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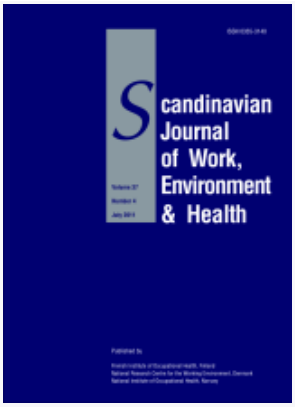

Original article

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Effectiveness of an exposure-based return-to-work program for workers on sick leave due to common mental disorders: a cluster-randomized controlled trial

by Noordik E, van der Klink JJ, Geskus RB, de Boer MR, van Dijk FJH, Nieuwenhuijsen K

Time to return to a full workload was longer for workers on sick leave due to common mental disorders who received an exposure-based return-to-work (RTW) intervention compared to guideline-directed care-as-usual (CAU) by occupational physicians (OP). OP should not apply an exposure-based RTW intervention but continue counseling these workers according to guideline-directed CAU.

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Corrections

See 2013;39(3):319 for a correction.

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Key terms: absenteeism; common mental disorder; exposure; occupational health; occupational health; randomized controlled trial; return to work; return-to-work program; RTW; sickness absence

Additional material

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Effectiveness of an exposure-based return-to-work program for workers on sick leave due to common mental disorders: a cluster-randomized controlled trial

by Erik Noordik, MSc,[1] Jac J van der Klink, PhD,[2] Ronald B Geskus, PhD,[3] Michiel R de Boer, PhD,[2] Frank J H van Dijk, PhD,[1] Karen Nieuwenhuijsen, PhD [1]

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Objectives In case of long-term sick leave, gradually increasing workload appears to be an effective component of work-directed interventions to reduce sick leave due to common mental disorders (CMD). CMD are defined as stress-related, adjustment, anxiety, or depressive disorders. We developed an exposure-based return-to-work (RTW-E) intervention and evaluated the effect on time-to-full return to work (RTW) among workers who were on sick leave due to CMD in comparison to those treated with care-as-usual (CAU). CAU is guideline-directed and consists of problem-solving strategies and graded activities.

Methods Using a two-armed cluster-randomized trial, we randomized 56 occupational physicians (OP). Of these, 35 OP treated 160 workers at the start of their sick leave: 75 workers received RTW-E and 85 workers received CAU. These workers were followed over a 12-month follow-up period. The primary outcome measure was time-to-full RTW lasting ≥28 days without recurrence. To evaluate differences between groups, we used intention-to-treat and multilevel Cox's regression analysis.

Results The median time-to-full RTW differed significantly between groups [hazard ratio (HR) 0.55; 95% confidence interval (95% CI) 0.33–0.89]. The workers receiving RTW-E (209 days; 95% CI 62–256) had a prolonged time-to-full RTW compared to workers receiving CAU (153 days; 95% CI 128–178).

Conclusions Workers on sick leave due to CMD treated with RTW-E showed a prolonged time-to-full RTW compared to those treated with CAU. We recommend that OP do not apply RTW-E but continue counseling workers on sick leave due to CMD according to CAU.

Key terms absenteeism; occupational health; sickness absence; RTW.

Common mental disorders (CMD), such as adjustment, anxiety, and depressive disorders are highly prevalent in the working population (1) and are associated with long-term sick leave and a loss of productivity (2). Regular clinical treatments, such as cognitive behavioral therapy or pharmacotherapy, can reduce anxiety and depressive symptoms effectively (3, 4), although the full recovery of work functioning often does not follow automatically (5, 6). Work-directed interventions appear to be a promising means of reducing the time-to-full return to work (RTW) for workers on sick leave due to CMD (7–9), although two studies reported no differences between the intervention and control group (10, 11). To understand the results of these two studies, one needs to take into account that both studies used a less intensive but still work-directed intervention as a control group.

We know little about how time-to-full RTW is reduced. We therefore identified three common elements of work-directed interventions in the abovementioned studies: improving the problem-solving skills of work-

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ers, restoring contact with the workplace, and gradually increasing the workload. Gradually increasing the workload means gradually increasing the number of working hours and the complexity of the work tasks. Restoring contact with the workplace and gradually increasing the workload are recommended policies for employers when supporting workers in their RTW after long-term sick leave (12). However, a potential disadvantage of gradually increasing the workload for workers on sick leave due to CMD is that work situations that evoke stress or strong emotions can be postponed until the final part of the RTW process. This offers workers who are inclined to avoid these situations the opportunity to be persistent in that avoidant behavior. If emotion-evoking work situations are an intrinsic part of the job that cannot be avoided – eg, a nurse who has become anxious to inject patients – avoidance could easily result in an unnecessary long time-to-full RTW. The findings of van Rhenen et al (13) provide support for the occurrence of avoidance and suggest that the avoidance behavior of workers, in contrast to an active problem-solving style, is associated with an increased frequency and duration of sick leave due to stress-related disorders. Moreover, there is moderate evidence that fear-avoidance belief is a negative predictor of RTW for workers on sick leave due to non-specific health complaints (14). Thus, as preventing avoidance behavior may enhance RTW, applying the principles of exposure in vivo as part of a work-directed intervention may be useful in reducing the time until full RTW.

