Underpowered results from the SoREAL Randomized Clinical Trial: Group Cognitive Behavioral Therapy with Virtual Reality Exposure Versus In-Vivo Exposure for Social Anxiety Disorder and Agoraphobia

Benjamin Arnfred, Fatime Zeka, Carsten Hjorthøj, Clas Winding Christensen, Kirsten Stengaard Moeller, Mette Pedersen Øllgaard, Nicole Rosenberg, Lars Clemmensen, Louise Birkedal Glenthøj, Merete Nordentoft

Submitted to: JMIR Mental Health
on: March 13, 2025

Table of Contents

Underpowered results from the SoREAL Randomized Clinical Trial: Group Cognitive Behavioral Therapy with Virtual Reality Exposure Versus In-Vivo Exposure for Social Anxiety Disorder and Agoraphobia

Benjamin Arnfred[1]; Fatime Zeka[1, 2]; Carsten Hjorthøj[1, 3]; Clas Winding Christensen[4]; Kirsten Stengaard Moeller[4]; Mette Pedersen Øllgaard[5]; Nicole Rosenberg[4]; Lars Clemmensen[1]; Louise Birkedal Glenthøj[1]; Merete Nordentoft[1]

[1]Copenhagen Research Center for Mental Health Mental Health Center Copenhagen Copenhagen University Hospital Hellerup DK
[2] Department of Psychology University of Copenhagen Copenhagen DK
[3] Department of Public Health University of Copenhagen Copenhagen DK
[4] Mental Health Centre Copenhagen Capital Region Psychiatry Copenhagen DK
[5] Mental Health Centre Stolpegaard Capital Region Psychiatry Copenhagen DK

Corresponding Author:
Benjamin Arnfred
Copenhagen Research Center for Mental Health
Mental Health Center Copenhagen
Copenhagen University Hospital
Gentofte Hospitalsvej 15
Hellerup
DK

Abstract

Background: Social anxiety disorder (SAD) and agoraphobia are common, impairing conditions often treated with cognitive behavioral therapy (CBT), in which exposure therapy is a core element. Virtual reality exposure (VRE) has shown promise as a flexible alternative to in-vivo exposure.

Objective: This trial evaluated the efficacy of group CBT with VRE (VR-CBT) versus CBT with in-vivo exposure for treating SAD and agoraphobia in clinical settings.

Methods: In this randomized, parallel-group, assessor-blinded trial, 177 participants with SAD or agoraphobia were assigned to either VR-CBT or traditional CBT across five Danish mental health outpatient clinics. Both groups received 14 weekly group sessions. Primary outcomes were phobic anxiety reductions, measured by the Liebowitz Social Anxiety Scale (LSAS) and the Mobility Inventory for Agoraphobia (MIA). Secondary outcomes included work and social functioning, depressive symptoms, and quality of life.

Results: Both groups showed significant reductions in primary, secondary, and exploratory outcomes, with no significant differences between groups. Baseline characteristics and attrition rates were balanced across groups.

Conclusions: Due to insufficient recruitment and substantial missing data, no definitive conclusions can be drawn regarding group differences between VR-CBT and traditional CBT in group settings. The feasibility issues encountered suggest that careful consideration of the benefits and limitations of VR technology is essential before implementation in clinical practice. Clinical Trial: NCT03845101

(JMIR Preprints 13/03/2025:73815)
DOI: https://doi.org/10.2196/preprints.73815

Preprint Settings

1) Would you like to publish your submitted manuscript as preprint?

✔ **Please make my preprint PDF available to anyone at any time (recommended).**
Please make my preprint PDF available only to logged-in users; I understand that my title and abstract will remain visible to all users.
Only make the preprint title and abstract visible.
No, I do not wish to publish my submitted manuscript as a preprint.

2) If accepted for publication in a JMIR journal, would you like the PDF to be visible to the public?

✔ **Yes, please make my accepted manuscript PDF available to anyone at any time (Recommended).**

Yes, but please make my accepted manuscript PDF available only to logged-in users; I understand that the title and abstract will remain v

Yes, but only make the title and abstract visible (see Important note, above). I understand that if I later pay to participate in <a href="http

No. Please do not make my accepted manuscript PDF available to anyone.

Original Manuscript

Title: Underpowered results from the SoREAL Randomized Clinical Trial: Group Cognitive Behavioral Therapy with Virtual Reality Exposure Versus In-Vivo Exposure for Social Anxiety Disorder and Agoraphobia

Authors:

Arnfred; Benjamin[1], Zeka; Fatime[1.2], Hjorthøj; Carsten[3.4], Christensen, Clas Winding[5]; Moeller, Kirsten Stengaard[5]; Øllgaard, Mette Pedersen[6]; Rosenberg, Nicole[5]; Clemmensen, Lars[1]; Glenthøj, Louise Birkedal[1]; Nordentoft, Merete[3.7]

Affiliations:

1 VIRTU Research Group, Copenhagen Research Center for Mental Health, Mental Health Center Copenhagen, Copenhagen University Hospital, Copenhagen, Denmark

2 Department of Psychology, University of Copenhagen, Copenhagen, Denmark

3 Copenhagen Research Center for Mental Health – CORE, Mental Health Center Copenhagen, Copenhagen University Hospital, Copenhagen, Denmark

4 Department of Public Health, University of Copenhagen, Copenhagen, Denmark

5 Mental Health Centre Copenhagen, Capital Region Psychiatry, Copenhagen, Denmark

6 Mental Health Centre Stolpegaard, Capital Region Psychiatry, Copenhagen, Denmark

7 Department for Clinical Medicine, Faculty of Health and Medical Science, University of Copenhagen, Copenhagen, Denmark

Corresponding author:

Benjamin Arnfred

Email: barn0006@regionh.dk

Keywords: Virtual Reality, Social Anxiety Disorder, Agoraphobia, Exposure Therapy, RCT, Virtual Reality Exposure Therapy

Abstract

Introduction: Social anxiety disorder (SAD) and agoraphobia are common, impairing conditions often treated with cognitive behavioral therapy (CBT), in which exposure therapy is a core element. Virtual reality exposure (VRE) has shown promise as a flexible alternative to in-vivo exposure. This trial evaluated the efficacy of group CBT with VRE (VR-CBT) versus CBT with in-vivo exposure for treating SAD and agoraphobia in clinical settings.

Methods: In this randomized, parallel-group, assessor-blinded trial, 177 participants with SAD or agoraphobia were assigned to either VR-CBT or traditional CBT across five Danish mental health outpatient clinics. Both groups received 14 weekly group sessions. Primary outcomes were phobic anxiety reductions, measured by the Liebowitz Social Anxiety Scale (LSAS) and the Mobility Inventory for Agoraphobia (MIA). Secondary outcomes included work and social functioning, depressive symptoms, and quality of life.

Results: Both groups showed significant reductions in primary, secondary, and exploratory outcomes, with no significant differences between groups. Baseline characteristics and attrition rates were balanced across groups.

Conclusion: Due to insufficient recruitment and substantial missing data, no definitive conclusions can be drawn regarding group differences between VR-CBT and traditional CBT in group settings. The feasibility issues encountered suggest that careful consideration of the benefits and limitations of VR technology is essential before implementation in clinical practice.

Significant Outcomes

- Both treatment groups saw reduced phobic anxiety and improved quality of life.
- Feasibility challenges highlight barriers to implementing VR in clinical settings.
- This study provides a foundation for future research on VR therapy in group formats.

