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Author(s)
Wortman, Margreet S.H.; van der Wouden, Johannes C. ; Twisk, Jos W.R.; Visser, Bart; Assendelft, Willem J.J.; van der Horst, Henriëtte E.; Olde Hartman, Tim C.

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Effectiveness of psychosomatic therapy for patients with persistent somatic symptoms: Results from the CORPUS randomised controlled trial in primary care

Margreet S.H. Wortman [a,b,*], Johannes C. van der Wouden [b], Jos W.R. Twisk [c], Bart Visser [a], Willem J.J. Assendelft [d], Henriëtte E. van der Horst [b], Tim C. Olde Hartman [d]

[a] Centre of Expertise Urban Vitality, Faculty of Health, Amsterdam University of Applied Sciences, Amsterdam, the Netherlands
[b] Department of General Practice, Amsterdam UMC, Vrije Universiteit Amsterdam, Amsterdam Public Health Research Institute, De Boelelaan, 1117 Amsterdam, the Netherlands
[c] Department of Epidemiology and Data Science, Amsterdam UMC, Vrije Universiteit Amsterdam, Amsterdam Public Health Research Institute, Amsterdam, the Netherlands
[d] Department of Primary and Community Care, Radboud Institute of Health Sciences, Radboud University Medical Center, Nijmegen, the Netherlands

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ABSTRACT

Objective: To evaluate the effectiveness of psychosomatic therapy versus care as usual in primary care for patients with persistent somatic symptoms (PSS).
Methods: We conducted a pragmatic, two-armed, randomised controlled trial among primary care patients with PSS in the Netherlands that included 39 general practices and 34 psychosomatic therapists. The intervention, psychosomatic therapy, consisted of 6–12 sessions delivered by specialised exercise- and physiotherapists. Primary outcome measure: patient's level of functioning. Secondary outcomes: severity of physical and psychosocial symptoms, health-related quality of life, health-related anxiety, illness behaviour and number of GP contacts.
Results: Compared to usual care ($n = 85$), the intervention group ($n = 84$) showed no improvement in patient's level of functioning (mean difference − 0.50 [95% CI -1.10 to 0.10]; $p = .10$), and improvement in health-related anxiety (mean difference − 1.93 [95% CI -3.81 to −0.04]; $p = .045$), over 12 months. At 5-month follow-up, we found improvement in physical functioning, somatisation, and health-related anxiety. The 12-month follow-up revealed no therapy effects. Subgroup analyses showed an overall effect in patient's level of functioning for the group with moderate PSS (mean difference − 0.91 [95% CI -1.78 to −0.03]; $p = .042$). In the year after the end of therapy, the number of GP contacts did not differ significantly between the two groups.
Conclusion: We only found effects on some secondary outcome measures, and on our primary outcome measure especially in patients with moderate PSS, the psychosomatic therapy appears promising for further study.
Trial registration: the trial is registered in the Netherlands Trial Registry, https://trialsearch.who.int/Trial2.aspx?TrialID=NTR7356 under ID NTR7356.

1. Introduction

The term Persistent Somatic Symptoms (PSS) refers to a heterogeneous group of physical symptoms such as chronic widespread pain, headache, dizziness, fibromyalgia, chronic fatigue and irritable bowel syndrome that cannot be directly attributed to detectable underlying diseases or an organic pathology [1]. The symptoms patients experience affect their health status and interfere with their quality of life [2]. They experience functional impairment, interference with functioning at work [3,4] and a reduced quality of life [5–7]. The prevalence of PSS in primary care depends on the severity of symptoms and on the definition used; in 40% of all patients complaining of at least one PSS, PSS is much more common than generally assumed [8]. Patients with PSS seek contact with primary care professionals to an above average extent [9].

* Corresponding author at: Van der Boechorststraat 7, 1081 BT, the Netherlands.
E-mail addresses: m.wortman@amsterdamumc.nl (M.S.H. Wortman), j.vanderwouden@amsterdamumc.nl (J.C. van der Wouden), jwr.twisk@amsterdamumc.nl (J.W.R. Twisk), b.visser2@hva.nl (B. Visser), pim.assendelft@radboudumc.nl (W.J.J. Assendelft), he.vanderhorst@amsterdamumc.nl (H.E. van der Horst), Tim.OldeHartman@radboudumc.nl (T.C. Olde Hartman).

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The Dutch GPs' guideline for treating PSS recommends a stepped-care approach [10], in which patients with mild PSS should be treated by the GP, patients with moderate PSS should be referred to a psychosomatic therapist or mental health nurse practitioner and patients with severe PSS should receive specialised multidisciplinary treatment. GPs consider performing specific additional testing, referrals, medication, follow-up consultations, and watchful waiting, a considerable part of their care for PSS [11]. They often experience patients with PSS as difficult to manage [12].

In the Netherlands, psychosomatic therapists are qualified psychosomatic exercise- and physiotherapists specialised in PSS [13,14]. The therapists focus on both the physical aspects and the mental aspects of PSS. This therapy is based on the biopsychosocial model in which illness is viewed as a result of interacting mechanisms at the biomedical, interpersonal, and environmental levels. It implies that patient's symptoms, illness, beliefs, anxiety, concerns, illness behaviour, and social environment are addressed in the therapy. It is a multi-component, stepped-care and tailored approach.

Results from various studies suggest that multimodal treatments, which address both physical and cognitive behavioural aspects of PSS, may be effective in patients with PSS [15,16]. Moreover, a recently published review concludes that a biopsychosocial stepped care approach and therapies that activate the patients are recommended for patients with PSS [17]. So far, little research has been carried out on the effectiveness of psychosomatic therapy in primary care [16,18,19] and there is little scientific evidence for its effectiveness in patients with PSS [20,21]. We therefore conducted a large randomised controlled trial, the CORPUS study. The aim of this study was to investigate the clinical effectiveness of psychosomatic therapy versus usual care for patients with PSS in primary care, in terms of improving symptoms and daily functioning, and of (a decrease in) the number of GP contacts in the year after the end of psychosomatic therapy. In addition, we aimed to examine whether the psychosomatic therapy benefits specific categories of patients.

