

ORIGINAL REPORT

EFFECTS OF ADDITIONAL INDIVIDUALLY TAILORED INTERVENTIONS ON SICK-LEAVE AND SYMPTOMS IN PATIENTS WITH EXHAUSTION DISORDER: A RANDOMIZED CONTROLLED TRIAL

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Objective: To evaluate the effects of adding individually tailored interventions to a standard treatment in patients with stress-related exhaustion disorder, with regard to sick-leave days and symptoms of burnout. The study design was a 2-armed randomized controlled intervention, with follow-up after 15 months. Data were obtained from patients referred to the Institute of Stress Medicine, and were collected between 2011 and 2014 in western Sweden.

Methods: Inclusion criteria were scoring above cut-off in at least 1 of 4 dimensions; mental and physical exhaustion, disturbed sleep, reduced cognitive function and perceived poor self-esteem. The total study population comprised 142 patients (112 females, 30 males) allocated through block randomization to either the intervention group ($n = 71$) or the control group ($n = 71$). The intervention group received 1–4 individually tailored interventions (physical activity, cognitive behaviour therapy for insomnia, computerized memory training, cognitive behavioural therapy for self-esteem), based on the results of screening assessments. The interventions were additional to a standard treatment. The control group received solely the standard treatment. The primary outcome measure was the proportion of participants not sick-listed at the 15-month follow-up.

Results: At the 15-month follow-up, 30% of subjects in the intervention group and 34% in the control group had 0% sick-listed ($p = 0.58$). No change between baseline and follow-up was seen in 42% of the intervention group and 39% of the control group, while an increased sick-leave rate was seen in 1% of the intervention group and 4% of the control group. However, no statistically significant difference was seen between groups.

Conclusion: Adding individually tailored interventions to a standard treatment in patients with stress-related exhaustion did not reduce sick-leave days or burnout symptoms.

Key words: stress-related exhaustion; randomized controlled trial; work-related stress; rehabilitation; mental health disorder; sick-leave; burnout symptoms.

Accepted: May 31, 2022; Epub ahead of print: July 8, 2022

LAY ABSTRACT

The aim of this randomized controlled study was to investigate whether individually tailored interventions, added to a standard treatment for patients diagnosed with stress-related exhaustion, could reduce sick-leave and symptoms of burnout more in the intervention group than in a control group. Patients were allocated randomly into either the intervention group or a control group. To be included in the study patients had to score above cut-off in 1 or more of the core dimensions characterizing stress-related exhaustion, mental and physical exhaustion, disturbed sleep, cognitive decline, or perceived poor self-esteem. Patients assigned to the intervention group received additional interventions as well as a standard treatment, while the control group received only standard treatment. The results showed no major differences between the intervention group and the control group, with respect to either sick-leave and symptoms of burnout at the 15-month follow-up. The clinical implication from this study is that individually tailored interventions added to the standard treatment are inefficient in reducing both sick-leave days and burden of disease in this patient group, and should be accompanied by interventions targeting the workplace and the work organization level.

J Rehabil Med: jrm00321

DOI: 10.2340/jrm.v54.2941

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Stress-related mental health disorders are a challenge in contemporary society and have a profound impact on health and work ability throughout all stages of life (1). Within the large group of people affected by these disorders is a subgroup of individuals with such pronounced symptom severity that contact with the healthcare sector is required. Some of these patients are diagnosed with exhaustion disorder (ED), which, since 2005, has been an established clinical diagnosis in Sweden under code F43.8A of the 10th revision of the International Classification of Diseases and Related

Health Problems (ICD-10). This disorder is characterized by a variety of symptoms, including extreme physical and mental fatigue, sleep disturbance, cognitive impairment, and reduced stress tolerance, often in combination with symptoms of depression, anxiety, and somatic symptoms such as non-generalized musculoskeletal pain, chest pain, and gastrointestinal problems (2, 3). The exposure leading to ED mostly originates from work-related factors, but exposures in subjects' private lives are also present (4). Moreover, it has recently been shown that patients diagnosed with ED have longer sick-leave duration than those diagnosed with other stress-related disorders (1).