Limitations

- Insufficient recruitment and missing data prevent conclusions about group differences.
- VR acceptability, technical issues, and limited training impacted VR-CBT implementation.

- The generalizability of findings is limited due to the naturalistic study design.

Introduction

Social anxiety disorder (SAD) and panic disorder with or without agoraphobia (PD/A) are prevalent [1,2] and impairing disorders associated with decreased quality of life [3], increased suicidality [4], and psychiatric comorbidity. They typically develop in early adolescence [1,2], are more common in women [5,6], and are often chronic if untreated [7,8].

Cognitive behavioral therapy (CBT) is a research-informed, time-limited psychotherapeutic intervention focused on modifying biased cognitions and dysfunctional behaviors [9,10]. It is the recommended first-line treatment for SAD and PD/A [11–14], demonstrating lasting efficacy [15–21], minimal side effects [15], and is generally preferred over psychopharmacological treatment [22]. Exposure therapy, a key component of CBT for SAD and PD/A, aims to modify patients' expectations about the likelihood and consequences of a feared outcome by exposing them to feared stimuli [23,24]. However, feared stimuli can sometimes be inaccessible, uncontrollable, or aversive, leading both patients and therapists to avoid exposure therapy [25–28].

Virtual reality (VR) technology offers a controlled and flexible way to expose patients to feared stimuli, potentially overcoming some challenges of traditional exposure therapy [29,30]. Meta-analyses suggest that virtual reality exposure (VRE)-based treatments are as effective as active control conditions for anxiety disorders [31–33]. However, VRE has primarily been studied in individual therapy rather than group settings and has not been extensively evaluated in naturalistic clinical settings.

In clinical practice, therapy for anxiety disorders is often conducted in groups, as group therapy has shown efficacy comparable to individual therapy [15,34,35] while being considered more cost-effective. In Danish mental health services, SAD and agoraphobia without panic disorder are treated in standardized "mixed anxiety" CBT groups. The aim of the SoREAL trial was to evaluate the efficacy of VRE-based therapy for SAD and agoraphobia in a naturalistic clinical setting. As such, this study was embedded in the Danish mental health services, where VRE-based CBT (VR-CBT) was implemented in a mixed anxiety group format.

We hypothesized that VR-CBT would result in greater reductions in phobic anxiety compared to traditional CBT, as we expected the VRE format to allow for more tailored and higher dosages of exposure than in-vivo exposure therapy.

Materials & Methods

Design

We conducted a 1:1 randomized, assessor-blinded, parallel-group superiority trial across five outpatient psychotherapeutic clinics offering standardized anxiety group therapy within the Danish mental health services.

We estimated that 302 participants were needed to detect the minimal clinically relevant differences in phobic anxiety severity reductions between groups [36]. Participant recruitment began in February 2019 and ended prematurely in December 2023 due to recruitment and feasibility issues, resulting in a sample size of 177. These issues are elaborated in the discussion section. Figure 1 illustrates the recruitment and assessment flow of the trial.

Design changes after trial registration

The SoREAL trial was initially designed to investigate the efficacy of group VR-CBT for SAD (ICD code F40.1), and this design was registered at ClinicalTrials.gov as NCT03845101 before inclusion began. However, to address severe recruitment problems, we implemented several changes to the trial's design. We revised the inclusion criteria, removing the Liebowitz Social Anxiety Scale (LSAS) score requirement of >65 and adding agoraphobia (ICD code F40.0) as a possible primary diagnosis. Therapy manuals and VR software were modified with agoraphobia-specific modules and VR environments. The primary outcome measure was changed to percentage of maximum points (POMP)-transformed total scores of the LSAS for patients with SAD and the Mobility Inventory for Agoraphobia (MIA) for patients with agoraphobia. POMP transforming two different measures of anxiety allowed us to include patients with different primary diagnoses in the same analysis [37,38]. Finally, we expanded from two to five clinical sites and adjusted randomization to allocate therapy groups (rather than individual participants), stratified by site, to minimize wait times and account for the geographical distance between sites. The randomization module was updated in March 2020 after 40 participants had been individually randomized. The final trial design is also described in the published trial protocol [36].

Participants

Patients were recruited from the five outpatient clinic sites while on the waitlist for treatment. Eligible participants had a primary diagnosis of SAD (ICD code F40.1) or agoraphobia (ICD code F40.0), were aged 18–75 years, had adequate proficiency in Danish, and were willing and able to provide informed consent. Patients were excluded if they had a drug or alcohol dependence.

Randomization and blinding

Therapy groups were randomly assigned (1:1) to either VR-CBT mixed anxiety groups or CBT with in-vivo exposure mixed anxiety groups. Randomization was performed using REDCap [39] by a trial coordinator uninvolved in data collection, who informed the relevant clinicians via email or telephone. Allocation tables were generated by a statistician using an online tool [40] with varying block sizes of two and four and stratification by treatment site. Trial assessors were blinded to group allocation, and if unblinded, another assessor conducted the assessment.

Procedures

Patients were assessed before treatment, approximately two weeks after treatment, and nine months after treatment by trained assessors. Assessments took place at the clinics where patients received treatment or via telephone if necessary due to COVID-19 restrictions. Eligibility was confirmed by assessors during the baseline interview. Self-reported questionnaires were answered by hand (on printed copies) or online using a secure link. Both interventions followed a standardized structure and included the same core elements: one hour of individual therapy in preparation for group sessions, 14 weekly two-hour group therapy sessions, and optional components consisting of next-of-kin involvement, pharmacological treatment planning, physical therapy, and coordination with social services. The group therapy in both interventions was manualized and based on established CBT approaches to treating anxiety [41–44]. The manual was flexible, allowing clinicians to change the order of sessions. However, the amount of time allocated for exposure in both interventions was fixed, encompassing all related processes such as setup, transport, and preparation. Therapy groups consisted of eight to nine patients and were led by two clinicians trained in CBT (e.g., psychologists, medical doctors, or physiotherapists trained in psychotherapy). Acute supplementary individual sessions were also available in both interventions. In session seven of the 14 sessions, 45 minutes were allocated to either VR or in-vivo exposure exercises. Both interventions included homework consisting of in-vivo exposure tasks between sessions and one session of "out-of-clinic" in-vivo exposure (e.g., taking the bus or going shopping). The exposure exercises aimed to foster adaptive responses to anxiety-provoking situations, reinforce cognitive restructuring, train general cognitive strategies (e.g., identifying negative automatic thoughts), and build social skills. The cognitive therapy strategies used in non-exposure sessions included psychoeducation, cognitive restructuring, shifting self-focused attention, and relapse prevention. The interventions differed only in the delivery method of exposure therapy.

VR exposure

Each patient received an Oculus Go head-mounted display and high-quality sound-blocking headphones for use throughout treatment. The VR environments were high-resolution, 360° stereoscopic films depicting salient, fear-inducing situations for SAD and agoraphobia. Patients chose from 13 scenarios with four to six scenes of increasing difficulty. Scenes transitioned to a looped, action-free sequence in the same environment to allow habituation as needed. Patients were introduced to the VR equipment and guided to select scenarios relevant to their anxieties. Exposure exercises were completed individually in the therapy room, with sessions typically including one or two breaks for group discussions. The exposure platform was developed collaboratively over 16 months with CBT experts, lived experience experts, and VR developers. Lived experience experts provided input on anxiety levels and scenario relevance, which guided adjustments. Details about the VR environments are available in supplemental file 1.

