Efficacy of eye movement desensitization and reprocessing therapy for fear of cancer recurrence among cancer survivors: a randomized single-case experimental design

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CLINICAL RESEARCH ARTICLE

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Efficacy of eye movement desensitization and reprocessing therapy for fear of cancer recurrence among cancer survivors: a randomized single-case experimental design

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ABSTRACT

Background: Fear of cancer recurrence (FCR) is one of the greatest problems with which cancer survivors have to deal. High levels of FCR are characterized by intrusive thoughts about cancer-related events and re-experiencing these events, avoidance of reminders of cancer, and hypervigilance, similar to post-traumatic stress disorder (PTSD). Eye movement desensitization and reprocessing (EMDR) therapy focuses on these images and memories. It is effective in reducing PTSD and may be effective in reducing high levels of FCR.
Objective: The aim of the present study is to investigate the effectiveness of EMDR for severe FCR in breast and colorectal cancer survivors.
Method: A multiple-baseline single-case experimental design ($n = 8$) was used. Daily repeated measurements for FCR were taken during the baseline phase and treatment phase, post-treatment, and at the 3 month follow-up. Participants answered the Cancer Worry Scale (CWS) and the Fear of Cancer Recurrence Inventory, Dutch version (FCRI-NL) five times, i.e. at the start and at the end of each phase (baseline, treatment, post-treatment, and follow-up). The study was prospectively registered at clinicaltrials.gov (NL8223).
Results: Visual analysis and effect size calculation by Tau-U were executed for the daily questionnaire on FCR. The weighted average Tau-U score was .63 ($p < .01$) for baseline versus post-treatment, indicating large change, and .53 ($p < .01$) between baseline and follow-up, indicating moderate change. The scores on the CWS and FCRI-NL-SF decreased significantly from baseline to follow-up.
Conclusion: The results seem promising for EMDR therapy as a potentially effective treatment for FCR. Further research is recommended.

Eficacia de la terapia de desensibilización y reprocesamiento por movimientos oculares para el miedo a la recurrencia del cáncer entre sobrevivientes de cáncer: Un diseño experimental aleatorizado de caso único

Antecedentes: El miedo a la recurrencia del cáncer (FCR por sus siglas en inglés) es uno de los mayores problemas con los que tienen que lidiar los sobrevivientes de cáncer. Los altos niveles de FCR se caracterizan por pensamientos intrusivos sobre eventos relacionados con el cáncer y la re-experimentación de estos eventos, la evitación de recuerdos del cáncer y la hipervigilancia similar al trastorno de estrés postraumático (TEPT). La terapia de Desensibilización y Reprocesamiento por Movimientos Oculares (EMDR) se centra en estas imágenes y recuerdos y es eficaz para reducir el TEPT y podría ser eficaz para reducir los altos niveles de FCR.
Objetivo: El objetivo del presente estudio es investigar la eficacia de la EMDR sobre la FCR grave en sobrevivientes de cáncer de mama y colorrectal.
Método: El diseño utilizado es un diseño experimental de línea de base múltiple y caso único (n=8) (SCED por sus siglas en inglés). En el presente estudio se realizaron mediciones diarias repetidas de FCR durante la fase inicial, la fase de tratamiento, el postratamiento y a los 3 meses de seguimiento. Los participantes respondieron 5 veces a la Escala de Preocupación por el Cáncer (CWS por sus siglas en ingles) y al Inventario de Miedo a la Recurrencia del Cáncer versión holandesa (FCRI-NL por sus siglas en ingles), al inicio y al final de cada fase (es decir, a nivel basal, tratamiento, postratamiento y seguimiento'). El estudio se registró prospectivamente (NL8223) en clinicaltrials.gov.

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Cancer; cancer survivors; eye movement desensitization and reprocessing; EMDR; fear of cancer recurrence; FCR; multiple-baseline case series design; oncology; single-case experimental design; SCED

PALABRAS CLAVE
Cáncer; Supervivientes de cáncer; Desensibilización y Reprocesamiento por Movimientos Oculares; EMDR; Miedo a la Recurrencia del Cáncer; FCR; diseño de serie de casos de referencia múltiple; Oncología; Diseño experimental de caso único; SCED

关键词
癌症; 癌症幸存者; 眼动脱敏和再加工; EMDR; 癌症复发恐惧; FCR; 多基线个案系列设计; 肿瘤学; 单个案实验设计; SCED。

HIGHLIGHTS

- Patients who experience high fear of cancer recurrence (FCR) often have intrusive memories and images about (future) cancer-related events.
- Eye movement desensitization and reprocessing (EMDR) therapy can focus on these intrusions.
- EMDR therapy is found to be a promising therapy for patients experiencing high FCR.

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Resultados: Se realizó un análisis visual y un cálculo del tamaño del efecto mediante Tau-U para el cuestionario diario FCR. La media ponderada de las puntuaciones de Tau-U es de 0,63 (p < 0,01) para el valor basal frente al postratamiento, lo que indica un gran cambio; y de 0,53 (p < 0,01) entre el valor basal y el seguimiento, lo que indica un cambio moderado. Las puntuaciones en el CWS y el FCRI-NL-SF disminuyeron significativamente desde el inicio hasta el seguimiento.
Conclusiones: Los resultados parecen prometedores para la terapia EMDR como tratamiento potencialmente eficaz para el FCR. Se recomienda seguir investigando.