The increased prevalence of ED, mostly among the working population, seems to be an important reason behind the generally increased sick-leave due to mental disorders in Sweden (1). Given the long duration of sick-leave and the heavy burden of disease connected to ED (5), effective treatments and interventions are urgently needed. Most of the interventions performed to date have been oriented towards the individual, with the most common treatments being cognitive-behavioural therapy (CBT) and different stress-management programmes. However, the results from these studies have indicated only minor effects on symptoms, and poor or no effects on sick-leave and return to work (RTW) (6–8). Several aspects have been suggested as possible reasons for the poor outcome of the comprehensive interventions used in earlier studies. Firstly, the patient groups studied have, in many cases, been heterogeneous with respect to symptom severity, sick-leave, and workplace context, making it difficult to draw generalized conclusions about the effectiveness of the interventions. This heterogeneity in study populations might be due to the difficulty of using the diagnostic criteria in clinical practice, leading to an uncertainty among medical doctors regarding differential diagnostics with other stress-related diagnoses, such as adjustment disorders and reactions to long-lasting severe stress. It seems reasonable to believe that these different patient groups also need different treatment strategies, and thus the problematic diagnostic procedure in clinical practice constitutes part of the heterogeneity problem.

The strategy for treatment of ED in general, regarding content, volume, timing, and duration, has been questioned. Thus, this study was particularly designed to evaluate whether adding extra treatment, focused on each patient's individual needs, to a basic standard treatment could result in higher effectiveness of the intervention with respect to both sick-leave and symptom reduction. Hence, the overall aim of this study was to systematically evaluate the effect of an additional individually tailored intervention in patients diagnosed with ED.

Specific research questions for the study were as follows:

- Is there a difference in sick-leave (defined as being on sick-leave or not), between the intervention group and the control group at the 15-month follow-up?
- Is there a difference in the total number of sick-leave days between the intervention group and the control group during the 15-month follow-up period?
- Is there a difference in part-time sick-leave (25%, 50%, 75%) between the intervention group and the control group at the 15-month follow-up?
- Is there a difference in reported symptoms of burn-out between the intervention group and the control group at the 15-month follow-up?

METHODS

Study design

The study was designed around a 2-armed randomized controlled intervention with follow-up after 15 months. Patients were recruited from the Institute of Stress Medicine (ISM) in Gothenburg, a clinic specialized in diagnosing and treating patients with ED. The included patients were referred to ISM from public primary care units, occupational healthcare centres, and private general practitioners in the western part of Sweden between May 2011 and August 2014. Inclusion criteria for being a patient at the clinic were: confirmed ED and at least 25% ongoing sick-leave due to symptoms of ED. Exclusion criteria were complicating somatic disorders (untreated), severe psychiatric disorders other than ED, depression and anxiety disorders, alcohol or drug abuse, and sick-leave duration longer than 6 months before the first visit to the clinic. Extended anamnesis and clinical examination were performed at the first visit by experienced physicians, to verify and set the diagnosis. The Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition—DSM-IV-based instrument Primary Care Evaluation of Mental Disorders (PRIME-MD) (a single-page patient questionnaire) was used to diagnose concurrent and relevant comorbidity, such as depression and/or anxiety disorders. A 2-step procedure was applied for inclusion into the intervention study. During the first step, immediately after the first visit to the clinic, all patients received a standard treatment elaborated in line with our clinical experience and offered to all patients referred to the clinic. During the second step, 3 months after their first appointment, all included patients were assessed by means of validated methods regarding symptoms of burnout, sleep disturbances cognitive function, and

perceived self-esteem. To be eligible for the intervention, patients had to score above cut-off for 1 or more of these 4 dimensions. These critical dimensions had previously been identified as crucial factors for sustainable recovery and return to work, both in other studies and in a clinical pilot study performed by our research group prior to the current study (9, 10). The assessments were performed according to specific protocols, which are described in detail below. Cut-off levels for each critical dimension were set in line with earlier research and clinical practice. It was thus possible to participate in more than 1 intervention. However, in these cases, the research nurse decided in consultation with each patient in which order the interventions should take place to avoid treatment overload. To discriminate differences in burden of disease due to comorbidity at baseline, the widely used Hospital Anxiety and Depression Scale (HADS) was used (11). A timeline for the study procedure is shown in Fig. 1.

Measures

Symptoms of burnout (mental and physical exhaustion). Symptoms of burnout were measured with the Shirom-Melamed Burnout Questionnaire (SMBQ) (12). Here we used it to target symptoms of mental and physical exhaustion. We used the 18-item scale, in line with modern measurement standards as recommended by Lundgren-Nilsson et al (13). A score of ≥ 4.4 was set as the cut-off for being eligible to the intervention part of the study. Patients scoring above the cut-off and allocated to the intervention group received additional graded physical activity, which is described in detail further below.

Another way to be allocated to graded physical activity was to score ≤ 20 on the vitality dimension of the 36-item Short Form Survey (SF-36) (14). The responses to SF-36 were interpreted and evaluated using the manual by Sullivan et al. (15).