In-vivo exposure

In-vivo exposure exercises included small-talk (among patients), behavioral experiments within the clinic (e.g., asking the receptionist for directions), roleplay (e.g., job interviews), and public speaking exercises (e.g., talking about a hobby in the group). Detailed intervention descriptions are available in the trial protocol [36].

Outcomes

Primary diagnoses and comorbidities were assessed with the Mini-International Neuropsychiatric Interview version 7 [45]. The primary outcome was a reduction in phobic anxiety, measured with POMP-transformed total scores of the LSAS [46] (clinician-rated) for patients with SAD and the MIA [47] for patients with agoraphobia.

Secondary outcomes included fear of negative evaluation, measured with the Brief Version of the Fear of Negative Evaluation Scale [48]; depression symptoms, measured with the six-item version of the Hamilton Depression Rating Scale [49]; work and social functioning, measured with the Work and Social Adjustment Scale [50]; treatment satisfaction, measured with the Client Satisfaction Questionnaire [51]; and quality of life, measured with the WHO-5 Well-Being Index [52]. SAD treatment response was defined as an LSAS score below 50 or a reduction of 15 points, and remission was defined as an LSAS score below 25. For agoraphobia, treatment response was defined

as an MIA score below 2 or a reduction of 0.5 points, and remission was defined as an MIA score below 1.5, assessed post-treatment and at follow-up.

Exploratory outcomes included social functioning, measured with the Personal and Social Performance Scale [53]; substance and alcohol use over the last month, measured with Timeline Followback [54]; self-efficacy, measured with the General Self-Efficacy Scale [55]; working alliance, measured with the Working Alliance Inventory [56]; SAD symptom severity for patients with SAD as a primary diagnosis, measured with the LSAS (clinician-rated); and agoraphobia symptoms for patients with agoraphobia as a primary diagnosis, measured with the MIA.

Other measures included simulation sickness from VR, assessed using the Simulation Sickness Questionnaire [57] after each exposure session. Deterioration and adverse effects of psychotherapy on SAD symptoms were defined as an increase of 6.8 points or more on the LSAS total score, while for agoraphobia, deterioration was defined as an increase of 0.3 points or more on the MIA total score, assessed post-treatment and at follow-up. Treatment fidelity was evaluated using a therapist self-report questionnaire administered five times throughout therapy, consisting of six Likert-style questions (ranging from 1 to 5) and questions about time spent on exposure therapy.

Statistical analysis

We aimed to enroll 302 patients based on the following parameters: an alpha of 0.05, 80% power, and a standard deviation of 21 to detect a difference of 6.8 on the LSAS, corresponding to a Cohen’s d of 0.33. After expanding inclusion to patients with agoraphobia, we retained the target N of 302, even though the lower variability of the MIA would have reduced the required sample size. All analyses were conducted using an intention-to-treat approach, with tests performed at a two-tailed 5% level of significance. Missing data were handled using multiple imputations (m=100), with predictors in the imputation model including baseline and post-treatment scores of primary, secondary, and exploratory outcomes; primary diagnosis (SAD or agoraphobia); degree of comorbidity; and session attendance. Group differences were examined using analysis of covariance (ANCOVA), with primary diagnosis, degree of comorbidity, and baseline severity as covariates. For POMP-transformed outcomes and analyses of specific diagnostic groups, primary diagnosis was not included as a covariate. Assumptions for ANCOVA were checked as follows: normality of the dependent variable via visual inspection of Q–Q plots, homogeneity of variance using Levene’s test, and homogeneity of regression slopes with univariate analysis of variance. Baseline severity was

excluded as a covariate for post-treatment analyses of the Fear of Negative Evaluation and Work and Social Adjustment Scales, and post-treatment severity was excluded as a covariate for follow-up analysis of the Hamilton Depression Rating Scale due to non-homogeneity of regression slopes. For dichotomous outcomes, multiple logistic regression analyses were performed using primary diagnosis, comorbidity, and baseline severity as predictors. Model fit was assessed using Hosmer-Lemeshow's test, and multicollinearity was evaluated using tolerance values and variance inflation factors. Due to the small number of drug use incidents (<5 in both groups), drug use was not analyzed.

Results

A total of 177 participants were analysed, with 81 randomized to VR-CBT and 96 to CBT. Sociodemographic and clinical characteristics were balanced between groups (Table 1).

Table 1: Baseline characteristics
Data are mean (SD) or n (%).

	VR-CBT (n=81)	CBT (n=96)
Age	29.5 (9.7)	28.5 (9.6)
Sex		
Male	34 (42%)	44 (45.8%)
Female	46 (56.8%)	51 (53.1%)
Other	1 (1.2%)	1 (1%)
Education		
Primary education	21 (28.4%)	17 (20.5%)
Secondary/vocational education	28 (37.8%)	38 (45.8%)
Post-secondary education	23 (31.1%)	28 (33.7 %)
Other	2 (2.7%)	0 (0%)
Civil status		
Partnered	27 (36%)	27 (31 %)
Not partnered	45 (60%)	53 (60.9%)
Other	3 (4%)	7 (8%)
Previous psychiatric treatment		
No	12 (16%)	26 (29.5%)
Yes	63 (84 %)	62 (70.5)
Number of psychiatric comorbidities		
0	32 (39.5%)	35 (36.5%)
1	21 (25.9%)	32 (33.3%)
2	18 (22.2%)	17 (17.7%)
3	10 (12.3%)	12 (12.5%)
Currently in psychopharmacological treatment		
No	32 (39.5%)	41 (42.7%)
Yes	49 (60.5)	55 (57.3%)
Primary diagnose		
Social Anxiety Disorder	71 (87.7%)	79 (82.3%)
Agoraphobia	10 (12.3%)	17 (17.7%)

Missing data rates for POMP scores were substantial at post-treatment (VR-CBT: 29.6%, CBT: 35.4%) and follow-up (VR-CBT: 48.1%, CBT: 49.0%). The only identifiable reason for missing data was participants not responding to contact attempts or failing to attend scheduled assessment sessions, with no specific reasons reported by the participants. Missing data rates were not significantly different between groups but were significantly associated with older age (*P*=.03),

having a primary diagnosis of agoraphobia, and fewer sessions attended (*P*<.001) (Table 2). On average, participants attended 9.0 therapy sessions in the VR-CBT group and 9.3 therapy sessions in the CBT group.

Table 2: Attrition analysis.
Continuous variables were analysed using independent t-tests. Categorical variables were assessed using Pearson's chi-square tests (asymptotic significance). All p-values are two-sided.

	Post-treatment attrition (primary outcome)		**Follow-up attrition (primary outcome)**	
	P	Effect	*P*	Effect
Group assignment	.41	-	.91	-
Primary diagnosis	.02	Agoraphobia as primary diagnosis associated with attrition	.43	-
Number of psychiatric comorbidities	.23	-	>.99	-
Previous psychiatric treatment	.25	-	.30	-
Sex	.76	-	.13	-
Age	.03	Older age associated with attrition	.10	-
Baseline anxiety severity	.46	-	.30	-
Number of sessions attended	<.001	Attending fewer sessions associated with attrition	<.001	Attending fewer sessions associated with attrition

Primary Outcomes

Both groups showed reductions in phobic anxiety severity. At post-treatment, the VR-CBT group had an adjusted mean POMP score of 47.4 (SE=2.3), and the CBT group had an adjusted mean of 46.8 (SE=2.3), with no significant between-group differences (*P*=.61). No statistically significant differences were observed between groups at follow-up, with an adjusted mean of 43.6 (SE=1.8) for VR-CBT and 45.2 (SE=1.7) for CBT (*P*=.47) (Table 3).