眼动脱敏和再加工疗法对癌症幸存者癌症复发恐惧的疗效：随机单个案实验设计

目的：癌症复发恐惧 (FCR)是癌症幸存者必须应对的最大问题之一。 高水平FCR 的特点是类似于创伤后应激障碍 (PTSD)的对癌症相关事件的闯入性想法和再体验这些事件，回避癌症提示物和的高警觉。眼动脱敏和再加工 (EMDR) 疗法关注这些图像和记忆，可有效减少 PTSD，并可能有效降低高水平 FCR。本研究旨在考查 EMDR 对乳腺癌和结直肠癌幸存者严重 FCR 的有效性。
方法：所使用的设计是多基线单个案实验设计 (n=8) (SCED)。 在本研究中，在基线阶段、治疗阶段、治疗后和 3个月的随访期间，每天重复测量 FCR。 参与者在每个阶段的开始和结束时（即基线、治疗、治疗后和跟进）5 次作答了癌症担忧量表(CWS) 和荷兰语版癌症复发恐惧量表 (FCRI-NL)。该研究在 clinicaltrials.gov 上进行了前瞻性注册 (NL8223)
结果：对每日问卷 FCR 进行了 Tau-U 的可视化分析和效应量计算。基线与治疗后的加权平均 Tau-U 评分为 0.63 (p < .01)，表明变化很大；基线和随访之间为 .53 (p < .01)，表明中度变化。CWS 和 FCRI-NL-SF 的分数从基线到随访显著降低。
结论：EMDR 疗法作为 FCR 潜在有效疗法的结果似乎很有希望。建议进一步研究。

1. Introduction

In recent years, early diagnosis through (mass) screening and improvements in multimodality treatment have led to a growing number of cancer survivors. One of the largest problems cancer survivors have to deal with is fear of cancer recurrence (FCR) (Koch et al., 2013; Simard et al., 2013; van de Wal, van de Poll-Franse, et al., 2016). FCR is defined as the 'fear, worry, or concern relating to the possibility that cancer will come back or progresses' (Lebel et al., 2017). While some concern about recurrence or progression is universal among cancer survivors and may even be adaptive, persistently high levels of FCR are not. Severe FCR has found to negatively impact patients' quality of life, mood, relationships, and ability to work. Moreover, severe FCR has been associated with inappropriate use of healthcare services (both overuse and underuse) and non-adherence to follow-up recommendations (Koch et al., 2013; van de Wal, van Oort, et al., 2016). Consequently, severe FCR may result in higher healthcare costs and lower surveillance rates, which may compromise health outcomes (Champagne et al., 2018; Otto et al., 2018) Previous research has shown that approximately half of cancer survivors and 70% of more vulnerable patient subsets (e.g. younger, female) report moderate FCR levels, while 10% experience high and disabling FCR (Butow et al., 2017). Severe FCR is characterized by intense worrying and frequent intrusive thoughts and images about illness-related traumatic events and future-orientated catastrophes, avoidance, and difficulties making plans for the future (Lebel et al., 2016). Severe FCR is one of the largest unmet support needs (Koch et al., 2013; Simard et al., 2013; van de Wal, van de Poll-Franse, et al., 2016) and without intervention it usually does not diminish over time, even when the actual risk of cancer recurrence is low (Ellegaard et al., 2017).

Recent trials have supported the efficacy of different psychological interventions for the management of FCR, such as psychoeducation, cognitive behavioural therapy (CBT), meta-cognitive therapy, and acceptance commitment therapy (Hodgkinson et al., 2007; Maheu et al., 2016; Sharpe et al., 2017, 2019; van de Wal et al., 2017). These interventions generally focus on maladaptive thoughts, rumination, and inappropriate monitoring and screening behaviours (Burm et al., 2019; Sharpe et al., 2019). Moreover, while effective for many, these interventions are not effective for all patients, are relatively time consuming, and may require specific cognitive and motivational skills of the patient. Hence, there is room for alternative treatments that may also be effective and explicitly target the intrusive images about the past and the future that are prevalent in patients with high FCR.

Eye movement desensitization and reprocessing (EMDR) therapy may be a good alternative treatment. With more than 25 randomized clinical trials, EMDR has been established as an evidence-based intervention for post-traumatic stress disorder (PTSD) and PTSD-like symptomatology, including physical symptoms and fear of future catastrophes (van Balkom et al., 2013).

As in PTSD, a high level of FCR is characterized by intrusive thoughts and re-experiencing events, avoidance of reminders of cancer, hypervigilance,

difficulty in making future plans, and increased emotional distress (Simonelli et al., 2017). In EMDR treatment, these symptoms are the core focus of the intervention. Therefore, EMDR seems to be a logical choice for processing cancer-related memories and intrusions that exacerbate FCR and to reduce high levels of FCR.

The primary aim of the present, eight-times-replicated, multiple-baseline, single-case experimental design (SCED) is to investigate the efficacy of EMDR on severe FCR in breast and colorectal cancer survivors. We hypothesize that EMDR will be effective in reducing severe FCR.

2. Method

2.1. Study design

The design used is a multiple-baseline SCED across eight participants. SCEDs evaluate treatment response at the level of the individual, and when combined, may provide information on how we should treat groups of patients with similar conditions (Vohra, 2016). SCEDs are useful to find effective treatments in healthcare applications, in which the individual is the unit of analysis and intervention (Vohra, 2016). SCEDs are a good alternative to a randomized controlled trial (RCT) for initial tests of a therapy in a different setting, or for different patient groups or problems than those for which the therapy was originally designed (Krasny-Pacini and Evans, 2018). SCEDs come with the additional advantage that they require fewer resources and are often practically more feasible (Kazdin, 2011). In a SCED, sufficient power is attained not by including many patients, as in an RCT, but by assessing the primary outcome measure frequently. By including randomization over baseline length in the multiple-baseline design, one can control for threats to internal validity (spontaneous recovery and fluctuations over time). In the present study, daily repeated measurements about FCR were taken during the baseline period, when no treatment was provided (phase T1), continued during EMDR treatment (phase T2) and post-treatment (phase T3/T4), and restarted 3 months after the end of treatment, during a 2 week follow-up period (phase T5) (see Figure 1). The length of baseline and hence the number of daily measures during the baseline phase are randomly assigned to the participants. For each participant, the primary outcome measure is assessed 98 times, with an additional 14 assessments 3 months after ending treatment (maximum 112 assessments). This way, a comparison can be made between the change in scores during baseline and the change in scores during the treatment phase, post-treatment phase, and follow-up phase. The effect of the EMDR treatment is expected to be found between baseline and post-treatment because it will take several EMDR sessions before FCR will diminish.