A third way of being allocated to additional graded physical activity was to score > 20 on the Mental Fatigue Scale (MFS) (16). This criterion was chosen because both our clinical experience from this patient group and

a systematic review (17) have indicated a relationship between mental fatigue and physical performance.

Sleep disturbance. Sleeping problems and sleep quality were measured with the well-established and validated Karolinska Sleep Questionnaire (KSQ) (18). This questionnaire covers different domains of sleep, sleepiness, and recovery, with the questions in each domain being used to form an index. This study used the insomnia index, which includes 4 items: difficulty sleeping, repeated awakenings during the night with subsequent difficulty falling asleep again, early waking in the morning, and generally disturbed sleep during the night. To be allocated to cognitive group therapy for sleep disturbances (“Sleeping school”), patients had to respond, “almost always” or “always” to at least 1 of the questions included in the insomnia index, and “poor” or “very poor” to the single-item question “How do you perceive your overall sleep?”

Self esteem. Perceived self-esteem was assessed using the Rosenberg Self-Esteem Scale (19), which produces a score ranging from 0 to 30. In this study, a score < 15 was used as a cut-off for being allocated to additional cognitive therapy for self-esteem. This cut-off was chosen based on clinical experience within the research team and the results from an earlier study among patients diagnosed with clinical burnout (10).

Cognitive function. Parts of the MFS were used to measure cognitive function. The cut-off to be allocated to the additional memory training was to score ≥ 2.5 (penultimate response alternative) on at least 2 of the following questions on the MFS:

- Does your brain become fatigued quickly when you must think hard? Do you become mentally fatigued from things such as reading, watching television, or taking part in a conversation with several people?
- If you must take a break, how long do you need to recover after you have worked “until you drop” or are no longer able to concentrate on what you are doing?
- Do you find it difficult to gather your thoughts and concentrate?
- Do you forget things more often than before; do you need to make notes, or do you have to search for things at home or at work?

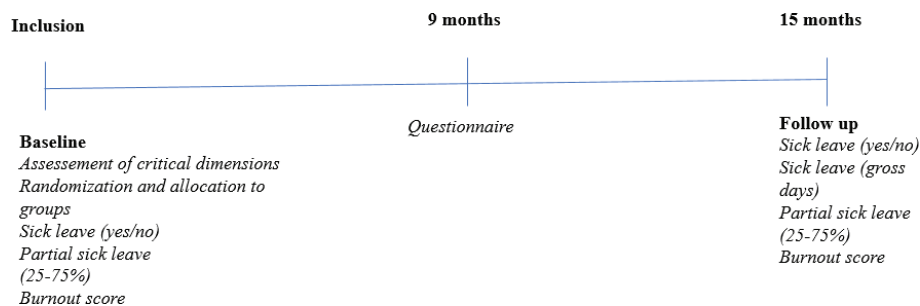


Fig. 1. Study time-line. Starting points for the intervention/interventions were individually adjusted.

- Do you feel slow or sluggish when you think about something? Do you feel that it takes an unusually long time to conclude a train of thought or solve a task that requires mental effort?

Interventions

Standard treatment. This treatment consisted of several components, including a comprehensive educational package aimed at increasing the patient's knowledge and understanding of both acute and long-lasting stress reactions involving mental, physical, and behavioural reactions. Moreover, core symptoms and functional difficulties connected to ED were discussed in combination with a wide-ranging knowledge about the impact of different exposures, work-related and private factors for the onset and severity of symptoms of ED, and corresponding decrease in self-perceived work ability. The influence of moderating lifestyle factors was also covered, including work–life balance and a well-structured everyday life in general, with specific reference to meals, sleep pattern, and regular physical activity. These issues were discussed during frequent appointments with the physician, psychologist, and/or physiotherapist. In addition, all patients were invited to join a stress-reduction programme comprising 7 group sessions lasting 1.5 h each. Psychological treatment and/or appropriate medication for concurrent comorbidity, such as depression and anxiety disorders were offered with respect to the different needs of each patient. Finally, people close to the patient (i.e. spouse, parents, friends), were offered group-based information about the disease and the consequences of the disease for everyday life. In some cases, on the initiative of the patients, employers and colleagues received the same information.

Physical activity. The individually adapted physical activity programme was based on a concept for graded activity used and evaluated at the clinic (20). Patients in the intervention group who scored above the cut-off for any of the instruments used to detect mental fatigue and exhaustion received the above-mentioned programme including individual information about the positive effects of graded physical activity through weekly coaching sessions during the first 4–6 weeks (based on individual needs) of the intervention. The coaching support was carried out by 2 specially trained physiotherapists through telephone calls in which an individually tailored and scheduled recommendation regarding the dose of physical activity was launched. All participants in the physical activity programme were offered fitness tests in connection with the baseline assessments and at both follow-ups.