Exposure in vivo is a behavioral therapy in which patients with anxiety disorders are gradually exposed to increasing levels of anxiety according to a hierarchy of anxiety-evoking situations (15). This therapy has been shown to have positive or neutral effects on work-related outcomes of patients with obsessive compulsive and post-traumatic stress disorders (16). Furthermore, there is limited evidence that a graded activity program based on in vivo exposure principles for patients on sick leave due to low-back pain is more effective than usual care in reducing long-term sick leave (17, 18). However, to our knowledge, the effectiveness of exposure in vivo has not yet been applied to RTW interventions for workers on sick leave due to CMD.

Therefore, we developed an exposure-based RTW (RTW-E) intervention to be integrated into usual care. With this intervention, we aimed to stimulate workers to use active problem-solving behavior and prevent avoidance behavior when dealing with stressful work situations during RTW. The objective of our study was to evaluate the effectiveness of the RTW-E intervention, applied by occupational physicians (OP), in reducing the time-to-full RTW of workers on sick leave due to CMD in comparison to care-as-usual (CAU). CAU is guideline-directed and consists of problem-solving strategies and graded activities (19). We conducted a cluster randomized controlled trial (RCT) in which we first hypothesized that the time-to-full RTW for workers receiving the RTW-E intervention is shorter than for workers receiving CAU. Second, in the protocol of the study, we hypothesized that the RTW-E intervention is more effective for workers on sick leave with anxiety disorders compared to workers with other CMD (20). The presupposed reason would be that exposure in vivo can reduce avoidance behavior among patients with anxiety disorders (21). Furthermore, we explored the effectiveness of the RTW-E intervention compared to CAU on mental health outcomes.

Methods

In the present study, we summarize the main elements of the design. For a detailed description of the methods, we refer to the study protocol (20). The items of the CONSORT statement (22) and its extension regarding cluster randomized trials (23) were used for reporting the design.

Setting

This study was conducted in the Netherlands, where most of the workers on sick leave due to CMD visit an OP. The OP offers RTW interventions to these workers according to the evidence-based (Dutch) guidelines (19). Although adherence to these guidelines can be improved (24), we considered CAU to consist of interventions according to these guidelines.

Design

The study was designed as a two-armed cluster RCT with randomization at the level of OP and a follow-up period of 12 months. The OP in the intervention group counseled their workers according to the RTW-E program. The OP in the control group counseled their workers according to CAU.

Study population

Workers. We included workers who were on sick leave due to CMD for ≥2 and ≤8 weeks. CMD were defined as stress-related, adjustment, anxiety or depressive disorders. Stress-related disorders were classified according to the Dutch guidelines for OP (19). Anxiety, depressive, and adjustment disorders were classified by the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV). Workers with a primary somatic disorder according to the OP and those who were not able to speak Dutch were excluded.

Workers eligible according to the OP were invited to participate. After signing an informed consent form, participants were interviewed over the telephone (MINI, 25) to verify the DSM IV diagnosis. In the RTW-E group, homework assignment forms were collected from the OP to assess compliance. All participants were asked to complete a baseline survey and follow-up surveys at 3, 6, 9, and 12 months after the first day of sick leave. Furthermore, on a daily basis, participants filled out diaries on hours at work, sick leave or vacation until the day they achieved their first full RTW. Medical records in the OP register were used to verify data on recurrences and sick leave.

Occupational physicians. The OP were recruited in the summer of 2006 from various occupational health services located throughout the Netherlands. The OP who agreed to participate were randomly assigned to the experimental (RTW-E) or control (CAU) groups. We performed a restricted randomization with blocks of four OP. Participating OP were requested to complete a seven-item questionnaire concerning personal (one item) and professional characteristics (six items). The OP in the RTW-E group received two days of training in the RTW-E program. Thereafter, we conducted three follow-up tutorial sessions during the inclusion period. During these sessions, difficulties with applying the RTW-E program were discussed with the session supervisor and other participating OP and ideas for practical solutions were exchanged for problems that had arisen. The OP in the control group received one day of training to update their skills in counseling workers with CMD according to the Dutch guidelines (19).

Sample size

We planned to include 60 OP who would in turn include 200 workers to be able to detect a statistically significant difference between groups on time-to-full RTW. The sample size of OP and workers needed in the study was not based on a power analysis as software for such an analysis of survival data was not available at the time. We used a comparable intervention study of van der Klink et al (8) as a point of reference. They found significant differences on time-to-full RTW in a study with 33 OP and 192 patients.

