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Exposure therapy consortium: Outcomes of the proof-of-principle study

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ABSTRACT

Background: This paper reports on the outcomes of a proof-of-principle study for the Exposure Therapy Consortium, a global network of researchers and clinicians who work to improve the effectiveness and uptake of exposure therapy. The study aimed to test the feasibility of the consortium's big-team science approach and test the hypothesis that adding post-exposure processing focused on enhancing threat reappraisal would enhance the efficacy of a one-session large-group interoceptive exposure therapy protocol for reducing anxiety sensitivity.
Methods: The study involved a multi-site cluster-randomized controlled trial comparing exposure with post-processing (ENHANCED), exposure without post-processing (STANDARD), and a stress management intervention (CONTROL) in students with elevated anxiety sensitivity. Feasibility was assessed using site performance metrics (e.g., timeline, sample size, missing data). Efficacy was assessed up to 1-month follow-up using the Anxiety Sensitivity Index-3.
Results: Despite challenges posed by unforeseen global crises, a standardized protocol for screening, assessment, and treatment at 12 research sites across four continents was successfully implemented, resulting in a total sample size of 400 with minimal missing data. Challenges in recruitment and adherence to the projected timelines were encountered. Significant reductions in anxiety sensitivity were observed in all conditions.

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Contrary to hypotheses, group differences were only observed at post-treatment, when ENHANCED and CONTROL outperformed STANDARD but were not significantly different from each other.
Conclusions: This study demonstrates the feasibility of the Exposure Therapy Consortium. Findings raise questions regarding the efficacy of large group exposure interventions and underscore the importance of careful research site selection and an iterative approach to treatment development.

1. Introduction

The Exposure Therapy Consortium (www.exposuretherapyinfo.org) was established to facilitate the goal of optimizing the effectiveness and implementation of exposure therapy (Smits et al., 2024). By adopting a big-team science approach - i.e., involving a large group of investigators from different labs around the world (Forscher et al., 2023) - the consortium promises to produce better data faster. This manuscript reports on the outcome of the consortium's first study, which was designed to test (1) the feasibility of this big-team science approach for the consortium and (2) the hypothesis that incorporating post-exposure processing focused on reappraising perceived threat would enhance symptom reduction with a large-group exposure therapy protocol (Smits et al., 2024).

The idea to incorporate clinical strategies to maximize threat reappraisal during exposure therapy is guided by theories positing that reestablishing a sense of safety around feared cues is a core mechanism in this intervention (Benito et al., 2024). That is, patients undergoing exposure therapy may experience symptom improvement when they start perceiving feared cues (e.g., situations, images, thoughts, memories) as less threatening or benign (Pittig et al., 2023). Studies assessing this mediation hypothesis have generally supported the hypothesis that changes in outcome (threat) expectancies predict treatment outcome, although evidence for causality often is missing (Smits et al., 2012). Small-scale experiments that directly manipulate threat reappraisal complement these correlational studies by showing that targeting threat reappraisal during exposure practice outperforms a control procedure that does not target this change mechanism (Ginat-Frolich et al., 2023; Kamphuis & Telch, 2000; Sloan & Telch, 2002). The current proof-of-principle study sought to build upon earlier work. Indeed, the need for the Exposure Therapy Consortium stems from limitations inherent in individual studies on exposure therapy (Smits et al., 2024). One such issue is that these investigations are often underpowered, making it difficult to draw definitive conclusions. A second limitation is that individual studies frequently rely on homogeneous samples, which restricts the generalizability of their findings. Such studies often fail to account for variations in cultural, socioeconomic, and demographic factors that can influence both the implementation and effectiveness of exposure therapy. By bringing together a diverse, global network of researchers and leveraging a big-team science approach, the consortium aims to address these gaps.