Cognitive behaviour therapy for insomnia. Patients in the intervention group with verified sleep disturbance according to the assessments received group-

based CBT for insomnia. This specialized CBT was developed in Stockholm, Sweden, and has been successfully used in clinical practice for several years as part of a multimodal treatment for patients with sleep disturbance and stress-related disorders (21). The treatment is divided into 7 group sessions spread over a period of 11 weeks. The first session lasts 2.5 h, and the 6 remaining sessions last 2 h each. Sleep registrations and individually adjusted “homework” were important parts of the intervention during the whole treatment period. The main aims of the intervention were to change the participants' attitudes towards their insomnia, to make them aware of how behaviours and feelings about sleeping problems influenced their sleep patterns, and to use discussions and reflections to enable interactions between the group members to facilitate a more favourable sleep pattern.

Computerized memory training (ReMemo). Patients in the intervention group who scored above the cut-off for decline in cognitive function received a computerized training programme (ReMemo) aimed at improving different dimensions of cognitive function through comprehensive daily training. This method was originally developed by Klingberg et al. for use in children with neuropsychological disorders (22), but has also been used for patients with brain injuries, which have effects on cognitive function, such as those apparent in ED (23).

Cognitive behavioural treatment for self-esteem. Patients in the intervention group who were assessed as having poor self-esteem participated in a cognitive psychotherapy treatment developed especially for this study. This manual-based therapy was predominantly aimed at addressing poor self-esteem, but parallel treatment effects were expected regarding symptoms of depression and anxiety, as shown in an earlier study (24). The CBT included 10 individual sessions, each lasting 60 min. The first 5 sessions were conducted once a week and the remaining 5 sessions were conducted every 2 weeks. The rationale for this procedure was to give more time for practice during the second part of the therapy. The patients were given a workbook for writing down their reflections and their own experiences, and to help them recollect previous sessions. The decreased cognitive function among patients with ED was taken into consideration, and so the workbook contained pictures, figures, many spaces, and very short texts to facilitate its use. Another advantage of both the manual and the workbook was that they helped to make the standard procedure more reproducible.

Randomization

Block randomization with random allocation rule was used to ensure the same number of patients in

each group. The randomization procedure was done as follows. First, 142 sealed envelopes were placed in a box. Half of the envelopes contained a paper where it was written “control” and the other half contained a paper note “intervention”. Every time a patient was eligible for the study, a sealed envelope was drawn by a research nurse from the box and not replaced into the box again (random sampling without replacement). The procedure was repeated until all patients were allocated in both groups.

Outcomes

Primary outcome measures. The primary outcome measures were differences in sick-leave between the intervention group and the control group, defined as yes/no sick-leave at the 15 months follow-up compared with baseline, and differences between the groups with respect to number of registered sick-leave days, both gross (number of sick days, irrespective of the extent of sick-leave) and net (number of sick days converted into whole days) during the 15 months following the baseline measurement. Data were obtained from the Swedish Social Insurance Agency (SSIA) Micro Database for Analysing Social Insurance (MIDAS).

Secondary outcome measures. The secondary outcomes measures were differences between the groups in part-time sick-leave (25%, 50%, 75%) at the 15-month follow-up compared with baseline, and remaining symptoms of burnout at the 15-month follow-up compared with baseline.

Statistical analysis

Both intention-to-treat and adhering-to-protocol analysis were carried out to evaluate the intervention. Patients fully adhering to the treatment protocol were included in the adhering-to-protocol analysis. Full adherence to each intervention was defined as participating in all coached sessions for promoting physical activity, all sessions of the CBT treatment for self-esteem, all computerized cognitive training sessions, and more than 80% of the group sessions for sleep disturbance. Per protocol analysis did not change the results and are therefore not presented. Pearson’s χ^2 test was used to compare proportions of patients with no sick-leave in the intervention and control groups at the 15-month follow-up and, moreover, the proportions of patients in each group scoring below or above the cut-off for burnout symptoms on the SMBQ-scale. Mean days of sick-leave were compared using independent *t*-test. Statistical power analysis was calculated on self-reported data measuring RTW (100% return with 0% sick-leave benefit). This was estimated to be 40% in the control group after 1 year. To see an increase of at least 30% in the intervention group compared

with the control group with a power of 80% and a 5% significance level, we estimated that each group would need to include 45 people. To compensate for possible dropouts, approximately 70 patients were included in each group.

