Nordic Journal of Psychiatry

ISSN: 0803-9488 (Print) 1502-4725 (Online) Journal homepage: https://www.tandfonline.com/loi/ipsc20

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To cite this article: Morten Fenger, Jane Lindschou, Christian Gluud, Per Winkel, Lise Jørgensen, Jan Hein Dybkjaer & Marianne Lau (2020): Internet-based therapy with FearFighter for anxiety disorders: a randomised clinical trial, Nordic Journal of Psychiatry, DOI: 10.1080/08039488.2020.1755363

To link to this article: https://doi.org/10.1080/08039488.2020.1755363

Published online: 13 May 2020.

NORDIC JOURNAL OF PSYCHIATRY
https://doi.org/10.1080/08039488.2020.1755363

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ARTICLE

Internet-based therapy with FearFighter for anxiety disorders: a randomised clinical trial

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ABSTRACT

Background: Internet-based cognitive behavioural self-help psychotherapy (ICBT) can be an important alternative or supplement to ordinary face-to-face therapy.
Aim: To assess effectiveness of ICBT for adults with an anxiety disorder.
Methods: Sixty-four participants were randomised to 9 weeks with the FearFighter ICBT program ($n = 32$) or no intervention ($n = 32$). Outcomes included complete remission, severity of symptoms and occurrence of adverse events.
Results: No difference ($p = 1.00$) in remission between groups following 10 weeks of intervention nor at 37 weeks follow-up was found. There was significant reduction in the severity of symptoms ($p < 0.05$) at end of intervention of ICBT compared to the control group, while the reduction in symptoms at 37 weeks follow-up was equal for the two groups. Two participants in the ICBT group and none in the control group reported adverse events.
Conclusion: We found no difference in remission, but a reduction of symptoms in the ICBT group compared with the control group at end of intervention. At six months follow-up the two groups showed the same level in the reduction of symptoms.

Trial registration: Clinicaltrials.gov: NCT02499055. Registered 01 July 2015.

ARTICLE HISTORY
Received 11 February 2019
Revised 22 February 2020
Accepted 1 April 2020

KEYWORDS
Anxiety; randomised clinical trial; cognitive behavioural therapy; internet-based psychotherapy

Background

Anxiety disorders are characterised by excessive worries and fear of situations, objects, and living creatures [1]. Reviews show that between 14% and 18% of European citizens fulfil the diagnostic criteria for anxiety disorder according to DSM-IV, or ICD-10 [2,3], and access to face to face treatment is insufficient.

Internet-based cognitive behavioural self-help psychotherapy (ICBT) for anxiety disorders is based on the same philosophy and treatment principles as face-to-face cognitive behavioural therapy (CBT) [4,5] and has in the latest meta-analysis shown better effect than no intervention and comparable effect to face to face CBT [6]. With the 2013 revision of the NICE guidelines for anxiety disorders, interventions with self-help resources are now recommended in stepped care model for anxiety in England [7–9]. FearFighter is an English developed and commercial ICBT programme for treatment of panic and phobia, and it is used in the mental health services in England [7]. Two randomised clinical trials from England have assessed FearFighter and found the programme better than relaxation and comparable to other treatment formats [10,11]. In Denmark, one randomised trial with a Danish version of FearFighter has been conducted [12,13]. The trial compared FearFighter with a waitlist control group. The authors found no significant difference between the two groups on their primary outcome measure for anxiety (e.g. Beck Anxiety Inventory). The authors reported that due to the chosen eligibility criteria, recruitment was poor, and the drop-out fraction was high: 50% in the intervention group and 20% in the waitlist group. The authors recommended a new randomised clinical trial to be conducted [13].

Aim of the study

The objective of the present randomised clinical trial is to assess the effectiveness of the ICBT programme FearFighter compared with no intervention in people with an anxiety disorder.

