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Self-Help for Medically Unexplained Symptoms: A Systematic Review and Meta-Analysis

Anne van Gils, MD, Robert A. Schoevers, MD, PhD, Irma J. Bonvanie, MD, Jeannette M. Gelauff, MD, Annelieke M. Roest, PhD, and Judith G.M. Rosmalen, PhD

ABSTRACT

Objective: Medically unexplained symptoms (MUS), which are highly prevalent in all fields of medicine, are considered difficult to treat. The primary objective of this systematic review and meta-analysis was to assess the efficacy of self-help for adults with MUS.

Methods: Four electronic databases were searched for relevant studies. Randomized controlled trials comparing self-help to usual care or waiting list in adults with MUS were selected. Studies were critically appraised using the Cochrane “risk of bias assessment tool.” Standardized mean differences (Hedges g) were pooled using a random-effects model. Outcomes were symptom severity and quality of life (QoL) directly posttreatment and at follow-up.

Results: Of 582 studies identified, 18 studies met all inclusion criteria. Studies were heterogeneous with regard to patient populations, intervention characteristics, and outcome measures. Compared with usual care or waiting list, self-help was associated with lower symptom severity (17 studies, $n = 1894$, $g = 0.58$, 95% confidence interval = 0.32–0.84, $p < .001$) and higher QoL (16 studies, $n = 1504$, $g = 0.66$, 95% confidence interval = 0.34–0.99, $p < .001$) directly posttreatment. Similar effect sizes were found at follow-up. A high risk of bias was established in most of the included studies. However, sensitivity analyses suggested that this did not significantly influence study results. Funnel plot asymmetry indicated potential publication bias.

Conclusions: Self-help is associated with a significant reduction in symptom severity and improvement of QoL. The methodological quality of included studies was suboptimal, and further research is needed to confirm the findings of this meta-analysis.

Key words: functional somatic symptoms, chronic fatigue syndrome, irritable bowel syndrome, fibromyalgia, somatoform disorders, self-administered.

INTRODUCTION

Medically unexplained symptoms (MUS) are physical symptoms that cannot be adequately explained by organic disease. MUS are highly prevalent and range from single, self-limiting complaints to constellations of chronic and disabling symptoms such as irritable bowel syndrome (IBS), fibromyalgia, and chronic fatigue syndrome (CFS) (1). Apart from the suffering and impairments these conditions impose on patients, they are also very costly for society due to the associated productivity losses and burden on health care (2–4). Patients with MUS visit their general practitioner, medical specialist, and emergency department approximately twice as often as other patients

(2), ranking their medical costs among the highest of all patient groups (4).

Physicians consider patients with chronic MUS among the most difficult patients (5), probably because treatment possibilities within somatic health care are limited (6). Psychological treatments such as cognitive behavioral therapy (CBT) have shown modest effects on symptom severity and quality of life (QoL) in patients with chronic MUS (7,8). However, psychological treatments are costly, time consuming, and often not easily available due to a shortage of

CFS = chronic fatigue syndrome, **IBS** = irritable bowel syndrome, **MUS** = medically unexplained symptoms, **QoL** = quality of life, **RCT** = randomized controlled trial, **WAD** = whiplash-associated disorder

SDC Supplemental Content

From the Interdisciplinary Center Psychopathology and Emotion regulation (ICPE) (van Gils, Schoevers, Bonvanie, Roest, Rosmalen) and Department of Neurology (Gelauff), University of Groningen, University Medical Center Groningen, Groningen, the Netherlands.

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qualified therapists. Furthermore, many patients with MUS are unwilling to visit a mental health professional because of the associated stigma (9). As a consequence, only a selected subgroup of patients with MUS benefits from psychological treatment. Self-help interventions, which are designed to be conducted largely independently of health care professionals, might overcome these problems and form a valuable addition to current treatment options. Self-help has shown to be effective for a number of conditions such as depression, anxiety, and alcohol abuse (10–12). Apart from three systematic reviews on specific forms of self-help for IBS (13–15), no overview has been published on the efficacy of self-help interventions for MUS in general.

Following the PRISMA statement (16), we report on a systematic review and meta-analysis of randomized controlled trials with the primary aim of assessing efficacy of self-help in adults with MUS with regard to symptom severity and QoL. Because we included a variety of MUS, investigating whether treatment efficacy varied according to the type of symptoms was a secondary aim. Studies in patients with depression and anxiety have indicated that guided self-help is associated with better outcomes than unguided self-help (17,18). Therefore, another secondary aim was to study the influence of therapist contact on treatment efficacy.

METHODS

Search Strategy

Relevant studies were identified by searching electronic databases and scanning reference lists of included articles and related reviews (13–15, 19–21). The following electronic databases were searched from their inception up to May 2014: PubMed, Embase, PsycINFO, and CINAHL. A combination of two sets of text words and indexing (MeSH) terms was used. The first set consisted of the terms MUS, IBS, fibromyalgia, CFS, somatoform disorder, somatization, conversion, and synonyms. In accordance with current recommendations, medical and psychiatric diagnostic concepts were incorporated in the search (22). The second set consisted of the terms self-help, self-management, self-care, self-administered, bibliotherapy, and synonyms (see Supplementary Text Document, Supplemental Digital Content 1, <http://links.lww.com/PSYMED/A281>, for exact search terms for each database). Where possible, a filter for randomized controlled trials was applied. To reduce risk of bias, searches were conducted without restrictions on language or publication date.

Study Selection

Two researchers (J.M.G. and A.G.) independently selected studies based on prespecified eligibility criteria. After removal of duplicates, articles that were identified through the literature search were screened for relevance on the basis of their title and abstract. Subsequently, full-text articles of potentially relevant studies were obtained and examined. During both stages, differences in study selection were resolved through consensus.

Inclusion Criteria

Studies were considered eligible if they were a) randomized controlled trials (RCTs) comparing the effects of b) a self-help intervention c) to a waiting list or usual care control condition d) in adults e) with MUS f) on symptom severity and QoL.