2. Methods

2.1. Trial design

We performed a pragmatic, two parallel groups, randomised controlled trial among patients aged 18–80 with PSS. The effectiveness of psychosomatic therapy was compared with usual care. The study design is described in more detail elsewhere [22]. The trial was registered in the Netherlands Trial Registry (NTR) under ID NTR7356, before the first patient was recruited. Unfortunately, the NTR is no longer available. The registration information, as registered in NTR, is automatically included in the International Clinical Trial Registry Platform (ICTRP) and will be accessible through the https://trialsearch.who.int/ and https://trialsearch.who.int/Trial2.aspx?TrialID=NTR7356. Moreover, the PDF proof of the protocol registered at NTR can be found as supplementary appendix (S1a).

We have followed the CONSORT reporting guidelines for non-pharmacologic treatments [23] (Supplementary data Table S1 CONSORT checklist).

2.2. Participants

2.2.1. Eligibility criteria

Participants aged 18 years and above with PSS. Exclusion criteria were: aged older than 80 years; having a Patient Health Questionnaire 15-item (PHQ-15) somatic symptom severity scale score of <5 [24,25]; receiving palliative care; having a severe psychiatric disorder (i.e. psychosis-related disorders, dementia and bipolar disorder); having a medical or psychological disorder explaining the symptoms; insufficient understanding of Dutch language; psychosomatic therapy not suitable for the patient, according to the GP.

2.2.2. Inclusion procedure

Participants were recruited from 39 general practices in the Netherlands participating in the academic networks of GPs of Amsterdam University Medical Center (UMC) and Radboud UMC. Through an electronic health record search, participating GPs selected, the 10% most frequently attending patients with PSS (aged 18 to 80 years) from the past two years. PSS was based on “Robbins list” of 23 physical complaints [22,26], of which one or more were present twice or more in the past three months. This selection procedure was proven effective in previous research [27,28]. GPs checked the list of selected patients for exclusion criteria. Potentially eligible participants received a brief information package by mail from their GP, including a consent form to provide their name and address to the researchers, to receive more information about the study and the PHQ-15. The PHQ-15 is a frequently used and validated questionnaire about physical symptoms [24,25]. Patients interested in participating in the study with a PHQ-15 score of at least 5 (low level of symptom severity) received extensive study information and an informed consent form. Upon receipt of the signed informed consent form, participants received an email with a link to the web-based baseline assessment.

2.2.3. Intervention, training psychosomatic therapist, and treatment protocol

The psychosomatic therapy was administered by psychosomatic therapists with special interest in PSS, registered with the Dutch Association of Exercise Therapists [14] and the Dutch Association for Psychosomatics in Physical Therapy [13], respectively. It includes the following elements: psychoeducation, relaxation therapy and mindfulness, cognitive-behavioural approaches and activating therapy. During the psychosomatic therapy sessions, the therapist explores somatic symptoms and integrates the physical, cognitive, emotional, behavioural and social dimensions of the symptoms together with the patient. The overall aim of the treatment is to improve patients' functioning by stimulating self-regulation and empowerment to regain control over own health [22]. The intervention consisted of 6 to 12 sessions of 30–45 min over a period of 4 to 5 months, depending on the number and severity of the patient's symptoms.

Prior to starting treatment of patients included in the CORPUS study, the therapists ($n = 34$) completed an accredited e-learning concerning PSS [29] and received two 4-h training sessions from the main researcher (MW) and a psychosomatic physical therapist specialised in PSS who was not involved in the trial. The training sessions consisted of an introduction to the CORPUS study and a training in the standardised CORPUS study treatment protocol. The therapists received an intervention manual describing the sessions. Although the therapists were provided with a standardised treatment protocol, they were allowed to change the intensity, frequency and order of the psychosomatic elements in order to deliver personalised care to their patient.

2.2.4. Usual care

Patients in the usual care group received care as usual provided by their GP and any other health care professionals they were referred to, without restrictions.

2.2.5. Treatment outcomes

Assessments were carried out at baseline, and 5- and 12-months after baseline. The primary outcome measure was patient's level of functioning, measured with the Patient-Specific Complaints instrument (PSC) [30], in which the patient chooses the three most important activities for which he/she perceives limitations, rated on an 11-point numeric rating scale (0 representing ‘not a problem at all’ and 10 ‘impossible‘). The PSC is similar to the Patient-Specific Functional Scale (PSFS) [31], both were developed to assess patient-specific functioning and can used interchangeably. Both instruments are thoroughly validated and responsive measurement instruments [32,33]. However, using the PSC is a deviation from our protocol where we originally

proposed the use of the PSFS. We selected the PSC over the PSFS, as it is widely used in the Netherlands and recommended in the majority of Dutch physiotherapy guidelines [34].

Secondary outcome measures were the Four Dimensional Symptom Questionnaire (4DSQ) [35], with four subscales: distress, somatisation, depression and anxiety; a Numeric Rating Scale (NRS) [36] measured patient's perceived severity of physical symptoms; the Short Form Health Survey-36 items (SF-36) [37], of which we used the nine subscales, which measure the following facets of health-related qualtity of life: physical functioning, role limitations caused by physical health problems, role limitations caused by emotional problems, social functioning, bodily pain, emotional well-being, energy/fatigue, general health and perceived change in health. In addition we used the two summary measures: the mental component summary (MCS) and the physical component summary (PCS) [38]. Hypochondriacal beliefs were measured with the Illness Attitude Scale (IAS) [39] using the total score and the scores on two subscales [40]. Illness beliefs were measured with the brief Illness Perception Questionnaire (IPQ—B) [41].

In addition, GPs reported the total number of contacts (consultations, house calls and telephone calls) with the participating patients in the twelve months after ending the psychosomatic therapy.

2.2.6. Patients' experiences

In order to get a better understanding of patients' opinions regarding psychosomatic therapy, we asked participants in the intervention group to complete questionnaires after the first and last treatment session to determine 1) the characteristics of the interaction between therapist and patient (such as Relationship; Goals and Topics; Approach and Methods) using the Session Rating Scale-Dutch Version (SRS-DV) [42]; 2) the strength of therapeutic alliance using the Working Alliance Inventory-Short Form (WAI-SF) [43,44] and, after the last session, 3) the patient's perceived recovery and satisfaction with psychosomatic therapy using the Global Perceived Effect (GPE) [45] (See Supplement S2.) In addition, we asked participants to evaluate their participation in the CORPUS study in 12 items with a Likert scale (See Supplement S3).