Methods

Trial design

The trial was an investigator-initiated randomised clinical trial in which 64 participants with an anxiety diagnosis were

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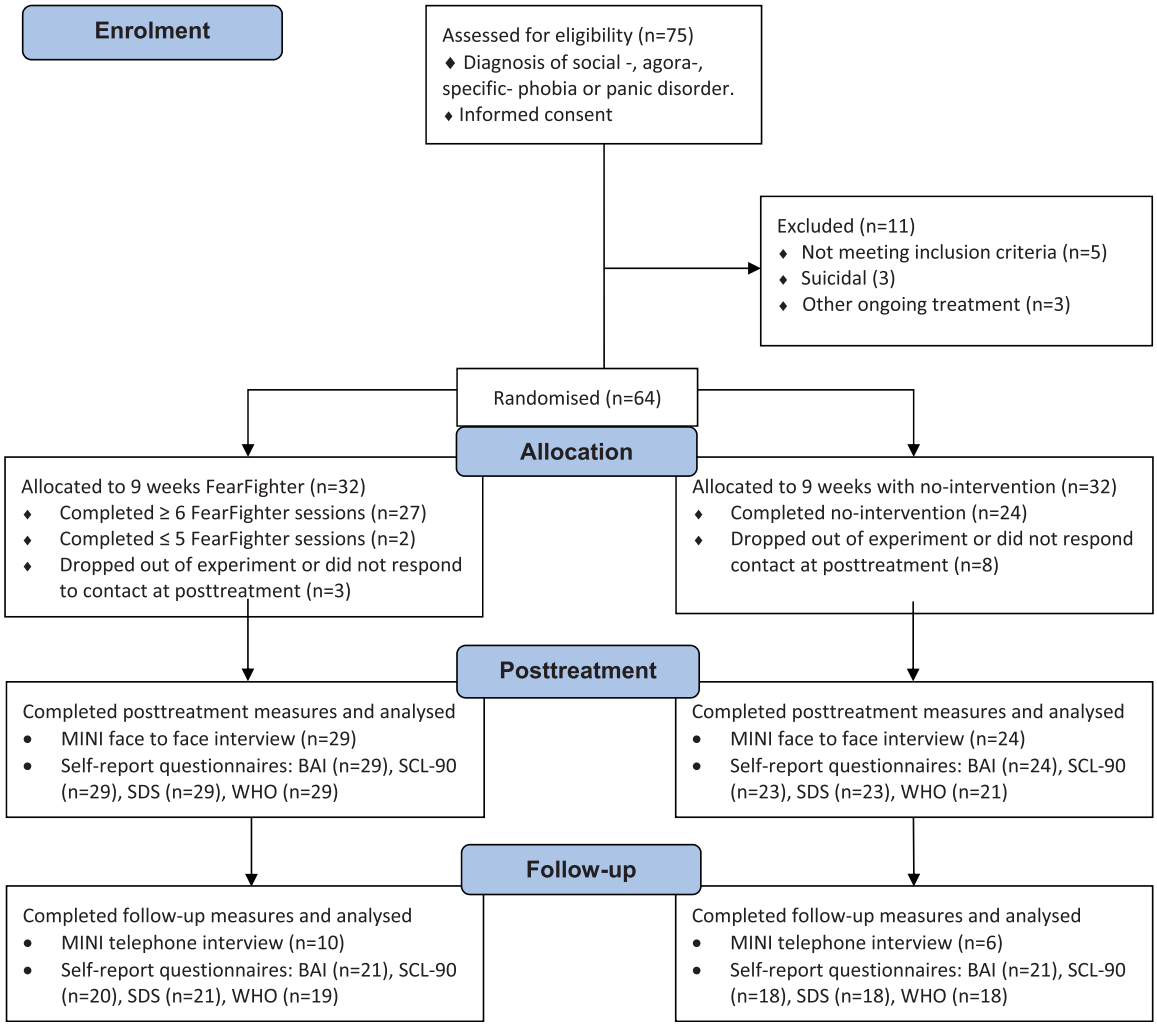

Figure 1. Flowchart.

randomised to ICBT with FearFighter ($n = 32$) versus no intervention ($n = 32$). The trial followed the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) 2013 statement for clinical trials [14], and a design article was published in Trials [15]. Assessment was conducted prior to randomisation and start of intervention (week 0), at end of intervention (week 10), and at follow-up (week 37) (see flow chart in Figure 1). The trial was approved by the regional ethics committee for the Capital Region of Denmark (journal number: H-15005836), and by the Danish Data Protection Agency (journal number; RHP-2015-009, I-Suite 03652). The trial was registered at Clinicaltrials.gov (registration number: NCT02499055. Registered 1 July 2015).

Randomisation

The Copenhagen Trial Unit (CTU) was responsible for the centralised randomisation. The randomisation was carried out according to a web-based computer-generated allocation sequence with varying block sizes kept unknown to the investigators. Once a participant was assessed eligible for the trial, the trial secretary used the web-based randomisation system to allocate the participant to an intervention group.

