Journal of Contemporary Psychotherapy (2024) 54:47–57
https://doi.org/10.1007/s10879-023-09597-4

ORIGINAL PAPER

Effectiveness of a Multicomponent Group-Based Treatment in Patients with Medically Unexplained Physical Symptoms: A Multisite Naturalistic Study

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Accepted: 18 August 2023 / Published online: 9 September 2023

Abstract

Psychotherapy is expected to be effective in the treatment of patients with medically unexplained physical symptoms (MUPS). However, evidence is scarce. The aim of this study was to examine the effectiveness of a multicomponent treatment based on group therapy in patients with MUPS in a naturalistic setting and to explore potential predictors of the outcomes. A multisite naturalistic uncontrolled effectiveness study. A total of 290 patients with MUPS participated in group psychotherapy across seven clinical sites. Somatic symptoms, depression, anxiety, general psychotherapy outcomes operationalized as the Outcome Rating Scale (ORS) score, well-being, role functioning interference, as well as a number of pretreatment predictors were measured using a battery of self-report measures. Multilevel modeling and lasso regression with bootstrapping were used for the analysis. Medium to large pre-post effects were found for somatic symptoms, ORS, depression, anxiety, well-being, role functioning interference found in completers after controlling for site and group effects, pretreatment outcome values, and treatment length. Changes reported at 6- and 12-month follow-up were higher for most variables. No substantial pretreatment predictors of the patients' posttreatment status were found in addition to the pretreatment level of outcome variables. Somatic symptoms seem to be less malleable in psychotherapy than psychological outcome variables. However, there was a trend of further improvement after treatment completion.

Registration This study was retrospectively registered with ISRCTN (Identifier 13532466).

Keywords Medically unexplained physical symptoms · Multicomponent treatment · Group psychotherapy · Effectiveness · Predictors

Introduction

Medically unexplained physical symptoms (MUPS) are a highly prevalent phenomenon in health care (Haller et al., 2015). Since MUPS is to be, at least partly, produced and/or maintained by psychological mechanisms (Van den Bergh et al., 2017), psychotherapy is often considered the treatment of choice. However, the efficacy of psychotherapy in the treatment of patients with MUPS remains rather low (Kleinstäuber et al., 2011; van Dessel et al., 2014) and needs to be further investigated. Experts agree that patients with MUPS best profit from multicomponent psychological treatments that include a safe therapeutic environment, generic interventions (e.g., motivating patients for therapy, providing explanations, and reassuring) and specific interventions (Heijmans et al., 2011). Typically, these specific interventions comprise psychotherapy, often supplemented with

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other interventions such as relaxation training, graded exercise, or physiotherapy (Kleinstäuber et al., 2011). Although existing meta-analyses did not focus on the effectiveness of multicomponent treatments for the general category of MUPS, they were shown to be effective with specific syndromes such as fibromyalgia (Häuser et al., 2009) and chronic fatigue syndrome (Thomas et al., 2006).

In this study, we focus on intensive multicomponent treatments provided in group settings, with group psychotherapy as the main component provided on a daily basis for several weeks. These treatments allow to address patients' complaints in a focused and condensed manner. Furthermore, the group format offers more opportunities for developing new relationships and sources of social support, identifying with other group members and normalizing one's complaints, receiving feedback and validation from others, and experiencing altruism during the treatment process (Holmes & Kivlighan, 2000), as well as learning new coping strategies from other patients and developing interpersonal skills (Claassen-van Dessel et al., 2015). Although these characteristics make multicomponent group-based treatments potentially effective, we are not aware of any study that would examine the effectiveness of this specific therapy format. We adhered to Kroenke's (2006) definition of MUPS as the presence of at least one somatic symptom that is not fully explained by a somatic or psychiatric disorder with a duration of at least six months. This is a broad definition that covers various functional somatic syndromes, such as chronic fatigue syndrome, irritable bowel syndrome, and fibromyalgia, as well as the area until recently known as somatoform disorders (American Psychiatric Association, 2000; World Health Organization, 2008). Recently, the field has shifted towards more descriptive terms, such as somatic symptom disorder (American Psychiatric Association, 2013) and bodily distress disorder (Gureje & Reed, 2016), that aim to overcome the body–mind dichotomy embedded in previous classifications. Although these patients may present with a variety of somatic symptoms, many authors argued that they tend to share many characteristics and, therefore, these patients can be meaningfully treated as a single group (Lacourt et al., 2013). Smith et al. (2005) found that by relying on the DSM-IV somatoform diagnosis, approximately three in four patients suffering from MUPS remain unrecognized. Therefore, we have accepted this inclusive view in our study and use the term MUPS as an overarching category because of its wide use and etiological neutrality.