Self-help was defined as a therapeutic intervention, administered through text (printed or online), audio, or video, and conducted (largely)

independently of a health care professional. Guided self-help interventions with minimal therapist contact of facilitative or supportive nature were also considered. Self-help groups were typically excluded because these usually involved sharing experiences rather than independently working through an intervention based on text, audio, or video. MUS, were defined as physical symptoms that, after appropriate medical assessment, could not be (fully) explained by a medical disease. Because this definition of MUS is incorporated into the diagnostic criteria for syndromes such as IBS, fibromyalgia, and CFS, they were automatically included. If other diagnostic concepts or terms were used, the authors' judgment was followed to determine whether it concerned MUS. The nature of these symptoms may vary considerably. However, research has shown that substantial overlap exists between syndromes such as IBS, fibromyalgia, and CFS (23). Assuming that similarities between patients with MUS outweigh their differences, we decided to include a broad array of MUS and syndromes into our review.

Data Extraction

Data were extracted independently by two researchers (I.J.B. and A.G.) using standardized forms that were developed a priori. Disagreements were resolved by discussion. The following data were extracted from each article: study details (first author, publication year, and country), design, sample size (numbers randomized and analyzed), sample characteristics (inclusion and exclusion criteria, recruitment setting, mean age, percentage of women, symptom duration and severity, and comorbidity), type of intervention (form, theoretical basis, duration, amount of therapist contact) and comparison group (waiting list or care as usual), timing of follow-up assessments, dropout and compliance, outcome measures, adverse events, and effects (mean and standard deviation of symptom severity and QoL for intervention and control group directly posttreatment and—if available—at follow-up). Some studies did not report all of these outcome data. We contacted seven authors to obtain missing outcome data. All of them responded and five were able to provide all of the requested data.

Risk of Bias Assessment

Eligible studies were critically appraised using the Cochrane “risk of bias assessment tool” (24). This tool determines possible sources of bias in the reporting of RCTs in six domains: a) allocation sequence generation; b) allocation concealment; c) blinding of participants, personnel, and outcome assessors; d) management of incomplete outcome data; e) selective outcome reporting; and f) other sources of bias such as extreme baseline imbalances. Each of these criteria was separately rated as “met,” “unmet,” or “unclear” by two independent researchers (I.J.B. and A.G.), corresponding with a low, high, or unclear risk of bias in that domain. Disagreements were resolved through consensus.

Data Analysis

Effect Size Calculation

Outcomes of interest were symptom severity and QoL. Most of the included studies reported both of these outcomes with continuous measures. However, different measurement instruments were used. Also, few studies reported effect sizes, and those that did used different methods to calculate effect estimates. Therefore, standardized mean differences were calculated for each study (Cohen d = difference in posttreatment means between intervention and control group divided by the pooled standard deviation) (25). Because Cohen d has a slight bias that overestimates the effect size in small samples, d was multiplied by a correction factor J , resulting in the unbiased estimate referred to as Hedges g (25). For each outcome, we distinguished between posttreatment and follow-up assessments. This led to a maximum of four effect estimates per study: symptom severity posttreatment, symptom severity at follow-up, QoL posttreatment, and QoL at follow-up. Summary statistics used to calculate these estimates (means, standard deviations, and number of participants for treatment and control groups) can be obtained from the corresponding author on request. The sign of some scores was reversed to ensure all scales were aligned (e.g.,

for QoL high values representing good health on all scales). For two studies, standard deviations were calculated from the reported 95% confidence interval (CI) (26,27). For one study (28), continuous outcome data on symptom severity were not available, but the numbers of patients with persistent symptoms at several follow-up moments were. We used these data to calculate odds ratios and converted these, via Cohen *d*, to Hedges *g* (25). For another study, posttreatment QoL data were not available, but follow-up data were (29). We replaced the missing posttreatment effect estimate by the follow-up effect estimate of that study.

Meta-analysis

The precalculated effect estimates were pooled using STATA 13.1. Because of the heterogeneous nature of study populations and interventions, the DerSimonian and Laird random-effects method was chosen. The *I*² statistic was used as a measure of heterogeneity. This is the percentage of between-study heterogeneity that is attributable to variability in the true treatment effect, rather than sampling variation (30). Roughly, an *I*² > 75% represents considerable heterogeneity (24). For the interpretation of effect sizes, we followed the rule of thumb as proposed by Cohen: 0.20–0.49 is considered small, 0.50–0.79 medium, and >0.80 large (31). To assess the influence of the risk of bias of individual studies on treatment effects, sensitivity analyses were performed using three meta-regression analyses with different sources of bias (low or unclear versus high risk) as covariates. To explore the possibility of publication bias, the symmetry of funnel plots was assessed visually as well as formally with Egger test. To investigate whether treatment efficacy would differ depending on symptom type, meta-regression was used. Symptoms were divided into four categories: chronic pain (including fibromyalgia, whiplash-associated disorder [WAD], or back pain), IBS, CFS, and functional neurological symptoms. Dummies for these four symptom types were used in separate analyses to test whether one of these showed larger treatment effects compared with the other symptom types. In addition, subgroup analyses were performed to illustrate potential differences in effectiveness. Finally, we also used meta-regression to study the influence of therapist involvement (none versus some form of therapist

contact) on treatment efficacy. For all meta-regression analyses, posttreatment outcomes were used.

RESULTS

Study Selection

The process of study selection is presented in Figure 1. Searching four electronic databases provided 582 unique citations. Of these, 538 studies were discarded because, after reviewing their title and/or abstract, they did not meet our criteria. Full-text articles of the remaining 44 citations were examined. During this stage, another 28 articles were excluded, leaving 16 eligible studies. Two more studies were identified through reference lists, resulting in a total of 18 studies meeting all eligibility criteria.

Characteristics of Included Studies

An overview of study characteristics can be found in Table 1. All 18 included studies were RCTs published in English during the last decade. Most studies were performed in the United States (8/18), followed by the United Kingdom (3/18) and the Netherlands (3/18).