2.2.7. Adherence to treatment protocol and delivery

To examine the extent to which the psychosomatic therapists adhered to the treatment protocol and treatment delivery, we used a treatment-delivery checklist. This checklist was developed in three steps based on the 'Method of Assessing Treatment Delivery (MATD)' [46]. In addition, we used the standardised treatment protocol (developed for the CORPUS study), and the therapists' audio recordings of the treatment sessions. See Supplement S4. for detailed information on the development of this checklist and the analysis of the adherence treatment protocol using this checklist.

2.3. Sample size

Based on previous research we aimed to detect a minimal relevant difference between the intervention group and usual care group of 1 point on PSC (range 0–10) with an SD of 2 points [32,47–49]. With an α of 0.05, a β of 0.20, and an estimated dropout rate of 20% after 1 year we needed at least 79 patients per treatment group.

2.4. Randomisation and blinding

Patients who completed the informed consent procedure and filled out the baseline questionnaire, were randomly assigned to one of the two groups using the computer-generated variable block size randomisation method in Castor [50]. All patients were informed about the treatment allocation by regular mail. In addition, the research assistant contacted patients in the intervention group by telephone, informed them about the psychosomatic therapy and referred them to one of the participating therapists. GPs were informed about the allocation of their participating patients by mail and therapists were telephoned by the research assistant. The randomisation sequence was masked for researchers and research assistant (concealed allocation). To balance the size of the groups in each region, randomisation was stratified according to regions (Amsterdam or Nijmegen). Due to the nature of the treatment, we could not blind patients and therapists.

We invited patients who did not consent to randomisation to participate in a parallel cohort. Only seven patients were included in this cohort, of whom five completed all follow-up measurements. We therefore do not report the data of these patients.

2.5. Statistical analyses

We used descriptive statistics to compare baseline characteristics. The effect of the intervention on primary and secondary outcomes was analysed according to the intention-to-treat (ITT) principle as outlined in the CONSORT Statement [51], in which we used all available data at baseline, 5 and 12 months.

Linear mixed-models analyses were carried out for both follow-up moments (at 5 and 12 months) and without imputing missing data [52]. We estimated the overall effect over time, and the effect at 5 and 12 months after baseline for each outcome variable. For the overall as well as time analyses, we performed a crude and an adjusted analysis for each outcome measure including the group variable, time, the interaction between the group variable and time, and the baseline value of the particular outcome. We used two adjusted models for potential confounders, namely 1) impairment of daily functioning, intensity of somatic symptoms, impeded by complaints and somatic symptom severity (PHQ-15) and 2) as 1 with age, gender, level of education added. We additionally performed a per-protocol (PP) analysis over time using the data of patients in the intervention group ($n = 72$) who completed at least four sessions, and all patients in the control group ($n = 81$) not attending psychosomatic therapy.

Subgroup analyses were performed in the 'moderate PSS' group compared to the 'severe PSS' group (based on PHQ-15 scores 5–13 and 14–30, respectively [53]) for 'somatic symptom severity', 'number of symptoms', and 'comorbidities' to determine whether subgroups responded differently to the intervention. Negative binomial regression was carried out to estimate differences in number of GP contacts during the year after the intervention. P values $< .05$ were considered statistically significant. SPSS 26.0 was used for all statistical analyses. We did not adjust for multiple testing.

2.6. Ethics

The study was conducted according to the declaration of Helsinki (version 2013) and in accordance with the Dutch Medical Research Involving Human Subjects Act (WMO). This study was approved by the Medical Ethics Committee of VU University Medical center (VUmc) (METc VUmc registration number 2018.011; 22 June 2018 (Amendment 13 March 2019). Written informed consent was obtained from all participating patients and therapists. Patients and therapists were able to withdraw their consent at any time.

3. Results

3.1. Recruitment

Participants were recruited between January 2019 and March 2020 from 39 general practices. Fig. 1 shows the patient flow during the trial.

3.2. Baseline characteristics

Socio-demographic and clinical baseline characteristics are provided in Table 1. The mean age was 52.5 years (sd = 16.3) and there were more female patients in the control group (72%) than in the intervention group (64%). In the control group the level of completed education was