RESULTS

Baseline results

A total of 167 patients were assessed for eligibility, 142 were randomized and participated in the intervention part of the study, 79% ($n = 112$) were female and 21% ($n = 30$) were male. The mean age for the whole group was 42 years. A total of 71 patients were randomized to the intervention group and 71 patients to the control group. A flow chart showing the enrolment into the study is shown in Fig. 2.

Among the 167 patients who were assessed with respect to the predefined 4 dimensions, 25 did not score above the cut-off for any of the functions tested. Of the remaining 142, 92% ($n = 131$) indicated low levels of mental and physical energy, 39% ($n = 56$) scored above the cut-off for sleep disturbances, 18% ($n = 26$) scored above the cut-off for decreased cognitive function, and 44% ($n = 63$) scored above the cut-off for poor self-esteem.

Baseline characteristics for the whole final study population ($n = 142$), and for the intervention and control groups separately, are shown in Table I. At baseline, 72% of the control group and 79% of the intervention group were on 100% sickness benefits according to the registry data from the Social Insurance Office (Table I). There were no statistical differences with respect to outcomes measures between the intervention group and the control group at baseline.

The numbers and proportions of patients in the intervention and control groups scoring above the cut-off, on 1 or more of the critical functions assessed are presented in Table II. No major statistical differences could be seen between the 2 groups with respect to individual needs for extra treatment, apart from sleep disturbance, with a higher percentage of patients in the intervention group scoring above the cut-off compared with the control group ($p = 0.039$) (Table II).

Follow-up results

Sick-leave (yes/no) at the 15-month follow-up. In the total study population, 57% of the patients had reduced their sick-leave days between baseline and the 15-month follow-up. No change between baseline and follow-up was seen in 42% of the intervention group and 39% of the control group, while an increased sick-leave rate was seen in 1% of the intervention group and

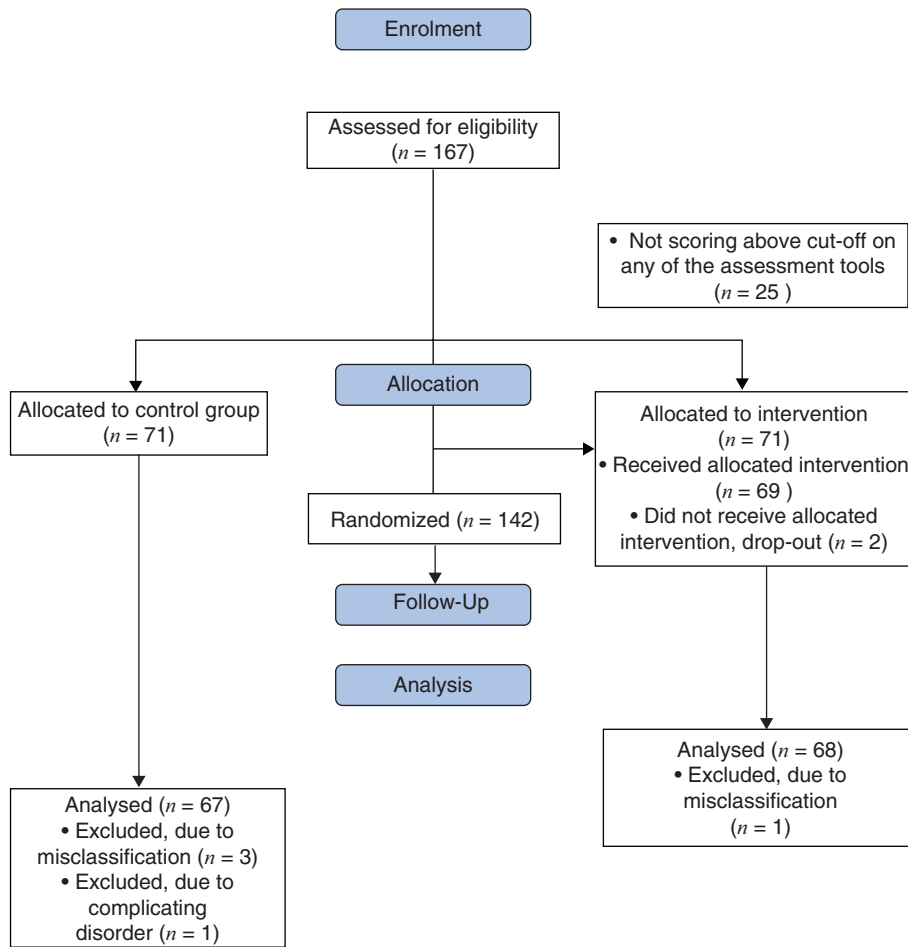


Fig. 2. Flow-chart for study enrolment.