Participants

Most studies focused on patients with IBS (7/18) or chronic pain (fibromyalgia, WAD, or back pain; 7/18). Three studies involved patients with CFS and one study focused on patients with functional neurological symptoms. Sample size ranged from 28 to 405 participants. Participants were

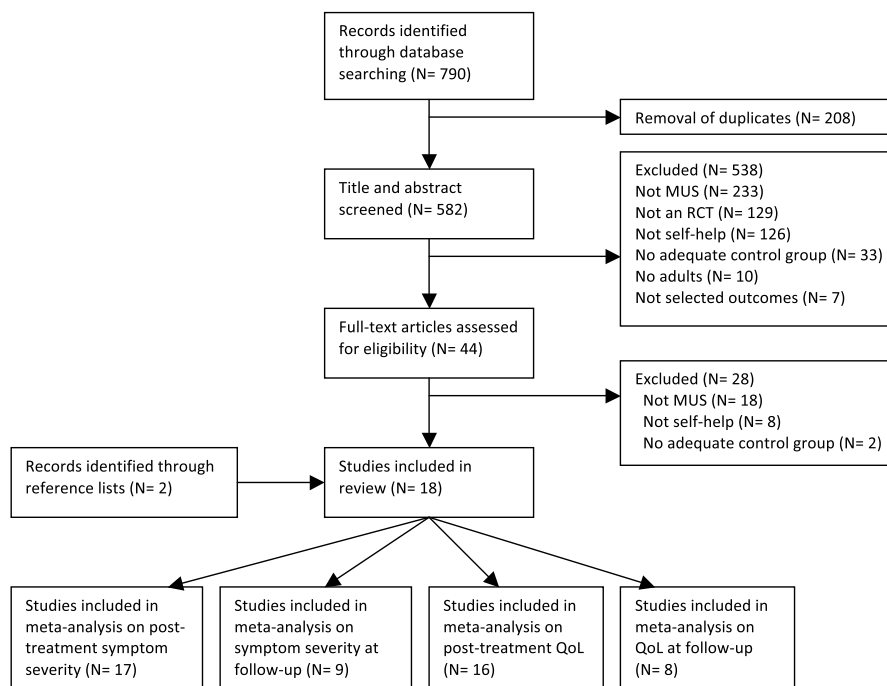


FIGURE 1. Flow diagram of study selection. MUS = medically unexplained symptoms; RCT = randomized controlled trial; QoL = quality of life.

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TABLE 1. General Characteristics of RCTs on Self-Help for MUS

| First Author, Year | N Randomized | Type of MUS | Recruitment Setting | Treatment Form | Theoretical Framework | Therapist Contact | Treatment Duration | Follow-up |
|--------------------------|-----------------|--------------|--|--------------------------------|-----------------------|---|--------------------|---------------------------|
| Bratberg, 2008 (32) | 86 | Fibromyalgia | Advertisements in newspaper and online discussion forums | Web site | EFT | E-mail contact 1 ×/wk | 8 wk | Posttreatment |
| Brison, 2005 (28) | 405 | WAD | Tertiary care (emergency departments) | Video | Educational | None | 20 min | 2, 6, 12, 24, and 52 wk |
| del Pozo-Cruz, 2012 (33) | 100 | Back pain | Advertisements | Web site with video | Educational | None | 9 mo | Posttreatment |
| Everitt, 2013 (26) | 135 | IBS | Primary care | Web site with video, and audio | CBT | 30 min telephone contact + e-mail support on request or technical e-mail support on request | 6 wk | Posttreatment and 12 wk |
| Friedberg, 2013 (34) | 73 ^a | CFS | Primary care | Booklet | CBT | Max. 2 × 1-h face-to-face contact | 3 mo | Posttreatment and 12 mo |
| Hunt, 2009 (35) | 54 | IBS | Online advertisements | Web site | CBT | E-mail contact 1 ×/wk | 5 wk | Posttreatment |
| Knoop, 2008 (36) | 171 | CFS | Tertiary care | Booklet | CBT | E-mail contact 1 ×/2 wk | ≥16 wk | Posttreatment |
| Lackner, 2008 (37) | 52 ^b | IBS | Secondary care (gastroenterology) and advertisements | Booklet | CBT | 4 × 1-h face-to-face + 2 × 10-min telephone contact | 10 wk | 12 wk |
| Lorig, 2008 (38) | NR ^c | Fibromyalgia | Advertisements Web sites, newsletters, and online forums | Web site | CBT | E-mail reminders | 6 wk | 6 and 12 mo |
| Menzies, 2006 (39) | 48 | Fibromyalgia | Secondary care | Audio | CBT: Guided imagery | None | 6 wk | Posttreatment and 10 wk |
| Moss-Morris, 2010 (29) | 64 | IBS | Primary care | Booklet | CBT | 1-h face-to-face + 2 × 1-h telephone contact | 7 wk | Posttreatment, 5 and 8 mo |
| Oerlemans, 2011 (27) | 76 | IBS | Advertisements IBS patient association | PDA | CBT | Feedback through text messages during 3 wk | 4 wk | Posttreatment and 3 mo |

Continued on next page

TABLE 1. (Continued)

| First Author, Year | N Randomized | Type of MUS | Recruitment Setting | Treatment Form | Theoretical Framework | Therapist Contact | Treatment Duration | Follow-up |
|---------------------|------------------|--------------|--|-------------------------------|-----------------------|--|--------------------|------------------------|
| Oliveira, 2006 (40) | 126 | WAD | Secondary care (emergency departments) | Video | Educational | None | 12 min | 1, 3, 6 mo |
| Robinson, 2006 (41) | 281 ^d | IBS | Primary care | Booklet | Educational | None | NR | 12 mo |
| Sanders, 2007 (42) | 28 | IBS | Secondary care (gastroenterology) and advertisements | Booklet | CBT | None | ≥10 wk | Posttreatment |
| Sharpe, 2011 (43) | 127 | Neurological | Secondary care (neurology) | Booklet | CBT | Max. 4 × 30-min face-to-face/telephone contact | 3 mo | Posttreatment and 6 mo |
| Tummers, 2012 (44) | 123 | CFS | Secondary care (psychiatry) | Booklet | CBT | E-mail contact 1 ×/2 wk | ≥20 wk | Posttreatment |
| Williams, 2010 (45) | 118 | Fibromyalgia | Primary and secondary care | Web site with video and audio | CBT | None | 6 mo | Posttreatment |

RCTs = randomized controlled trials; MUS: medically unexplained symptoms; EFT = Emotional Freedom Techniques; WAD = whiplash-associated disorder; IBS = irritable bowel syndrome; CBT = cognitive behavioral therapy; CFS = chronic fatigue syndrome; NR: not reported.