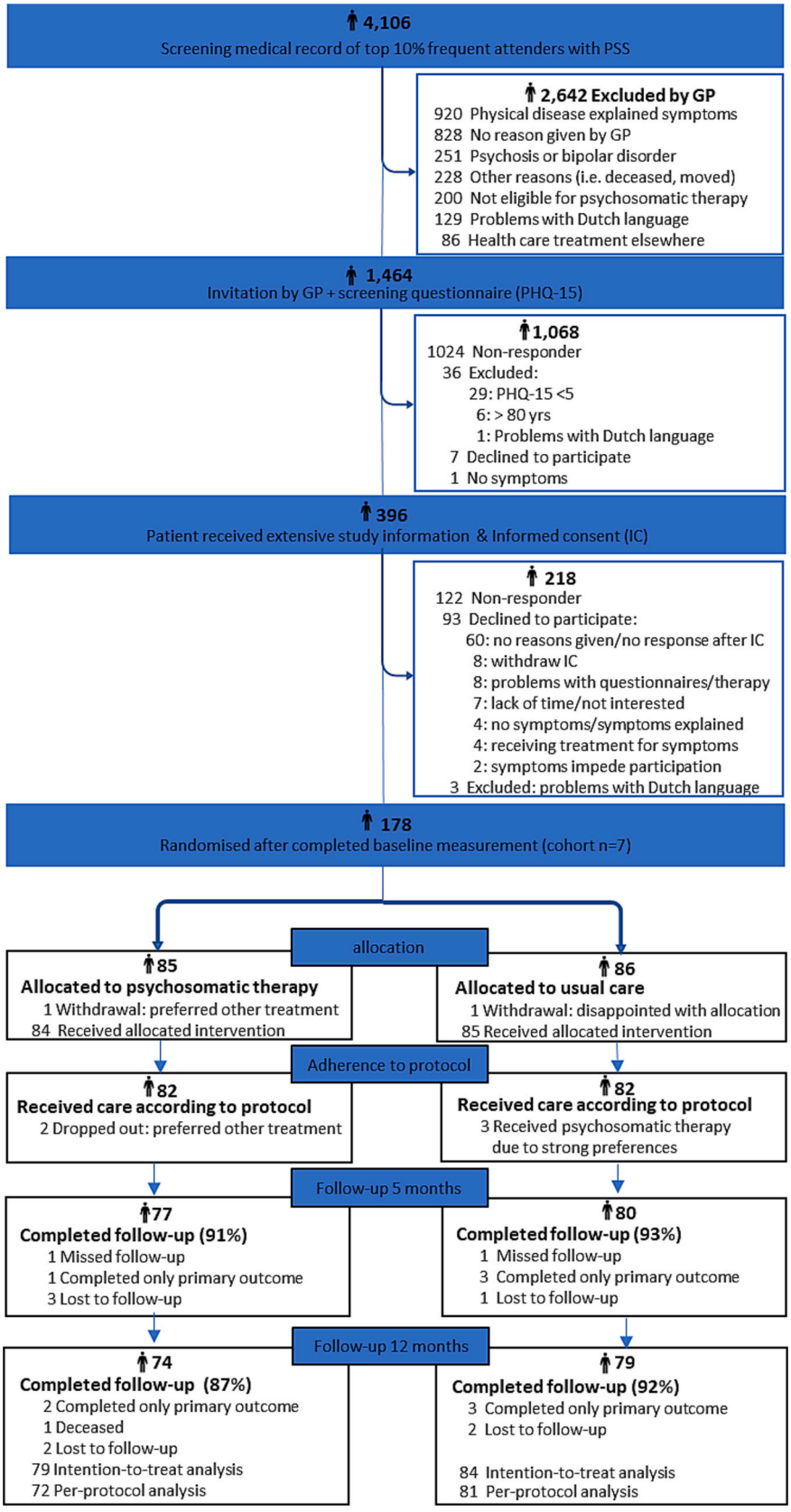


Fig. 1. Patients flow during the trial.
PSS = persistent somatic symptoms; GP = General practitioner; PHQ-15 = Patient Health Questionnaire-15 somatic symptom severity, exclusion score < 5. The cohort patients were not included in the analyses.

Table 1
Patient characteristics at baseline. Values are numbers (percentages) unless stated otherwise.

Characteristics	**Intervention group (n = 84)**	**Control group (n = 85)**
Age, mean (SD)	52.5 (16.3)	54.8 (16.9)
Female	54 (64)	61 (72)
Living situation		
Alone	25 (30)	27 (32)
Not alone	59 (70)	58 (68)
Country of birth		
the Netherlands	66 (79)	71 (83)
Other countries	18 (21)	14 (17)
Education level		
Low	16 (19)	16 (19)
Middle	32 (38)	38 (45)
High	36 (43)	31 (36)
Work status		
Employed	34 (40)	29 (34)
Unemployed	50 (60)	56 (66)
Main physical symptoms		
Fatigue	8 (10)	11 (13)
Pain	66 (79)	70 (82)
Multisite	38 (45)	34 (40)
Head	6 (7)	12 (14)
Back	9 (11)	9 (11)
Neck/Shoulder	4 (5)	6 (7)
Stomach/abdominal	1 (1)	6 (1)
Hip, knee, foot	6 (7)	2 (2)
Most frequently reported complaints/comorbidities		
Musculoskeletal	18 (21)	25 (29)
Rheumatic	18 (21)	7 (8)
Cardiological/Pulmonary	11 (13)	12 (14)
Psychological	9 (11)	12 (14)
Digestive	5 (6)	5 (6)
Auto immune diseases	7 (8)	2 (2)
Hormonal	1 (1)	2 (2)
Neurological	2 (2)	0 (0)
Sleeping problems	0 (0)	1 (1)
Other	3 (4)	4 (5)
Impairment daily functioning[a]*	2.5 (0.5)	2.4 (0.6)
Expected prognosis symptoms[b]*	3.4 (2.7)	3.9 (2.9)
Expected effect of treatment[c]*	5.5 (2.1)	5.2 (2.8)
Intensity somatic symptoms[d]*	6.9 (1.9)	6.4 (2.1)
Impeded by complaints[e]*	6.6 (2.4)	5.7 (2.6)
PSC*	7.00 (1.7)	6.95 (2.2)
Activity 1	6.76 (2.1)	6.75 (2.1)
Activity 2	6.66 (2.2)	6.72 (2.0)
Activity 3		
4DSQ*	16.1 (8.7)	14.1 (8.3)
Distress	3.3 (3.9)	2.5 (3.3)
Depression	5.3 (6.0)	3.8 (4.9)
Anxiety	16.4 (7.0)	13.5 (7.0)
Somatisation		
NRS*	7.1 (1.7)	6.5 (1.8)
SF-36 PCS*	48.6 (9.2)	51.4 (10.0)
SF-36 MCS*	49.7 (10.0)	50.3 (10.4)
PHQ-15, mean (SD)	14.3 (5.5)	13.0 (5.2)

* mean (SD); a. 0–3: no impairment-severe impairment; b. 0–10: no improvement-complete improvement; c. 0–10: not at all-very much; d. 0–10: no symptoms at all-most serious symptoms; e. 0–10: not at all-complete impeded; PSC = Patient Specific Complaint instrument: (0–10; 0 represents 'not a problem at all' and 10 'impossible'); 4DSQ = 4 Dimensional Symptom Questionnaire (higher scores represent worse health); distress and somatisation range 0–32 (low: 0–10; moderate: 11–20; high: 21–32); anxiety range 0–24 (low: 0–7; moderate: 8–12; high: 13–24); and depression range 0–12 (low: 0–2; moderate: 3–5, high: 6–12); NRS = Numeric Rating Scale (0–10; 10 represents most severe symptoms); SF-36 = Short-Form-36 (0–100; higher scores represent better health-related quality of life), PCS = physical component summary; MCS = mental component summary; PHQ-15 = Patient Health Questionnaire-15 somatic symptom severity, exclusion score < 5; 0–30; higher scores indicating higher somatic symptom severity.

lower and fewer participants had a paid job. The main physical symptom in both groups was pain (80%), and musculoskeletal complaints (25%) were reported most frequently.

3.3. Numbers analysed

At baseline, 171 participants were randomised: 85 to the intervention group and 86 to the usual care group. Follow-up data on the primary outcome was complete at 5 and 12 months for 161 (94%) and 158 (92%) of participants, respectively. Fig. 1 provides details on withdrawals and drop-out.