In uncontrolled naturalistic studies, change is usually reported in terms of pre-post effects. While such effect sizes do not allow researchers to disentangle the treatment effect from natural recovery and other confounding variables (Cuijpers et al., 2017), they are more easily generalizable to everyday practice, as they represent the average amount of change patients may expect when they participate in a treatment (Schmitz et al., 2013). Two meta-analyses revealed that, as far as symptom intensity is considered, estimates of the pre-post effect sizes vary between $d = 0.70$ (Kleinstäuber et al., 2011) and $d = 0.80$ (Koelen et al., 2014). Since at least one-third of patients suffering from MUPS have comorbid depressive or anxiety disorders (Löwe et al, 2008; Toft et al., 2005), depression and anxiety are often reported as secondary outcomes. While the pre-post effects size for depression was reported to be $d = 0.65$ (Kleinstäuber et al., 2011), the pre-post effect for anxiety was not reported in any meta-analysis. The pre-post effect for functioning was reported to range from $d = 0.38$ (Kleinstäuber et al., 2011) to 0.45 (Koelen et al., 2014).

When outcomes were assessed at follow-up, patients tended to report better outcomes compared to posttreatment assessment in terms of somatic symptoms and functional impairment, but not in terms of depression (Kleinstäuber et al., 2011; Koelen, 2014). For instance, change in symptom intensity increased from $d = 0.70$ after therapy to 0.80 at follow-up, but change in depression dropped from $d = 0.65$ after therapy to 0.40 at follow-up (Kleinstäuber et al., 2011).

Predictors of Medically Unexplained Physical Symptoms

There is ample evidence that MUPS is associated with various psychological characteristics. These include higher levels of dissociation (Gupta et al., 2017), which typically occur in the context of extreme psychosocial stress and a history of severe abuse/neglect during early life (Roelofs & Spinhoven, 2007). MUPS are also connected with alexithymia (Mattila et al., 2008), poorer emotional regulation skills (Schwarz et al., 2017) and poorer interoceptive awareness (Schaefer et al., 2012), which do not allow patients to interpret their somatic signals and emotions adequately. Patients with MUPS also tend to have difficulties tolerating somatic sensations (Kleinstäuber et al., 2019) and to react with increased anxiety (Creed, 2011). Furthermore, patients' perceptions of bodily dysfunction and their pain sensitivity are related to the lack of psychological mindedness (Denollet & Nyklíček, 2004). In terms of patients' interpersonal relationships, MUPS are often connected with interpersonal difficulties (Hilbert et al., 2010) and attachment problems (Riem et al., 2018). Since these variables were found to be related to the occurrence of MUPS, we expected that they may also predict treatment outcome. However, empirical evidence related to predictors of treatment outcome in patients with MUPS is still missing.

Aim of Study

The aim of this multisite study was to assess the effectiveness of multicomponent group-based treatments in patients

with MUPS in the naturalistic context. While the treatments shared many characteristics across the sites, such as intensity and predominant psychodynamic orientation, they were non-manualized. Roubal et al. (2021) demonstrated that in the naturalistic context, psychotherapists tend to differ in their style of working with MUPS even when they self-identify with the same therapeutic approach. Although this prevents us from making conclusions about the effectiveness of specific treatment ingredients, it shows the amount of change reported by patients in the typical context in which these treatments are delivered.

We hypothesized that the intensity of somatic symptoms (primary outcome), depression, and anxiety would decrease and that general psychotherapy outcomes (as operationalized by the Outcome Rating Scale, Miller et al., 2003), well-being (operationalized as positive affect) and role functioning in daily life would increase after psychotherapy. Furthermore, we hypothesized that the gains will be at least partially maintained after six and 12 months after treatment completion. As a second, exploratory (i.e., nonregistered) aim, we tested whether the above-listed variables predict patients' posttreatment status on each of the outcome variables. Given the lack of empirical literature on outcome predictors in patients with MUPS, we decided to include a range of potential predictors. This study did not focus on potential mechanisms of change, which were addressed in a separate study (Řiháček et al., 2022).

Method

We used the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines (von Elm et al., 2007) to structure the report of the study.

