely focused on enhancing psychological flexibility may not yield similar outcomes across these groups. In their study, Leonidou et al. (2019) observed a decrease in physical quality of life among individuals with somatization, suggesting that thoughts of physical problems may limit physical activity and contribute to increased

Table 4 Unadjusted (M, SD) and adjusted (EMM, 95%CI) of Health-Related quality of life values measured by 15D questionnaire among all study participants, between study groups and summary of analyses of covariances

	All	IE	Chronic fatigue	Both	Ancova (F)	df	*p*	η_p^2	Adjusted R^2
Unadjusted (M, SD)	0.80 (0.08)	0.84 (0.08)	0.78 (0.07)	0.79 (0.09)					
Adjusted for age and gender	0.79 (0.77, 82)	0.84 (0.80, 0.87)	0.77 (0.75, 0.80)	0.79 (0.75, 0.83)	5.67	(2, 98)	0.005	0.10	0.07
Additionally adjusted for covariate:									
Group	0.79 (0.78, 0.81)	0.81 (0.78, 0.83)	0.80 (0.77, 0.82)	0.78 (0.74, 0.81)	1.22	(2, 97)	0.301	0.02	0.37
Covariate: Symptoms of depression (PHQ-9)					47.56	(1.97)	*p* <.001	0.33	
Group	0.80 (0.78, 0.82)	0.83 (0.79, 0.86)	0.78 (0.75, 0.81)	0.79 (0.75, 0.82)	3.57	(2, 97)	0.032	0.07	
Covariate: Symptoms of general anxiety (GAD-7)					12.31	(1.97)	*p* =.001	0.11	0.17
Group	0.80 (0.78, 0.82)	0.82 (0.79, 0.86)	0.79 (0.76, 0.81)	0.79 (0.76, 0.82)	2.37	(2, 97)	0.10	0.05	0.23
Covariate: Symptoms of insomnia (ISI)					21.19	(1.97)	*p* <.001	0.18	
Psychological flexibility									
Group	0.80 (0.78, 0.82)	0.83 (0.80, 0.87)	0.78 (0.76, 0.81)	0.79 (0.76, 0.83)	4.09	(2, 97)	0.02	0.08	0.16
Covariate: Psychological flexibility (CompAct)					11.87	(1.97)	*p* =.001	0.11	
Psychological inflexibility									
Group	0.80 (0.77, 0.82)	0.83 (0.80, 0.86)	0.78 (0.75, 0.81)	0.79 (0.75, 0.82)	3.89	(2, 97)	0.024	0.07	0.14
Covariate: Cognitive fusion (CFQ-7)					9.27	(1.97)	*p* =.003	0.09	
Group	0.80 (0.77, 0.82)	0.83 (0.80, 0.86)	0.78 (0.75, 0.81)	0.79 (0.76, 0.83)	3.71	(2, 97)	0.028	0.07	
Covariate: Thought suppression (WBSI)					8.60	(1.97)	*p* =.004	0.08	0.14

M = Mean; SD = Standard deviation; EMM = Estimated marginal mean; Ancova = HRQoL differences between inclusion groups; Analyses are additionally adjusted for participants' age and gender

CFQ-7 = Cognitive Fusion Questionnaire; CompACT = Comprehensive assessment of Acceptance and Commitment Therapy; GAD-7 = General Anxiety Disorder-7; ISI = Insmnia Severity Index; PHQ-9 = Patient Health Questionnaire-9; WBSI = White Bear Suppression Inventory

feelings of being unwell [21]. This points out a difference between our study groups: where individuals with IE-associated PPS react to perceived harmful environments [7], individuals with chronic fatigue attribute their symptoms to physical illness [63, 64]. Such variations in illness perceptions may influence behavioral responses aimed at symptom management, with illness behavior differing based on illness perceptions [7, 65] and leading to different outcomes [66] as our results suggest. Furthermore, the influence of psychiatric symptoms on illness behavior and outcomes, along with illness perceptions, should be acknowledged. Depression is associated with challenges in emotion regulation, as well as reduced variability in behavioral responses across different situations and rigid cognitions [33]. In addition to challenges in emotion and cognitive regulation, depression-related inflexibility has been linked with a loss of normal physiological variability [33]. Thus, considering the higher prevalence of depressive symptoms among individuals with chronic fatigue-associated PPS compared to other groups, it can be suggested that depressive state influences HRQoL outcomes via multiple pathways. Additionally, it should be kept in mind that IE-related health -issues from minor comfort complaints to severe functional impairment are rather common in Finland with nearly a quarter of the population reporting complaints at some level [67]. As such, those with IE-associated PPS might represent a more heterogeneous population in earlier phases of the illness process whereas those with chronic fatigue-associated PPS may represent a more selected group of individuals with more severe health effects. Such comorbidity and complexity might diminish the impact of psychological flexibility on health.

This study provides valuable insights that expand upon previous research. While it is commonly assumed that PPS share similar underlying mechanisms, our findings suggest that the predisposing and perpetuating processes linked with PPS are somewhat distinct. Instead of a unified category, PPS may exist along a continuum where the burden of comorbid symptoms increases, while the impact of psychological processes on HRQoL decreases. Complementing the depression-related inflexibility discussed above, it should be noted that inclusion criteria for chronic fatigue include neurological and cognitive symptoms which might be linked to a diminished repertoire of cognitive and emotion regulation strategies. As such, the comparison between conditions in this study offers important insights into the factors influencing quality of life among individuals with PPS. Consequently, interventions aimed at improving functioning in these individuals should address different aspects of their overall condition. It is worth noting that there are no existing studies assessing the role of psychological flexibility in individuals with PPS associated with indoor environments. Therefore, this study contributes to previous research by identifying characteristics that can be targeted and improved through psychosocial interventions.