Table 3: Primary, secondary, and exploratory results from ANCOVA analysis

Treatment effects (i.e., the interaction of time and treatment condition) are shown. Positive B values indicate an effect in favour of the CBT group. Results are pooled from 100 imputations. Unless otherwise noted, covariates are primary diagnose, comorbidity, and baseline severity. For all follow-up analysis, post-treatment severity was added as a covariate. Phobic anxiety severity included sessions attended as a covariate.

Outcome measure		Post-treatment						1 year follow-up					
		B	95 % CI	SE	t	*P*	Cohen's d	B	95 % CI	SE	t	*P*	Cohen's d
Primary outcomes													
Phobic anxiety severity[a]	LSAS and MIA POMP transformed	-1.328	-6.384 to 3.728	2.579	-.515	.61	-0.026	1.619	-2.740 to 5.977	2.222	0.728	.47	0.097
Secondary outcomes													
Fear of negative evaluation[b]	FNES	-0.64	-0.342 to 0.213	.142	-0.454	.65	-0.061	0.047	-0.215 to 0.309	1.33	0.352	.73	0.039
Depressive symptoms[c]	HAM-6	0.279	-0.975 to 1.533	0.639	0.437	.66	0.063	0.214	-1.214 to 1.643	0.728	0.294	.77	0.037
Work and social adjustment[d]	WSAS	-0.214	-0.839 to 0.411	0.318	-0.673	.50	-0.094	-0.22	-0.679 to 0.635	0.335	-0.065	.95	-0.007
Quality of life	WHO-5	1.883	-5.488 to 9.254	3.755	0.501	.62	0.069	0.245	-6.563 to 7.053	3.469	0.071	>.99	0.008
Acceptability and satisfaction with treatment	CSQ	0.069	-1.636 to 1.774	0.869	0.080	.94	0.011	n/a					
Exploratory outcomes													
Social functioning	PSP	1.257	-2.241 to 4.754	1.783	0.705	.48	0.102	-0.262	-4.233 to 3.709	2.024	-0.129	.90	-0.016
Alcohol use	TLFB (Units of 12g of alcohol last 30 days)	0.215	-0.173 to 0.788	0.197	0.993	.32	0.145[d]	0.154	-0.221 to 0.711	0.201	0.714	.48	0.097[d]
Self-belief of coping	GSE	-0.194	-2.024 to 1.635	0.932	-0.209	.84	−0.027	-0.152	-2.131 to 1.828	1.008	-0.150	.88	-0.017
Working alliance[b]	WAI	0.023	-0.276 to 0.321	0.152	0.149	.88	0.018	n/a					
Social anxiety symptoms[a] (Participants with primary diagnosis of SAD)	LSAS	2.017	-5.489 to 9.523	3.829	0.527	.60	0.085	1.708	-4.881 to 8.296	3.358	0.509	.61	0.085
Agoraphobia symptoms[a] (Participants with primary diagnosis of agoraphobia)	MIA	-0.193	-0.846 to 0.459	0.332	-0.582	.56	0.114						

[a]Primary diagnoses not included as a covariate. [b]Baseline severity violated assumption of homogeneity of regression slopes, thus not included as covariate. [c]Post-treatment severity violated assumption of homogeneity of regression slopes, thus not included as covariate. [d]Calculated with logarithmic means and SDs

LSAS=Leibowitz Social Anxiety Scale. MIA=Mobility Inventory for Agoraphobia. FNES=Fear of Negative Evaluation Scale. HAM-6=Hamilton Depression Scale. WHO-5=World Health Organization Wellbeing Index. WSAS=Work and Social Adjustment Scale. CSQ=Client Satisfaction Questionnaire. GSE=General Self-Efficacy Scale. PSP=Personal and Social Performance Scale. TLFB=Timeline Followback for alcohol consumption. WAI=Working Alliance Inventory. SAD=Social Anxiety Disorder.

Secondary Outcomes

Depressive symptoms decreased in both groups, with no statistically significant between-group differences (post-treatment adjusted means: VR-CBT=4.8, SE=0.4; CBT=5.1, SE=0.4; *P*=.66; follow-up adjusted means: VR-CBT=5.1, SE=0.6; CBT=5.3, SE=0.5; *P*=.77). Fear of negative evaluation also decreased similarly in both groups (post-treatment adjusted means: VR-CBT=3.7, SE=0.1; CBT=3.6, SE=0.1; *P*=.65; follow-up adjusted means: VR-CBT=3.7, SE=0.1; CBT=3.8, SE=0.1; *P*=.73) (Tables 3 and 4). Work and social adjustment scores improved slightly in both groups, with no significant between-group differences (post-treatment adjusted means: VR-CBT=3.7, SE=0.2; CBT=3.5, SE=0.2; *P*=.50; follow-up adjusted means: VR-CBT=3.4, SE=0.3; CBT=3.4, SE=0.2; *P*=.95). Quality of life also improved, but differences between groups were not statistically significant (post-treatment adjusted means: VR-CBT=41.5, SE=2.9; CBT=43.4, SE=2.8; *P*=.62; follow-up adjusted means: VR-CBT=42.8, SE=3.5; CBT=43.1, SE=2.9; *P*=.99) (Tables 3 and 4). At post-treatment, the odds of treatment response did not differ significantly between groups (*P*=.65), and no statistically significant differences were observed for the odds of remission at post-treatment (*P*=.49) or follow-up (*P*=.51) (Table 5).

Table 4: Adjusted means of outcome measures
Standard error in parenthesis. 95 % confidence interval in brackets. Data is pooled from 100 imputations. Covariates are identical to the ANCOVA models.