The present study opted to focus on anxiety sensitivity reduction as the outcome variable. Anxiety sensitivity reflects the fear of anxiety and related sensations based on the belief that such sensations are dangerous (Reiss et al., 1986), and is an empirically established risk and maintaining factor for panic attacks and panic disorder, as well as for other fear- and anxiety-related disorders (Schmidt et al., 2006). Hence, anxiety sensitivity reduction is an important target for the prevention and treatment of these conditions (Smits et al., 2018). Interventions that guide patients to systematically and repeatedly approach somatic arousal (e.g., racing heart, dizziness, sweating, etc) without escaping, a process known as interoceptive exposure therapy, have shown to be effective in reducing anxiety sensitivity (Fitzgerald et al., 2021; Smits et al., 2008). Building on the successful implementation of one-session large-group exposure therapy in Germany (Wannemueller et al., 2018, 2020), a protocol was developed for large-group interoceptive exposure therapy for anxiety sensitivity. To investigate whether the inclusion of post-exposure processing enhances the efficacy of exposure therapy, the study compared two protocol variants: (1) STANDARD, which includes psychoeducation and interoceptive exposure therapy modeling and practice, and (2) ENHANCED, which is identical to STANDARD but adds post-exposure processing focused on facilitating threat reappraisal. A general stress reduction intervention was added to the design to serve as a control condition (CONTROL). Participants with elevated anxiety sensitivity signed up for groups that were randomly assigned to one of the three conditions. Anxiety sensitivity was assessed at pre-treatment, post-treatment, and at 1-week and 1-month follow-ups.

The manuscript reports on two types of outcomes. The first outcome pertains to the establishment of a new consortium for big-team science. Study feasibility was examined by collecting performance metrics, including elements like timeline adherence, participating study sites, achieved sample size, and the presence of missing data. The second outcome involves the tests of the pre-registered study hypotheses (Smits et al., 2024): (1) participants in the two exposure conditions (combined) would demonstrate greater reduction in anxiety sensitivity from pre-treatment to post-treatment (primary endpoint) and from pre-treatment to the 1-month follow-up (secondary endpoint) compared to the control condition, and (2) participants in the enhanced exposure condition would exhibit a greater reduction in anxiety sensitivity from pre-treatment to post-treatment (primary endpoint) and from pre-treatment to the 1-month follow-up (secondary endpoint) compared to those in the standard exposure condition.

2. Method

The trial was registered (https://clinicaltrials.gov/study/NCT05225740) in May, 2021 and data collection occurred between September, 2022 and July, 2024. All participants provided written informed consent prior to participation, and the protocol was approved by the Institutional Review Boards and Ethics Committees of participating research sites. A protocol paper (Smits et al., 2024) details the study methodology, including the pre-registered hypotheses and data analysis plan (see https://osf.io/uw3zs).

2.1. Research Sites

Because the current study was not funded, the study was limited to sites that could achieve participant enrollment with university students and complete the study in one term. In addition, all sites had to have the capacity to collect data using a REDCap interface (Harris et al., 2009, 2019).[1] Twelve sites were recruited in November, 2019, and one additional site (Georg-August-Universität Göttingen) was recruited in April, 2023. Of the 13 sites, 6 were in the United States of America (The University of Texas at Austin, The University of Colorado Boulder, The University of Mississippi, The University of Miami, Boston University, and The University of North Carolina), 4 were in Germany (Ruhr-Universität Bochum, Technische Universität Dresden, Philipps-Universität Marburg, Georg-August-Universität Göttingen), 2 were in Australia (The University of New South Wales, Curtin University), and 1 site was in Israel (The Hebrew University of Jerusalem).

[1] One site (The Hebrew University of Jerusalem) ultimately chose to use Qualtrics instead.

2.2. Participants

Eligibility criteria included ages 18–70, elevated anxiety sensitivity defined as a total score of 23 (Allan et al., 2014) or higher on the Anxiety Sensitivity Index-3 (ASI-3; Taylor et al., 2007), and the absence of any respiratory or cardiovascular conditions, neurological disorders, pregnancy, or other medical issues that might hinder participation in interoceptive exposure procedures (e.g., severe back pain or asthma). Eligibility was confirmed through self-report measures, requiring participants to report an ASI-3 score of 23 or above on two separate administrations (Marsic et al., 2010). All participating sites utilized established data acquisition platforms (e.g., Sona Systems, REDCap) to facilitate the collection of written consent, screening, and enrollment of participants. Participants received course-related credit for their involvement in research.

2.2.1. Sample size determination.

Sample size targets were based on *a priori* power analyses to detect a small effect (a mean difference of 0.2 standard deviation) between ENHANCED and STANDARD (Smits et al., 2024). Power estimates with an average of 20 participants per group per site across 10–14 sites (600–840 participants total), yielded 81–92 % power, respectively (Smits et al., 2024).