Blinding

The assessment of symptoms and recovery at posttreatment and at follow-up was performed by blinded assessors. Participants were instructed to withhold information of their allocation group when assessed. Statistical analyses were conducted blinded with the two intervention groups coded as X and Y. Two abstracts with conclusions were prepared by the blinded investigators, one assuming X is the experimental group and Y is the control group, and one conclusion assuming the opposite [16,17]. After consensus on the two abstracts was reached, the code was broken.

Assessors

A co-author, LJ (MS in Psychology), was trained by a senior psychiatrist in conducting the Mini International Neuropsychiatric Interview (MINI) for diagnostic assessment. LJ performed the initial interview and the diagnostic MINI face to face with all participants on a central location at the University of Copenhagen. LJ trained and instructed the end of intervention and the follow-up assessors (graduate students in psychology) in the use of MINI. It was optional for the participants to have the interview at week 10 and at

week 37 face to face or by telephone. Besides performing the diagnostic interview, the assessors also asked the participants if they had experienced any adverse events in connection with the trial and if they had received any other psychological treatment in the trial period.

Recruitment and included participants

Participants were recruited *via* advertisements through the Danish Student Counselling Service and their website (www.srg.dk), with a link to a website created by us for the trial. Our trial website contained information on the trial and a contact form for the prospective trial participants. Co-author LJ contacted and invited the interested participants to a face-to-face interview at the university for their eligibility to participate in the trial. The inclusion criteria were: age 18 or older; panic disorder, specific phobia, agoraphobia, or social phobia according to DSM-IV [18] assessed with the MINI [19], and signed informed consent. Criteria for exclusion were: suicidal risk, ongoing episode of bipolar disorder or psychosis, concurrent psychological treatment for the anxiety disorder, considered unable to attend the intervention as planned (due to vacation, work/study placement, sickness, or similar occurrences), or lack of informed consent (Figure 1). As MINI did not identify or screen for personality disorders, Standardised Assessment of Personality Abbreviated Scale (SAPAS) was used as a screening instrument [20]. SAPAS was only used for background information to indicate the possible presence of co-morbid personality disorders. The majority of the participants were students and females with an average age of 27 years and the majority had suffered from anxiety over five years. Table 1 displays characteristics of the included and randomised participants.

Table 1. Characteristics of the participants.

	Internet-based cognitive behavioural therapy ($n = 32$)	No intervention control group ($n = 32$)
Sex, n (%)		
Women	26 (81%)	26 (81%)
Men	6 (19%)	6 (19%)
Age, years		
Mean (s.d.)	26.3 (5.6)	27.9 (7.3)
Minimum–maximum	19–51	19–52
Marital and parental status, n (%)		
Single	16 (50%)	10 (31%)
Boy/girlfriend	12 (38%)	17 (53%)
Married	4 (13%)	5 (16%)
Parent, yes	3 (9%)	9 (28%)
Occupational status, n (%)		
Student	31 (97%)	27 (84%)
Other	1 (3%)	5 (15%)
Social relations – see 1–3 friends, n (%)		
In a week	26 (81%)	23 (72%)
In 14 days	3 (9%)	4 (13%)
In a month	3 (9%)	5 (15%)
Anxiety – duration of symtoms, n (%)		
Under 2.5 year	7 (22%)	4 (13%)
Between 2.5 and 5 years	3 (9%)	2 (6%)
Over 5 years	22 (69%)	26 (81%)
Earlier treatment , n (%)		
Privat psychologist	26 (81%)	27 (84%)
Mental health service	6 (19%)	7 (22%)
Other clinical information, n (%)		
Present psychotropic medication	5 (16%)	2 (6%)
SAPAS positive*	13 (39%)	16 (50%)

*SAPAS = Standardised Assessment of Personality Abbreviated Scale contains 8 screening questions. SAPAS has a cut off score on 3 for the presence of a personality disorder.