^a A total of 111 participants were randomized into three groups. For our analyses, we only included two groups (self-management and usual care).

^b A total of 75 participants were randomized into three groups. For our analyses, we only included two groups (minimal contact CBT and waiting list).

^c A total of 855 participants were randomized, but these are patients with different types of chronic pain, including rheumatoid arthritis and osteoarthritis. For the meta-analysis, we only included participants with fibromyalgia (no other rheumatologic conditions).

^d A total of 420 participants were randomized into three groups. For our analyses, we only included two groups (guidebook and control group).

predominantly female (58%–100%) and middle-aged (mean age = 36–52 years). Mean duration of symptoms was reported in approximately half of the studies and ranged from 4.5 to 16.5 years, suggesting that most participants had chronic MUS. Comorbidity, somatic and psychiatric, was rarely reported.

Interventions

Nearly all interventions contained educational elements. For some interventions, these were their main ingredient (5/18); for others, these formed the base for self-administered CBT (12/18). The study by Robinson et al. (41) is an example of a purely educational intervention. In this study, IBS patients were provided with a guidebook containing information about life-style, diet, pharmacological, and alternative therapies. In two other studies (28,40), patients presenting to an emergency department with a whiplash injury were shown a short educational video. The video provided information about expected duration of symptoms and advice on posture, return to regular activities, exercise, and pain-relief methods. This is somewhat similar to an online intervention (33), in which office workers with low back pain received daily e-mail reminders linked to information and videos on posture and physical exercise. Most studies, however, also included elements of CBT. The treatment components used in each of these studies are described in Table 2. One study investigated a specific component of CBT called “guided imagery.” Using audiotapes, participants were taught to “imagine and experience an internal reality in the absence of external stimuli” (39). Finally, Brattberg (32) examined the self-administration of “emotional freedom techniques” in patients with fibromyalgia. This intervention combines elements of cognitive therapy, acupuncture, and eye movement desensitization and reprocessing. It involves focusing on a disturbing memory, emotion, or sensation, while simultaneously tapping meridians, ending with a series of eye movements. Apart from the two studies in which treatment consisted of watching a single video (with a duration of 12–20 minutes), duration of treatment varied from 4 weeks to 9 months. Seven studies did not involve any therapist contact. In the remaining studies, various forms and quantities of therapist contact were incorporated.

Control

Six studies used a waiting list control group (32,35–37,42,44). In 11 studies, the control group received “care as usual” (27–29,33,34,38–41,43,45). Very few articles provided information on the nature or content of care as usual. Two studies described that patients in both groups received a factsheet containing information on their diagnosis and/or advice on managing their symptoms (29,40). Finally, one study had a slightly different control group (26). In this study, participants with IBS were randomized into nine

groups. Groups were based on a combination of self-help (no Web site, Web site, or Web site + e-mail support) and medication (bulk-forming laxative, antispasmodic, or placebo). Because these medications are commonly prescribed for IBS, we chose to consider these as “usual care” and divided the groups as follows: intervention (Web site and Web site + e-mail support) versus control (no Web site), regardless of the medication groups.

Outcomes

Although most studies included one or more follow-up assessments, seven studies only assessed outcomes directly posttreatment. Duration of follow-up ranged from 2 weeks to 1 year. All studies evaluated symptom severity as an outcome, but because different types of MUS were studied, different measurement instruments were used. Three of seven studies on IBS used the IBS symptom severity scale. The checklist individual strength was used to assess fatigue in two of three studies on CFS. Various instruments were used to assess pain. Seventeen studies evaluated QoL as an outcome, using a variety of instruments. Most instruments, for example, the IBS QoL questionnaire, which is used in 6 studies, evaluated several aspects of physical, mental, and/or social functioning. The 36-item Short Form Health Survey physical functioning scale was also a commonly used instrument (five studies). This is a subscale of the 36-item Short Form Health Survey, which specifically focuses on physical impairments due to health problems. None of the studies explicitly defined adverse events as an outcome. Occasionally, it was reported that no adverse events occurred in the intervention group (33,37,43).

Risk of Bias Within Studies

Because blinding of participants with regard to self-help interventions is impossible and nearly all studies used self-report measures, a high risk of bias in this domain (“blinding of participants, personnel, and outcome assessors”) was inevitable. Regarding the other five domains, a high risk of bias was established in 11 studies (Fig. 2). All of these 11 studies showed an imbalance in dropout rates across groups or did not adequately address missing outcome data. In addition, allocation sequence was not adequately generated and concealed in two studies. Two other studies had a high risk of bias due to selective outcome reporting: based on published protocols, we concluded that not all of their prespecified outcomes were reported.

Meta-regression showed that the risk of bias of included studies (low or unclear versus high) did not significantly influence our main results (see Supplementary Table, Supplemental Digital Content 2, <http://links.lww.com/PSYMED/A282>, for the results of sensitivity analyses). This applies to all relevant sources of bias: randomization, management of incomplete outcome data, and selective outcome reporting.

TABLE 2. Components of CBT-Based Self-Help Interventions

| | Everitt (26) | Friedberg (34) | Hunt (35) | Knoop (36) | Lackner (37) |
|--|--------------|----------------|-----------|------------|--------------|
| Education about physiology, diagnosis, possible precipitating and perpetuating factors, and/or treatment options | ✓ | ✓ | ✓ | ✓ | ✓ |
| Assessing symptoms, thoughts, feelings, and behaviors through daily diaries | ✓ | ✓ | | | ✓ |
| Goal setting | ✓ | | | ✓ | |
| Identifying and challenging unhelpful thoughts and beliefs | ✓ | ✓ | ✓ | ✓ | ✓ |
| Identifying avoidance behavior, exposure | | | ✓ | | |
| Identifying unhelpful activity patterns, scheduling activities and exercise | ✓ | ✓ | | ✓ | |
| Relaxation exercises | ✓ | | ✓ | | ✓ |
| Practicing a regular sleep pattern | ✓ | ✓ | | ✓ | |
| Practicing a regular, and healthy diet | ✓ | | | | |
| Problem solving | | | | | ✓ |
| Communicating about symptoms | | | | ✓ | |
| Relapse prevention, managing flare-ups | ✓ | ✓ | | ✓ | ✓ |

Publication Bias

Visual assessment and Egger test showed that the funnel plots for symptom severity (4.00, 95% CI = 0.34–7.66, $p = .03$) and QoL (5.22, 95% CI = 0.92–9.51, $p = .02$) displayed significant asymmetry (see Supplementary Figures, Supplemental Digital Content 3, <http://links.lww.com/PSYMED/A283>, for funnel plots).