2.3. Randomization

Groups of participants were randomized to one of the three study conditions, using cluster randomization sequences (blocks of 3 stratified by site) generated such that each block of 3 sequential groups included one of each study condition. Accordingly, eligible participants did not know which intervention they would receive. The study biostatistician (SP) remained blind to group assignment while completing analyses. However, study personnel were not blind to assignment.

2.4. Interventions

All interventions were delivered in group-format, in a classroom setting by a team of clinicians trained in the delivery of exposure therapy and in the study procedures. To ensure consistency across sites, clinicians implemented the interventions using a series of videos featuring one of the investigators guiding the participants through the steps of the interventions (e.g., education, modeling, completing forms). Study materials (e.g., manuals, videos, and forms) are available for download in multiple languages (e.g., English, German, Hebrew; https://www.exposuretherapyinfo.org/file-share/022d11a8-23ca-4210–89c7-ee5d1518addb).

2.4.1. ENHANCED

The ENHANCED intervention began with an orientation and psychoeducation (approximately 20 min), which was followed by exposure practice (approximately 75 min) and post-exposure processing (approximately 15 min).

Orientation/Psychoeducation: After a general orientation, participants watched a brief video that (1) described anxiety sensitivity and its relation with anxiety disorders, along with the rationale for interoceptive exposure, and (2) provided an overview of the intervention. Next, they viewed a brief video of a clinician and patient discussing the rationale for interoceptive exposure and demonstrating three safe and effective exercises for evoking particular somatic sensations: (1) spinning, (2) straw breathing, and (3) voluntary hyperventilation (Antony et al., 2006). After watching the videos, participants answered a series of questions about their concerns and fear level going into the exercise. Clinicians provided corrective feedback to ensure that participants fully understood both the model and the procedures involved in exposure therapy.

Exposure Practice: Participants then completed five trials each of three different exposure exercises: 30 seconds of spinning, 1 minute of straw breathing, and 1 minute of hyperventilation. Each exercise was led by a team of clinicians to ensure that participants completed each one properly and according to protocol. Before each exercise, participants indicated their specific threat expectancy, i.e., what feared outcome they expected to happen during the exercise. At the end of each exercise, the participants answered three questions specifically targeting any expectancy violations (e.g., "Did what you were concerned about happen?", "How do you know that has not happened?", and "How convinced are you that [exposure exercise] and its related sensations are not harmful?"). Research sites that were able to recruit larger samples, completed these rotations in smaller subgroups.

Post-Exposure Processing: This exercise started with a brief video featuring a clinician and patient discussing the outcome of an exposure practice and focusing on the discrepancy between anticipated and actual feared outcomes during the exposure practice. After the video, study participants (1) wrote their own responses to questions aimed at facilitating such safety learning (e.g., "Did what you were most worried about occur?", "What actually happened compared to what you predicted would happen?") and (2) engaged in a brief discussion led by clinicians to assist with processing this information. After post-exposure processing, clinicians debriefed participants and offered assistance in regulating any distress resulting from the exposure practice among participants who requested that.

2.4.2. STANDARD

Participants assigned to the STANDARD condition received the identical exposure practice intervention as did those in the ENHANCED condition, but without answering the 3 questions at the end of each exercise or the post-exposure processing. To account for time spent on the post-processing in the ENHANCED condition, participants assigned to the STANDARD condition responded to a set of questions about exposure practice and participated in discussion (approximately 15 min) without specifically highlighting the discrepancy between anticipated and actual outcomes (e.g., "How would you describe exposure therapy to a friend?", "What do you think were some of the advantages of completing the exercise in a group?", "Which of these exercises was most similar to the anxiety symptoms you most fear?").

2.4.3. CONTROL

Participants assigned to this condition watched videos about, and discussed, (1) the physiological stress response, including its positive and negative consequences, and (2) strategies for maintaining a healthy lifestyle focused on nutrition, exercise, and sleep hygiene. The CONTROL condition was equated for time with the exposure conditions, lasting approximately 1 hour and 50 minutes in total.

2.4.4. Quality Assurance

To facilitate standardization, staff and clinicians completed brief training modules (see https://www.exposuretherapyinfo.org/large-group-exposure-training). These modules covered procedures (e.g., screening, assessment, treatment) and systems (REDCap). Clinician training also included a brief video workshop. Site investigators ensured that staff and clinicians completed the relevant training before participating in the study.