Outcome measure		VR-CBT			CBT		
		Baseline	Post-treatment	Follow-up	Baseline	Post-treatment	Follow-up
Primary outcomes							
Phobic anxiety severity	LSAS and MIA (POMP transformed)	58.78 (1.68) [55.50, 62.07]	47.45 (2.30) [42.88, 52.02]	43.63 (1.82) [40.05, 47.21]	58.83 (1.53) [55.83, 61.82]	46.88 (2.37) [42.18, 51.59]	45.25 (1.75) [41.80, 48.69]
Secondary outcomes							
Fear of negative evaluation	FNES	4.13 (0.07) [4.00, 4.27]	3.72 (0.11) [3.51, 3.94]	3.76 (0.12) [3.53, 3.99]	4.07 (0.06) [3.94, 4.19]	3.66 (0.10) [3.45, 3.86]	3.80 (0.10) [3.60, 4.01]
Depressive symptoms	HAM-6	6.65 (0.37) [5.92, 7.39]	4.84 (0.48) [3.91, 5.77]	5.14 (0.62) [3.93, 6.35]	6.38 (0.34) [5.70, 7.05]	5.12 (0.46) [4.22, 6.02]	5.35 (0.59) [4.20, 6.50]
Work and social adjustment	WSAS	4.32 (0.17) [3.98, 4.66]	3.77 (0.25) [3.28, 4.26]	3.48 (0.30) [2.88, 4.07]	4.25 (0.16) [3.94, 4.56]	3.55 (0.23) [3.09, 4.01]	3.46 (0.28) [2.90, 4.01]
Quality of life	WHO-5	35.56 (1.89) [31.86, 39.26]	41.56 (2.99) [35.68, 47.44]	42.86 (3.59) [35.78, 49.94]	34.17 (1.76) [30.73, 37.62]	43.44 (2.80) [37.95, 48.94]	43.10 (2.98) [37.24, 48.97]
Acceptability and satisfaction with treatment	CSQ	n/a	24.77 (0.68) [23.44, 26.10]	n/a	n/a	24.84 (0.71) [23.44, 26.23]	n/a
Exploratory outcomes							
Social functioning	PSP	63.54 (1.25) [61.10, 65.99]	67.67 (1.34) [65.05, 70.29]	69.55 (1.78) [66.06, 73.04]	63.43 (1.14) [61.19, 65.67]	68.93 (1.28) [66.42, 71.43]	69.29 (1.62) [66.11, 72.47]
Alcohol use	TLFB (Units of 12g of alcohol last 30 days)	10.48 (2.08) [6.42, 14.55]	5.01 [3.51, 7.03]	5.65 [3.81, 8.22]	11.14 (1.89) [7.44, 14.85]	6.32 [4.56, 8.62]	6.68 [4.74, 9.28]
Self-belief of coping	GSE	21.86 (0.61) [20.66, 23.06]	23.99 (0.77) [22.48, 25.50]	24.49 (0.95) [22.62, 26.36]	22.06 (0.58) [20.93, 23.19]	23.80 (0.71) [22.41, 25.19]	24.34 (0.91) [22.55, 26.12]
Working alliance	WAI	n/a	3.58 (0.12) [3.35, 3.81]	n/a	n/a	3.60 (0.12) [3.38, 3.83]	n/a
Social anxiety symptoms (Participants with primary diagnosis of SAD)	LSAS	89.48 (2.33) [84.92, 94.04]	68.96 (2.76) [63.55, 74.38]	66.47 (2.67) [61.24, 71.71]	87.09 (2.21) [82.77, 91.42]	70.98 (2.72) [65.65, 76.32]	68.18 (2.66) [62.96, 73.40]
Agoraphobia symptoms (Participants with primary diagnosis of agoraphobia)	MIA	2.67 (0.35) [1.98, 3.35]	2.18 (0.31) [1.57, 2.79]	2.15 (0.32) [1.51, 2.79]	3.00 (0.23) [2.54, 3.46]	1.99 (0.21) [1.57, 2.40]	2.23 (0.24) [1.77, 2.70]

LSAS=Leibowitz Social Anxiety Scale. MIA=Mobility Inventory for Agoraphobia. FNES=Fear of Negative Evaluation Scale. HAM-6=Hamilton Depression Scale. WHO-5=World Health Organization Wellbeing Index. WSAS=Work and Social Adjustment Scale. CSQ=Client Satisfaction Questionnaire. GSE=General Self-Efficacy Scale. PSP=Personal and Social Performance Scale. TLFB=Timeline Followback for alcohol consumption. WAI=Working Alliance Inventory. SAD=Social Anxiety Disorder.

Table 5: Results of logistic regression analysis on categorical outcomes.
Positive B values indicate higher odds of the outcome for the CBT group compared to the VR-CBT group. Results are pooled from 100 imputations. Predictors included in the models were baseline severity, comorbidity, and primary diagnoses.

Outcome measures		Post-treatment					Follow-up				
		B	SE	*P*	Exp(B)	95 % CI for Exp (B)	B	SE	*P*	Exp(B)	95 % CI for Exp (B)
Secondary outcomes											
Response to treatment	LSAS below 50 or a 15 drop / MIA below 2 or a 0.5 drop	0.157	0.346	.65	1.170	0.593 to 2.307	n/a				
Remission	LSAS below 25 / MIA below 1.5	-0.449	0.654	.49	0.638	0.177 to 2.300	-0.625	0.953	.51	0.535	0.083 to 3.472
Other measures											
Deterioration of phobic anxiety symptoms	6.8 or higher increase in LSAS score / 0.3 or higher increase in MIA score	0.224	0.538	.68	1.251	0.435 to 3.594	-0.285	0.436	.51	0.752	0.319 to 1.771

Exploratory Outcomes

Social functioning and self-belief in coping improved in both groups, with no statistically significant between-group differences at post-treatment or follow-up (post-treatment social functioning adjusted means: VR-CBT=67.6, SE=1.3; CBT=68.9, SE=1.2; follow-up social functioning adjusted means: VR-CBT=69.5, SE=1.7; CBT=69.2, SE=1.6; all *P*>.05). Similarly, no statistically significant between-group differences were found for alcohol use or treatment satisfaction (all *P*>.05) (Tables 3 and 4).

Other Measures

No statistically significant group differences were observed regarding deterioration of phobic anxiety symptoms (all *P*>.05) (Table 5). The average total exposure time per therapy course was not statistically significantly different between groups (*P*=.09): 85 minutes for VR-CBT groups (SD=76.5) and 120.7 minutes for CBT groups (SD=76.5), which were overall less than a third of the 360 minutes specified in the treatment manuals. Therapist-reported fidelity scores did not differ significantly between groups (*P*=.24), with a mean of 4.0 (SD=0.3) for VR-CBT and 4.1 (SD=0.5) for CBT, suggesting that therapists adhered closely to the manualized treatment protocols. Among participants receiving VR-CBT, the mean simulation sickness score was high, with an average score of 36.2 (SD=27.9) across 51 participants. There were no reported serious adverse events or reactions.

Discussion

This trial evaluated the effects of group-based VR-CBT with 360° video exposure versus traditional in-vivo group CBT for treating SAD and agoraphobia in a naturalistic clinical setting. Both groups showed reductions in symptoms, with no statistically significant differences observed in primary, secondary, or exploratory outcomes. However, due to the limited statistical power of the study, these results must be interpreted with caution. We cannot conclude that VR-CBT and traditional CBT are equally effective, nor can we exclude the possibility of differences in efficacy between the two treatments. Despite the lack of statistically significant differences on primary outcomes, this trial provides valuable insights into the practical implementation of VR-CBT in naturalistic clinical settings and highlights critical factors influencing its feasibility and acceptability.

Failure to reach N

Being fully embedded in the Danish Mental Health Services, the SoREAL trial could only recruit

patients referred by their GPs to the standardized anxiety treatment package. Based on clinical intake and experience from previous trials at the two initial sites, we expected to reach N in 36 months. However, changes to GP guidelines for psychiatric referrals, designed to reduce the case load of psychotherapeutic outpatient hospitals, resulted in most SAD patients being referred to practicing psychologists instead. To offset the slower-than-anticipated recruitment rate, we expanded the study to include three additional clinic sites, which also entailed the design changes described elsewhere.

Shortly after including the new sites, Denmark entered lockdown due to the COVID-19 pandemic. This meant that psychotherapeutic treatment was conducted via telephone and/or individually. A notable drop in referrals to treatment sites also occurred, possibly because SAD and agoraphobia symptoms are less functionally impairing during a national lockdown.

After the lockdown ended, the clinical sites decided not to continue with the trial for several reasons. The primary concern raised by the clinics was the ethicality of continuing a treatment perceived as unsuitable for the population and group format. These concerns stemmed from observations that patients found VR distressing in a group setting and struggled to focus on VR scenarios due to the social dynamics within the therapy room. Clinicians also raised concerns about the lack of interactivity in the virtual environments, which made it difficult to expose patients to core SAD fears, such as conversation. These concerns are consistent with prior findings [57] and align with the notion that therapeutic context, patient characteristics, and VR characteristics can influence the experience of VR environments [58,59]. Group settings, in particular, may introduce stressors like performance anxiety, which could potentially diminish immersion and thus the therapeutic value of VR environments. Addressing these concerns may require the use of VR technology that accounts for group settings and the need for flexible social interactions. Examples include multi-user VR, in which all patients engage in the same shared virtual environments; augmented reality, where the therapy room remains visible but virtual objects are overlaid to simulate therapeutic scenarios; or large language model-based avatars to engage in conversation.