3.4. Primary outcome

The ITT and PP analyses, crude analyses as well as both adjusted analyses, showed no overall effect of the intervention in patient's level of functioning ((adjusted) analyses: mean difference − 0.50 [95% CI -1.10; 0.10]; $p = .10$ and − 0.60 [95% CI -1.22; 0.02]; $p = .06$, respectively) (Table 2, Fig. 2, Appendix A and B). Also at 5 and 12 months after baseline, no intervention effect was shown (mean difference − 0.56 [95% CI -1.27; 0.16]; $p = .13$ and − 0.43 [95%CI -1.14; 0.28]; $p = .24$, respectively). Compared to 'severe PSS', an overall intervention effect was found for the subgroup 'moderate PSS' (mean difference − 0.91 [95% CI -1.78;-0.03]; $p = .042$]. Results are provided in more detail in Table 3 and Appendix C. No statistically significant differences over 12 months were found per subgroup 'number of symptoms' and 'comorbidities'.

3.5. Secondary outcomes

Statistically significant intervention effects over 12 months were found on SF-36 subscales energy/fatigue (mean difference 4.28 [95% CI 0.02; 8.54]; $p = .049$) and perceived change in health (mean difference 8.23 [95% CI 1.02; 15.44]; $p = .026$). Health-related anxiety (mean difference − 1.93 [95% CI -3.81; −0.04]; $p = .045$) and comprehension of illness (mean difference − 0.73 [95% CI -1.45; −0.01] $p = .048$) measured with the IAS and IPQ—B, respectively, also showed a statistically significant intervention effect (Table 2 and Fig. 2). The results of the PP analyses showed similar effect and are presented in Appendix B.

At 5 months after baseline the intervention effect showed improvement on 4DSQ subscale somatisation (mean difference − 1.46 [95% CI -2.83; −0.09]; $p = .037$), SF-36 Physical Component Summary (PCS) (2.36 [95% CI 0.27; 4.45]; $p = .027$) and SF-36 subscales energy/fatigue (mean difference 7.40 [95% CI 2.48; 12.31]; $p = .003$) and perceived change in health (mean difference 9.04 [95% CI 0.76; 17.33]; $p = .033$). Comprehension of illness measured with IPQ-B (mean difference − 1.24 [95% CI -2.15; −0.34] $p = .007$) as well as illness behaviour measured with the IAS (mean difference − 3.50 [95% CI -6.66; −0.34]; $p = .03$) also showed a statistically significant intervention effect with the largest difference for health-related anxiety (mean difference − 3.00 [−5.13; −0.87] $p = .006$) at 5 months after baseline (Appendix A). No statistically significant differences were found for the remaining domains of health-related quality of life, psychosocial symptoms, and perceived severity of physical symptoms (Appendix A; Supplement S5). Data about how outcomes have changed over time within each group are provided in Appendix D.

The median number of treatment sessions was 9 (IQR = 6–12) over a median duration of 18.6 weeks (IQR = 12.4–28.1), with 54% of patients having finished therapy at 5-month follow-up. In the year after the end of therapy, the median number of GP contacts in the intervention group ($n = 75$) and control group ($n = 76$) was 9 (IQR = 5.0–14.0) and 10 (IQR = 4.0–16.8), respectively. Intervention and control group did not significantly differ regarding the number of contacts with the GP. The corresponding rate ratio was 1.24 ([95%CI 0.96; 1.62]; $p = .11$).

Table 2
Difference in outcome between intervention and control group over the 12 months period: intention-to-treat analyses.

Primary outcome	Crude analyses		Adjusted analyses[a]		Adjusted analyses[b]	
PSC	95% CI	*p*-value	95% CI	p-value	95% CI	p-value
Activity 1	−0.25 (−0.87 to 0.36)	0.42	−0.50 (−1.10 to 0.10)	0.10	−0.44 (−1.04 to 0.15)	0.14
Activity 2	0.14 (−0.48 to 0.76)	0.66	−0.06 (−0.68 to 0.56)	0.86	0.02 (−0.59 to 0.64)	0.94
Activity 3	−0.26 (−0.99 to 0.46)	0.47	−0.46 (−1.17 to 0.26)	0.21	−0.42 (−1.14 to 0.30)	0.25
Secondary outcomes						
4DSQ						
Somatisation	−0.83 (−2.00 to 0.34)	0.16	−1.00 (−2.17 to 0.17)	0.09	−0.88 (−2.03 to 0.27)	0.13
Distress	−0.74 (−2.28 to 0.81)	0.35	−0.85 (−2.42 to 0.72)	0.29	−0.75 (−2.33 to 0.82)	0.35
Depression	−0.20 (−0.81 to 0.41)	0.52	−0.18 (−0.79 to 0.43)	0.56	−0.17 (−0.78 to 0.45)	0.59
Anxiety	−0.42 (−1.35 to 0.51)	0.38	−0.37 (−1.31 to 0.57)	0.44	−0.35 (−1.30 to 0.59)	0.46
Severity symptoms NRS	−0.07 (−0.64 to 0.50)	0.82	−0.25 (−0.79 to 0.28)	0.36	−0.21 (−0.75 to 0.33)	0.45
SF-36						
Physical functioning	1.37 (−3.17 to 5.91)	0.55	1.81 (−2.78 to 6.39)	0.44	1.23 (−3.33 to 5.79)	0.59
Role functioning physical	4.77 (−4.73 to 14.27)	0.32	7.40 (−1.99 to 16.78)	0.12	6.41 (−2.86 to 15.68)	0.17
Role functioning emotional	1.20 (−8.70 to 11.09)	0.81	2.84 (−7.18 to 12.85)	0.58	2.20 (−7.80 to 12.21)	0.66
Social functioning	1.34 (−4.47 to 7.16)	0.65	3.35 (−2.45 to 9.14)	0.26	3.08 (−2.77 to 8.92)	0.30
Bodily pain	1.99 (−2.85 to 6.82)	0.42	3.17 (−1.62 to 7.96)	0.19	2.14 (−2.54 to 6.82)	0.37
Emotional well-being	1.08 (−2.97 to 5.14)	0.60	1.44 (−2.70 to 5.58)	0.49	1.29 (−2.89 to 5.46)	0.54
Energy/fatigue	2.67 (−1.67 to 7.01)	0.23	4.28 (0.02 to 8.54)	0.049*	3.58 (−0.67 to 7.82)	0.10
General health	2.34 (−1.52 to 6.19)	0.23	3.07 (−0.78 to 6.91)	0.12	3.16 (−0.65 to 6.97)	0.10
Health change	7.47 (0.28 to 14.66)	0.04*	8.23 (1.02 to 15.44)	0.026*	6.58 (−0.44 to 13.61)	0.07
PCS	1.31 (−0.50 to 3.11)	0.15	1.68 (−0.12 to 3.48)	0.07	1.35 (−0.40 to 3.11)	0.13
MCS	0.62 (−1.53 to 2.78)	0.57	0.88 (−1.33 to 3.08)	0.43	0.74 (−1.44 to 2.92)	0.50
IPQ-B						
1. Consequences of illness	−0.21 (−0.76 to 0.35)	0.46	−0.28 (−0.84 to 0.28)	0.32	−0.24 (−0.81 to 0.32)	0.40
2. Expected timeline of illness	0.23 (−0.46 to 0.92)	0.51	0.18 (−0.52 to 0.88)	0.62	0.13 (−0.58 to 0.83)	0.72
3. Personal control	−0.30 (−0.96 to 0.35)	0.36	−0.44 (−1.10 to 0.23)	0.20	−0.41 (−1.07 to 0.25)	0.22
4. Treatment control	0.25 (−0.43 to 0.93)	0.47	0.20 (−0.50 to 0.89)	0.58	0.20 (−0.49 to 0.90)	0.56
5. Identity	−0.16 (−0.74 to 0.42)	0.58	−0.27 (−0.83 to 0.30)	0.35	−0.30 (−0.86 to 0.27)	0.30
6. Concern about illness	−0.01 (−0.65 to 0.63)	0.98	−0.15 (−0.80 to 0.50)	0.65	−0.13 (−0.78 to 0.53)	0.71
7. Comprehension of illness	−0.51 (−1.24 to 0.21)	0.16	−0.70 (−1.42 to 0.02)	0.06	−0.73 (−1.45 to −0.01)	0.048*
8. Emotional response	−0.01 (−0.69 to 0.68)	0.99	−0.19 (−0.87 to 0.49)	0.58	−0.23 (−0.91 to 0.45)	0.50
IAS						
IAS total	−1.87 (−4.62 to 0.88)	0.18	−1.91 (−4.70 to 0.87)	0.18	−1.60 (−4.40 to 1.19)	0.26
Health-related anxiety	−1.91 (−3.77 to −0.04)	0.045*	−1.93 (−3.81 to −0.04)	0.045*	−1.63 (−3.51 to 0.25)	0.09
Illness behaviour	0.22 (−0.72 to 1.15)	0.65	0.14 (−0.80 to 1.08)	0.77	0.20 (−0.75 to 1.15)	0.68