Interventions

The participants in the experimental group received internet-based therapy using the programme FearFighter, developed by professor Isaac Marks from the Maudsley Psychiatric Hospital in England [21]. A Danish version of the programme was developed in 2013 [13,22]. The FearFighter programme is based on principles derived from the cognitive behavioural therapy. The programme aims to teach people how to tackle negative thoughts and stand up against avoidance behaviours due to anxiety disorders. FearFighter consists of nine sessions. In each session, a video-filmed therapist gives psychoeducation and explains the rationale for the training, followed by a number of exercises and tasks for homework. Important points in psychoeducation are illustrated with video clips with four patients telling about their anxiety disorder, their symptoms and their treatment of the anxiety.

A whole week is assigned to do the homework. Homework is done between each session, and it is estimated to take one to three hours, depending on the invested effort by the individual. Each online session excluding the homework takes about 30 to 40 min. In all, the FearFighter programme recommends that participants use 5 to 8 h with the FearFighter programme and do 32 to 35 h on practicing the assignments and exposure exercises. The recommendations are set for an average participant and are indicative. The purpose is to understand or achieve the intended idea, experience or state as instructed in the exercises. The participants have to watch and complete all elements in a session before they can progress to the next and new session. All elements in earlier sessions are open to be revisited if needed. The participants' activity on FearFighter is logged and can be monitored by the support person. The content of the nine sessions is described below.

- *Session 1*: Psychoeducation about anxiety, cognitive behavioural therapy, and the programme. The homework is to find a person who can encourage the patient to complete the sessions in the programme.
- *Session 2*: Psychoeducation about anxiety symptoms and safety behaviour. The homework is to register episodes with anxiety in an electronic diary built within the programme.
- *Session 3*: Psychoeducation about panic disorder and interoceptive exposure. Demonstration of three interoceptive exercises, flash cards, progressive relaxation, and applied tension. The homework is to do one or more of the exercises on a daily basis.
- *Session 4*: Psychoeducation about automatic negative thoughts. The homework is to challenge the negative thoughts with rational questions, write answers, and thoughts in a schema.

- *Session 5*: Psychoeducation about core beliefs about oneself. The homework is to challenge the negative core beliefs with rational questions and to try to replace it with positive core beliefs.
- *Session 6*: Psychoeducation about exposure and the hierarchy model of anxiety provoking situations. The homework is to make a hierarchy of anxiety provoking situations, including goal setting.
- *Session 7*: Psychoeducation about how to prepare for exposure by pictures, sound, and video. The homework is to prepare the exposure plan.
- *Session 8*: Support for the participant in the exposure exercises. The exposure exercises have to be repeated until the patient fulfils their exposure plan and goal setting.
- *Session 9*: Sum-up and counselling on how to master setbacks and prevent relapse. Continue exposure exercises if necessary.

Each trial participant in the ICBT group was contacted over the telephone by a support person once a week during the nine weeks of intervention. The purpose of the contact was to secure compliance, and also to assist the participant to adhere to the program. The support person was instructed not to engage in a psychotherapeutic dialogue with the participants. The 32 participants received each 6.4 (standard deviation (SD) 1.8) telephone contacts of average 6.3 (SD 4.2) minutes' duration – in all 57 min per participant. The participants in the control group did not receive intervention or telephone contact and had accepted to refrain from seeking other treatment in the trial period as far as their condition with anxiety allowed it.

Outcomes

We assessed the proportion of participants who no longer fulfilled the diagnostic criteria for an anxiety disorder at the end of the intervention with the MINI [19]. Other clinical outcomes were the severity of psychiatric symptoms measured with Beck Anxiety Inventory (BAI) [23]; Symptom Checklist-90-R (SCL-90-R) – the dimensions reported from SCL-90-R are the global severity index (GSI), the anxiety dimension (ANX), the interpersonal sensitivity dimension (IS), the phobic anxiety dimension (PHOB), and the depression dimension (DEP) [24]; level of functional impairment measured with Sheehan Disability Scale (SDS) [25]; and well-being measured with WHO Well-Being Index [26]. We also assessed the proportion of adverse events in the two groups. Finally, the proportion in the groups of experimental and control participants that were compliant with the randomised intervention defined as the lack of any psychological treatment during the 9-week intervention period and follow-up was registered, although no restrictions were imposed on the participants during the follow-up period.

Statistical analyses

The clinical outcomes were analysed using the general linear model (GLM), logistic regression, or the proportional odds model for ordinal outcomes as appropriate, adjusting for the stratification variable and baseline scores of the outcomes. We calculated two-sided tests and used the resulting P values (threshold is $p < 0.05$) to select hypothesis-generating outcomes.