Beyond this, staff turnover limited clinicians' ability to gain experience with VR-CBT. Overall, 39 therapists delivered VR-CBT, most of whom could only receive very limited training in conducting VRE due to time constraints. Frequent technical malfunctions and limited time for in-session troubleshooting also impacted feasibility. These factors likely contributed to the low mean exposure time per VR-CBT group (85 minutes).

Lastly, the extended inclusion period strained the resources of the clinics, which had agreed to participate for limited periods (e.g., two years) and had obligations to other clinical trials. The factors that led clinics to opt out of the trial are important to consider for future studies examining VR-based psychotherapy in naturalistic clinical settings. They also underscore the importance of pilot studies for both design and intervention feasibility [57], which could have identified challenges related to recruitment rates, the group format, technical issues, and clinician training requirements before conducting the full-scale RCT.

Beyond incomplete recruitment, the trial's substantial missing data further impede interpretation, as data is likely missing due to factors associated with the intervention (i.e., it is not missing at random [58]). As such, the missing data likely impacts the accuracy of the results. However, since data is missing equally across both groups and the variables associated with missing data are balanced between groups, any influence on the results is likely comparable for both groups.

Conclusion

Due to the study's underpowered analysis and substantial missing data, we are unable to draw definitive conclusions about group differences between VR-CBT and CBT in group therapy. The feasibility challenges encountered underscore the need to carefully evaluate both the benefits and limitations of VR technology before clinical implementation. Future research could explore the VR technologies that account for the group therapy context, such as multi-user VR or augmented reality.

Statements

Statement of Ethics

The SoREAL trial received approval from the Regional Ethics Committee of Zealand (H-6-2013-015) and the Danish Data Protection Agency (RHP2014-009-02670). All participants were informed about the study procedures and provided written informed consent prior to participation. The individuals appearing in the supplemental material are professional actors who were hired for this study. Written consent has been obtained from all actors for the use of their images in this publication.

Conflict of Interest Statement

The authors declare no conflicts of interest related to this study.

Acknowledgements

The Novo Nordisk Foundation awarded the SoREAL trial 5,000,000 DKK [NNF17OC0027780]. Additionally, the trial received a grant of 3,517,500 DKK from TrygFonden [ID: 146169]. The project is fully independent of both the Novo Nordisk Foundation and TrygFonden. Neither funding body influenced the study's design, data collection, analysis, interpretation, or manuscript preparation.

Data and Procedures Availability

The trial’s anonymized data will be made available upon reasonable request and in compliance with the Danish Data Protection Act. Materials related to the interventions, including the treatment manual, will also be available upon reasonable request. Data will be stored securely in accordance with ethics and legal regulations under the Danish Health Authorities.

[1] Roest AM, Vries YA de, Lim CCW, Wittchen HU, Stein DJ, Adamowski T, et al. A comparison of DSM-5 and DSM-IV agoraphobia in the World Mental Health Surveys. Depression and Anxiety 2019;36:499–510. https://doi.org/10.1002/da.22885.
[2] Stein DJ, Lim CCW, Roest AM, Jonge P de, Aguilar-Gaxiola S, Al-Hamzawi A, et al. The cross-national epidemiology of social anxiety disorder: Data from the World Mental Health Survey Initiative. BMC Medicine 2017;15:1–21. https://doi.org/10.1186/s12916-017-0889-2.
[3] Olatunji BO, Cisler JM, Tolin DF. Quality of life in the anxiety disorders: A meta-analytic review. Clinical Psychology Review 2007;27:572–81. https://doi.org/10.1016/j.cpr.2007.01.015.
[4] Vega DDL, Giner L, Courtet P. Suicidality in Subjects With Anxiety or Obsessive-Compulsive and Related Disorders: Recent Advances. Current Psychiatry Reports 2018;20. https://doi.org/10.1007/s11920-018-0885-z.
[5] Wittchen HU, Gloster AT, Beesdo-Baum K, Fava GA, Craske MG. Agoraphobia: A review of the diagnostic classificatory position and criteria. Depression and Anxiety 2010;27:113–33. https://doi.org/10.1002/da.20646.
[6] Lijster JMD, Dierckx B, Utens EMWJ, Verhulst FC, Zieldorff C, Dieleman GC, et al. The age of onset of anxiety disorders: A meta-analysis. Canadian Journal of Psychiatry 2017;62:237–46. https://doi.org/10.1177/0706743716640757.
[7] Bruce SE, Yonkers KA, Otto MW, Eisen JL, Weisberg RB, Pagano M, et al. Influence of psychiatric comorbidity on recovery and recurrence in generalized anxiety disorder, social phobia, and panic disorder: A 12-year prospective study. American Journal of Psychiatry 2005;162:1179–87. https://doi.org/10.1176/appi.ajp.162.6.1179.
[8] PMG E, Wittchen H-U. Specific phobias. In: Andrews G, Charney DS, Sirovatka PJ, Regier DA, editors. Stress-Induced and Fear Circuitry Disorders: Refining the Research Agenda for DSM-V, American Psychiatric Publishing; 2009.
[9] Beck JS. Cognitive behavior therapy: Basics and beyond, 2nd ed. Guilford Press; 2011.
[10] Hofmann SG, Asmundson GJG, Beck AT. The Science of Cognitive Therapy. Behavior Therapy 2013;44:199–212. https://doi.org/10.1016/j.beth.2009.01.007.
[11] Health NI for, Excellence C. NICE Guidelines: Social Anxiety Disorder: Assessment and Treatment. National Institute for Health and Care Excellence 2013. https://doi.org/10.1002/9781118775349.ch47.
[12] NKR S. Treatment of Anxiety Disorders A Systematic Review 2005;12 Suppl 1:1–29.
[13] Katzman MA, Bleau P, Blier P, Chokka P, Kjernisted K, Ameringen MV, et al. Canadian clinical practice guidelines for the management of anxiety, posttraumatic stress and obsessive-compulsive disorders. BMC Psychiatry 2014;14:1–83. https://doi.org/10.1186/1471-244X-14-S1-S1.
[14] Bandelow B, Werner AM, Kopp I, Rudolf S, Wiltink J, Beutel ME. The German Guidelines for the treatment of anxiety disorders: first revision. European Archives of Psychiatry and Clinical Neuroscience 2021. https://doi.org/10.1007/s00406-021-01324-1.
[15] Mayo-Wilson E, Pilling S, Dias S, Mavranezouli I, Kew K, Clark DM, et al. Psychological and pharmacological interventions for social anxiety disorder in adults: A systematic review and network meta-analysis. The Lancet Psychiatry 2014;1:368–76. https://doi.org/10.1016/S2215-0366(14)70329-3.
[16] Carpenter JK, Andrews LA, Witcraft SM, Powers MB, Smits JAJ, Hofmann SG. Cognitive behavioral therapy for anxiety and related disorders: A meta-analysis of randomized placebo-controlled trials. Depression and Anxiety 2018;35:502–14. https://doi.org/10.1002/da.22728.
[17] Powers MB, Sigmarsson SR, Emmelkamp PMG. A meta–analytic review of psychological treatments for social anxiety disorder. International Journal of Cognitive Therapy 2008;1:94–113. https://doi.org/10.1521/ijct.2008.1.2.94.
[18] Imai H, Tajika A, Chen P, Pompoli A, Ta F, Imai H, et al. Panic disorder with or without agoraphobia in adults 2016. https://doi.org/10.1002/14651858.CD011170.pub2.www.cochranelibrary.com.
[19] Papola D, Ostuzzi G, Tedeschi F, Gastaldon C, Purgato M, Giovane CD, et al. Comparative efficacy and acceptability of psychotherapies for panic disorder with or without agoraphobia: systematic review and network meta-analysis of randomised controlled trials. The British Journal of Psychiatry 2021:1–13. https://doi.org/10.1192/bjp.2021.148.