Effect of Self-Help on Symptom Severity and QoL

Posttreatment outcome data on symptom severity were available for 17 studies, with a total of 2067 participants randomized and 1894 analyzed. Compared with control, self-help was associated with lower symptom severity ($g = 0.58$, 95% CI = 0.32–0.84, $p < .001$) directly posttreatment (Fig. 3). Strong evidence of heterogeneity was observed ($I^2 = 85\%$, 95% CI = 78–90%, $p < .001$). At follow-up, self-help was still associated with lower symptom severity compared with control (9 studies, $n = 922$, $g = 0.52$, 95% CI = 0.18–0.86, $p = .002$).

For QoL, posttreatment data from 16 studies were used, with a total of 1662 participants randomized and 1504 analyzed. Compared with control, self-help was associated with a higher QoL ($g = 0.66$, 95% CI = 0.34–0.99, $p < .001$), directly posttreatment (Fig. 4). Strong evidence of heterogeneity was observed ($I^2 = 89\%$, 95% CI = 83%–92%, $p < .001$). At follow-up, self-help was still associated with a higher QoL compared with control (8 studies, $n = 581$, $g = 0.73$, 95% CI = 0.25–1.21, $p = .003$).

Type of Symptoms

Meta-regression showed that the effect of self-help on symptom severity was not significantly influenced by symptom type. The effect of self-help on QoL was significantly larger in patients with chronic pain (fibromyalgia, WAD, and back pain) compared with other symptom types ($\beta = 1.00$, 95% CI = 0.23–1.77, $p = .02$).

Therapist Contact

Whether the interventions included some form of therapist contact did not significantly influence effects on symptom severity ($\beta = -0.22$, 95% CI = -0.90 to 0.47, $p = .51$) or QoL ($\beta = -0.77$, 95% CI = -1.59 to 0.04, $p = .06$).

DISCUSSION

This is the first study to quantify the effects of self-help interventions for various types of MUS. Meta-analysis showed that self-help significantly reduced symptom severity and improved QoL compared with usual care or waiting list. Overall, we found medium effect sizes. However, these should be interpreted with caution because statistical heterogeneity between studies was considerable.

This meta-analysis has several methodological strengths. Four databases were searched with broad selection criteria. To reduce risk of bias, searches were conducted without restrictions on language or publication date. Study selection, data extraction, and risk of bias assessment were conducted independently by two researchers. After obtaining missing data from the original researchers, we were able to use data

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| Lorig (38) | Moss-Morris (29) | Oerlemans (27) | Sanders (42) | Sharpe (43) | Tummers (44) | Williams (45) |
|------------|------------------|----------------|--------------|-------------|--------------|---------------|
| ✓ | ✓ | | ✓ | ✓ | ✓ | ✓ |
| ✓ | ✓ | ✓ | ✓ | ✓ | | |
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CBT = cognitive behavioral therapy.

| | |
|--|----------------------|
| | Low risk of bias |
| | Unclear risk of bias |
| | High risk of bias |

| | Random Sequence Generation | Allocation concealment | Blinding of Participants, Personnel, and Assessors | Incomplete Outcome Data | Selective Outcome Reporting | Other Sources of Bias |
|--------------------------|----------------------------|------------------------|--|-------------------------|-----------------------------|-----------------------|
| Brattberg, 2008 (36) | Low | Low | High | High | Low | Low |
| Brison, 2005 (28) | Low | Low | High | High | Low | Low |
| del Pozo-Cruz, 2012 (34) | Unclear | Unclear | High | High | High | Low |
| Everitt, 2013 (26) | Low | Unclear | High | Low | Low | Low |
| Friedberg, 2013 (42) | Low | Low | High | Low | Low | Low |
| Hunt, 2009 (37) | High | High | High | High | Low | Low |
| Knoop, 2008 (38) | Low | Low | High | Low | Low | Low |
| Lackner, 2008 (39) | Low | Low | High | Low | Low | Low |
| Lorig, 2008 (43) | Unclear | Low | High | High | Low | Low |
| Menzies, 2006 (35) | Low | Unclear | High | Low | Low | Low |
| Moss-Morris, 2010 (29) | Low | Low | High | Low | Low | Low |
| Oerlemans, 2011 (27) | Unclear | Unclear | High | High | High | Low |
| Oliveira, 2006 (33) | High | High | High | High | Low | Low |
| Robinson, 2006 (32) | Low | Low | High | Low | Low | Low |
| Sanders, 2007 (40) | Low | Low | High | Low | Low | Low |
| Sharpe, 2011 (44) | Low | Low | High | High | Low | Low |
| Tummers, 2012 (41) | Low | Low | High | Low | Low | Low |
| Williams, 2010 (45) | Low | Low | High | Low | Low | Low |

FIGURE 2. Assessment of risk of bias. Color image is available only in online version (www.psychosomaticmedicine.org).