Results

Twenty-nine participants in the intervention group and 24 participants in the control group completed the posttreatment measurement. Hereby did 27 participants in the intervention group complete 6 or more sessions in FearFighter (84.4%; lower limit of 95% CI 71.8%). The average number of FearFighter sessions completed for the 29 participants was 8.3 sessions (SD = 1.3).

As seen in Figure 1, a number of participants did not respond at posttreatment and at follow-up. The MINI interview had 10 missing respondents at posttreatment (16%) and 48 missing respondents at follow-up (75%). For the self-reported questionnaires (BAI, SCL-90-R, WHO, SDS) around 12 respondents were missing at posttreatment (19%) and around 26 respondents were missing at follow-up (41%).

Outcomes and adverse events

At the end of the intervention, 13 out of 29 participants (44.8%) were cured (no longer meeting the diagnostic criteria for anxiety disorder) in ICBT group. In the control group 10 out of 24 (41.7%) were cured (P of Fisher's exact test = 1.00). Three values (9.4%) were missing in the ICBT group and 8 values (25%) in control group. The result of the adjusted logistic regression with the control group as reference was OR 1.13, 95% CI 0.37 to 3.41, and $p = 0.83$.

At follow-up, 7 out of 10 (70%) were cured in the ICBT group versus 4 out of 6 (66.7%) in the control group (P of Fisher's exact test = 1.00). Twenty-two values (68.8%) in the ICBT group versus 26 (81.3%) in the control group were missing. The result of the adjusted logistic regression was OR 1.13, 95% CI 0.13 to 10.2, and $p = 0.91$.

Table 2 shows the least square mean (lsmean) in the two intervention groups and the differences between these means at end of intervention (week 10) for the Beck Anxiety Inventory score (BAI-score), and for five of the dimensions in the Symptom Checklist-90 revised (SCL-90-R). The dimensions are the global severity index (GSI), the anxiety dimension (ANX), the interpersonal sensitivity dimension (IS), the phobic anxiety dimension (PHOB), and the depression dimension (DEP). The results reported for the functional scores using the Sheehan Disability Scale (SDS) are also shown in the table. It is noted that the WHO Well-Being score results are included in the table as well and treated as a continuous variable. This is because the results range from 28 to 96.

[Differences between least square means (lsmeans) of control group and ICBT group]

Table 2. Differences between least square means (lsmeans) of control group and ICBT group of the outcomes as measured at end of intervention (week 10) and at follow-up (week 37). The results were calculated based on a regression of each outcome on intervention, the protocol specified stratification variable, and the outcome value measured at baseline.

OUTCOME	Ls mean							
	Internet-based cognitive behavioural therapy group		No intervention control group		Difference between ls means at mean of baseline values			
End of intervention (week 10)	Lsmean	95% CI	Lsmean	95% CI	Mean difference	95% CI	P of difference	Percent missing values
BAI-sum	9.66	6.39 to 12.9	19.6	15.9 to 23.3	9.94	4.96 to 14.9	0.0002	18.8%
SCL-90-R (GSI)	0.447	0.316 to 0.579	0.784	0.633 to 0.935	0.336	0.135 to 0.537	0.0015	20.3%
SCL-90-R (ANX)	0.511	0.338 to 683	0.904	0.706 to 1.103	0.394	0.129 to 0.658	0.0044	20.3%
SCL-90-R (IS)	0.806	0.579 to 1.033	1.084	0.823 to 1.34	0.278	−0.069 to 0.625	0.11	20.3%
SCL-90-R (PHOB)	0.303	0.151 to 0.455	0.620	0.446 to 0.795	0.318	0.086 to 0.549	0.0081	20.3%
SCL-90-R (DEP)	0.571	0.373 to 0.769	1.055	0.827 to 1.282	0.483	0.182 to 0.785	0.0023	20.3%
WHO-5	59.0	52.4 to 65.6	47.9	39.9 to 55.8	−11.1	−21.5 to −0.787	0.036	23.4%
SDS	5.97	4.12 to 7.81	9.00	6.88 to 11.1	3.03	0.197 to 5.87	0.037	20.3%
Follow-up (week 37)								
BAI-sum	9.01	5.43 to 12.6	9.52	5.75 to 13.3	0.515	−4.79 to 5.81	0.84	37.5%
SCL-90-R (GSI)	0.486	0.327 to 0.646	0.449	0.275 to 0.622	−0.038	−0.27 to 0.20	0.75	42.2%
SCL-90-R (ANX)	0.549	0.338 to 0.759	0.496	0.267 to 0.724	−0.053	−0.366 to 0.260	0.73	42.2%
SCL-90-R (IS)	0.691	0.439 to 0.943	0.736	0.462 to 1.009	0.044	−0.328 to 323	0.81	42.2%
SCL-90-R (PHOB)	0.405	0.205 to 0.605	0.431	0.214 to 0.649	0.026	−0.270 to 0.323	0.86	42.2%
SCL-90-R (DEP)	0.626	0.374 to 0.878	0.567	0.293 to 0.846	−0.060	−0.434 to 0.315	0.75	42.2%
WHO-5	62.0	55.4 to 68.7	65.0	7.9 to 72.1	2.97	−6.80 to 12.7	0.54	43.8%
SDS	5.08	3.39 to 6.77	5.49	3.61 to 7.37	0.411	−2.14 to 2.96	0.75	40.6%