PSC = Patient specific complaint instrument, higher scores reflect more problems with the activity; 4DSQ = 4 Dimensional Symptom Questionnaire, higher scores reflect worse health; NRS = Numeric Rating Scale, higher scores represent more severity of symptoms; SF-36 = Short-Form-36, higher scores represent better health-related quality of life; PCS = Physical component summary score; MCS = Mental component summary score; IPQ-B = Illness Perception Questionnaire-Brief, higher scores reflect more threatening view of the illness; IAS = Illness Attitude Scale, higher scores reflect higher health-related anxiety and illness behaviour (i.e., effects of symptoms and treatment experiences). a: Adjusted for impairment of daily functioning, intensity of somatic symptoms, impeded by complaints and somatic symptom severity (PHQ-15); b: Adjusted for age, gender, level of education, impairment of daily functioning, intensity of somatic symptoms, impeded by complaints and somatic symptom severity (PHQ-15).

3.6. Patients' opinions

A total of 72 patients (88%) completed the patient evaluation questionnaire and the GPE after completion of therapy, and the SRS-DV, WAI-SF after the first and last session. Three patients had only an intake session and seven patients were lost to follow-up. The selected results of the evaluation questionnaire are provided in Table 4. The majority of patients (76%) reported some or much improvement after the psychosomatic therapy.

The total score of the SRS-DV and the WAI-SF was 34.1 (sd = 4.0) and 45.8 (sd = 7.9), respectively. Scores on subscales of WAI-SF: Task, Goals and Bond were 14.4 (sd = 3.1); 15.0 (sd = 3.0) and 16.4 (sd = 3.0), respectively. The total scores indicate good quality of working alliance between therapist and patient (See Supplement S2). Most patients (95%) were (very) satisfied with the psychosomatic therapy and most patients (82%) reported that psychosomatic therapy helped them deal (a lot) better with their physical complaints.

3.7. Adherence treatment protocol and delivery

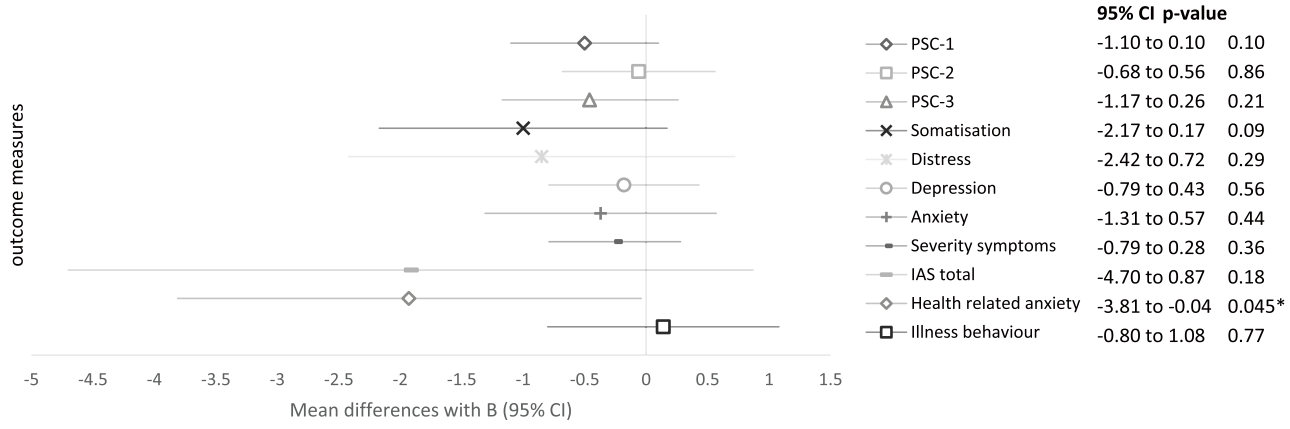
We received 73 audio recordings and 72 treatment reports, of which we analysed 21 recordings and 24 reports. Analysis of the audio recordings showed a range of adherence to protocol in percentages for the diagnostic, treatment, and evaluation phases of between 48 and 92%, 56–95%, and 75–97%, respectively. The extent to which therapists used other treatment approaches not in accordance with the protocol (treatment deviation) was lower for the diagnostic and evaluation phases than for the treatment phase, i.e., 3%, 0% and 11%, respectively.