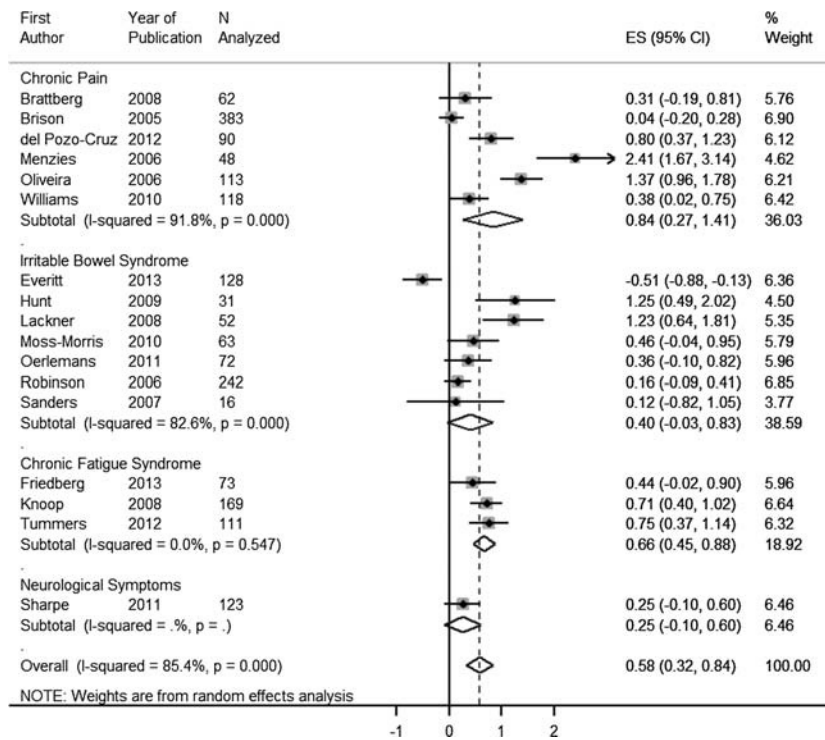


FIGURE 3. Forest plot showing effects of self-help on symptom severity ($n = 1894$). Markers represent point estimates of standardized mean differences; marker size represents study weight in random-effects meta-analysis. Horizontal bars indicate 95% CIs. Results are stratified by type of symptom. ES = effect size; CI = confidence interval.

from all of the 18 studies that were identified during the systematic literature review. Although we included a substantial number of studies into our meta-analysis, it should be taken into account that heterogeneity between these studies with regard to patient populations, intervention characteristics, and outcome measures was substantial. Specifically, the variety in QoL outcome measures has to be considered an important limitation. Although most studies used instruments that assess several aspects of QoL, others used specific subscales assessing, for example, only physical functioning. Like for most meta-analyses, the results of our study are also limited by possible biases in included studies. First, the inevitable lack of blinding of participants causes a possible bias in all included studies. Furthermore, a high risk of bias in other domains was established in 11 studies (61%). These studies might have overestimated treatment effects because of inappropriate randomization and selective outcome reporting, or because incomplete outcome data were not adequately addressed. However, sensitivity analyses showed that our main results were not significantly influenced by the risk of bias of individual studies. We also assessed potential publication bias. Asymmetrical funnel plots suggested that selective reporting might have led to an overestimation of effect sizes in small trials.

In addition to three systematic reviews demonstrating positive effects of “minimal contact” psychological treatments for patients with IBS (13–15), we have shown that

a broad array of self-help interventions reduces symptom severity and improves QoL in patients with different types of MUS. The effect sizes we found were larger than those found for conventional psychotherapies. A recent Cochrane review on psychological treatments for MUS and somatoform disorder demonstrated small effect sizes for symptom severity ($d = 0.34$, 95% CI = 0.16–0.53) and QoL ($d = 0.17$, 95% CI = 0.03–0.32) (8). Similar results were found by another recent meta-analysis on psychotherapy for MUS (7). We found medium effect sizes for both outcomes ($g = 0.58$ [95% CI = 0.32–0.84] and $g = 0.66$ [95% CI = 0.34–0.99]). This difference might be explained by the stricter inclusion criteria of those meta-analyses, resulting in patients with more severe symptoms and disabilities. Thus, self-help might be a useful additional treatment option, especially for patient with less severe, chronic, and debilitating symptoms.

Considerable heterogeneity in treatment effects was observed. We investigated two factors that might explain this heterogeneity. First, we explored the role of the type of symptoms. We found that the impact of self-help on symptom severity did not differ according to symptom type. However, the effect of self-help on QoL was larger in patients with chronic pain compared with other symptom types. Second, we explored the role of therapist contact. In our study, the level of therapist contact did not influence treatment outcomes. This contradicts the findings of studies on self-help in patients with depression and anxiety, for

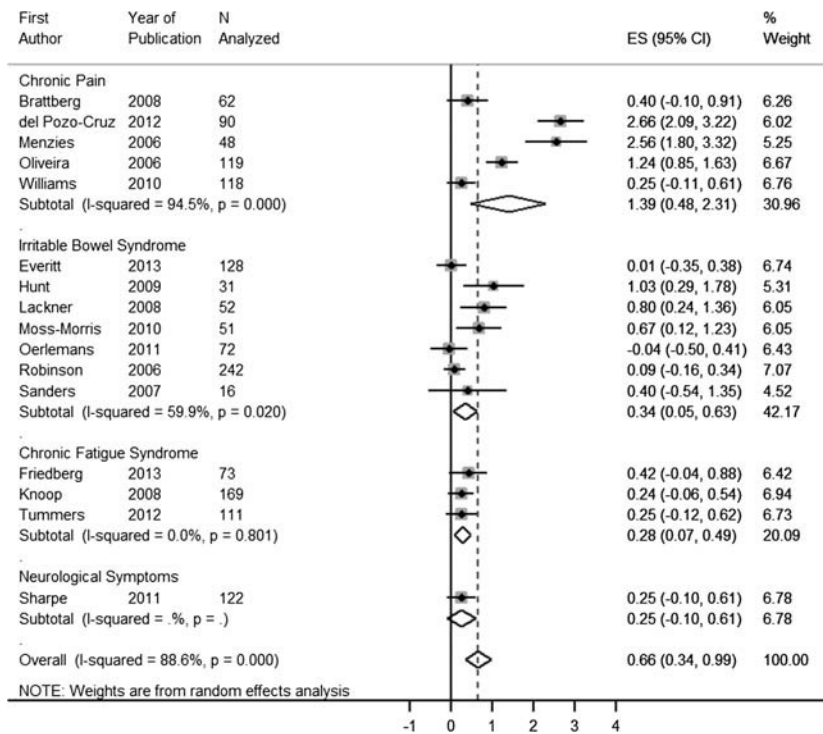


FIGURE 4. Forest plot showing effects of self-help on quality of life ($n = 1504$). Markers represent point estimates of standardized mean differences; marker size represents study weight in random-effects meta-analysis. Horizontal bars indicate 95% CIs. Results are stratified by type of symptom. ES = effect size; CI = confidence interval.