Patients

This study was a naturalistic multisite study (7 sites) without any control conditions. A total of $N = 290$ adult patients recruited from seven clinical sites and suffering from MUPS (75.5% women) participated in the study. Their ages ranged from 19 to 74 ($M = 40.6$, $SD = 11.1$). In terms of the ICD-10 diagnoses, 75.9% were diagnosed with a neurotic, stress-related, or somatoform disorder, 16.9% had an affective disorder, and 14.1% had a personality disorder. About 9% of the patients had multiple diagnoses. The most often reported somatic symptoms included feeling tired or having low energy (93.8%), trouble sleeping (86.6%), back pain (82.8%), headaches (79.0%), nausea, gas, or indigestion (77.2%), pain in arms, legs, or joints (71.7%), feeling one's heart pound or race (70.7%), constipation, loose bowels, or diarrhea (67.6%), and stomach pain (60.7%). Most patients were Czech (95.5%); 41.4% had university-level education, 54.8% had secondary, and 2.4% had primary education.

Treatment

The treatment was comparable across the seven sites with some degree of variation. The treatment length varied between four and 12 weeks, with the most common length being 6 weeks. At five sites, patients received five sessions of face-to-face group psychotherapy per week, while at two sites, they received three and four sessions, separately. Typically, a session lasted 90 min (except for one site, where sessions lasted 75 min). At three sites, the groups were "open" (i.e., new patients were incorporated as they were accepted to treatment), while they were "closed" at another three sites (i.e., their composition did not change during treatment, except for dropouts). At the remaining site, both formats were used in different groups. The treatment was non-manualized, mostly psychodynamic, with the integration of humanistic and experiential approaches. Since not all patients participating in the therapeutic groups suffered from MUPS, the treatment was not exclusively focused on somatic symptoms. Instead, somatic symptoms were treated as one of possible types of patients' reactions to life distress.

The group therapy aimed mainly to develop a better understanding of the patients' problems, raise patients' awareness of their needs and life situation, learn how to better utilize their strengths and resources, strengthen patients' resilience, and develop a follow-up care plan. Aims of the treatment were discussed with the patients in the group. Group psychotherapy was supplemented with other therapeutic activities, such as art therapy or relaxation training. The time allocation of these supplementary activities varied between 3 and 23.5 h per week ($Mdn = 11.38$; participation of the individual participants not documented). At four sites, the treatment was designed as an inpatient program, while at three sites, patients attended day-care-based outpatient programs. See Supplement 1 for a detailed description of each site's treatment program and client demographics.

Therapists

The group therapy was performed by 16 female and 9 male therapists. Their age ranged from 25 to 59 years ($M = 44.13$, $SD = 10.29$), and their length of practice varied between 1 and 25 years ($M = 12.21$, $SD = 7.30$). Psychotherapists' self-classified theoretical orientations included psychoanalysis and psychoanalytic psychotherapy ($n = 9$), psychodynamic psychotherapy ($n = 6$), gestalt therapy ($n = 4$), person-centered approach ($n = 3$), Daseinsanalysis ($n = 1$), and integrative psychotherapy ($n = 2$).

Measures

Patient Health Questionnaire-15-modified (PHQ-15-modified). Somatic symptom intensity was measured by a self-report questionnaire derived from the Patient Health Questionnaire-15 (PHQ-15, Kroenke et al., 2002). The PHQ-15 is a 15-item self-report measure developed to assess somatization. Each item represents a somatic symptom or symptom cluster. Using a Likert-type scale, patients rate the degree to which they have been bothered by each of these symptoms over a specified period. The PHQ-15 has shown good concurrent validity with the Short-Form General Health Survey (Kroenke et al., 2002). In our study, the measure used had two modifications. First, patients were asked to rate the intensity of their symptoms over the last week (instead of four weeks, as used in the original version) to allow for weekly measurements. Second, a five-level scale ranging from "not at all" to "very severe" (instead of the three-level scale used in the original version) was used to rate the items to offer a response scale potentially more sensitive to change. The symptom intensity score was computed as the average of all items. In this study, the Cronbach's α at baseline was α = 0.81.

Within the pretherapy assessment, patients were also asked three questions about each item: (1) Was the symptom one of the main reasons why you sought therapy? (2) Has the symptom been present for more than six months? (3) Was your physician unable to find a cause of this symptom? Patients' responses to these questions were used to classify patients into either the MUPS or non-MUPS group (see the "Procedure" section).