Interventions

CAU aims to help workers regain control and rebuild social and occupational contacts and activities, according to the guidelines for CMD (19, 26). The OP can reach this goal by using recommended methods such as stress inoculation training, cognitive restructuring, graded activity, and time contingency during the RTW.

In the RTW-E program, workers received CAU and were gradually exposed in vivo to more demanding work situations structured by a hierarchy of tasks evoking increasing levels of anxiety, stress, or anger. The RTW-E program provided workers with several homework assignments aimed at preparing, executing, and evaluating an exposure-based RTW plan. The homework assignment forms and the worker information brochure can be downloaded from http://www.psychischenwerk.nl/datafiles/patientinformationbrochure_RTW-E_english_okt%202006(1).pdf and http://www.psychischenwerk.nl/datafiles/Homework_RTW-E_A-F_%20english_%20febr%202007(1).pdf.

Outcome measures

Primary outcome. The time-to-full RTW was the primary outcome evaluated in this study and was calculated as the number of calendar days from the first day of sick leave to the first day of full RTW. Full RTW was defined as the total number of contracted working hours per week lasting ≥28 calendar days without a recurrence of sick leave. The calculated time-to-full RTW was based on workers' diaries and OP medical records.

Secondary outcomes. The following were considered to be secondary outcomes: time to partial RTW, the number of recurrences of sick leave, symptoms of distress, anxiety, depression and somatization [Four-Dimensional Symptom Questionnaire (4DSQ) (27)], and satisfaction with the OP, all within the one-year follow-up period. The 4DSQ is a Dutch self-report questionnaire that consists of 50 items distributed over 4 subscales. The distress subscale contains 16 items and the total score ranges from 0–32; the depression subscale contains 6 items and the total score ranges from 0–12; the anxiety subscale contains 12 items and the total score ranges from 0–24; and the somatization subscale contains 16 items and the total score ranges from 0–32. Higher scores indicate more distress, depression, anxiety, or somatization. The 4DSQ appears to be a valid and reliable self-report questionnaire for primary care patients. The Cronbach's alpha for the 4 subscales ranged from 0.84–0.90.

Process measures

Compliance with the RTW-E program, the frequency of consultations of the worker with the OP, and the reported communication between the worker and his or her supervisor were considered to be process measures. We measured the compliance of the counseling process of OP and their patients with the RTW-E program by scoring the presence and quality of completed homework assignment forms. The presence of six completed forms was scored

by yes or no. Two researchers classified the quality of the forms independently. The quality of each form was rated on a 3-point Likert scale: 0=not in accordance with the purpose of the form, 1=partly in accordance with the purpose of the form, and 2=in accordance with the purpose of the form. The total quality score of compliance was classified for each worker as low (0–4), moderate (5–8), or high (9–12), which was an adaptation of the classification as proposed in the study protocol.

Statistical analysis

Baseline measurements of OP, workers, and costs were compared between the two intervention groups using descriptive statistics. These analyses were performed using SPSS, version 16.0.1 (SPSS Inc, Chicago, IL, USA). To evaluate differences between groups on time-to-full RTW (the primary outcome) and time to partial RTW, we calculated Kaplan-Meier time-to-event curves and fitted Cox proportional hazards regression models. Because the OP, rather than the workers, were randomized, we corrected for clustering in the Cox models by including a "frailty" random effect (28). We performed an intention-to-treat analysis and used the Wald test to assess differences between groups. To evaluate the confounding effect of having an anxiety disorder on time-to-full RTW, we included anxiety disorders as a covariate in the model. By including an interaction between anxiety and time-to-full RTW, we also evaluated whether the anxiety disorder was an effect modifier.

We evaluated differences between groups on all secondary outcome scores and process measures using mixed models. For symptoms of somatization and distress, a linear mixed model (LMM) was used with three levels of random effects, namely OP, patients within OP, and measurements within patients. At the patient level, both the intercept and the slope were included as random effects. For anxiety and depressive symptoms, there were many zero values. Therefore, we used a generalized LMM assuming a Poisson distribution. We again included a random effect for intercept and slope at the patient level. The Cox regression analysis and the LMM were performed using the R statistical program versions 2.10.1 and 2.11.0 (29). To evaluate the effectiveness of RTW-E and CAU over time, we calculated the mean anxiety change score as the difference between the anxiety score at baseline and at 3, 6, 9, and 12 months, respectively. We adjusted the change scores for the floor-effects by calculating the relative change scores. These scores are the percentage of the ratio between the anxiety changes scores and the difference between the baseline anxiety score and the lowest value of the scale, which is zero (30). Furthermore, we also adjusted the change scores for the effects of potential confounding in the association between anxiety change scores and the intervention groups, eg, age and the presence of mixed anxiety-depressive disorder (31). Moreover, the presence of mixed-depressive disorder was unevenly distributed between the RTW-E and CAU groups. The differences in the anxiety change score between the RTW-E and CAU group were evaluated by linear regression analyses.