2.5. Assessment

Data collection and entry procedures were standardized across sites. Prescreens and follow-up surveys were collected electronically, while data collected during the session (baseline, within-session, and post-intervention measures) were recorded on paper and later entered into

REDCap by research teams.[2] To ensure data integrity, the primary outcome measure (ASI-3) was double-coded, and all paper-and-pencil entries were checked by multiple research team members.

2.5.1. Outcome Measure

The ASI-3 (Taylor et al., 2007) is a psychometrically-sound 18-item self-report measure of anxiety sensitivity. Responses are rated on a 5-point Likert scale ranging from 0 (very little) to 4 (very much) and summed to yield a total score ranging from 0 to 72.

2.6. Data Analysis

Trial outcome data analyses were pre-registered on the Open Science Framework (https://osf.io/uw3zs). Since ignoring cluster effects (participants within groups within sites) can bias the estimation of treatment effects (Feaster et al., 2011), multilevel modeling was used to account for the nested structure of the data. Random (as opposed to fixed) effects were used for clustering variables (e.g., site) because this approach yields more efficient estimation of treatment effects in the presence of cluster imbalances (Feaster et al., 2011) and is robust to missing data (Schielzeth et al., 2020). All analyses were conducted in *R* version 4.4.2 (R Core Team, 2023) using the *lmer* function of the lme4 package (Bates et al., 2015), which follows intention-to-treat principles and includes all participants in analyses regardless of missing outcome data. The primary outcome model (ASI-3) included fixed effects of phase (pre-treatment, post-treatment, 1-week follow-up, 1-month follow-up), condition (ENHANCED, STANDARD, CONTROL) and a condition-by-phase interaction. Models that treated phase as a linear, exponential, quadratic, or factor variable were compared; the best-fitting model (based on Akaike information criterion [AIC]) was used across analyses. Helmert coding was used to test the hypotheses: (1) The two exposure conditions (ENHANCED and STANDARD) will experience greater reduction in ASI relative to CONTROL from pre- to post-treatment and from pre- to 1-month-follow-up; and (2) ENHANCED will experience greater reduction in ASI relative to STANDARD from pre- to post-treatment and from pre- to 1-month-follow-up. Post-treatment served as the primary endpoint for the hypotheses, and follow-up served as the secondary endpoint. Estimates are reported along with 95 % confidence intervals. Cohen's d effect sizes were also calculated using model estimates and pooled SDs. Group differences were considered significant at $p < .05$. We also report random effect variances.

3. Results

3.1. Big-Team Science Feasibility

As can be seen in Table 1, 12 of 13 sites (92 %) provided data for the trial. Reasons for delays between the trial registration date (2021) and data collection (2022–2024) included unforeseen crises (e.g., the COVID-19 pandemic, Israel-Gaza conflict) and their restrictions on in-person group data collection, and unexpected challenges recruiting students for in-person studies (Smits et al., 2024). Because of a reduced interest in in-person studies observed at universities, conducting a large-group exposure trial with a select sample proved to be impossible. Specifically, although all sites aimed to enroll groups of 25 or greater ($\geq$75 total) only 1 site achieved that aim and only one-third of sites achieved a sample size of 50. As a result, the actual study-wide sample size (N = 400; a mean sample size per site of 33.3) was smaller than what had been planned (N = 600). Despite provision of all study materials to sites at the time, there was substantial variability in the date of study initiation, with some sites delayed a year and a half from the lead sites.

In terms of adherence to the study protocol, all sites completed screening, enrollment, intervention, data collection and data transfer per the specified procedures. No serious adverse events were reported; however, two participants in CONTROL reported discomfort arising from content related to the eating and physical activity recommendations in the educational videos. Three participants (0.8 %; one in each treatment) did not complete the protocol or post-treatment measures. Of these, two reported scheduling conflicts, and one reported feeling ill after completing the baseline measures but before initiation of the treatment protocol. Rates of online completion of follow-up surveys were high with 90.75 % adherence at 1-week follow-up (88.9 % CONTROL, 92.3 % STANDARD, and 90.9 % ENHANCED) and 88.75 % completion rate at 1-month follow-up (89.7 % CONTROL, 88 % STANDARD, and 88.6 % ENHANCED). Group differences in follow-up adherence were not significant at 1-week ($p = .64$) and 1-month ($p = .91$).

3.2. Clinical Trial Hypothesis Testing

3.2.1. Participant characteristics

Fig. 1 illustrates participant flow into the study. Table 2 summarizes the demographic and baseline anxiety sensitivity of the randomized participants.