Hypothesis-generating differences ($p < 0.05$) were found for all measures except the SCL-90-R interpersonal sensitivity (IS).

The lower part of Table 2 shows the corresponding results obtained at follow-up (week 37). The differences between the ICBT group versus the control group had a P larger than 0.5 for all measures. It is noted that now the means of the control group have dropped to the same low levels as those of the ICBT group. By contrast the means in the ICBT group have not changed as compared to the low values they had at week 10.

Paired *t*-tests comparing the 37-week values to the corresponding baseline values gave P values <0.05 for all outcomes on symptoms in both groups. Thus, we hypothesise that whether intervention is given or not the anxiety levels of the participants return to the same low level which is lower ($p < 0.05$) than that characterising the two groups at entry in the experiment. But the effect of the intervention seems to be to speed up this process. In the control group the effect may be explained by the regression towards the mean effect.

One participant in each intervention group received psychological treatment during the 9 weeks.

In the statistical analysis plan (SAP) it was stated that a general linear model should be used to analyse continuous data collected at week ten and that the same model should be used for an independent analysis of data collected at week 37. We have followed the SAP. However, an alternative would have been to use a mixed model with repeated measures. We have also used this model and the results (not shown) are almost identical to the results presented here.

It is noted that none of covariates in any analysis had missing values. So, unless the data are missing not at random the results should not be biased.

Adverse events

At week ten, two participants in the ICBT group (6.9%) reported an adverse event during the trial: one participant reported to be very stressed but managed to calm down. Another reported suicidal ideation and had to call the help service 'lifeline' to talk to somebody to get calmed. There was no report of adverse events in the control group (P of Fisher's exact test = 0.50). At week 37, no participant with whom contact had been established reported an adverse event.

Discussion

The aim of our trial was to investigate the effectiveness of the ICBT programme FearFighter for people with anxiety disorders in Denmark. We wanted to do this investigation of internet-based therapy, as an earlier conducted Danish trial on FearFighter demonstration project failed to recruit the intended number of participants and suffered from a drop-out rate of 50% of the participants in the intervention group [12,13].

Our randomised clinical trial showed that the recruitment of eligible participants (85.3%) and the number of participants that completed the intervention (84.4%) were satisfying. Our high rate in recruitment and completion compared to the former Danish trial may be explained by the setting and the self-efficacy in participants. We recruited participants from a non-clinical setting among students at Danish universities, and students are assumed to be highly self-efficacious and self-efficacious people have better prognosis in getting things done [27], while the other trial recruited participants from a clinical setting at district psychiatry centres, where patients had failed earlier treatment and more than the half

were unemployed [12,13] – these patients are assumed likely to be less self-efficacious than university students.

The number of missing data due to not responding participants is unacceptable high at follow-up. At the MINI posttreatment interview 14% did not respond and at the MINI follow-up interview 75% did not respond. About 19% of participants did not fill out the self-reported questionnaires at posttreatment and 41% of the participants at follow-up.