Results

Participants and baseline data

Overall, 74 OP participated in the study, 18 of whom withdrew; the remaining 56 OP were randomized into two groups (figure 1). Recruitment of workers started in November 2006 and ended in December 2007. The OP asked 200 workers to participate in the study, all of whom signed an informed consent form. Forty workers were excluded. In the RTW-E intervention and CAU groups, 3 and 11 workers, respectively, were excluded due to a sick leave duration of >8 weeks. Moreover, 3 and 4 workers, respectively, refused to participate, and OP excluded 6 and 2 workers, respectively, for unknown reasons. After the telephone diagnostic interview, another 3 workers were excluded from the RTW-E group due to post-traumatic stress disorder (PTSD), 1 due to substance abuse, and 1 due to psychosis. From the CAU group, another 5 were excluded due to PTSD and 1 due to poor mastery of the Dutch language.

As a result, we included 75 workers from 21 OP in the RTW-E intervention group and 85 workers from 14 OP in the CAU control group. In both groups, the workers' responses rates decreased during the four follow-up questionnaires. The proportion of workers lost during the follow-up was 34% and 28% in the RTW-E and CAU groups, respectively. Analyses of the primary outcome were based on workers' diaries and medical records of OP and could be performed in both groups for 63 (18% lost to follow-up) and 80 (11% lost to follow-up) workers in the RTW-E and CAU groups, respectively. Baseline data for several characteristics of the workers and their OP are shown in table 1. The characteristics of the workers and OP did not differ significantly between both groups.

Work-related outcomes

In figure 2, the differences between the groups on time-to-full RTW (lasting ≥28 days) are presented as Kaplan-Meier time-to-event curves. The median time-to-full RTW differed significantly between the groups (P=0.02). For workers receiving RTW-E, the median time-to-full RTW was 209 days [95% confidence interval (95% CI) 162–256], whereas for workers receiving CAU, the median time-to-full RTW was 153 days (95%