3.2.2. Model fit and omnibus test

Treating phase as a factor yielded the best-fitting model, as indicated by the lowest AIC (factor AIC = 11105; exponential model AIC = 11112; quadratic model AIC = 11141; linear model AIC = 11156). In this model, there was a significant group-by-phase interaction, $F(6, 1110.76) = 2.20$, $p = .04$. Fig. 2 illustrates the model estimated means for each group across the phases of the study.

3.2.3. Primary endpoint

Across all three groups, change in ASI from pre- to post-treatment was significant (ENHANCED M = −4.78, 95 % CI [-6.37, −3.20], $d = -0.40$, $p < .001$; STANDARD M = −2.03, 95 % CI [-3.56, −0.51], $d = -0.17$, $p = .01$; CONTROL M = −4.96, 95 % CI [-6.58, −3.34], $d = -0.41$, $p < .001$). The reduction in ASI in the exposure groups (ENHANCED + STANDARD) was not significantly different from the reduction in the CONTROL group (M = 1.55, 95 % CI [-0.41, 3.51], $d = 0.13$, $p = .12$). Although the reduction in ASI in the ENHANCED group was significantly greater than the reduction in the STANDARD group (M = −2.75, 95 % CI [-4.95, −0.55], $d = -0.23$, $p = .01$), ENHANCED was not significantly different from CONTROL (M = 0.18, 95 % CI [-2.09, 2.45], $d = 0.01$, $p = .88$). Moreover, the CONTROL group had significantly greater reduction in ASI than the STANDARD group (M = −2.93, 95 % CI [-5.15, −0.70], $d = -0.24$, $p = .01$).

3.2.4. Secondary endpoint

Across all three groups, change in ASI from pre-treatment to 1-month-follow-up was significant (ENHANCED M = −5.18, 95 % CI [-6.83, −3.53], $d = -0.43$, $p < .001$; STANDARD M = −5.44, 95 % CI [-7.04, −3.85], $d = -0.45$, $p < .001$; CONTROL M = −6.92, 95 % CI [-8.60, −5.23], $d = -0.58$, $p < .001$). The reduction in ASI in the exposure groups (ENHANCED + STANDARD) was not significantly different from the reduction in the CONTROL group (M = 1.61, 95 % CI [-0.43, 3.64], $d = 0.13$, $p = .12$). Moreover, all pairwise group comparisons were not significant (ENHANCED - STANDARD M = 0.27, 95 % CI [-2.03, 2.56], $d = 0.02$, $p = .82$; ENHANCED - CONTROL M = 1.74, 95 % CI [-0.61, 4.09], $d = 0.14$, $p = .15$; STANDARD - CONTROL M = 1.48, 95 % CI [-0.84, 3.79], $d = 0.12$, $p = .21$).

3.2.5. Random effects

Participants accounted for most of the random effect variance ($\sigma^2 = 127.28$), with group ($\sigma^2 = 2.99$) and site ($\sigma^2 = 4.31$) accounting for a relatively smaller proportion; residual variance was 42.74. Likelihood ratio tests based on the comparison between a model without random

[2] One site (The Hebrew University of Jerusalem) entered data directly into Qualtrics.

Table 1
Research site enrollment data.

Site	CTRL	STANDARD	ENHANCED	Total			
	n	n	n	n	%	Recruitment Period	Subgroups*
Austin	21	17	13	51	12.8	Sep 2022 - ov 2023	1
Boulder	11	19	25	55	13.8	Feb 2023 - Sep 2023	0
Oxford	4	2	4	10	2.5	Jan 2024 - Mar 2024	0
Miami	11	8	5	24	6	Sep 2022- Mar 2024	0
Boston	16	19	19	54	13.5	Oct 2022 - Dec 2022	1
Bochum	5	3	3	11	2.8	Jan 2023- June 2023	0
Dresden	10	6	4	20	5	Dec 2022 - Mar 2023	0
Marburg	5	6	4	15	3.8	Dec 2022 - May 2023	0
Göttingen	14	18	15	47	11.8	Feb 2024 - Jun 2024	0
Perth	2	7	8	17	4.3	Apr 2023 - May 2024	0
Sydney	25	33	29	87	21.8	Oct 2023 - Apr 2024	1
Jerusalem	2	4	3	9	2.3	Jan 2024 - July 2024	0

* A 1 indicates the site broke up their exposure conditions into subgroups, and a 0 indicates that they did not break up conditions into subgroups.