which guided self-help was found to be superior to unguided interventions (17,18). This inconsistency might be explained by differences in study populations; patients with depression or anxiety disorders may have lower intrinsic motivation, which increases the additional value of therapist guidance. Other factors that might explain heterogeneity of treatment effects are differences in study populations, such as the duration of complaints; differences in the form, content, duration, and intensity of interventions; differences in the content and amount of care that is received in (usual care) control conditions; and differences in the duration of follow-up. Unfortunately, because of the relatively small number of included studies, it was not possible to explore the role of these factors using statistical analyses. Further research will have to show which patients benefit most from self-help and which characteristics and elements of self-help interventions are associated with the best outcomes.

In conclusion, self-help is a promising form of treatment for patients with MUS. Especially when offered online, self-help can be made widely available at relatively low costs. Unguided, Internet-based interventions might be implemented in primary care as a first step in a stepped care approach (46). If symptoms persevere, self-administered CBT with minimal therapist contact might offer an alternative to psychotherapy for patients who are unwilling or unable to visit a mental health care facility. Because the

quality of research designs and reporting of included studies was far from optimal, further research is needed to confirm the findings of this study. To ensure transparency and consistency in the reporting of trials, the CONSORT statement and checklist should be followed (47). The content of intervention and control conditions should be described in detail. Furthermore, future studies should use uniform and validated measurement instruments. We strongly recommend the use of intention-to-treat analyses instead of completers-only analyses. Also, follow-up assessments are encouraged to study long-term effects of self-help interventions. Furthermore, future research should focus on the effectiveness of self-help in various clinical care settings and identification of moderators to optimize treatment effects and overcome potential barriers for implementation.

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REFERENCES

- Burton C. Beyond somatisation: a review of the understanding and treatment of medically unexplained physical symptoms (MUPS). *Br J Gen Pract* 2003;53:231–9.
- Barsky AJ, Orav EJ, Bates DW. Somatization increases medical utilization and costs independent of psychiatric and medical comorbidity. *Arch Gen Psychiatry* 2005;62:903–10.
- Konnopka A, Schaefer R, Heinrich S, Kaufmann C, Lupp A, Herzog W, König HH. Economics of medically unexplained symptoms: a systematic review of the literature. *Psychother Psychosom* 2012;81:265–75.
- Zonneveld LN, Sprangers MA, Kooiman CG, van 't Spijker A, Busschbach JJ. Patients with unexplained physical symptoms have poorer quality of life and higher costs than other patient groups: a cross-sectional study on burden. *BMC Health Serv Res* 2013;13:520.
- Hahn SR, Kroenke K, Spitzer RL, Brody D, Williams JB, Linzer M, deGruy FV 3rd. The difficult patient: prevalence, psychopathology, and functional impairment. *J Gen Intern Med* 1996;11:1–8.
- Kleinstaub M, Witthoft M, Steffanowski A, van Marwijk H, Hiller W, Lambert MJ. Pharmacological interventions for somatoform disorders in adults. *Cochrane Database Syst Rev* 2014;11:CD010628.
- Kleinstaub M, Witthoft M, Hiller W. Efficacy of short-term psychotherapy for multiple medically unexplained physical symptoms: a meta-analysis. *Clin Psychol Rev* 2011;31:146–60.
- Van Dessel N, Den Boeft M, van der Wouden JC, Kleinstaub M, Leone SS, Terluin B, Numans ME, van der Horst HE, van Marwijk H. Non-pharmacological interventions for somatoform disorders and medically unexplained physical symptoms (MUPS) in adults. *Cochrane Database Syst Rev* 2014;11:CD011142.
- Freidl M, Spitzl SP, Prause W, Zimprich F, Lehner-Baumgartner E, Baumgartner C, Aigner M. The stigma of mental illness: anticipation and attitudes among patients with epileptic, dissociative or somatoform pain disorder. *Int Rev Psychiatry* 2007;19:123–9.
- Lewis C, Pearce J, Bisson JI. Efficacy, cost-effectiveness and acceptability of self-help interventions for anxiety disorders: systematic review. *Br J Psychiatry* 2012;200:15–21.
- Riper H, Spek V, Boon B, Conijn B, Kramer J, Martin-Abello K, Smit F. Effectiveness of E-self-help interventions for curbing adult problem drinking: a meta-analysis. *J Med Internet Res* 2011;13:e42.
- Cuijpers P, Donker T, Johansson R, Mohr DC, van Straten A, Andersson G. Self-guided psychological treatment for depressive symptoms: a meta-analysis. *PLoS One* 2011;6:e21274.
- Ahl A, Mikocka-Walus A, Gordon A, Andrews JM. Are self-administered or minimal therapist contact psychotherapies an effective treatment for irritable bowel syndrome (IBS): a systematic review. *J Psychosom Res* 2013;75:113–20.
- Dorn SD. Systematic review: self-management support interventions for irritable bowel syndrome. *Aliment Pharmacol Ther* 2010;32:513–21.
- Pajak R, Lackner J, Kamboj SK. A systematic review of minimal-contact psychological treatments for symptom management in irritable bowel syndrome. *J Psychosom Res* 2013;75:103–12.
- Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *J Clin Epidemiol* 2009;62:1006–1012.
- Spek V, Cuijpers P, Nyklicek I, Riper H, Keyzer J, Pop V. Internet-based cognitive behaviour therapy for symptoms of depression and anxiety: a meta-analysis. *Psychol Med* 2007;37:319–28.
- Palmqvist B, Carlbring P, Andersson G. Internet-delivered treatments with or without therapist input: does the therapist factor have implications for efficacy and cost? *Expert Rev Pharmacoecon Outcomes Res* 2007;7:291–7.
- Beatty L, Lambert S. A systematic review of Internet-based self-help therapeutic interventions to improve distress and disease-control among adults with chronic health conditions. *Clin Psychol Rev* 2013;33:609–22.
- Du S, Yuan C, Xiao X, Chu J, Qiu Y, Qian H. Self-management programs for chronic musculoskeletal pain conditions: a systematic review and meta-analysis. *Patient Educ Couns* 2011;85:e299–310.
- Macea DD, Gajos K, Daglia Calil YA, Fregni F. The efficacy of Web-based cognitive behavioral interventions for chronic pain: a systematic review and meta-analysis. *J Pain* 2010;11:917–29.
- Schröder A, Sharpe M, Fink P. Medically unexplained symptom management. *Lancet Psychiatry* 2015;2:587–8.
- Wessely S, Nimnuan C, Sharpe M. Functional somatic syndromes: one or many? *Lancet* 1999;354:936–9.
- Higgins JPT, Green S. *Cochrane handbook for systematic reviews of interventions*. Version 5.0.1 [updated March 2011]. Oxford: The Cochrane Collaboration; 2008.
- Borenstein M, Hedges LV, Higgins JPT, Rothstein HR. *Introduction to Meta-Analysis*. Chichester: Wiley; 2009.
- Everitt H, Moss-Morris R, Sibelli A, Tapp L, Coleman N, Yardley L, Smith P, Little P. Management of irritable bowel syndrome in primary care: the results of an exploratory randomised controlled trial of mebeverine, methylcellulose, placebo and a self-management Web site. *BMC Gastroenterol* 2013;13.
- Oerlemans S, van Cranenburgh O, Herremans PJ, Spreeuwenberg P, van Dulmen S. Intervening on cognitions and behavior in irritable bowel syndrome: a feasibility trial using PDAs. *J Psychosom Res* 2011;70:267–77.
- Brisson RJ, Hartling L, Dostaler S, Leger A, Rowe BH, Stiell I, Pickett W. A randomized controlled trial of an educational intervention to prevent the chronic pain of whiplash associated disorders following rear-end motor vehicle collisions. *Spine* 2005;30:1799–807.
- Moss-Morris R, McAlpine L, Didsbury LP, Spence MJ. A randomized controlled trial of a cognitive behavioural therapy-based self-management intervention for irritable bowel syndrome in primary care. *Psychol Med* 2010;40:85–94.
- Harris R, Bradburn M, Deeks J, Harbord R, Altman D, Sterne J. *Metan: fixed- and random-effects meta-analysis*. *Stata J* 2008;8:3–28(26).
- Cohen J. *Statistical Power Analysis for the Behavioral Sciences*, Hillsdale, NJ: L. Erlbaum Associates; 1988.
- Brattberg G. Self-administered EFT (Emotional Freedom Techniques) in individuals with fibromyalgia: a randomized trial. *Integr Med* 2008;30–5.
- del Pozo-Cruz B, Parraca JA, del Pozo-Cruz J, Adsuar JC, Hill J, Gusi N. An occupational, Internet-based intervention to prevent chronicity in subacute lower back pain: a randomized controlled trial. *J Rehabil Med* 2012;44:581–7.
- Friedberg F, Napoli A, Coronel J, Adamowicz J, Seva V, Caikauskaitė I, Ngan MC, Chang J, Meng H. Chronic fatigue self-management in primary care: a randomized trial. *Psychosom Med* 2013;75:650–7.