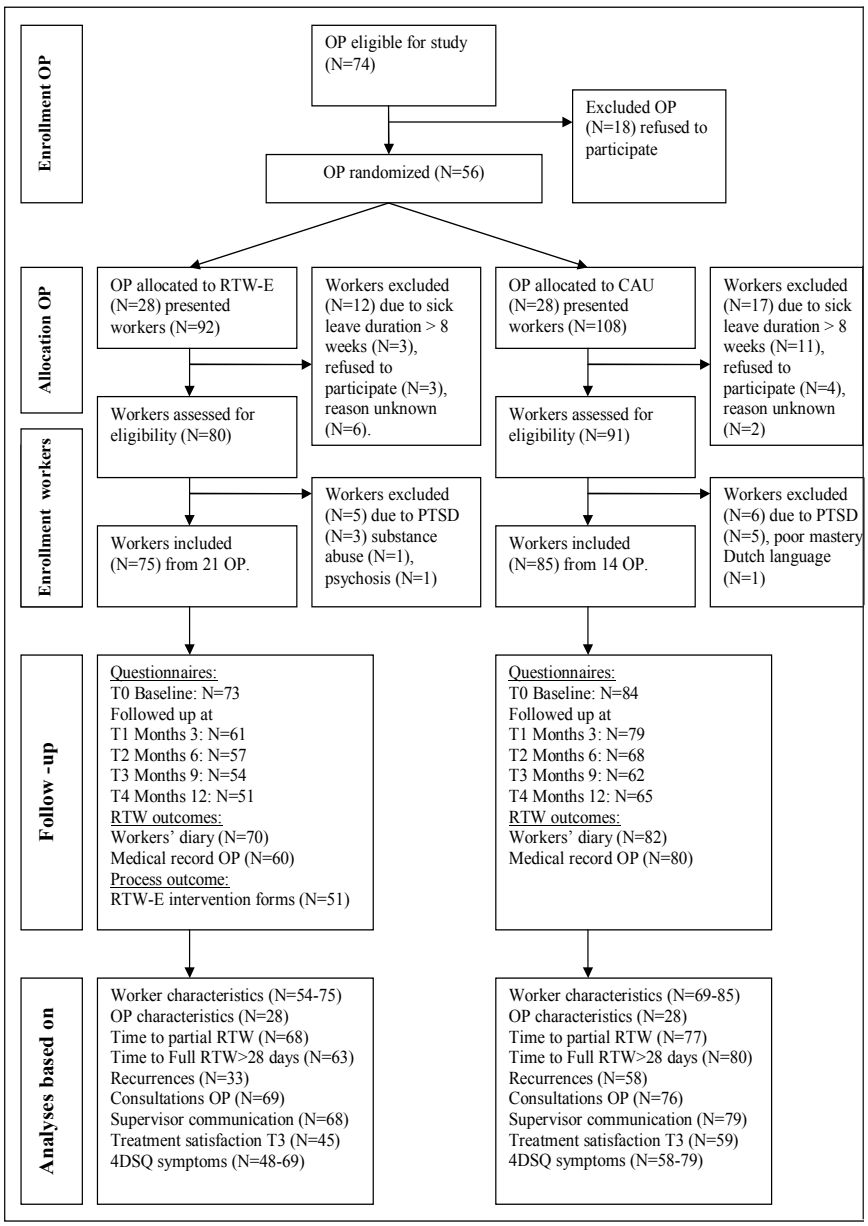

Figure 1. Flowchart of the study. [CAU=care-as-usual; OP=occupational physician; PTSD=post traumatic stress disorder; RTW-E=exposure-based return to work; 4DSQ=4-dimensional symptom questionnaire]

CI 128–178). The hazard ratio (HR) of the RTW-E group compared to that of the CAU group was 0.55 (95% CI 0.33–0.89), indicating that they had a lower likelihood of reaching full RTW.

For the subgroup of workers with anxiety disorders (N=76), the effect of RTW-E versus CAU group on the time-to-full RTW was not significantly different from that of workers with other CMD (there was no interaction effect: P=0.97). Also, the effect of RTW-E versus CAU group did not change if we corrected for the confounding effect of the presence of anxiety disorders.

The median time-to-partial RTW was 78 (95% CI 60–95) and 70 days (95% CI 60–80) for workers receiving RTW-E and CAU, respectively. The HR for this difference was 0.89 (95% CI 0.62–1.29), so both interventions did not differ significantly. The mean number of recurrences of sick leave within a one-year follow-up also did not differ between both interventions (P=0.96). The median and interquartilerange (IQR) of the number of recurrences among workers receiving RTW-E were 0 and 2, respectively, and 1 and 2 for workers receiving CAU.

Treatment characteristics

No significant differences (P=0.07) were found in the mean number of consultations with the OP between the RTW-E [3.9; standard deviation (SD) 2.2] and the CAU groups (3.4; SD 1.9). The frequency of communication

Table 1. Characteristics of the study population. The number of the worker characteristics ranges from 54–74 for the RTW-E group and from 69–84 for the care-as-usual (CAU) group due to missing values; the number of the occupational physician (OP) characteristics ranges from 15–21 for the exposure-based return-to-work (RTW-E) group and from 7–14 for the CAU group due to missing values. [SD=standard deviation.]

Worker characteristics	RTW-E				CAU			
	Mean	SD	N	%	Mean	SD	N	%
Age in years	44.9	9.8			45.9	9.8		
Gender								
Male			18	24.3			28	33.3
Female			56	75.7			56	66.7
Educational level								
Low			6	8.7			14	17.9
Middle			17	24.6			18	23.1
High			46	66.7			46	59.0
Duration of sick leave before inclusion in days	36.0	13.2			34.1	13.3		
Diagnosis inclusion								
Stress-related disorder			11	15.1			25	29.8
Depressive disorder			18	24.7			19	22.6
Anxiety disorder			17	23.3			20	23.8
Mixed anxiety-depressive disorders			27	37.0			20	23.8
Adjustment disorder			0	0.0			0	0.0
OP characteristics								
Age in years	52.9	7.0			48.3	8.4		
Gender								
Male			12	57.1			7	50
Female			9	42.9			7	50

with the supervisor during the first three months of sick leave (T1) and the satisfaction of the workers with the treatment of the OP after 9 months (T3) also did not differ significantly between groups; the P-values for these differences were 0.74 and 0.99, respectively. We found that 28 workers were treated as intended with the RTW-E program, which is 55% of the workers who completed their RTW-E homework assignments. Compliance with the RTW-E program was rated moderate or high quality in these cases. Furthermore, during the tutorial sessions and the 12-month follow-up period, OP did not report adverse events or side effects that were specifically related to the RTW-E program.

Health-related outcomes

Table 2 presents the mean health-related outcomes at the beginning of the study and at the 3-, 6-, 9- and 12-month follow-up periods for both groups, and the P-values for the total group effects (ie, the main effect and the interaction) based on the mixed model. The overall differences between groups on the mean distress, depression, and somatization scores were not statistically significant. Within both groups, the mean distress, depression, anxiety, and somatization scores decreased significantly over time. The overall difference between groups on the mean anxiety score was statistically significant (P=0.004). The overall mean anxiety score for the RTW-E group was higher than that for the CAU group. The interaction term between group and time however was not statistically significant (P=0.66). The mean anxiety change scores from baseline until 12-month follow-up, differed significantly between the RTW-E and CAU groups (P=0.01). However, after adjustment for the floor-effects and the effects of potential confounding of differences in the presence of mixed anxiety-depressive disorders and in age, the mean anxiety change score did not differ significantly between groups (P=0.27).