Outcome Rating Scale (ORS). The ORS (Miller et al., 2003) is a brief evaluation of psychotherapy outcomes and is particularly suited for repeated assessment. The individual items were derived based on measurement domains of other existing instruments and are composed of four visual analog scales that allow patients to rate their individual, relational, and social well-being and functioning. In this study, the Cronbach's α at baseline was α = 0.82.

Patient Health Questionnaire-9 (PHQ-9). The PHQ-9 (Kroenke et al., 2001) is a nine-item self-report measure for screening the severity of depressive symptoms over the past 2 weeks. In this study, the Cronbach's α at baseline was α = 0.81.

Generalized Anxiety Disorder Screener (GAD-7). The GAD-7 (Spitzer et al., 2006) is a seven-item self-report measure of anxiety symptoms over the last 2 weeks. In this study, the Cronbach's α at baseline was α = 0.86.

Well-Being Index (WHO-5). The WHO-5 (Bech et al., 2003) is a self-report measure of well-being operationalized as positive affect. In this study, the Cronbach's α at baseline was α = 0.85.

Role functioning interference. The following single item adopted from the full Patient Health Questionnaire (PHQ, Kroenke et al., 2010) was used to measure role functioning: "If you checked off any problems on this questionnaire, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?" Patients were asked this question three times in the context of the PHQ-15-modified, PHQ-9, and GAD-7. The score was computed as the sum of the three items, quantifying interindividual differences in how much overall role functioning is affected by somatic, depressive, and anxiety symptoms (Cronbach's α = 0.82 at baseline).

Demographic Questionnaire. The demographic questionnaire included questions about patients' age, gender, education, household, nationality, occupation, and marital status.

Procedure

Recruitment and Data Collection

The study was approved by the Research Ethics Committee of Masaryk University (ref. no. EKV-2017-029-R1). Patients were recruited at seven psychotherapeutic clinics by the local staff during the years 2018 and 2019 and follow-up data collection proceeded until January 2021. All patients who were admitted to the treatment were invited to participate in the study. In case they agreed, they were administered a pretreatment battery (all outcome and predictor measures), a weekly assessment battery (PHQ-15-modified, ORS, MAIA, ERSQ, CPAQ-modified, and RNSS), a posttreatment assessment battery (all outcome measures plus MAIA, ERSQ, CPAQ-modified, and RNSS), and a follow-up battery (all outcome measures except for ORS). The batteries also included other measures not analyzed in this study. The data were collected in a paper-and-pencil form during treatment and online in case of the follow-up measurement (18% of the sample declined to provide an e-mail contact and could not be reached for the follow-up measurement). The sample size was not predetermined but based on the knowledge of the patient flow in the sites, we expected a sample of 500 patients willing to participate and approximately 50% of them to suffer from MUPS. The study was registered 4 months after the data collection began (at the time of registration, data from 24 patients were collected but were neither transcribed nor analyzed).

Patients were included in the sample if they (1) were at least 18 years old, (2) had at least one MUPS (i.e., a somatic symptom with a duration of at least 6 months that was not fully explained by any somatic or psychiatric disorder), (2) did not have a diagnosis of a severe mental disorder that would make participation in this kind of treatment impossible.

The MUPS vs. non-MUPS status of each patient was determined based on the following procedure. All patients who were diagnosed by their local clinical staff with a somatoform disorder (F45, World Health Organization, 2008) were considered MUPS ($n = 82$). In the remaining patients, the status was determined based on a triangulation of patients' self-report data and data obtained from the local clinical staff. Patients who marked at least one somatic symptom in the PHQ-15-modified as "lasting for at least 6 months" and, at the same time, as "one of the main reasons for seeking psychotherapy" were provisionally classified as "self-identified MUPS". Patients who were found to comply with Kroenke's (2006) definition of MUPS by the local clinical staff were provisionally classified as "site-identified MUPS". When two classifications agreed with each other, patients were placed in the MUPS group ($n = 47$). In cases of a conflict between the two classifications, the patients' records were reviewed by two physicians (a psychiatrist and a general practitioner) who were not familiar with any of the patients' process and outcome data to determine the patients' MUPS status (this resulted in $n = 161$ patients also being placed into the MUPS group).