In addition to the daily measures, secondary outcome measures included much-used and well-validated standard measures of FCR, and were assessed at the beginning of the baseline phase, start of the intervention phase, end of the intervention phase, end of post-treatment, and at 3 months' follow-up.

2.2. Participants

During a period of 10 months (January 2020 to October 2020) potential participants were recruited at the 9 month follow-up appointment after curative treatment for breast or colorectal cancer at the Department of Oncology and Department of Surgery of Leiden University Medical Center (LUMC). After signing informed consent, they received an online link to complete the Cancer Worry Scale (CWS). Those with a score above the cut-off (CWS ≥ 14) were included in the study. Moreover, to be eligible to participate in this study, patients needed to meet all of the following criteria: adult (aged 18–70 years) survivors of breast cancer (female) or colon cancer (male/female) after ending treatment. Participants must have been able to report on a daily basis on an online questionnaire, so minimal computer skills were necessary. Participants with a low to normal score would not participate in the treatment phase of the study. Participants with a score of ≥ 14 on the CWS were included for the treatment phase of the study. Signed informed consent was necessary to participate. All patients participating in the study met the inclusion criteria. Patients who met the following criteria were excluded from participation in this study: age under 18 years or over 70 years, obvious intellectual impairment, insufficient knowledge of the Dutch language, or acute psychiatric problems such as acute psychotic disorders or suicidality. Patients using medication that has an effect on anxiety needed to be on stable medication for at least 3 months and to keep their medication unchanged during the study. Only one patient was excluded because of her age (> 70 years) and the impossibility of reporting using an online questionnaire on a daily basis. This particular patient was referred to the Department of Psycho Oncology for psychological treatment.

2.3. Measurements

2.3.1. Daily Questionnaire Fear of Cancer Recurrence (DQ-FCR)

Participants answered this five-item questionnaire (five-point Likert scale) about the degree of FCR and the existence of intrusive thoughts or images. Questions were: To what degree do you suffer from (1) fear of cancer recurrence; (2) thoughts about cancer