Ancillary analysis

In an ancillary analysis, diagnosis (ie, stress-related, anxiety, depressive, mixed anxiety-depressive disorder), distress, somatization, anxiety and depressive symptoms (4DSQ), and self-efficacy to RTW at baseline were included as a correction for potential confounding in the association between the intervention and the time-to-full RTW (32–34). Inclusion of diagnosis, symptoms (4DSQ), and self-efficacy did not cease the significant difference between RTW-E and CAU on the time-to-full RTW; the HR for the diagnosis was 0.51 (95% CI 0.30–0.86), for the symptoms (4DSQ) they were 0.46 (95% CI 0.24–0.86), 0.47 (95% CI 0.27–0.80), 0.47 (95% CI 0.26–0.87), 0.48 (95% CI 0.28–0.82), respectively, and for self-efficacy it was 0.44 (95% CI 0.25–0.74). We also assessed interactions between both groups and the potential confounding variables, but no interactions were found to be significant. Furthermore,

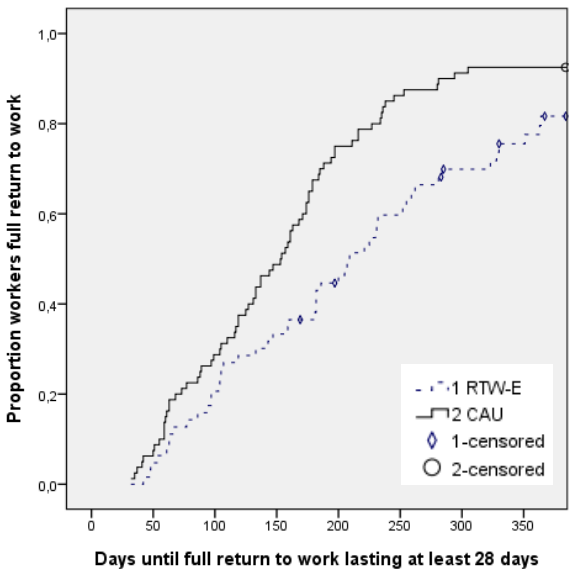

Figure 2. Cumulative probability of time-to-full return to work (RTW) lasting ≥28 days for both the exposure-based RTW (RTW-E) (N=63) and care-as-usual (CAU) group (N=80). Data were censored if the time-to-full RTW was >365 days or if full RTW was not accomplished before the working hours stopped being registered. At 12-months follow-up, N=56 and 79 in the RTW-E and CAU group, respectively.

we performed a per protocol analysis in which we corrected for compliance, good compliance was defined as having a moderate or high quality score on the RTW-E intervention forms. The HR we found between groups on time-to-full RTW was 0.71 (95% CI 0.42–1.19). So, the difference between the RTW-E and CAU groups was no longer significant.

Discussion

Main findings

In contrast to our hypothesis, compared to CAU, RTW-E prolonged the time-to-full RTW for workers on sick leave due to CMD. Also, in contrast to our hypothesis, in terms of the time-to-full RTW, RTW-E was not more effective than CAU for workers on sick leave due to anxiety disorders compared to workers with other CMD. Furthermore, the prolonged time-to-full RTW that we observed in the RTW-E group was not associated with a lower number of recurrences during the one year follow-up period, which would have been advantageous later in the RTW process.

To understand better the prolonging effect of RTW-E on time-to-full RTW, we performed several unplanned ancillary analyses. Only the results of the per protocol analysis indicated that a better compliance to RTW-E could possibly neutralize the prolonging effect of RTW-E on time-to-full RTW. However, we could not exclude the possibility that the results of the per protocol analysis were due to a lack of power. All other results of the ancillary analyses did not change our main finding on time-to-full RTW.

By exploring the effectiveness of RTW-E on mental health outcomes we found that RTW-E was not more effective in reducing anxiety symptoms compared to CAU after adjustment for the floor-effects and the effect of potential confounding. This finding was unexpected as we would hypothesize, based on a systematic review (4), that RTW-E was more effective in reducing anxiety symptoms, compared to CAU.

Furthermore, we did not find any adverse events or side-effects of the application of the RTW-E program in our study. This is in accordance with the application of exposure in vivo treatments for anxiety disorders in general (35).

Strengths and limitations

This study can be considered to be a pragmatic trial in which many requirements for a high quality trial were met. The validity of the results was enhanced by the following features of the study: workers were recruited over the same period of time; the OP in both groups were allocated using block randomization; the researchers were blind to the allocation and outcome measurement; the workers were blind to the differences in RTW-E and CAU; the chance of contamination of RTW-E between the OP in both groups was minimal; there was an intention-to-treat analysis at the level of the participating workers; and there was sufficient power to detect an effect on the primary outcome at a 5% significance level. Furthermore, the OP in both groups were trained to apply the intervention program. The validity of the results of this study may have been limited due to a selection bias because of the absence of allocation concealment of the OP and attrition of workers.