Statistical Analysis

The analysis was conducted using R software version 4.0.3 (R Core Team, 2021). Total scores for each scale were computed. If a patient skipped some items but answered at least 80% of the scale's items, the total score was computed as the average of the answered items times the total number of items in the scale. Otherwise, the patient's response was considered missing data. The first aim was to test the effectiveness of the intervention using multilevel modeling (Tasca & Gallop, 2009) with the use of the lme4 package (Bates et al., 2015) using the Restricted Maximum Likelihood method. We fitted two two-level multilevel models for each outcome variable and each measurement point (i.e., posttreatment, 6-month follow-up, and 12-month follow-up). In Model 1, the pre- and posttreatment scores were modeled nested within patients and controlled for the group effect (random effect) and site effect (fixed effect) only. In Model 2, the pre- and postscores were further controlled for the pretreatment level of the outcome variable and the length of treatment, operationalized as the number of days of attendance (fixed effects). See Supplement 2 for the formulation of the statistical models.

To explore the effect of the baseline severity (i.e., the pretreatment level of the outcome variables) in more detail, we added the interaction between baseline severity and measurement point in Model 3. We used the sjPlot package (Lüdecke, 2022) to plot the results. However, due to the space limitation we present these analyses in the Supplement 3.

To standardize the effect size, the regression coefficient of the "measurementPoint" variable was divided by the standard deviation of the outcome variable (Lorah, 2018). Furthermore, the proportion of the variance of the outcome variable explained by a site was calculated as an intraclass correlation coefficient (ICC; Lorah, 2018). In case of outcome variables that were measured only at pre- and posttreatment, the analysis was conducted using a subsample of patients for whom a posttreatment measurement existed. However, two outcome variables were measured with a weekly frequency, and for these, the same analysis was also conducted using the last observation as the final value.

Additionally, we used one type of sensitivity analyses to explore the potential impact of drop-out, namely inverse probability weighting (Gomila & Clark, 2022). Using logistic regression, we predicted the dropout probability for each patient at posttherapy, 6-month follow-up, and 12-month follow-up (see Supplement 4). We then repeated the multilevel analysis using inverse probability weighting (Seaman & White, 2014).

Furthermore, we conducted an exploratory analysis aimed at the prediction of patients' posttreatment status. Due to space limitations, this analysis is described in Supplement 5.

Results

Descriptive Statistics

From the 736 patients accepted for treatment, 444 (60%) agreed to participate in the study. There was a high variability in the recruitment rate per site (35–91%, $Mdn = 63\%$). Altogether, there were 78 therapeutic groups. The number of groups varied between five and 22 per site ($Mdn = 10$). The number of patients from each group who participated in this study ranged from one to 12 ($Mdn = 6$). While 290 patients were classified as MUPS and were included in the study, only $N = 280$ commenced the treatment, $N = 222$ completed the treatment, and $N = 159$ completed the 6-months follow-up measurement, and $N = 131$ completed the 12-months follow-up measurement (see Supplement 6 for the flow diagram). The treatment length ranged from 1 to 60 sessions ($Mdn = 32$). Most patients (84%) participated in outpatient programs. The descriptive statistics of the outcome variables are reported in Table 1. The differences in the pretreatment level of the outcome variables were negligible between outpatient and inpatient programs ($d = 0.07$ to 0.28 for somatic symptoms, depression, anxiety, ORS, well-being, and role functioning interference); therefore, the analyses were conducted using the total sample.

Table 1 Description of outcome variables

Variable	Pre-treatment		Last observation[a]		Posttreatment		Follow-up 6 months		Follow-up 12 months	
	Mean (*SD*)	n	Mean (*SD*)	n	Mean (*SD*)	n	Mean (*SD*)	n	Mean (*SD*)	n
Somatiwec symptoms	22.5 (9.6)	268	18.9 (10.2)	277	17.7 (10.1)	217	16.65 (9.0)	122	16.1 (9.2)	81
ORS	139.4 (86.3)	281	227.2 (102.1)	281	239.8 (99.9)	220				
Depression	14.9 (5.7)	287			10.8 (5.4)	222	9.7 (6.3)	126	8.6 (6.0)	81
Anxiety	12.1 (4.9)	284			8.6 (4.7)	223	7.4 (5.0)	126	6.7 (5.3)	81
Well-being	6.7 (4.3)	286			10.5 (4.5)	221	10.4 (6.2)	125	10.9 (5.8)	81
Role functioning	5.7 (2.0)	238			4.2 (2.0)	162	3.8 (2.1)	107	3.6 (2.1)	67

Total scores calculated as means of item scores. Empty cells mean that the variable was not measured at that measurement point

ORS Outcome Rating Scale

[a]Last observation is reported for weekly administered measures only

Change After Treatment Completion

The results of the effectiveness analysis are reported in Table 2. For completers, the pre-post change in somatic symptom intensity (i.e., the primary outcome) was small to medium. The change in ORS score was large, and the change in the remaining outcome variables (i.e., depression, anxiety, well-being, and role functioning interference) was medium to large. The decrease in effect size when controlling for the pretreatment outcome value and treatment length was minimal. The group effect ranged from 5 to 13%, but it disappeared after controlling for the pretreatment outcome value and treatment length. The analysis of the interaction between the measurement point and the baseline level of the outcome variable showed that patients with a worse baseline status tended to report larger changes compared to those with a better baseline status (see Supplement 3 for details).