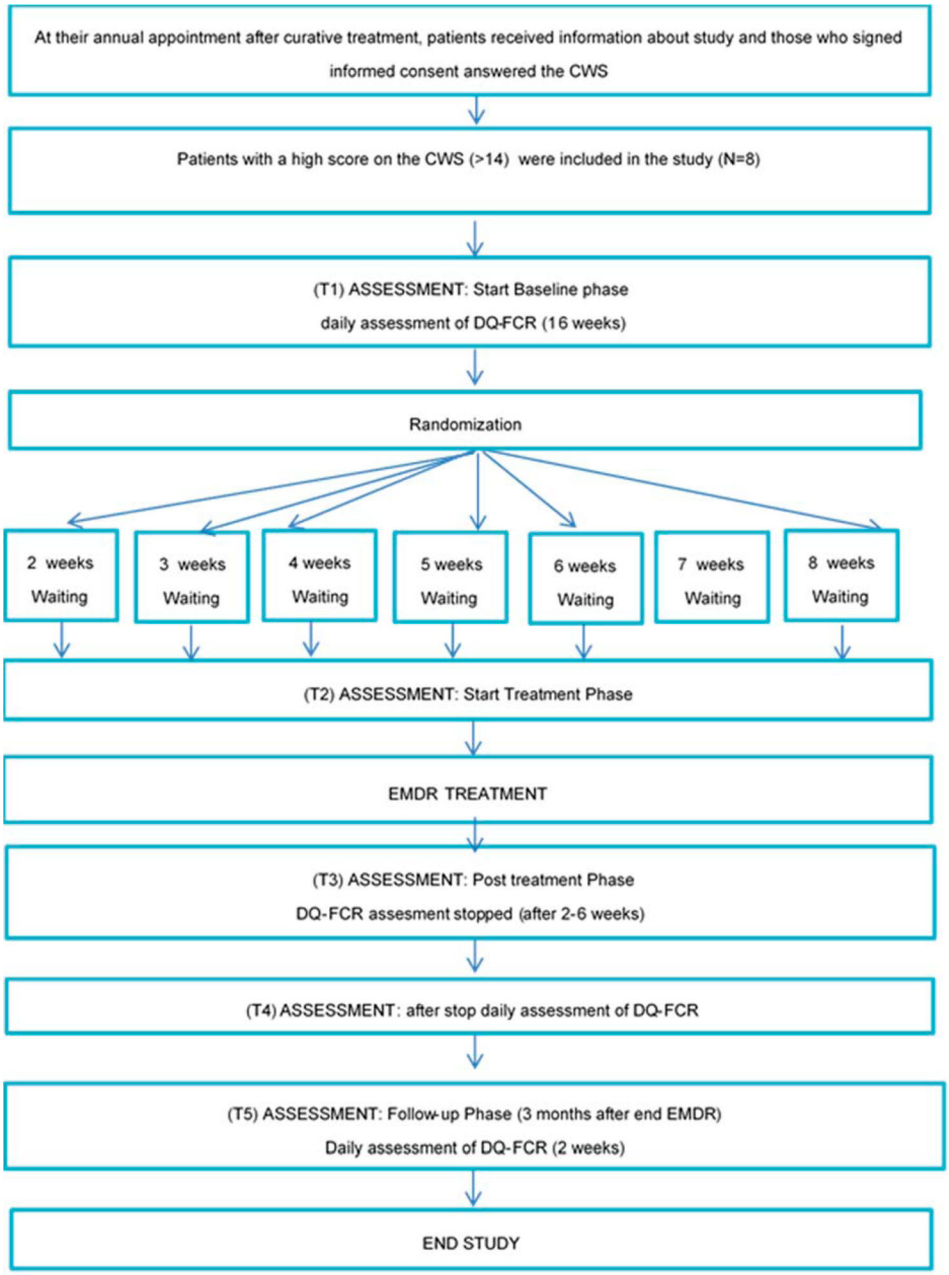

Figure 1. Flowchart of study design and main procedures. CWS = Cancer Worry Scale; DQ-FCR = Daily Questionnaire Fear of Cancer Recurrence; EMDR = eye movement desensitization and reprocessing.

recurrence; (3) intrusive images of cancer?; (4) How much time do you spend thinking about cancer?; and (5) To what degree are you limited today by thoughts about cancer? The DQ-FCR is the primary outcome measure. The DQ-FCR was designed by the research group based on questions of the CWS but adapted to be used on a daily basis. The DQ-FCR has good internal consistency (Cronbach's $\alpha = 0.91$). Participants received a link on a daily basis for online assessment.

2.3.2. Cancer Worry Scale (CWS)

The CWS is an eight-item questionnaire used to detect high levels of FCR (four-point Likert scale). Total scores range from 8 to 24. The CWS is a much-used, reliable, and valid questionnaire to assess FCR in cancer survivors (Custers et al., 2014). A score of 14 or higher indicates a severe level of FCR (Custers et al., 2014). The CWS has good internal consistency (Cronbach's $\alpha = 0.86$).

2.3.3. Fear of Cancer Recurrence Inventory, Dutch version (FCRI-NL)

The FCRI-NL is a 46-item questionnaire (five-point Likert scale) to assess FCR and has acceptable psychometric properties (van Helmondt et al., 2017). Total scores range from 0 to 184. The FCRI-NL has good internal consistency (Cronbach's $\alpha = 0.92$ for the total scale and $\alpha = 0.96$ and sufficient reliability for the severity subscales).

2.3.4. PTSD Checklist for DSM-5 (PCL-5)

The PCL-5 was used to assess the number of PTSD symptoms. The PCL-5 outcomes are not considered as outcome measures, but as descriptive variables between patients. The PCL-5 is a 20-item self-report questionnaire assessing the 20 symptoms of PTSD according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5). Initial psychometric evaluation showed a strong internal consistency (Cronbach's $\alpha = 0.94$) (Blevins et al., 2015).

2.4. Procedures

Figure 1 shows an overview of the study design and the main procedures.

2.4.1. EMDR therapy

EMDR therapy was carried out by two level II trained EMDR therapists who are members of the Dutch association of EMDR (VEN). Each therapist treated two colorectal cancer survivors and two breast cancer survivors. During treatment, the therapists received monthly supervision sessions of 1 h by an accredited EMDR consultant, using video recordings of the sessions. Additional supervision was provided via e-mail and telephone upon request. Another EMDR supervisor reviewed the videotaped EMDR sessions on protocol checklists. A total of 12 videotapes (32%) of treatment sessions were randomly selected and rated for adherence by an accredited EMDR consultant using EMDR-specific fidelity checklists. The level of treatment adherence was 93.5%.

In this study, the EMDR intervention consisted of one case conceptualization session of 90 min followed by weekly EMDR sessions of 60–90 min. In this session, all of the participating patients were considered stable and EMDR treatment was able to start directly. Participants received a minimum of three and a maximum of six sessions. The sessions were planned to be face to face, but during the coronavirus disease 2019 (COVID-19) pandemic we partly switched to online treatment, depending on the national and institutional regulations concerning the COVID-19 pandemic at different times. Four participants completed a face-to-face treatment, two participants received online video-consulting treatment only, and two participants received a combination of both. There are limited data available on whether online EMDR is as effective as face-to-face EMDR, but the results seem promising (Spence et al., 2013).

The key component of EMDR is that the patient holds an emotionally disturbing negative memory in their mind while simultaneously taxing working memory by tracking with the eyes a lightbar that is moving horizontally back and forth, following tones in the left and right ears produced by headphones, holding buzzers in the left and right hands, or by the therapist tapping with both hands on the patient's knees or shoulders (Shapiro, 2014). In this study, we used all of these methods for taxing working memory.

The standard EMDR protocol was used to desensitize patients' most disturbing images of past events and representations of future cancer-related catastrophes. After a set of eye movements (duration: about 30 s), the patient was asked what came to mind. What came up became the focus for the next set. This procedure was repeated until this memory no longer generated any distress. When all negative cancer-related experiences had been desensitized, the future catastrophe became the target for the EMDR. This is called the flashforward procedure. Unprocessed traumatic past experiences may also generate future-oriented anxiety-provoking images ('flashforwards') (Engelhard et al., 2011). These intrusive images can be ameliorated by taxing working memory using eye movements in the same way as disturbing memories can be desensitized (Logie and de Jongh, 2014). Targets are characterized by cancer-related experiences (e.g. feeling a lump in the breast, hearing the diagnosis from the oncologist, complications in the treatment phase), memories about prior loss or death of a loved one (e.g. seeing a friend in pain when dying of cancer, losing one's mother after unsuccessful reanimation), and future catastrophes when the cancer has recurred. In the future catastrophes, images about dying a horrible death (e.g. being in unbearable pain, suffocation, emaciation, or being fully dependent for care) or having to say farewell to loved ones (e.g. seeing young children grieving at one's deathbed) are often mentioned.