35. Hunt MG, Moshier S, Milonova M. Brief cognitive-behavioral Internet therapy for irritable bowel syndrome. *Behav Res Ther* 2009;47:797–802.
36. Knoop H, Van Der Meer JWM, Bleijenberg G. Guided self-instructions for people with chronic fatigue syndrome: randomised controlled trial. *Br J Psychiatry* 2008; 193:340–1.
37. Lackner JM, Jaccard J, Krasner SS, Katz LA, Gudleski GD, Holroyd K. Self-administered cognitive behavior therapy for moderate to severe irritable bowel syndrome: clinical efficacy, tolerability, feasibility. *Clin Gastroenterol Hepatol* 2008;6: 899–906.
38. Lorig KR, Ritter PL, Laurent DD, Plant K. The Internet-based arthritis self-management program: a one-year randomized trial for patients with arthritis or fibromyalgia. *Arthritis Care Res* 2008;59:1009–17.
39. Menzies V, Taylor AG, Bourguignon C. Effects of guided imagery on outcomes of pain, functional status, and self-efficacy in persons diagnosed with fibromyalgia. *J Altern Complement Med* 2006;12:23–30.
40. Oliveira A, Gevirtz R, Hubbard D. A psycho-educational video used in the emergency department provides effective treatment for whiplash injuries. *Spine (Phila Pa 1976)* 2006; 31:1652–7.
41. Robinson A, Lee V, Kennedy A, Middleton L, Rogers A, Thompson DG, Reeves D. A randomised controlled trial of self-help interventions in patients with a primary care diagnosis of irritable bowel syndrome. *Gut* 2006;55:643–8.
42. Sanders KA, Blanchard EB, Sykes MA. Preliminary study of a self-administered treatment for irritable bowel syndrome: comparison to a wait list control group. *Appl Psychophysiol Biofeedback* 2007;32:111–9.
43. Sharpe M, Walker J, Williams C, Stone J, Cavanagh J, Murray G, Butcher I, Duncan R, Smith S, Carson A. Guided self-help for functional (psychogenic) symptoms: a randomized controlled efficacy trial. *Neurology* 2011;77:564–72.
44. Tummers M, Knoop H, van Dam A, Bleijenberg G. Implementing a minimal intervention for chronic fatigue syndrome in a mental health centre: a randomized controlled trial. *Psychol Med* 2012;42:2205–15.
45. Williams DA, Kuper D, Segar M, Mohan N, Sheth M, Clauw DJ. Internet-enhanced management of fibromyalgia: a randomized controlled trial. *Pain* 2010;151:694–702.
46. Henningsen P, Zipfel S, Herzog W. Management of functional somatic syndromes. *Lancet* 2007;369:946–55.
47. Schulz KF, Altman DG, Moher D, CONSORT Group. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. *Int J Surg* 2010;9:672–7.