Overall, treatment elements 'essential and unique or essential and not unique features' regarded as important, such as psychosomatic education, physically focussed therapy, cognitive behavioural approaches and activating therapy, were actually applied (maximal protocol adherence), while elements not appropriate and not considered in accordance with the protocol were minimally applied during the sessions (low treatment deviation).

4. Discussion

4.1. Summary of findings

Patient's level of functioning and most secondary treatment outcomes improved in both groups, these improvements did not statistically significant differ between the two groups. At the 5-month measurement point, effectiveness was demonstrated in somatisation, physical functioning, energy/fatigue, health-related anxiety and comprehension of illness. Especially individuals with moderate PSS seemed to benefit from the therapy compared to individuals with severe PSS. Although the change in the severe symptom group is not significant, possibly because



Negative values represent improvement. PSC = Patient specific complaint instrument; IAS = Illness Attitude Scale.

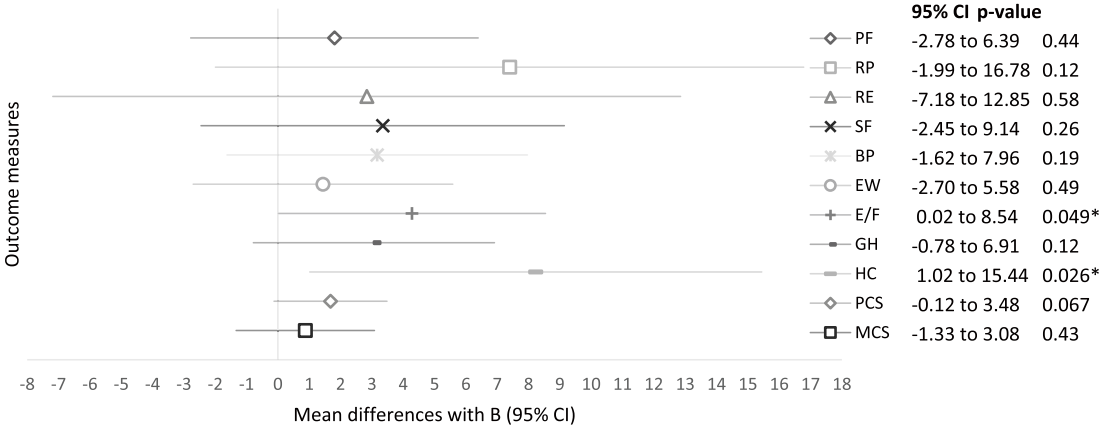


Fig. 2. Differences in outcome between psychosomatic therapy and care as usual over the 12 months period: ITT.*
Negative values represent improvement. PSC = Patient specific complaint instrument; IAS = Illness Attitude Scale.
Positive values represent improvement. SF-36 subscales: PF = Physical Functioning; RP = Role functioning Physical; RE = Role functioning Emotional; SF = Social Functioning; BP = Bodily Pain; EW = Emotional Well-being; E/F = Energy/Fatigue; GH = General Health; HC = Health Change; PCS = Physical Component Summary; MCS = Mental Component Summary.
*Adjusted analyses for impairment of daily functioning, intensity of somatic symptoms, impeded by complaints and somatic symptom severity (PHQ-15).

Table 3
Difference in primary outcome between intervention and control group over 12 months, per subgroup 'somatic symptom severity' (based on PHQ-15 scores).

Primary outcome (PSC-1)	Moderate PSS group (n = 87)		Severe PSS group (n = 76)		Difference			
	Intervention group (n = 37) Mean (SD)	Control group (n = 50) Mean (SD)	Intervention group (n = 42) Mean (SD)	Control group (n = 34) Mean (SD)	Moderate PSS group (n = 87)		Severe PSS group (n = 76)	
Baseline	6.69 (1.99)	6.67 (2.28)	7.25 (1.44)	7.37 (1.94)	95% CI	P-value	95% CI	P-value
5 months	4.97 (2.92)	5.82 (2.34)	6.31 (2.39)	6.25 (1.69)	n/a	n/a	n/a	n/a
12 months	4.60 (2.66)	5.50 (2.49)	6.07 (2.59)	5.52 (2.14)	n/a	n/a	n/a	n/a
Overall effect	n/a	n/a	n/a	n/a	−0.91 (−1.78 to −0.03)	0.042	0.32 (−0.53 to 1.18)	0.45

PHQ-15 = Patient Health Questionnaire-15**;** higher scores indicating higher somatic symptom severity. Moderate PSS group = PHQ-15 scores: 5–13; Severe PSS group = PHQ-15 scores: 14–30. PSC-1 = Patient specific complaint instrument, activity mentioned first (most important), higher scores reflect more problems with the activity.

the analyses in the subgroups are underpowered, there is a drop in the mean values. The number of GP contacts in the year after the end of therapy did not statistically significant differ between the two groups.

4.2. Comparison with existing literature

For patients with moderate PSS, psychosomatic therapy seems to be effective compared with patients with severe PSS. This is in agreement with a previous study with an individual, nurse-led CBT-based intervention for patients with PSS [28] that was particularly suitable for patients with symptoms that had been present for a limited number of years and with few comorbid physical diseases. Our findings are in agreement with the recommendation of the Dutch GPs' guideline for treating PSS [10].

Table 4
(Selected) results from the patient evaluation questionnaire (n = 72).