2.4.2. Statistical analysis

Analysis of the DQ-FCR consisted of visual analysis of all assessment points per participant followed by statistical analysis to detect whether EMDR therapy impacted FCR over time, by Tau-U effect size calculation. Tau-U is an effect size for analysing SCED data that can address problematic trend issues, is robust enough for small data sets, maintains non-overlap in the evaluation of a treatment effect, and uses all the data in the design (Parker et al., 2011). Tau-U is directly interpretable as a continuous index of improvement. As with Cohen's *d*, a Tau-U effect size of .20 improvement may be considered a small change, .20–.60 a moderate change, .60–.80 a large change, and above .80 a large to very large change (Parker et al., 2011). The analyses were performed using the online Single Case Data Analysis (SCDA) software, version 2.8 (https://tamalkd.shinyapps.io/scda/). The secondary outcome measures, CWS and FCRI-NL-SF, were analysed with SPSS. Mean differences on the CWS and the FCR between T1 and T4/T5 and Cohen's *d* with

Hedges' correction were calculated using paired-sample *t*-tests.

3. Results

3.1. Patients' characteristics

Three females and one male survivor of colorectal cancer ($n = 4$) and four female survivors of breast cancer ($n = 4$) participated in the study. The mean age was 47.3 (*SD* 13.5) years, seven of them were married or living together with a partner, and one participant was single. All participants had average or high levels of education. The mean score of participants on the CWS was 22.6 (*SD* 3.66) before inclusion, ranging from 17 to 27. Therefore, all participants had severe FCR at the start of the study. Time since the cancer diagnosis ranged between 1 year ($n = 5$) and 3 years ($n = 3$). All patients had completed their cancer treatment (e.g. radiotherapy, chemotherapy, or surgery) and were disease free at the time of inclusion. None of the participating patients met the DSM-5 criteria for PTSD measured with the PCL-5 at the start of the EMDR treatment.

Four participants received five EMDR sessions of 90 min, two received six EMDR sessions, one participant had four EMDR sessions, and one received only two sessions of EMDR. They all started treatment with a case conceptualization session of 90 min.

For some patients, the circumstances for successful treatment were complicated by comorbid conditions. Participant 8 was confronted with metastatic disease during the follow-up and did not complete the daily measurements 3 months after the EMDR ended, no follow-up data are available.

3.2. DQ-FCR

The primary outcome measure was analysed by visual analysis and with statistical analysis by Tau-U.

3.2.1. Visual analysis

Figure 2 displays the results for the DQ-FCR per participant for the baseline, treatment, post-treatment, and follow-up phases.

3.2.2. Statistical analysis: Tau-U

Table 1 presents the Tau-U scores for each participant (Parker et al., 2011; Vannest, 2015). The Tau-U scores for participants 6 and 7 were corrected for significant baseline trend in the therapeutic direction. Negative Tau-U values indicate an effect in the contra-therapeutic direction. In the following paragraphs, the visual analyses and the Tau-U effect sizes are described.

Visual and statistical analyses showed that six out of eight participants reported a moderate to (very) large effect in decrease in FCR at post-treatment. The weighted average Tau-U scores for all participants were .34 ($p < .01$) for baseline versus intervention, indicating moderate change; .63 ($p < .01$) for baseline versus post-treatment, indicating large change; and .53 ($p < .01$) for baseline versus follow-up, indicating moderate change.

A detailed description of the results for each participant can be found in the Appendix. Here, we present participant 2 as an example. All visual and Tau-U effect sizes of the other participants are analysed and described in the same way.

For participant 2, the data are low in variability. No discernible trend is visible during the baseline phase. During the intervention phase, a decreasing trend can be observed, as well as a decrease in the level of FCR. This decrease does not occur immediately after changing from baseline to intervention. There is some degree of overlap between the baseline and intervention phases. The post-treatment phase shows no immediate change compared to the preceding intervention phase. There is no discernible trend during the post-treatment phase. The follow-up phase follows the same pattern. There is no visible change in the level of FCR between the post-treatment and follow-up phases. The Tau-U between the baseline and intervention phases equals .68, indicating a large change; the Tau-U between baseline and post-treatment equals .92, indicating a very large change; and the Tau-U between baseline and follow-up equals .86, indicating a large to very large effect. Immediately after start of treatment, the FCR scores start to decline. The results were maintained after treatment and at follow-up.

3.2.3. CWS and FCRI-NL-SF

Paired-sample *t*-tests showed that the mean difference on the CWS between T1 and T4 was 6.83 ($SD = 2.48$) [$p = .001$, with Cohen's $d = 2.54$, 95% confidence interval (CI) 0.83–4.26]. Between T1 and T5 (follow-up), the mean difference was 5.83 ($SD = 1.84$) ($p < .001$, Cohen's $d = 2.93$, 95% CI 1.02–4.83). Similar results were found on the FCRI-NL. The mean difference between T1 and T4 was 36.57 ($SD = 18.61$) ($p = .002$, Cohen's $d = 1.84$, 95% CI 0.59–3.05). The mean difference between T1 and T5 was 31.00 ($SD = 20.01$) ($p = .013$, Cohen's $d = 1.43$, 95% CI 0.27–2.54).