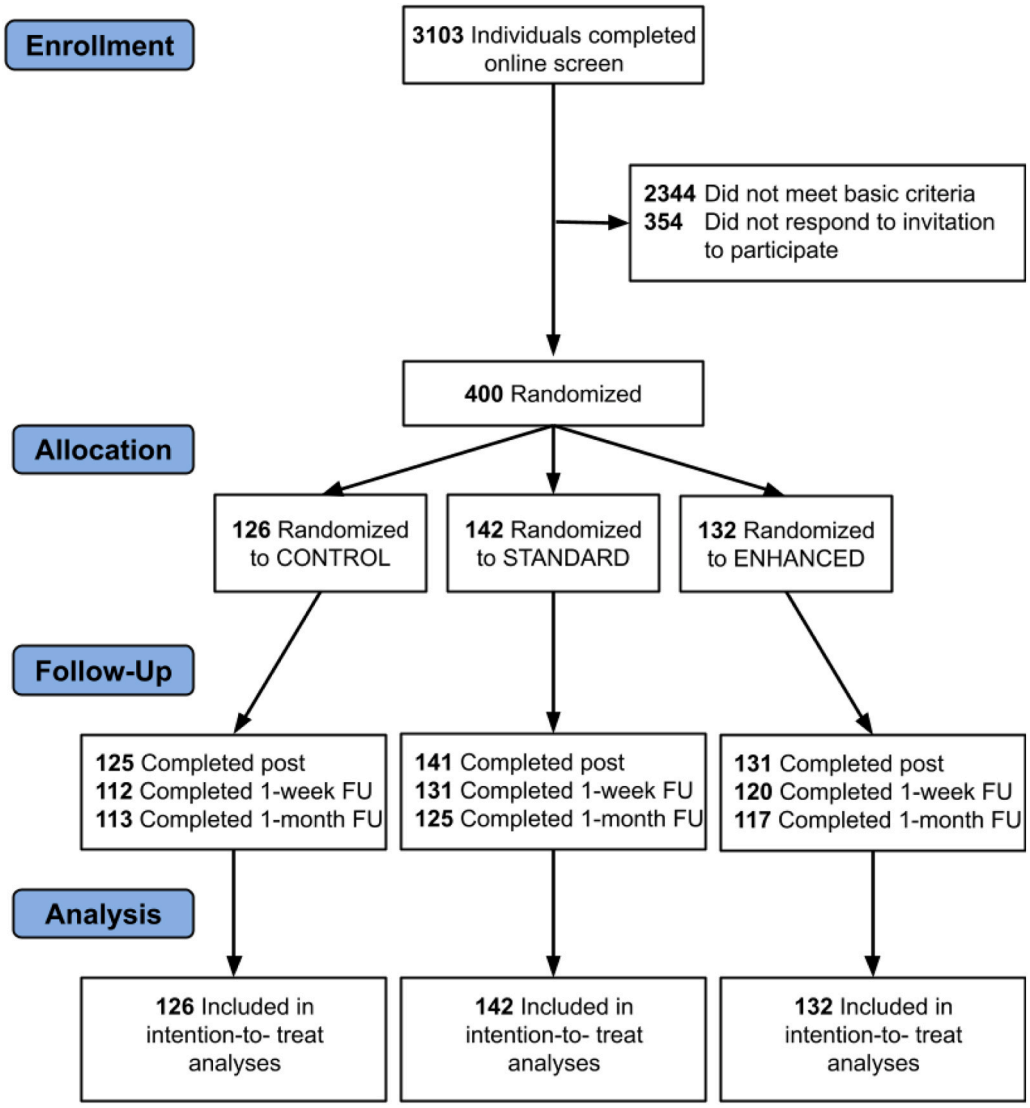

Fig. 1. Participant flow.

effects and one with a random effect of participant indicated that the participant-level random effect was significant ($p < .001$). However, after taking this participant-level random effect into account, random effects for additional levels were not significant (group only $p = 1$; site only $p = 0.06$; groups within sites $p = 0.16$). Together, this suggests that the groups participants were clustered in, and the sites in which the groups took place, contributed to approximately 1.7 % and 2.4 % of the total variance, respectively.

Table 2
Sample characteristics.