4% of the control group. There were no statistically significant differences between the 2 groups regarding the percentage of patients who had no ongoing sick-leave registered at the 15-month follow-up (Table III).

Part time sick-leave. There were no statistically significant differences between the percentage of patients on part-time sick-leave at the 15-month follow-up, or in mean number of days of sick-leave registered during the 15-month period.

Symptoms of burnout. There were no statistically significant differences between the 2 groups regarding remaining symptoms of ED at the 15-month follow-up. The percentage of patients who scored above the cut-off at the 15-month follow-up with respect to symptoms of ED was 46% for the intervention group and 44% for the control group.

DISCUSSION

Principal findings

The main result from this study is that no statistically significant differences could be seen between the

groups for any of the outcome measures, indicating that adding extra individual tailored interventions as supplement to the basic standard treatment, had no major effects on sick-leave days or symptoms of burnout at the 15-month follow-up.

Results in relation to other studies

Several aspects need to be discussed regarding these results. First, we cannot exclude the possibility that other treatment components (interventions) would have been more effective. However, in line with our results, recent studies and reviews have indicated that rehabilitation programmes frequently used in clinical practice for patients with stress-induced ED seem to have marginal effects on sick-leave patterns and symptoms (25). These rehabilitation programmes often contain, at least to some extent, components such as those used in our study, although in a more “clustered” context and not necessarily differentiated by individual needs. The interventions evaluated in this study are well-established and almost axiomatic components in so-called multimodal treatment for patients with ED in the primary care setting. Many intervention studies

Table I. Baseline characteristics for all patients (*n* = 142) divided by group. Means and standard deviations (SD) are presented

| Baseline characteristics | <i>N</i> | Total group (<i>n</i> = 142) | Control group (<i>n</i> = 71) | Intervention group (<i>n</i> = 71) |
|---|----------|-------------------------------|--------------------------------|-------------------------------------|
| Sex, <i>n</i> (%) | 142 | | | |
| Female | | 112 (79) | 53 (75) | 59 (83) |
| Male | | 30 (21) | 18 (25) | 12 (17) |
| Age, years, mean (SD) | 142 | 42 (8,72) | 42 (8,54) | 42 (8,94) |
| BMI, kg/m ² , mean (SD) | 141 | 25 (4,43) | 24 (4,12) | 25 (4,71) |
| Years of education, mean (SD) | 142 | 15 (2.9) | 15 (3.0) | 16 (2.9) |
| Co-morbid anxiety, <i>n</i> (%) | 142 | | | |
| Yes | | 124 (87) | 64 (90) | 60 (85) |
| No | | 18 (13) | 7 (10) | 11 (16) |
| Co-morbid depression, <i>n</i> (%) | 142 | | | |
| Yes | | 114 (80) | 56 (79) | 58 (82) |
| No | | 28 (20) | 15 (21) | 13 (18) |
| Any co-morbid depression and/or anxiety, <i>n</i> (%) | 142 | | | |
| Yes | | 134 (94) | 67 (94) | 67 (94) |
| No | | 8 (6) | 4 (6) | 4 (6) |
| SMBQ-18, <i>n</i> (%) | 142 | | | |
| < 4.4 | | 23 (16) | 10 (14) | 13 (18) |
| ≥ 4.4 | | 119 (84) | 61 (86) | 58 (82) |
| HADS depression, <i>n</i> (%) | 140 | | | |
| ≤ 10 | | 98 (70) | 47 (68) | 51 (72) |
| > 10 | | 42 (30) | 22 (32) | 20 (28) |
| HADS anxiety, <i>n</i> (%) | 139 | | | |
| ≤ 10 | | 70 (50) | 37 (54) | 33 (47) |
| > 10 | | 69 (50) | 31 (46) | 38 (54) |
| Sick leave, <i>n</i> (%) | 142 | | | |
| 25% | | 3 (2) | 1 (1) | 2 (3) |
| 50% | | 15 (11) | 9 (13) | 6 (9) |
| 75% | | 16 (11) | 10 (14) | 6 (9) |
| 100% | | 108 (76) | 51 (72) | 57 (79) |

SD: standard deviation; BMI: body mass index; SMBQ: Shirom-Melamed Burnout Questionnaire; HADS: Hospital Anxiety and Depression Scale.