3.3. Patients' reports on the EMDR treatment

Using the SCED, it is possible to add detailed information about the EMDR treatment and the patients' experience of participation, the treatment itself, and the effect after 3 months' follow-up. All eight patients reported a significant reduction in FCR at the last EMDR treatment. They reported less fear, and fewer fear-related thoughts and images, and mentioned that the cancer experience was more in the

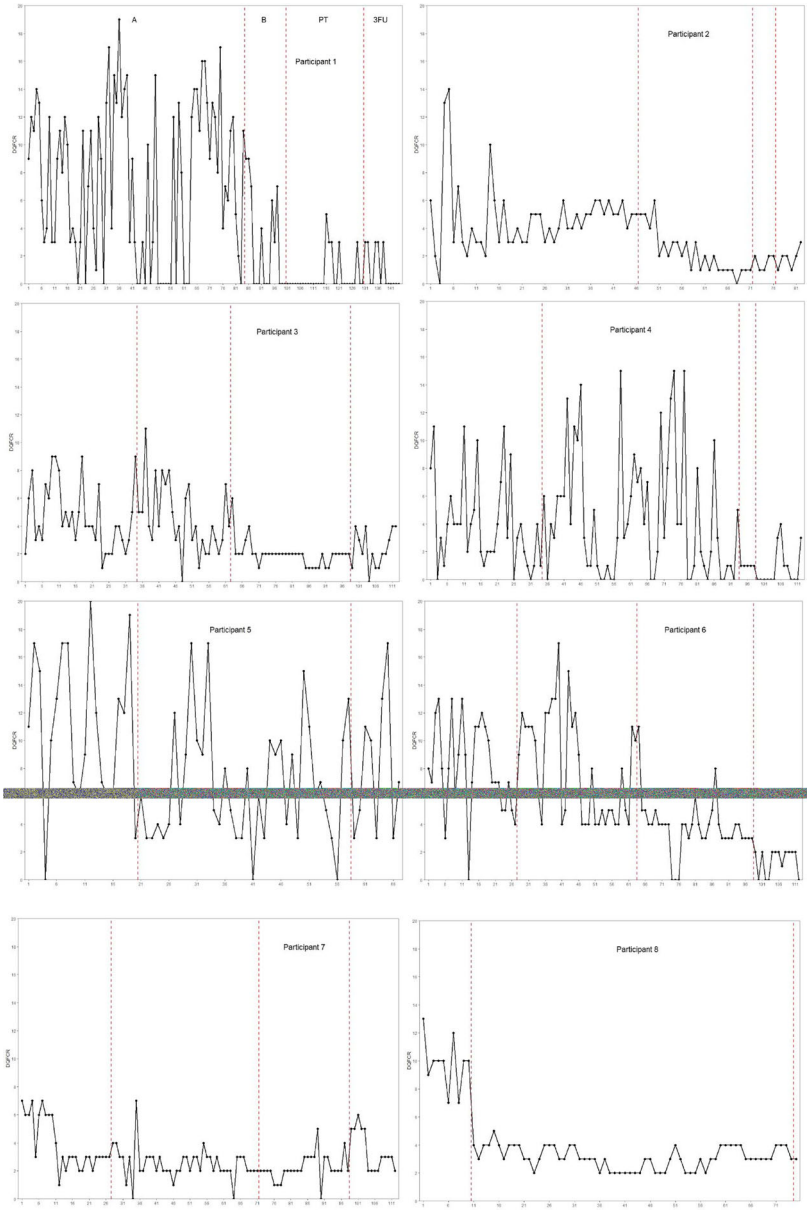

Figure 2. Results for the Daily Questionnaire Fear of Cancer Recurrence (DQ-FCR) per participant. A = baseline; B = intervention; PT = post-treatment; 3FU = 3 month follow-up.

background in their lives. Some of them were able to make changes in their avoidance behaviour (e.g. stopping obsessively checking for cancer on the skin, stopping obsessively checking stools for signs of blood, drinking or eating 'unhealthily' without being overly worried that this would lead to cancer recurrence). Some participants were able to have a healthier relationship with their body (e.g. looking in the mirror without being scared of cancer signs, taking a bath and looking at scars, thinking about the body as strong) or reported a better sleeping pattern and being able to feel more relaxed.

Table 1. Tau-U effect sizes for the Daily Questionnaire Fear of Cancer Recurrence (DQ-FCR) per participant.

Participant	Baseline vs intervention	Baseline vs post-treatment	Baseline vs follow-up	Type of treatment
1	.48*	.71*	.65*	Face-to-face
2	.68	.92*	.86*	Face-to-face
3	.04	.77*	.59*	Face-to-face
4	0	.68**	.69*	Online/face-to-face
5	.46*	.33	N/A	Face-to-face
6	−.04	.66*	.68*	Online
7	.33*	.39*	−.20	Online
8	1*	Missing	Missing	Online/face-to-face

Note: *$p < .01$, **$p < .05$.

On top of the evaluation with all participants, five of the eight participants were able to respond in an interview by telephone about this topic. They answered questions on a five-point Likert scale about different aspects of the EMDR treatment. The contentment of the effect of the EMDR treatment was scored as 'good' (score of 5) by three participants, one scored a 4, and one chose 'neutral' (score of 3). Three out of five would highly recommend EMDR as a treatment for FCR, one would probably recommend EMDR, and one chose 'maybe'. The

evaluation on how much of a burden the EMDR was experienced as had a wide range (1–5); each participants gave a different score from 'highly burdensome' to 'not a burden at all'. All participants answered that the EMDR treatment had a high (1), great (3), or reasonable (1) impact on their daily functioning or quality of life.