The study has several limitations. Firstly, the sample was recruited through various sources and relied on self-reports, which introduces the possibility of selection bias. Additionally, participants were not clinically examined, and the inclusion was based on screening questionnaires and structured video-based medical assessment, potentially contributing to sample heterogeneity. The study nature, conducted remotely, may have influenced the selection of participants who had the practical possibility (i.e. skills to use eHealth application and technical possibility to engage in the intervention) and motivation to engage without face-to-face interactions. Furthermore, the study design was cross-sectional, limiting our ability to draw causal conclusions about the relationships between HRQoL, psychiatric symptoms, and psychological flexibility. The cause-effect relationship and whether the associations are related to other confounding factors should be examined in further longitudinal studies. Another limitation is the relatively small sample size, which prevented further analyses of potential covariates and moderating effects between process-based factors, psychiatric symptoms, and quality of life. For instance, the study could not explore whether psychological inflexibility is a precursor or cause of psychiatric symptoms [33] due to the limited sample size and cross-sectional nature. In addition, as this study focused on examining the association between psychological flexibility, symptoms and HRQoL across participants representing different socioeconomic (SES) groups, we did not formulate a hypothesis regarding the impact of SES on these associations. Although there were no differences between the PPS groups in SES in this study, further studies should consider the potential moderating effects of SES on the associations. Future longitudinal studies are necessary to investigate whether enhancing psychological process-based factors can improve the quality of life in individuals with PPS with various symptom profiles.

Overall, the divergent associations between psychological flexibility and HRQoL among examined groups suggest the need for personalized treatment approaches. Thus, interventions like acceptance and commitment therapy (ACT) aimed at increasing adaptive functioning and behavior change towards psychological flexibility and well-being [20]. Methods based on ACT could be integrated by improving psychological flexibility skills. Treatment strategies should pay special attention to maladaptive cognitive strategies. The current study highlighted two strategies that should be observed in treatment planning. Strategies for how to deal with the suppression of certain thoughts and fusion with thoughts. In other words, it is essential to observe the impact of avoidance of thoughts and not letting your thoughts dictate your actions. However, this seems to be true only with PPS associated with the IE. It may be important to systematically assess individual intervention needs among patients with PPS to target processes of psychological flexibility that are most central for each person. One approach could be using case formulation that considers individual differences in factors that have predisposed, triggered and maintain the PPS to improve treatment targeting and communication between the clinician and the patient regarding the relevant treatment strategies [68]. This is especially important as the results contradict the hypothesis that psychological inflexibility serves as a unified mechanism that may explain symptoms across different topographies of PPS and suggest a need for a more individualized, multifactorial approach to care which should be integrated into policies to improve healthcare for PPS. Additionally, factors of psychological illbeing such as depression, insomnia, and anxiety significantly influence HRQoL, emphasizing the importance of addressing these comorbidities in treatment plans. However, one should keep in mind that the cross-sectional nature of this study and the small sample size limit the generalization of the results. Some data suggests that men and women differ in their strategies involved with initiation, maintenance and modification of feelings with women showing a wider repertoire of strategies and flexibility in their use [69]. As such, considering that our study sample was based on predominantly women, further studies are required to assess whether gender moderates the associations between psychological flexibility and HRQoL. Thus far relatively little attention has been paid to processes that translate bodily sensation

into PPS [70]. A recent review calls for action in healthcare systems in Europe to create care standards that are adaptable for different subgroups of PPS [71]. Our results however emphasize a need for further research on symptom group-tailored care plans. Such information could guide policy flexibility in developing healthcare resource allocation for various PPS groups.

Conclusions

In summary, this study suggests that the role of psychological flexibility on health-related quality of life might be more predominant among those with persistent physical symptoms related to environmental factors, while its role among those with chronic fatigue or both conditions appeared to be minor. As such, an individualized, multifactorial approach to care and further research should be considered to enhance intervention outcomes.

Abbreviations

ANCOVA	Analysis of covariance
CFQ	Cognitive Fusion Questionnaire
CompACT	Commitment Therapy processes
FIOH	Finnish Institute of Occupational Health
GAD-7	General Anxiety Disorder-7
HRQoL	Health-related quality of life
IE	Indoor environment
ISI	Insomnia Severity Index
PHQ-9	Patient Health Questionnaire-9
PPS	Persistent physical symptoms
WBSI	White Bear Suppression Inventory Declarations

Supplementary Information

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Supplementary Material 1

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Author contributions

Conceptualisation and methodology SS in collaboration with AV, PL, KK and RL; writing-original draft preparation: SS; statistical analyses SS; writing-review and editing: SS, AV, PL, KK, RL, MS, and TP. All authors provided feedback on the drafts and have read and approved the final version of the manuscript.

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Data availability

The data are not publicly available to protect the participants' privacy and the sensitive nature of the data. In addition, all the study participants did not give written consent for their data to be shared publicly. The data can be applied through FIOH: s data access permit process, in which the request and terms for sharing the data will be evaluated (https://www.ttl.fi/en/data-access-permits-information-materials-finnish-institute-occupational-health).

Declarations

Ethical approval and consent to participate

The Ethics Committee of the Hospital District of Helsinki and Uusimaa, Finland, has granted approval for this study in 2020 (ID: HUS/915/2020). The research permission was granted on 25.6.2020 (ID: HUS 60/20/2020). The Ethics Committee of the Hospital District of Helsinki and Uusimaa approved the protocol amendments (latest 8.9.2021). Participation was voluntary, and participants were free to leave the study at any time. All participants provided informed consent.

Consent for publication

Not applicable.

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). MS works as a part-time medical adviser to the Finnish Patient Insurance Centre (in accordance with the Patient Injuries Act). The remaining authors declare that they have no conflict of interest.

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