Table II. Distribution of patients scoring above the cut-offs for the 4 dimensions used in the study and *p*-values for differences between groups

| Critical dimensions | Intervention group | | <i>p</i> -value |
|----------------------------|-------------------------------|--------------|-----------------|
| | Control group <i>n</i> (%) | <i>n</i> (%) | |
| Mental and physical energy | 67 (94) | 64 (90) | 0.35 |
| Sleep disturbance | 22 (31) | 34 (48) | 0.04* |
| Cognitive function | 10 (14) | 16 (23) | 0.19 |
| Perceived self-esteem | 30 (42) | 34 (48) | 0.50 |

have likewise used programmatic and uniform interventions, such as group-based physical activity and/or extensive CBT programmes for all patients, which carries a risk of “overshooting” the target by offering more treatment than necessary without considering the pronounced low energy levels and extensive fatigue defining this patient group.

Study populations in intervention studies with respect to mental health problems often comprise a variety of closely-related diagnoses put together and labelled as “common mental disorders” (26, 27). This leads to a risk that selection bias might affect the results, since both the burden of disease and sick-leave patterns might vary in this heterogeneous patient group. The current study focused solely on patients who were given a diagnosis of ED via detailed clinical assessments by experienced physicians in combination with self-reported data obtained from validated questionnaires. The current study population thus consisted of a more homogeneous patient group, leading to a minor risk of selection bias.

Both practitioners and researchers are still predominantly focusing on interventions on the individual

Table III. Mean values, standard deviations (SD), *p*-values and 95% confidence intervals (95% CI) for the differences (0% sick-leave), total number of sick-leave days (gross and net), and remaining symptoms of burnout, for the whole study population and for the intervention and control group, respectively, at the 15-month follow-up

| | Total group (<i>n</i> = 135) | Intervention group (<i>n</i> = 68) | Control group (<i>n</i> = 67) | <i>p</i> -value | Diff (95% CI) |
|--------------------------------------|-------------------------------|-------------------------------------|--------------------------------|-----------------|---------------------|
| 0% sick-leave, % (<i>n</i>) | 32 (43) | 30 (20) | 34 (23) | 0.58 | 4.5 (-11.1; 19.8) |
| Sick-leave gross days, mean (SD) | 389 (108.43) | 390 (102.95) | 389 (114.82) | 0.97 | -1.1 (-38.3; 35.9) |
| Sick-leave net days, mean (SD) | 319 (141.31) | 332 (134.47) | 306 (147.86) | 0.39 | -25.2 (-73.3; 22.9) |
| Part-time sick-leave, % (<i>n</i>) | | | | | |
| 0% | 32 (43) | 30 (20) | 34 (23) | 0.60 | |
| 25% | 10 (14) | 8 (5) | 13 (9) | | |
| 50% | 12 (16) | 15 (10) | 9 (6) | | |
| 75% | 5 (7) | 8 (5) | 3 (2) | | |
| 100% | 40 (54) | 40 (27) | 40 (27) | | |
| SMBQ at 15 months, mean (SD) | 45 (55) | 46 (28) | 44 (27) | 0.79 | 2.4 (-14.8; 19.3) |

SD: standard deviation; 95% CI: 95% confidence interval; SMBQ: Shirom-Melamed Burnout Questionnaire.

level for this patient group. A plausible reason for the choice of interventions in earlier studies might have been that, according to the literature, each of the components alone has shown some positive effects on core symptoms of ED (28, 29). Thus, the current results also raise questions regarding the effectiveness of other common treatment components, on the individual level, offered to patients with ED in clinical practice. One lesson to be learned from the current results might be that neither universal interventions focused solely on the individual level nor individual tailored additional training of critical dimensions seem to be effective in reducing the number of sick-leave days or the burden of disease in this patient group. Hence, there is an increasing need for concurrent interventions aimed at reducing hazardous exposures in the work environment, in order to reduce sick-leave and symptoms for this patient group. In line with the current conclusions, other scholars have recommended a cohesive and work-focused rehabilitation programme involving several stakeholders for patients with stress-related disorders, such as ED and other common mental disorders (30, 31). Furthermore, in line with the current findings, at least 1 study focusing on the importance of various stress exposures in the development of ED concluded that work environmental factors seem to be deeply involved in the development of severe stress-related disorders, and thus should constitute a main target for interventions (32). However, in contrast, some recent reviews have found no or very limited support for work-directed interventions with respect to RTW in workers with stress-related diagnoses (33, 34). Thus, no univocal conclusions can be drawn from these reviews.