4. Discussion

The primary aim of this study was to test the efficacy of EMDR therapy for severe FCR among cancer survivors. In accordance with the hypothesis, we found large effect sizes between baseline and post-treatment, and these were maintained during follow-up with moderate effect sizes. To the best of our knowledge, this is the first intervention study to demonstrate the effects of EMDR therapy on FCR reduction in cancer survivors. Visual and statistical analyses showed that six out of eight patients reported a moderate to very large effect in decrease in FCR at post-treatment.

We hypothesized that the effect of the EMDR therapy would appear in post-treatment, and the results showed that for some participants the first effects were already detectable during EMDR treatment.

Comparing the results of this EMDR therapy with blended cognitive behavioural therapy (bCBT) for FCR, the mean difference on the CWS for these patients (6.6) was larger than that found in the study investigating bCBT (3.48) (van de Wal et al., 2017).

In this study, the treatment consisted of three to six 90 min EMDR sessions. The average treatment time (including a 90 min case conceptualization session) was 517 min. Comparing this to bCBT with six sessions of 60 min and three sessions of 15 min, in total 405 min average treatment time, supplemented with homework assignments between sessions, the durations of which are not specified (Maheu et al., 2016), EMDR may be comparable with bCBT with regard to time investment (Hall et al., 2018).

The present study has several strengths. It is the first to use EMDR as a treatment for FCR. SCEDs are a good alternative to RCTs when a therapy is found to be effective and needs to be tested in an alternative setting or to test the intervention on patients or problems other than those for which the intervention was originally designed (Krasny-Pacini and Evans, 2018). The multiple-baseline design with randomization over baseline length in this study controlled for threats to internal validity (spontaneous recovery and fluctuations over time) and the effect was replicated across heterogeneous individuals (psychological comorbidity, cancer type), which also increases the generalizability of the study. The potential for confounding by covariates is eliminated by given that each patient served as his or her own control. By assessing the primary outcome measure frequently on a daily basis for 112 days, we attained sufficient power.

The use of two therapists limited therapist bias. Therapists and patients were blind to assessment outcomes. The therapists used a manualized treatment protocol, session checklists, and video-recorded sessions, which were evaluated and discussed during supervision to enhance treatment integrity. None of the participants dropped out of the EMDR therapy and no adverse events were reported. This indicates that EMDR therapy is both bearable and safe to use among cancer patients.

4.1. Study limitations

This study has several limitations. During the study, the COVID-19 pandemic made it necessary to shift from face-to-face to online treatment, resulting in different circumstances for different participants. The possible impact on the results of the EMDR treatment is unclear. There were only follow-up data for six of the eight participants, and the post-treatment data of one participant (participant 8) could not be analysed because there were not enough observations. Having chosen a SCED, it is difficult to make a comparison with the results of RCTs. Finally, the results of the secondary outcome measures (CWS and FCRI-NL) need to be interpreted with caution, because of the small sample size.

Although this study supports the use of EMDR therapy in patients with FCR, the issues of external validity, the small sample size, and the ratio of females to males (1:7) may limit its generalizability. Larger scale studies with appropriate control groups are warranted.

The variation in follow-up after cancer treatment between the patients (from 1 to 3 years after diagnosis) is another possible limitation in this small sample.

In addition, in future research, it is recommended to assess broader outcome measures, such as depression, anxiety, distress, and adverse childhood events, as they are related to the construct of FCR, and to investigate the generalization of the effect of EMDR on these outcomes.

Nevertheless, the small sample size allowed us to focus on each participant's individual clinical characteristics, providing rich detail about the change, and we were able to closely monitor our participants. Therefore, some comments about the circumstances of the participants can be made. Participant 7 was confronted with the loss of a close family member to cancer before starting EMDR. Their grief may have interfered with the results of EMDR therapy.

For all participants, a limitation applies in that the study was executed during the COVID-19 pandemic. This forced us to change the original protocol, in which only face-to-face sessions were planned, to

blended or fully online video treatment sessions. The effect on the study results is uncertain, because limited research is available about online EMDR treatment. The experience of the therapists was that participants appreciated that the EMDR treatment continued online instead of being postponed or cancelled during the COVID-19 pandemic. Only one participant reported afterwards that she would prefer face-to-face treatment if she had a choice.

4.2. Clinical implications

Overall, this study provides new evidence highlighting the potential of EMDR as a feasible, effective, and acceptable treatment for FCR among cancer survivors. Further research on EMDR as a treatment for FCR is necessary. We propose investigating EMDR as treatment for FCR in a randomized waiting-list controlled trial as the next step. Future research on EMDR versus CBT interventions for FCR, and which intervention is most suitable for which type of (patients with) FCR, is recommended.

5. Conclusions

This study is, to the best of our knowledge, the first trial to investigate the efficacy of EMDR as a therapy for FCR. In this SCED, we found initial evidence that EMDR therapy could be an effective and efficient treatment for FCR. More research on this specific intervention should be conducted, preferably in an RCT.

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Disclosure statement

C. de Roos receives income for training postdoctoral professionals in EMDR. No potential conflict of interest was reported by the other authors.

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Ethics approval

The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Medical Ethics Committee South West Holland (P19.058 13-11-2019). The trial was registered at the Dutch Trial Register (NTR) (NL68358.058.19) as the FREE study: Effectiveness of EMDR for Fear of cancer Recurrence. Informed consent was obtained from all subjects involved in the study.

Data availability

The data sets generated during and/or analysed during the current study are available from the corresponding author upon reasonable request. The study protocol has been published with the original article.