[20] Pompoli A, Furukawa TA, Imai H, Tajika A, Efthimiou O, Salanti G. Psychological therapies for panic disorder with or without agoraphobia in adults: a network meta-analysis. The Cochrane Database of Systematic Reviews 2016;4:CD011004. https://doi.org/10.1002/14651858.CD011004.pub2.
[21] van Dis EAM, van Veen SC, Hagenaars MA, Batelaan NM, Bockting CLH, van den Heuvel RM, et al. Long-term Outcomes of Cognitive Behavioral Therapy for Anxiety-Related Disorders: A Systematic Review and Meta-analysis. JAMA Psychiatry 2020;77:265. https://doi.org/10.1001/jamapsychiatry.2019.3986.
[22] McHugh RK, Whitton SW, Peckham AD, Welge JA, Otto MW. Patient Preference for Psychological vs Pharmacologic Treatment of Psychiatric Disorders: A Meta-Analytic Review. J Clin Psychiatry 2013;74:595–602. https://doi.org/10.4088/JCP.12r07757.
[23] Abramowitz JS, Deacon BJ, Whiteside SPH. Exposure Therapy for Anxiety: Principles and Practice. 2nd ed. The Guilford Press; 2019.
[24] Neudeck P, Wittchen HU. Exposure therapy: Rethinking the model – Refining the method. In: Neudeck P, Wittchen H -u, editors. Exposure Therapy: Rethinking the Model - Refining the Method, Springer; 2012, p. 1–358. https://doi.org/10.1007/978-1-4614-3342-2.
[25] Pittig A, Kotter R, Hoyer J. The Struggle of Behavioral Therapists With Exposure: Self-Reported Practicability, Negative Beliefs, and Therapist Distress About Exposure-Based Interventions. Behavior Therapy 2019;50:353–66. https://doi.org/10.1016/j.beth.2018.07.003.
[26] Hedman E, Mörtberg E, Hesser H, Clark DM, Lekander M, Andersson E, et al. Mediators in psychological treatment of social anxiety disorder: Individual cognitive therapy compared to cognitive behavioral group therapy. Behaviour Research and Therapy 2013;51:696–705. https://doi.org/10.1016/j.brat.2013.07.006.
[27] Neudeck P, Einsle F. Dissemination of Exposure Therapy in Clinical Practice: How to Handle the Barriers? In: Neudeck P, Wittchen HU, editors. Exposure Therapy Rethinking the Model - Refining the Method. 1st ed., Springer; 2012, p. 23–34.
[28] Butler G. Exposure as a treatment for social phobia: Some instructive difficulties. Behaviour Research and Therapy 1985;23:651–7. https://doi.org/10.1016/0005-7967(85)90060-9.
[29] Botella C, Fernández-Álvarez J, Guillén V, Garc\'\ia-Palacios A, Baños R. Recent Progress in Virtual Reality Exposure Therapy for Phobias: A Systematic Review. Current Psychiatry Reports 2017;19. https://doi.org/10.1007/s11920-017-0788-4.
[30] Freeman D, Reeve S, Robinson A, Ehlers A, Clark D, Spanlang B, et al. Virtual reality in the assessment, understanding, and treatment of mental health disorders. Psychological Medicine 2017;47:2393–400. https://doi.org/10.1017/S003329171700040X.
[31] Wechsler TF, Mühlberger A, Kümpers F. Inferiority or even superiority of virtual reality exposure therapy in phobias? - A systematic review and quantitative meta-analysis on randomized controlled trials specifically comparing the efficacy of virtual reality exposure to gold standard in vivo e. Frontiers in Psychology 2019;10. https://doi.org/10.3389/fpsyg.2019.01758.
[32] Morina N, Kampmann I, Emmelkamp P, Barbui C, Hoppen TH. Meta-analysis of virtual reality exposure therapy for social anxiety disorder. Psychological Medicine 2021:12–4. https://doi.org/10.1017/S0033291721001690.
[33] Kampmann IL, Emmelkamp PMG, Morina N. Meta-analysis of technology-assisted interventions for social anxiety disorder. JOURNAL OF ANXIETY DISORDERS 2016;42:71–84. https://doi.org/10.1016/j.janxdis.2016.06.007.
[34] Gould RA, Buckminster S, Pollack MH, Otto MW, Yap L. Cognitive-behavioral and pharmacological treatment for social phobia: A meta-analysis. Clinical Psychology: Science and Practice 1997;4:291–306. https://doi.org/10.1111/j.1468-2850.1997.tb00123.x.
[35] Sánchez-Meca J, Rosa-Alcázar AI, Marín-Martínez F, Gómez-Conesa A. Psychological treatment of panic disorder with or without agoraphobia: A meta-analysis. Clinical Psychology Review 2010;30:37–50. https://doi.org/10.1016/j.cpr.2009.08.011.
[36] Arnfred B, Bang P, Hjorthøj C, Christensen CW, Stengaard Moeller K, Hvenegaard M, et al. Group cognitive behavioural therapy with virtual reality exposure versus group cognitive behavioural therapy with in vivo exposure for social anxiety disorder and agoraphobia: a protocol for a randomised clinical