What did you think of the quality of the PST that you followed?	*Excellent*	*Good*	*Medium*	*Poor*	*Very poor*
	26.40%	69.40%	2.80%	1.40%	0.00%
Did the PST meet yourexpectations or whishes?	*All my expectations or wishes were met*	*Most of my expectations or wishes were met*	*Some of my expectations or wishes were met*	*Only a few of my expectations or wishes were met*	*None of my expectations or wishes were met*
	27.80%	36.10%	30.60%	2.80%	2.80%
Did the PST help you deal better with your physical complaints?	*Yes, it helped me a lot*	*Yes, it helped me somewhat*	*Neutral*	*No, it did not help me*	*No, it aggravated my complaints*
	33.30%	48.60%	12.50%	5.60%	0.00%
How satisfied are you in general with the PST you received?	*Very satisfied*	*Somewhat satisfied*	*Not satisfied nor unsatisfied*	*Somewhat unsatisfied*	*Very unsatisfied*
	55.60%	38.90%	4.20%	0.00%	1.40%
Imagine that someone you know happens to have unexplained physical complaints, would you recommend this PST?	*Yes, definitely*	*Yes, I think so*	*Maybe*	*No, I don't think so*	*No, definitely not*
	56.90%	27.80%	13.90%	1.40%	0.00%
Imagine that you encounter unexplained physical symptoms again in the future, would you follow this PST again?	*Yes, definitely*	*Yes, I think so*	*Maybe*	*No, I don't think so*	*No, definitely not*
	34.70%	37.50%	20.80%	6.90%	0.00%

PST = psychosomatic therapy.

Almost all patients were (very) satisfied with the psychosomatic therapy and they reported that the quality of this intervention was good or excellent, that it helped them to deal (a lot) better with their physical complaints. In addition, the working alliance between therapist and patient was also judged to be of good quality. These findings are important for the success of an intervention, as suggested in a previous study that emphasised the importance of a good patient-therapist relationship [54]. Furthermore, a shared biopsychosocial disease model, and the patient feeling respected, taken seriously, heard, seen and validated are prerequisites for a succesful intervention [55]. These conditions were also mentioned by patients in a qualitative study on psychosomatic therapy [56].

Due to our selection procedure we may have included patients who did not always expect a psychosomatic approach. Some patients may need more explicit attention to a shared biopsychosocial disease model, more focus on understanding and acceptance of the symptoms as well as on their personal possibilities, which might reduce patients focussing on pain or complaints [55]. In addition, psychosomatic therapy aims at behavioural change and readiness to change might influence a positive outcome [57]. Some patients may lack this readiness to change. Furthermore, for the 30% of patients who were older than 66 years it might be more difficult to obtain a real change in symptoms and functioning. This needs to be verified in future studies.

As indicated in previous studies, CBT was particularly beneficial with a longer duration and frequency of treatment, and with sessions lasting longer than 50 min [58]. This is consistent with previous studies that suggested that negative cognitions, maladaptive behaviour and mood states need a structured treatment plan and session time to be reframed and modified [59,60]. Our intervention, which also focusses on behaviour change, with 6–12 sessions of 30–45 min, may therefore be too short to realise effective improvement in patients with severe symptoms.

4.3. Strengths and limitations

This randomised controlled trial is a pragmatic real-life trial, and the first study to investigate the effectiveness of psychosomatic therapy compared to usual care for patients with PSS in primary care. The dropout rate in our study was very low. We used the quantitative data from process evaluation surveys to better understand which specific patients might benefit from the psychosomatic therapy, to identify which treatment elements were actually applied, and to gain insight into patient satisfaction and experience with the therapy. To examine the extent to which the therapists adhered to the treatment protocol, we carefully monitored the implementation fidelity of the psychosomatic therapy. However, selection bias may have occurred as therapists were allowed to choose the three sessions that they wanted to audio record.

Some limitations must be considered as well. Firstly, we experienced that several participants had trouble completing the PSC. Prior to the intervention, patients had to report the three activities that impeded them most. For some patients, however, the importance of an activity apparently decreased or over time changed, or they considered other activities more important. Although we deliberately chose the patient-centered outcome measure PSC- as it is a measurement instrument frequently used by therapists in the Netherlands and because the PSC focusses particularly on patients' functioning instead of on patients' pain or symptoms- the PSC seems less suitable when used without guidance and explanation from the therapist [61,62]. Furthermore, we used part of the core set outcome measures as recommended by Rief and colleagues (2017), such as symptom intensity, symptom interference with daily activities and illness consequences. These outcomes might have been also suitable as primary outcome [63].

Secondly, the COVID-19 pandemic started during this study. Due to this crisis, we know that some participating patients became ill and developed various persistent physical symptoms and/or psychosocial problems, and some patients faced major life events. During the lockdown in spring 2020, the continuity of therapy was interrupted for at least six weeks for a quarter of the intervention group participants. Some participants (n = 36) were therefore still receiving treatment at the 5-month point. To date, limited information is available on the impact of COVID-19 on patients with a history of persistent somatic symptoms, but it is conceivable that the COVID-19 pandemic may have had consequences for the effect of the psychosomatic therapy.

Thirdly, in the CORPUS study, GPs had no role in preparing and informing the patient about the biopsychosocial explanation of the patient's symptoms and the psychosomatic approach. At baseline, less than half of the intervention group patients embraced a biopsychosocial understanding of their symptoms or seemed open to a biopsychosocial explanation. Patients did not always seem to expect a psychosomatic biopsychosocial approach and they had therapy goals that did not align with psychosomatic therapy, such as getting rid of their complaints. According to therapists and patients, it is essential that patient and therapist agree on the biopsychosocial explanation of the symptoms and try to find common ground on the psychosomatic approach [56]. At 5-month follow-up, a proportion of patients (25%) still held a more biomedical illness belief and therefore possibly benefited less from the intervention. GPs might enhance patient willingness to embrace a biopsychosocial approach by paying more attention to psychosocial exploration and providing a good explanation of patient's symptoms [64], but further research is needed. Whether patient's illness understanding is a predictor of the effectiveness of psychosomatic therapy will also require further research.

Finally, our study was conducted in the Netherlands, where patients

with PSS can be referred to psychosomatic therapists in primary care. Our results may not be easily generalised to countries with different healthcare systems.

5. Conclusion

Overall it is a negative study with some interesting secondary findings that generate hypotheses for further study. Although patient's level of functioning and most secondary outcomes improved in both groups, only for patients with moderate PSS significant group differences on the primary outcome were found. For this subgroup, psychosomatic therapy might contribute to psychologically informed healthcare. It might be an important treatment as part of a stepped-care approach, as recommended in the Dutch GPs' guideline for treating PSS, to improve the management of patients with PSS but further study is needed.

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Declaration of Competing Interest

The authors have declared no competing interests.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jpsychores.2023.111178.

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