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Appendix

A detailed description of the results per participant

For participant 1, a large variability is present throughout the baseline and intervention phases. The scores range from 0 to 19 during the baseline phase and from 0 to 9 during the intervention phase. No clear trend is visible during either the baseline or the intervention phase. There is no immediate change

in responding between the baseline and intervention phases, and a high degree of overlap between the two phases. However, during the post-treatment phase the data pattern is much less variable and a decrease in the level of FCR can be observed compared to the baseline and intervention phases. No discernible trend is visible during the post-treatment phase, and a decreasing trend with moderate variability is observed during the follow-up. The last three data points of the intervention phase have a score of 0, which continues into the post-treatment. The last five data points in the follow-up phase also have a score of 0. The Tau-U between baseline and intervention equals .48, indicating a moderate change; the Tau-U between baseline and post-treatment equals .71, indicating a large change; and the Tau-U between baseline and follow-up equals .65, indicating a large change.

For participant 2, the data are less variable. No discernible trend is visible during the baseline phase. During the intervention phase, a decreasing trend can be observed, as well as a decrease in the level of FCR. This decrease does not occur immediately after changing from baseline to intervention. There is some degree of overlap between the baseline and intervention phases, but less than for participant 1. The post-treatment phase shows no immediate change compared to the preceding intervention phase. There is no discernible trend during the post-treatment phase. The follow-up phase follows the same pattern. There is no visible change in the level of FCR between the post-treatment and follow-up phases. The Tau-U between the baseline and intervention phases equals .68, indicating a large change; the Tau-U between baseline and post-treatment equals .92, indicating a very large change; and the Tau-U between baseline and follow-up equals .86, indicating a large to very large effect.

For participant 3, the baseline phase shows high variability and no discernible trend. The intervention phase also shows high variability, but with an initially decreasing trend. There is no immediate change in responding between the two phases, which was consistent with the hypothesis that change will occur during the treatment phase and continue to decrease in the post-treatment phase. There is a high proportion of overlapping data points between the baseline and intervention phases. During the post-treatment phase, there is much less variability present in the data and a decrease in the level of FCR. With the exception of the first data point in the post-treatment phase, the scores range from 0 to 4. Towards the end of the follow-up phase, there seems to be an increasing trend, whereas the preceding data points show no trend. The follow-up phase also shows higher variability again. The Tau-U between baseline and intervention equals .04, indicating no change; the Tau-U between baseline and post-treatment equals .77, indicating a large change; and the Tau-U between baseline and follow-up equals .59, indicating a moderate change.

Participant 4 also shows very high variability in responding during the baseline and intervention phases. The scores in the baseline phase range from 0 to 11 and in the intervention phase from 0 to 15. Neither phase shows a discernible trend. Despite the large variability, the level of FCR in the intervention phase seems to be somewhat higher. There is no immediate change in responding between the baseline and intervention phases, and there is a high proportion of overlapping data points between the baseline and intervention phases. Responding in the post-treatment phase shows no variability and a much lower level of FCR than in either the baseline or intervention phase. The level during the follow-up phase is also lower but more variable, with an increasing trend overall. The Tau-U between baseline and intervention equals 0, indicating no change; the Tau-U between baseline and post-treatment equals .68, indicating a large change; and the Tau-U between baseline and follow-up equals .69, indicating a large change.

For participant 5, the scores range from 0 to 20 during the baseline phase and from 0 to 17 the during intervention phases, indicating very high variability. Neither the baseline nor the intervention phase shows a clear trend, but there seems to be a decrease in the level of FCR during the intervention phase. At treatment onset, there appears to be an immediate decrease in FCR, which subsequently increases again and is subject to large variability. Owing to the high variability, there is a large proportion of overlapping data points between the baseline and intervention phases. The high variability continues into the follow-up phase, with scores ranging from 3 to 17. There is no obvious change in the level of FCR or trend between the intervention and follow-up phases. The Tau-U between baseline and intervention equals .46, indicating moderate change; and the Tau-U between baseline and follow-up equals .33, indicating a moderate change.

For participant 6, the scores range from 0 to 13 during the baseline phase and from 4 to 17 during the intervention phase. Thus, both phases are subject to considerable variability. It appears that there is no noticeable change in the level of FCR between the two phases. In spite of the large variability, a decreasing trend in the therapeutic direction is visible in the baseline phase. There is an immediate increase in FCR after changing from baseline to intervention. A high proportion of overlapping data points between the baseline and intervention phases is present. When changing from intervention to post-treatment, there is an immediate decrease in FCR, with a decreasing trend over time. The proportion of overlapping data points between intervention and post-treatment is lower than that observed for the change between the baseline and intervention phases. In addition, the scores during the post-treatment phase are less variable than during baseline and intervention phases. There is again an immediate decrease in FCR between post-treatment and follow-up, with little overlap between the two phases. There is no discernible trend during follow-up. The Tau-U between baseline and intervention equals −.04, indicating no change; the Tau-U between baseline and post-treatment equals .66, indicating a large change; and the Tau-U between baseline and follow-up equals .68, indicating a large change.

The scores of participant 7 are much less variable, ranging only from 0 to 7 throughout the whole study. During the beginning of the baseline phase, there appears to be a decreasing trend in the therapeutic direction. For the remainder of the study, FCR appears to be consistent, without any noticeable changes in level, trend, or variability. Furthermore, there are no immediate changes between any of the phases. The Tau-U between baseline and intervention equals .33, indicating a moderate change; the Tau-U between baseline and post-treatment equals .39, indicating a moderate change; and the Tau-U between baseline and follow-up equals −.20, indicating a small change in the contra-therapeutic direction.

For participant 8, there is a clear and sustained decrease in the level of FCR between the baseline and intervention phases. This change appears immediately after the phase change from baseline to intervention. There is some variability in the baseline phase, but very little variability during the intervention phase. There are no overlapping data points between baseline and intervention. The Tau-U between the baseline and intervention phases equals 1, indicating a very large effect. No Tau-U was calculated between baseline and post-treatment and follow-up owing to a lack of data points.