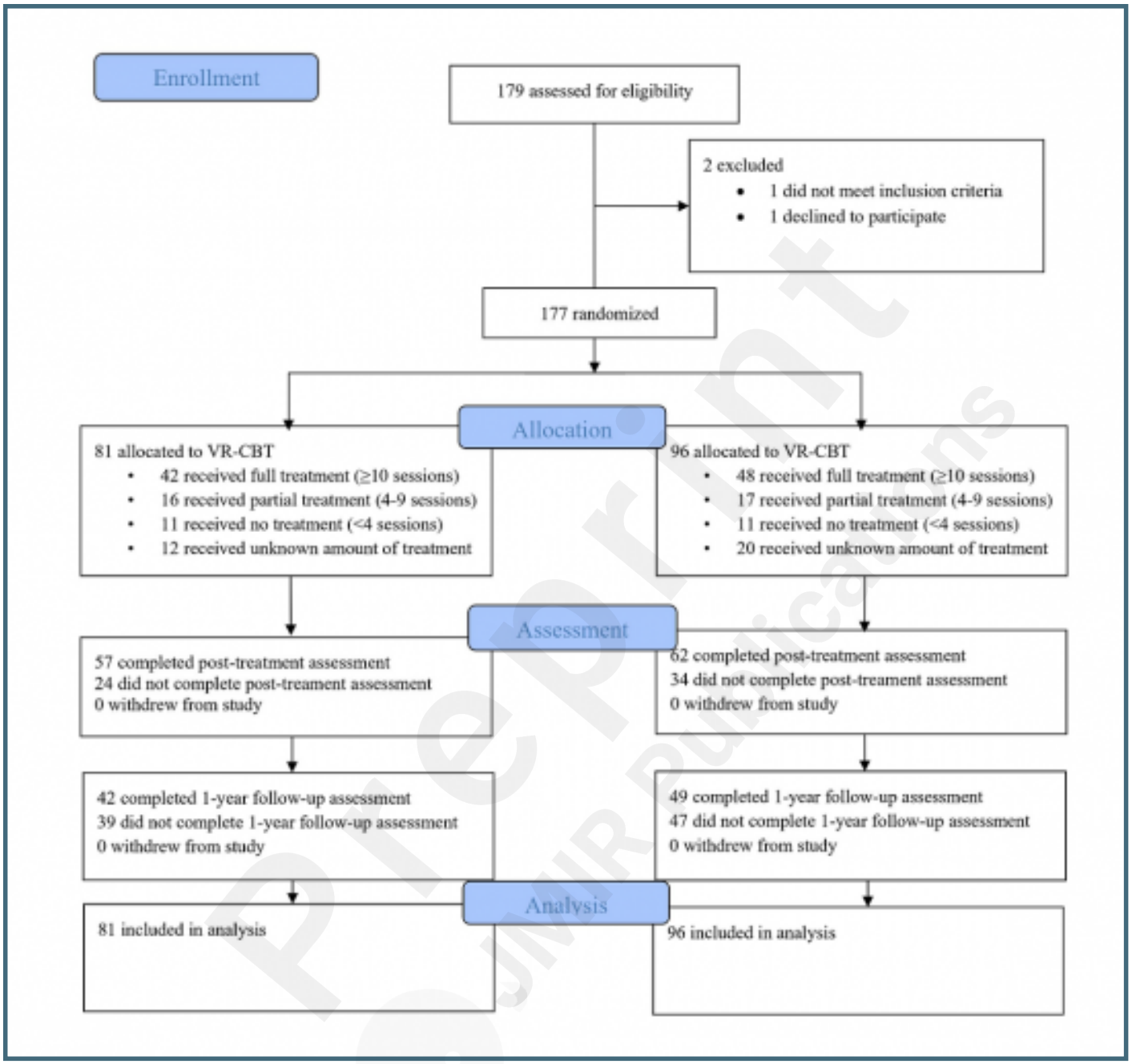
trial. BMJ Open 2022;12:e051147. https://doi.org/10.1136/bmjopen-2021-051147.
[37] Moeller J. A word on standardization in longitudinal studies: don't. Front Psychol 2015;6. https://doi.org/10.3389/fpsyg.2015.01389.
[38] Cohen P, Cohen J, Aiken LS, West SG. The Problem of Units and the Circumstance for POMP. Multivariate Behavioral Research 1999;34:315–46. https://doi.org/10.1207/S15327906MBR3403_2.
[39] Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)—A metadata-driven methodology and workflow process for providing translational research informatics support. Journal of Biomedical Informatics 2009;42:377–81. https://doi.org/10.1016/j.jbi.2008.08.010.
[40] Create a blocked randomisation list. n.d.
[41] Turk CL, Heimberg RG, Magee L. Social anxiety disorder. In: Barlow DH, editor. Clinical handbook of psychological disorders: A step-by-step treatment manual, Guilford Press; 2008, p. 123–63.
[42] Graske MG, Barlow DH. Panic Disorder and Agoraphobia. In: Barlow DH, editor. CLINICAL HANDBOOK OF PSYCHOLOGICAL DISORDERS. 4th ed., The Guilford Press; 2008, p. 1–65.
[43] Rosenberg NK, Mørck MM, Arendt M. Kognitiv terapi. Nyeste udvikling. Kognitiv terapi. Nyeste udvikling, 2012.
[44] Bouchard S, Robillard G, Larouche S, Loranger C. Description of a treatment manual for in virtuo exposure with specific phobia. Virtual Reality in Psychological, Medical and Pedagogical Applications 2012:81–108. https://doi.org/10.5772/46417.
[45] Lecrubier Y, Sheehan DV, Weiller E, Amorim P, Bonora I, Sheehan KH, et al. The Mini International Neuropsychiatric Interview (MINI). A short diagnostic structured interview: Reliability and validity according to the CIDI. European Psychiatry 1997;12:224–31. https://doi.org/10.1016/S0924-9338(97)83296-8.
[46] Heimberg RG, Horner KJ, Juster HR, Safren SA, Brown EJ, Schneier FR, et al. Psychometric properties of the Liebowitz Social Anxiety Scale. Psychological Medicine 1999;29:199–212. https://doi.org/10.1017/s0033291798007879.
[47] Chambless DL, Caputo GC, Jasin SE, Gracely EJ, Williams C. The Mobility Inventory for Agoraphobia. Behaviour Research and Therapy 1985;23:35–44. https://doi.org/10.1016/0005-7967(85)90140-8.
[48] Leary MR. Brief Fear of Negative Evaluation Scale 1983:1983.
[49] O'Sullivan RL, Fava M, Agustin C, Baer L, Rosenbaum JF. Sensitivity of the six-item Hamilton Depression Rating Scale. Acta Psychiatrica Scandinavica 1997;95:379–84. https://doi.org/10.1111/j.1600-0447.1997.tb09649.x.
[50] Mundt JC, Marks IM, Shear MK, Greist JM. The Work and Social Adjustment Scale: a simple measure of impairment in functioning. Br J Psychiatry 2002;180:461–4. https://doi.org/10.1192/bjp.180.5.461.
[51] Attkisson CC, Zwick R. The client satisfaction questionnaire. Evaluation and Program Planning 1982;5:233–7. https://doi.org/10.1016/0149-7189(82)90074-X.
[52] Bech P, Olsen LR, Kjoller M, Rasmussen NK. Measuring well-being rather than the absence of distress symptoms: a comparison of the SF-36 Mental Health subscale and the WHO-Five well-being scale. Int J Method Psychiat Res 2003;12:85–91. https://doi.org/10.1002/mpr.145.
[53] White S, Dominise C, Naik D, Killaspy H. The reliability of the Personal and Social Performance scale – informing its training and use. Psychiatry Research 2016;243:312–7. https://doi.org/10.1016/j.psychres.2016.06.047.
[54] Sobell LC, Sobell MB. Timeline follow-back: A technique for assessing self-reported alcohol consumption. Measuring alcohol consumption: Psychosocial and biochemical methods., Humana Press; 1992, p. 41–72. https://doi.org/10.1007/978-1-4612-0357-5_3.
[55] Cuevas CD las, Peñate W. Validation of the General Self-Effi cacy Scale in psychiatric outpatient care. Psicothema 2015:410–5. https://doi.org/10.7334/psicothema2015.56.
[56] Horvath AO. Working Alliance Inventory 1992:1–5.
[57] Eldridge SM, Lancaster GA, Campbell MJ, Thabane L, Hopewell S, Coleman CL, et al. Defining Feasibility and Pilot Studies in Preparation for Randomised Controlled Trials: Development of a Conceptual Framework. PLoS ONE 2016;11:e0150205. https://doi.org/10.1371/journal.pone.0150205.

[58] Jakobsen JC, Gluud C, Wetterslev J, Winkel P. When and how should multiple imputation be used for handling missing data in randomised clinical trials – a practical guide with flowcharts. BMC Med Res Methodol 2017;17:162. https://doi.org/10.1186/s12874-017-0442-1.

Supplementary Files

Figures

Recruitment and assessment flow of the trial.



Multimedia Appendixes

Descriptions and screenshots of virtual environments.
URL: http://asset.jmir.pub/assets/5ba963d587361b61f40c9aca31b56f20.pptx