Future interventions to improve RTW and reduce sick-leave days in this patient group must focus primarily on interventions and actions aimed at eliminating hazardous exposures in the work environment. Special consideration must be paid to the organizational context and preconditions relevant for each individual patient. Various attempts have been made to evaluate the effect of employer involvement in stress rehabilitation in a Swedish context, some of which seem to have had some beneficial effects on RTW (35, 36). In a recent study, patients being treated in primary care for common mental disorders (over 70% of whom had ED or adjustment disorder) were randomized to 1 of 3 groups: CBT, a workplace intervention including early contact with the employer and graded exposure to the workplace, or a combination of both (37). However, 1 year after the intervention there was no difference in number of days on sick-leave between the 3 treatment groups. Research on workplace involvement in the rehabilitation of patients with stress-related disease is thus also inconclusive in a Swedish context. Another important factor relevant to the current results is the

effectiveness of the specialist treatment received during the first 3 months after the first visit to the clinic before the intervention study was performed. No scientific evaluation of this treatment has been performed, but considering the positive results gained in clinical practice on both symptoms of ED and a parallel continuous reduction of sick-leave days (5), it is plausible that the standard treatment, used in this study, is an effective standalone treatment for these patients, and thus additional interventions are not likely to add more than minor effects on sick-leave and burden of disease. Moreover, the current research group recently presented results on a long-term follow-up (7 years) of patients diagnosed with ED and concluded that, although one-third of patients struggled with residual symptoms of ED, only 3% were on 100% sick-leave. Most of the patients (87%) were not sick-listed at all despite health-related problems connected with ED (38). The clinical implication of that study is that the process of the disease and the burden of disease seem to be quite independent of the sick-leave rate over time. Hence, in concordance with the results from the current study, meeting the needs of this patient group with universal treatment intervention on the individual level seems to be a rather inefficient treatment strategy with respect to the poor outcome on sick-leave over time. It is reasonable to believe that interventions focusing on the workplace will be more efficient, as mentioned previously. In line with this assumption, a study performed by Eskilsson et al. confirmed the significance of an early and well-functioning collaboration between patient, healthcare provider, and employer to achieve early RTW for patients with ED (30). However, in contrast, a study from Norway showed that an intervention on the individual level (inpatient rehabilitation for 3.5 weeks) for patients with either pain or common mental disorders reduced sick-leave at the 12-month follow-up significantly more in comparison with 6 weekly sessions of psychological treatment (39). Due to the sometimes-contrasting results in earlier studies, it is important to perform more high-quality intervention studies in well-defined study populations to reveal yet-unknown complicating and contextual factors of importance for the outcome of intervention studies with respect to sick-leave, RTW, and symptoms of burnout among patients diagnosed with ED.

Strengths and limitations

The major strengths of this study are the low number of dropouts, the high proportion of patients adhering to the protocol, and the use of register data instead of self-reported data in the analysis of the primary outcome measure. Other strengths include the individually designed interventions, based on the specific needs of each patient instead of a standard intervention similar

for all patients, and the fact that all the interventions were clinically well-established and evaluated in clinical practice.

One limitation that became apparent during the study period was the capability of the patients to take part in the different treatment components. The combination of symptoms, such as fatigue, low energy level, and cognitive failure, resulted in a delay of the time-point where the patients could mobilize enough energy to enter the different interventions, particularly the computerized training programme and the CBT therapy. However, once patients had begun the interventions, the adherence to protocol was good. Due to the time delay, some patients were still attending 1 or more of the interventions 1 year after the randomization. This fact stresses the importance of right “timing” between different treatment components with respect to the burden of disease in this patient group. For example, a lack of energy due to the condensed timeframe of the interventions might have negatively affected the ability to comply with some of the more demanding interventions, such as the computerized cognitive training programme.

Finally, an additional follow-up performed later than the 15 months used in this study would have been appropriate to evaluate potential long-term effects of the intervention on the outcome measures. However, no indication of a delayed effect has been revealed so far either in scientific studies or in clinical practice.

Conclusion

The main conclusion from this study is that adding individually tailored interventions to the standard treatment for patients diagnosed with stress-related exhaustion disorder did not reduce sick-leave days or symptoms of burnout more in the intervention group compared with the control group.

Clinical implications

Future interventions to reduce sick-leave and symptoms of burnout in patient diagnosed with ED should be accompanied by interventions targeting the workplace and work organizational level.

Ethical considerations

The study was approved by the regional ethics committee Gothenburg reference number Dnr 067-11. Date of approval 9th of May 2011. Informed consent was obtained from all subjects involved in the study.

ACKNOWLEDGEMENTS

This study was financed by the Swedish government within the REHAM research programme that was launched in 2008 to encourage development of

evidence-based methods (reference: S2014/5621/SF), and by grants from the Swedish state under the ALF agreement between the Swedish government and the county councils (reference: ALFGBG-431391).

The authors have no conflicts of interest to declare.

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