We considered two explanations for the high attrition rate. First, researchers in internet-based therapy acknowledge that attrition in e-health intervention is very high and probably intrinsic to the media [28]. The combination of limited human contact and the easiness of engaging and disengaging with the media are considered to be main factors for the attrition [28]. To secure compliance and to prevent unforeseen problems most of the ICBT programmes are guided [6]. In our trial we had a weekly telephone call to the participants in the intervention group to maintain compliance during the intervention. Unfortunately, we did not consider or forecast problems with compliance in the assessment. The second explanation concerns attenuation of obligation mediated by the assessors. The initial interview at baseline was performed of co-author LJ, where the participants met her face to face. LJ also made the contact to the participants for the posttreatment assessment but due to have blinded assessors two psychology students were trained to perform the assessment at week 10 and at week 37. This change from a known person to two unknown persons may have attenuated the participants feeling of trust and obligation to make the final effort to fulfil the diagnostic interview and the symptom questionnaire.

If the data are not missing at random, the results are prone to 'incomplete outcome bias' hereby lowering the validity of the results. This can be illustrated by an example. A Danish randomised clinical trial on the well-being of patients with cancer found that the probability of nonresponse decreased with increasing anxiety score in the intervention group, but it increased with increasing anxiety score in the control group leading to an underreport of the effect in the intervention group [29]. Missing data and possible bias should therefore be considered and prevented in future trials to secure a high validity. It is recommended that effort to prevent missing data is given in the design of the trial, and that investigators are trained with a specific focus on strategies to maximize and secure participant adherence and data gathering during the trial [30]. Moreover, participants should be instructed before signing the informed consent on the essential value to complete all scheduled follow ups to make the trial results meaningful to other people [31].

The outcomes and adverse events

In the outcomes, we found that 44.8% of the participants in the ICBT group did no longer fulfil the diagnostic criteria on MINI for at anxiety disorders at end of intervention and 70.0% at follow-up, which was comparable to the control group (41.7% at end of intervention and 66.7% at follow-up). Due to the many missing values at follow-up, these results are difficult to interpret. However, the data support the null-hypothesis that intervention with ICBT gives no more remission than no intervention neither at end of intervention nor at follow-up.

The severity of symptoms on BAI, SCL-90-R [except the dimension interpersonal sensitivity (IS)], WHO, and SDS were lower ($p < 0.05$) in the ICBT group than in the control group at end of intervention, which can support that ICBT is effective in relieving anxiety over a short period of time. Another interpretation is that the disappointment with no intervention in the control group sustains anxiety much longer. As the mean values of the anxiety symptoms end up being almost identical in the two groups after 37 weeks of follow-up, but at levels that are clearly lower than the corresponding baseline mean values, one may hypothesise that when the participants are left untreated the mean levels will eventually return to a level well below the levels characterising the participants when they were diagnosed due to a regression toward the mean effect [32]. The same effect may be obtained when they receive acute treatment by FearFighter, but the effect seems to be faster.

Limitations

Although we conducted this randomised clinical trial in concordance with the SPIRIT recommendations [14], the validity and generalisability of our trial may be limited. First and most important is the high amount of missing data in our trial, which may imply that the result suffers from incomplete outcome bias and therefore lowering the validity of the trial.

Second, other studies have shown that higher self-efficacy predicts a better outcome for patients with anxiety [27]. Our recruitment was done in a university setting and 58 (91%) of the 64 participants were therefore students. We assume students to be more self-efficacious than patients in ordinary clinical settings and therefore more suited to successfully engage in and complete an intervention that are based on self-directed (self-help) performance rather than therapist-directed performance. Thus, the special group of included participants in our trial may limit the generalisability to the more inhomogeneous or disabled patients in standard clinical settings.

The objective of this trial was to assess the effectiveness of ICBT. We found no difference in remission, but a reduction of symptoms in the ICBT group compared with the control group at end of intervention. At six months follow-up the two groups showed the same level in the reduction of symptoms. Further research is needed to explore the effectiveness of ICBT and ways to improve ICBT for the benefit of the patients [33].

Acknowledgements

The authors thank TrygFonden for the funding.

Disclosure statement

The authors declare to have no interests in the study and no involvement or partnership with the software company behind FearFighter.

Authors contributions

MF, CG, JL, and ML conceived and designed the trial. MF drafted the manuscript. CG, PW and JL provided critical contribution and review of the manuscript. PW planned and performed the statistical analyses. LJ and JHD were principal investigators for recruitment and LJ for initial assessment. All authors read and approved the manuscript.

Funding

The project is financed by the non-profit foundation TrygFonden, Lyngby Hovedgade 4, 2.sal. DK-2800 Kongens Lyngby, Denmark [Grant journal no. 7-10-0642].

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