Selection bias

In this trial, the allocation of treatment was predetermined for each OP. As a result, the potential for the selective inclusion of workers was rather high (36). To minimize the possibility of selection bias, during the OP training and tutorial sessions and in newsletters, we emphasized OP should present all workers who met the inclusion criteria. Furthermore, the researcher acted as a blind and independent assessor of the diagnostic interview for inclusion, which could have further minimized the selection bias (36). However, we could not prevent some OP from including zero workers, which could

Table 2. Overall differences between the exposure-based return-to-work (RTW-E) intervention and care-as-usual (CAU) groups on health-related outcomes concerning four-dimensional symptom questionnaire (4DSQ) symptoms measured at baseline and at 3-, 6-, 9-, and 12-month follow-up. The number of the health-related outcomes of the RTW-E and CAU group ranges from 48–69 and from 58–79 respectively, at the 5 measurements due to missing values. [SD=standard deviation]

Health-related outcomes baseline and follow-up	Group	N	Baseline		3 months		6 months		9 months		12 months		P-value of total group
			Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Distress	RTW-E	48–69	19.0	7.9	13.0	8.2	10.1	7.8	8.4	7.4	6.3	6.0	0.14
	CAU	58–79	17.4	7.9	11.6	7.8	8.6	6.5	7.4	6.4	7.3	7.7	
Depressive	RTW-E	48–69	2.7	2.9	1.6	2.5	1.4	2.6	1.1	2.8	0.6	1.5	0.13
	CAU	58–79	2.0	2.8	1.1	2.0	0.8	1.9	0.5	1.5	0.9	2.0	
Anxiety	RTW-E	48–69	5.5	4.8	3.8	4.8	2.5	3.2	2.0	3.8	1.5	2.4	0.004
	CAU	58–79	4.1	5.0	2.3	3.4	1.6	2.6	1.4	3.0	1.6	3.5	
Somatization	RTW-E	48–69	12.4	6.3	8.9	5.9	7.4	5.5	7.2	5.8	5.2	5.0	0.55
	CAU	58–79	11.5	6.6	9.2	6.1	6.7	5.1	5.9	5.3	6.2	5.9	

have introduced selection bias (36). The tendency that workers in the RTW-E group were found to have mixed anxiety-depressive disorders more often and stress-related disorders less often compared to workers receiving CAU could be indicative of a selection bias but also of an unintended consequence of the randomization process. As stress-related disorders can be considered to be a less severe CMD, we cannot exclude the possibility that the OP in the RTW-E group may have selected more severe cases. However, after correction of potential confounding of diagnosis (ie, stress-related, anxiety, depressive or mixed anxiety-depressive disorder), distress, somatization, anxiety, or depressive symptoms, or self-efficacy associated with time-to-full RTW, we still found a significant difference on time-to-full RTW between the RTW-E and CAU groups.

Analyses of the primary outcome (ie, time-to-full RTW) were based on workers' diaries and OP medical records and could be performed in both groups for 63 (16% lost to follow up) and 80 (6% lost to follow up) workers in the intervention and control groups, respectively. For 3 secondary outcome measures (ie, the number of recurrences, the health-related outcome 4DSQ, and the satisfaction of the workers with the treatment of the OP after 9 months) the loss to follow up varied from 31% to 56% in both the RTW-E and CAU groups. So, attrition could have introduced a low risk of bias in the estimated median time-to-full RTW and a higher risk of bias in the secondary outcome measures.

Generalization

The external validity of the results of this study depends on the similarities between the population and conditions of this study and those in the situation of interest. The study was conducted in the Netherlands with a sociocultural context in which OP have a central role in occupational healthcare that gives a high priority to RTW issues in cases of sick leave. A substantial group of OP were already familiar with the professional guidelines on sick leave due to CMD, which we considered to be CAU (19). Another relevant characteristic may be that there is a relatively low stigma on sick leave due to CMD in the Netherlands compared to many other countries. Furthermore, the majority of the included workers in this study were working in the healthcare, education, or public governance sectors.

Comparison with other studies and interpretation of main results

This study is the first trial to evaluate the effectiveness of a work-directed exposure in vivo procedure for workers on sick leave due to CMD. In the literature, only studies evaluating the effectiveness of a non-work-directed exposure in vivo procedure were available. Furthermore, in other studies, effectiveness was not evaluated in terms of time-to-full RTW (16). Developing a work-directed exposure in vivo procedure seems to be an innovation in itself, as Linden et al (37) deemed it hardly possible. We did not expect to find a prolonged time-to-full RTW of RTW-E compared to CAU.