When all patients who began the treatment were considered and their last outcome observation was used as a proxy of their final status (last observation carried forward), the effect sizes were expectedly lower compared to completers. In terms of somatic symptom intensity, the amount of change was in the small to medium range, while the change in the ORS score was still classified as large. The remaining outcome variables were not measured on a weekly basis, and therefore, no data were available for them.

Furthermore, we explored the change in interoceptive awareness, emotional regulation skills, symptom acceptance, and relational needs satisfaction. These variables were used as predictors of change in our study but may be considered outcomes on their own. See Supplement 7 for the descriptive statistics. For completers, the pre-post change was large in emotional regulations skills, medium to large in interoceptive awareness, medium in symptom acceptance, and small to medium in relational needs satisfaction (see Supplement 8 for details).

Change Six and Twelve Months After Treatment Completion

In case of somatic symptom intensity, depression, and well-being, effects sizes were higher at both follow-up measurements compared to posttreatment. In case of anxiety, change remained stable across measurement and role functioning slightly worsened in the follow-up measurements. The group effect ranged from 2 to 17%, but it disappeared after controlling for the pretreatment outcome value and treatment length.

Sensitivity Analysis

We refitted the abovementioned models using inverse probability weighting. The resulting standardized effect sizes (see Supplement 9) were comparable to (and often higher than) those obtain from the unweighted multilevel analysis. Therefore, our sensitivity analysis did not suggest any substantial influence of systematic attrition given the available predictors. Nevertheless, the explanatory power of the regressions to determine the weights was low (Hosmer & Lemeshow $R2 = 0.19; 0.06; 0.06$, respectively) and only very few predictive variables were found (see Supplement 4).

Table 2 Effectiveness of the intervention (multilevel models with 'group' as random effect)

Outcome variable	Last observation			Posttreatment			Follow-up 6 months			Follow-up 12 months		
	n	d [95%-CI]	group	n	d [95%-CI]	Group	n	d [95%-CI]	Group	n	d [95%-CI]	group
Somatic symptoms	255	−0.38 [−0.54; −0.22]	0.06	204	−0.48 [−0.65; −0.31]	0.05	133	−0.61 [−0.82; −0.40]	0.05	117	−0.61 [−0.83; −0.38]	0.07
(controlled)	252	−0.37 [−0.47; −0.26]	0.00	201	−0.43 [−0.54; −0.32]	0.00	133	−0.58 [−0.73; −0.43]	0.00	117	−0.58 [−0.75; −0.42]	0.00
ORS	267	0.86 [0.72; 1.00]	0.12	215	0.93 [0.78; 1.08]	0.10		−0.81 [−1.01; −0.62]	0.11		−0.91 [−1.12; −0.71]	0.09
(controlled)	264	0.85 [0.74; 0.96]	0.00	212	0.92 [0.81; 1.03]	0.00		−0.82 [−0.97; −0.68]	0.00		−0.90 [−1.05; −0.74]	0.00
Depression				220	−0.69 [−0.85; −0.53]	0.10	144	−0.84 [−1.03; −0.65]	0.15	125	−0.82 [−1.02; −0.61]	0.17
(controlled)				217	−0.65 [−0.75; −0.55]	0.00	144	−0.84 [−0.99; −0.69]	0.00	125	−0.80 [−0.96; −0.64]	0.00
Anxiety				219	−0.69 [−0.84; −0.53]	0.13	140	0.65 [0.45; 0.86]	0.07	123	0.70 [0.47; 0.93]	0.02
(controlled)				216	−0.64 [−0.75; −0.53]	0.00	140	0.63 [0.47; 0.79][a]	0.00	123	0.68 [0.50; 0.86]	0.00
Well−being				219	0.80 [0.64; 0.95]	0.11	141	−0.84 [−1.05; −0.63]	0.10	124	−0.86 [−1.10; −0.63]	0.02
(controlled)				216	0.77 [0.66; 0.88]	0.00	141	−0.84 [−1.00; −0.68]	0.00	124	−0.88 [−1.06; −0.70]	0.00
Role functioning				146	−0.70 [−0.88; −0.52]	0.10	106	−0.61 [−0.82; −0.40]	0.05	94	−0.61 [−0.83; −0.38]	0.07
(controlled)				143	−0.64 [−0.76; −0.52]	0.00	106	−0.58 [−0.73; −0.43]	0.00	94	−0.58 [−0.75; −0.42]	0.00