To understand the prolonged time-to-full RTW, it is important to consider that our comparison treatment is already rather effective in reducing the time-to-full RTW for workers on sick leave due to stress-related disorders (8). This suggests that the effectiveness of work-directed interventions for workers on sick leave due to CMD may have reached its optimum.

A first interpretation of the prolonged time-to-full RTW could be that workers who are in the first phases of a mostly work-related mental health disorder characterized by high levels of work-related stress symptoms and substantial elevated feelings of depression and anxiety (ie, a crisis), are not in the optimal mental condition to be confronted with difficult situations at work that they

left only a number of weeks before. It might be a more effective strategy to suspend this confrontation until the mental condition has improved. A second, more simplistic interpretation is that the RTW schedule according to RTW-E consists of more and smaller steps compared to CAU. For the OP and workers, this might create the actual situation that they need to take more time until full RTW. A third interpretation is that the exposure-based intervention we developed was not suitable for the included group of workers as the duration of sick leave differed from 2 to 8 weeks. RTW-E may be better suited to workers who are on sick leave >3 months (partially), are motivated to implement their solutions, and have already received CAU (38). In the per protocol analysis, we found no significant differences on time-to-full RTW between the workers who were compliant with the RTW-E program (N=28) and workers in the CAU group. This result suggest a fourth alternative interpretation namely that RTW-E is too complicated for many OP to apply after two days of training and three follow-up tutorial sessions. Or, in other words, the OP just started to learn RTW-E. They may have needed more time to become competent to apply RTW-E. Possibly RTW-E would have had better results if it was applied by professionals who were experts in applying exposure in vivo. However, we could not exclude the possibility that the results of the per protocol analysis were due to a lack of power.

The fact that there was no difference between RTW-E and CAU on time-to-partial or first RTW or on the recurrence of sick leave but only on time-to-full RTW could imply that something keeps workers within the RTW-E program from proceeding from partial to full RTW. A fifth interpretation may be that workplaces were possibly not ready or able to accommodate the changes in the work situation associated with the RTW-E program. In this sense, workers in the CAU group could have had a head start compared to those in the RTW-E group because the workplaces are accustomed to CAU and it may require less effort from the supervisors and colleagues.

To better understand the prolonged time-to-full RTW and the complex pathway from intervention to the outcomes, we discuss our intervention study according to the theoretical model of key elements in occupational intervention studies of Kristensen (39). According to this model, first of all we need to discuss the RTW-E program's integrity; second, we need to discuss to what extent the RTW-E program has generated an actual change of behavior (ie, less avoidance behavior). In terms of the model, this association is called the impact of the program (or program failure). And third, we need to discuss to what extent the changed behavior has generated changes in outcome (ie, time-to-full RTW). In terms of the model, this association is called the etiology of the disease or theory. First, looking at our per protocol analysis for integrity, our RTW-E intervention was performed as intended among at least 28 workers, which is 55% of the workers who completed their RTW-E homework assignments. Second, with regard to behavior change, we found no indications that the RTW-E program has generated less avoidance behavior compared to CAU. However, we could not find a suitable instrument to measure avoidance behavior at work, therefore we explored this by asking workers: "Do you avoid emotional or stress-evoking work situations?" This question was scored on a 4-point Likert scale ranging from 1 (seldom or never) to 4 (very often). Third, we do not know to what extent the change of behavior has generated a prolonged time-to-full RTW. So, in our intervention study, it is hard to distinguish program from theory failure.

Recommendations for future research

In this study, we hypothesized that countering the potential avoidance of difficult situations or tasks at work would reduce the time-to-full RTW among workers with CMD. While this study showed no such effect, it may be premature to discard this type of intervention completely. The early onset of the RTW-E intervention may not have been optimal. It may still be worthwhile to evaluate the efficacy of RTW-E or a similar program applied to workers who were unable to reach a full RTW during the first months of absence, despite having received CAU from their OP. Preferably, professionals who have experience in applying exposure in vivo procedures should perform such an intervention.

We further believe that future research should focus on improving the understanding of the mechanisms of the RTW process and the optimal timing of RTW interventions. With regard to the mechanism of RTW, exploring the role of self-efficacy in the RTW process seems worthwhile (34). With regard to the timing of RTW interventions, new interventions for workers who have started the RTW process but have not yet been able to achieve a full RTW are needed (38).

Concluding remarks

Counseling workers on sick leave due to CMD with an in vivo work-directed exposure procedure executed by OP resulted in a longer time-to-full RTW. We recommend that OP do not use a RTW program that is based on in vivo exposure principles but continue with CAU that is in accordance with the existing Dutch professional guidelines for CMD.

See Appendix (http://www.sjweh.fi/data_repository.php) for details on economic evaluation.

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