The overall effect was positive for all variables (the negative sign in some variables reflects the fact that a decrease in scores represents improvement). Site = the proportion of variance explained by the site (random effect). Group = the proportion of variance explained by the group, nested in site (random effect). Controlled = effect controlled for pre-treatment outcome value and treatment length (number of days). All effects were significant at $p < .001$

ORS Outcome Rating Scale

[a]The model failed to converge

Prediction of Posttreatment Status

Complete information was available for 120 patients (41%). The variables for which data were most often missing included posttreatment assessment of role functioning interference (42%), other outcome variables (missingness between 21 and 23%), and pretreatment assessment of role functioning interference (18%). The high proportion of missing data in case of role functioning interference is likely related to the fact that the corresponding items were easier to overlook in the questionnaire. The remaining missingness in outcome data corresponds to the proportion of patients who did not complete their treatment (or dropped out from the study before treatment completion). In addition, there was no distinct pattern of missing data that would suggest the existence of a systematic bias, and the missingness of no other variable exceeded 7%.

The patients' posttreatment status on the outcome variables was consistently predicted by the pretreatment status on the respective variables (β's ranging from 0.13 to 0.31). In addition, the prediction analysis was largely unable to find any relationships that received a high level of replication across the imputed data sets and bootstrap draws. Exceptions included pretreatment depression positively predicting the posttreatment status in role functioning interference ($\beta = 0.15$), pretreatment ORS score positively predicting posttreatment status in well-being ($\beta = 0.11$), and pretreatment relational needs satisfaction predicting the posttreatment ORS ($\beta = 0.12$) and well-being ($\beta = 0.10$) status. Furthermore, the treatment length predicted the posttreatment well-being status ($\beta = 0.11$). See Supplement 10 for the detailed results of the posttreatment status prediction.

Discussion

The aim of this study was to examine the effectiveness of a multicomponent treatment with intensive group psychotherapy as its central component in patients with MUPS. We hypothesized that the intensity of somatic symptoms (primary outcome), depression, and anxiety would decrease and that the ORS scores, well-being, and role functioning in daily life would increase after psychotherapy. Furthermore, we hypothesized that the gains will be at least partially maintained after six and 12 months after treatment completion.

In terms of somatic symptom intensity, we found a small to medium pre-post effect, which is considerably lower than the effects reported in previous studies (Kleinstäuber et al., 2011; Koelen et al., 2014). In contrast, we found a large effect on the ORS score and medium to large effects on depression, anxiety, well-being, and role functioning interference, which surpassed the results reported in existing meta-analyses (Kleinstäuber et al., 2011; Koelen et al., 2014). The relatively low change in somatic symptoms is consistent with Moreno's (2013) finding that group therapy tends to be less effective than individual treatment in patients with abridged somatization disorder. However, this conclusion was not confirmed in Liu et al.'s (2019) meta-analysis, which found that group therapy was more effective than individual treatment. The presumed inferiority of group therapy also does not explain the above-average results in other outcome variables. A more plausible explanation for this observation may be the fact that the therapeutic group included patients with diverse complaints, and therefore, the treatment did not focus on MUPS exclusively. The results also suggest that psychotherapy can influence psychological variables more easily than somatic symptoms. This is consistent with the recommendations to focus on stress reduction (e.g., Aktaas et al., 2019) and symptom acceptance (e.g., Kleinstauber, et al., 2019) rather than trying to work directly with the symptoms.

Patients' status tended to improve further after treatment completion in some outcome variables (i.e., symptom intensity, depression, and well-being). As far as symptom intensity is considered, the continuing improvement corresponds to the existing meta-analyses (Kleinstäuber et al., 2011; Koelen, 2014). However, continuing improvement in terms of depression and well-being was not expected and can be probably attributed to the intensity of the psychological treatment.

Except for the pretreatment status of the outcome variables themselves, we found almost no support for the anticipated pretreatment predictors of the patients' posttreatment status. Therefore, we must conclude that the therapeutic change in patients with MUPS is barely predictable from self-reported baseline psychological variables and, except for well-being, by the treatment length. In the case of two of the predictor variables, namely, the symptom willingness subscale of the CPAQ-modified and the global avoidance subscale of the ECR-RS, the lack of any substantial relationship may be attributable to the low reliability of the scales in our sample.

Strengths and Limitations

This study possessed high ecological validity, because it represented the naturalistic conditions under which these treatments are typically delivered. Furthermore, recruiting a relatively large sample of patients from multiple clinical sites provided a level of robustness to the findings. However, the generalizability is limited by the predominant psychodynamic orientation of the treatment. The findings may thus not generalize to therapeutic settings in which cognitive-behavioral therapy and other approaches are used.

The study did not include a control group; therefore, the treatment effect could not be disentangled from other influences, such as natural recovery. The non-manualized nature of the treatments prevented us from making conclusions about the effectiveness of specific treatment ingredients. However, we controlled for the potential effect of baseline severity, treatment length, group effect, and site effect in the statistical analyses.

The sample had a range of somatic complaints, and it is possible that the effects of psychotherapy differ for different kinds of somatic complaints, but as a naturalistic study, this reflects the reality of treatments in services (Delfstra & van Rooij, 2015). Furthermore, as only between 77% (posttreatment) and 45% (12-months follow up) contributed to the measurement of outcomes, attrition could have biased the results. Our analyses were conditioned on the pre-treatment levels of our outcomes, which could in part correct for systematic drop-out due to severity. Additionally, our sensitivity analysis did not suggest any substantial influence of systematic attrition given the available predictors. However, the amount of missing data was high and could have biased our findings in ways we were unable to detect.

Conclusions and Future Directions

We may conclude that, after a multicomponent treatment, patients reported an appreciable change in somatic symptoms and a substantial change in depression, anxiety, and well-being, as well as in their role functioning. Furthermore, the change persisted, and even increased 6 and 12 months after the treatment. The lack of a control group did not allow us to fully attribute this change to the intervention. This means that other factors, including spontaneous remission, could have played a role in the process of change. However, the effect sizes clearly outperformed those found in other studies' control groups (e.g., Koelen et al., 2014) and were homogeneous across the seven sites. This provides robust evidence of the effectiveness of multicomponent group-based treatment in patients with suffering from MUPS.

The change in somatic symptoms was smaller compared to psychosocial outcomes (i.e., depression, anxiety, well-being, and role functioning). This challenges the traditional assumption that MUPS stem from mental difficulties, as embedded in the concept of somatoform disorders (American Psychiatric Association, 2000; World Health Organization, 2008). However, newer concepts assume a more bidirectional relationship between the "body" and the "mind", in which genetic, neurophysiological, and environmental actors may render individuals more vulnerable to MUPS (Luyten et al., 2012). From this perspective, treatments that emphasize the psychological component can only address a part of this complexity.

Future research should focus on identifying potential subgroups of patients both in terms of disorder-related difficulties and other characteristics, and also in terms of their response to psychological treatment. Studies should also focus on identifying predictors that would have a more pronounced impact on outcome in psychological treatment than those used in our study.

Although we provided evidence that patients suffering from MUPS, on average, report substantial positive changes after multicomponent group-based treatment, data from our project also showed high rates of negative treatment effects (Pourová et al., 2022). Clinicians should thus be aware of these potentially harmful aspects of the treatment. Using a routine outcome monitoring system (Lambert & Lo Coco, 2013) will help detect patients who do not profit from the treatment.

Author contributions MP conducted the analysis and wrote the manuscript. TŘ designed the study, conducted the analysis, and wrote the manuscript. JRB conducted the analysis and revised the manuscript. JŠ, MS, JK, and PŠ all organized and supervised the data collection and revised the manuscript.

Funding Open access publishing supported by the National Technical Library in Prague. Czech Science Foundation Grant GA18-08512S funded this work.

Availability of data and material The data, R code, and Supplemental Materials are available at https://osf.io/dfrma/.

Declarations

Conflict of interest No potential conflict of interest was reported by the authors

Ethical approval and consent to participate The project was approved by the Research Ethics Committee of the Masaryk University (ref. no. EKV-2017-029-R1) and all participants provided a written informed consent.

Consent for publication The authors give their consent for this manuscript to be published in *Research in Psychotherapy: Psychopathology, Process and Outcome*.

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