	CONTROL (N = 126)	STANDARD (N = 142)	ENHANCED (N = 132)	Total (N = 400)
Age, mean (SD)	19.50 (2.12)	19.70 (2.17)	19.70 (2.42)	19.70 (2.24)
Gender, n (%)				
Male	23 (18.3 %)	25 (17.6 %)	27 (20.5 %)	75 (18.8 %)
Female	97 (77.0 %)	110 (77.5 %)	101 (78.8 %)	311 (77.8 %)
Transmale	1 (0.8 %)	2 (1.4 %)	0 (0 %)	3 (0.8 %)
Transfemale	0 (0 %)	1 (0.7 %)	0 (0 %)	1 (0.3 %)
Non-binary	4 (3.2 %)	3 (2.1 %)	0 (0 %)	7 (1.8 %)
Other	1 (0.8 %)	0 (0 %)	1 (0.8 %)	2 (0.5 %)
Decline to state	0 (0 %)	1 (0.7 %)	0 (0 %)	1 (0.3 %)
Race, n (%)				
American Indian/Alaska Native	1 (0.8 %)	0 (0 %)	1 (0.8 %)	2 (0.5 %)
Asian	34 (27.0 %)	39 (27.5 %)	37 (28.0 %)	110 (27.5 %)
Black or African American	1 (0.8 %)	2 (1.4 %)	2 (1.5 %)	5 (1.3 %)
White	47 (37.3 %)	58 (40.8 %)	55 (41.7 %)	160 (40.0 %)
More than one race or Other	4 (3.2 %)	5 (3.5 %)	8 (6.1 %)	17 (4.3 %)
Decline to State	3 (2.4 %)	1 (0.7 %)	0 (0 %)	4 (1.0 %)
not collected*	36 (28.6 %)	37 (26.1 %)	29 (22.0 %)	102 (25.5 %)
Ethnicity, n (%)				
Hispanic/ Latino	17 (13.5 %)	17 (12.0 %)	7 (5.3 %)	41 (10.3 %)
Black/African Origins	1 (0.8 %)	3 (2.1 %)	2 (1.5 %)	6 (1.5 %)
White/ Caucasian	31 (24.6 %)	40 (28.2 %)	48 (36.4 %)	119 (29.8 %)
Asian	35 (27.8 %)	36 (25.4 %)	37 (28.0 %)	108 (27.0 %)
Arab/Middle Eastern	1 (0.8 %)	7 (4.9 %)	0 (0 %)	8 (2.0 %)
Jewish	2 (1.6 %)	3 (2.1 %)	4 (3.0 %)	9 (2.3 %)
Aboriginal or Torres Strait Islander	1 (0.8 %)	0 (0 %)	0 (0 %)	1 (0.3 %)
Other	4 (3.2 %)	3 (2.1 %)	8 (6.1 %)	15 (3.8 %)
not collected*	34 (27.0 %)	33 (23.2 %)	26 (19.7 %)	93 (23.3 %)
Screening ASI, mean (SD)	37.7 (11.1)	36.0 (9.65)	37.9 (9.71)	37.1 (10.2)

* Sites in Germany (Bochum, Dresden, Goettingen, and Marburg) did not collect race or ethnicity data. Jerusalem collected ethnicity but not race

4. Discussion

4.1. Summary of Findings

Analyses of performance metrics suggest that a standardized protocol for screening, assessment, and treatment was successfully implemented at 12 research sites across four continents. The multi-site cluster-randomized controlled trial achieved a robust total sample size of 400 with minimal missing data. However, the aspiration to yield better data faster was not achieved. Specifically, most research sites were unable to achieve targeted enrollment numbers and completing the study required more time than planned. As a result, sample sizes varied considerably across clusters, the total sample size was smaller than planned (N = 600). Although multilevel modeling is an efficient approach in the presence of cluster imbalance (Feaster et al., (2011), the precision of site-level treatment effect estimates is impacted when site-level recruitment is low. The non-significance of the random effect of site should not be interpreted as evidence of equivalence across sites; nevertheless, the relatively small proportion of variability that was attributable to sites would be consistent with successful standardization of procedures across diverse university settings. The time to complete the study was longer than anticipated. That stated, the COVID-19 pandemic hit at the start of this study, which severely delayed and then hindered the ability to recruit participants, particularly to an in-person group study with a select sample. Thus, the pandemic likely obscured the ability to assess the true potential of conducting large-group studies within the consortium.

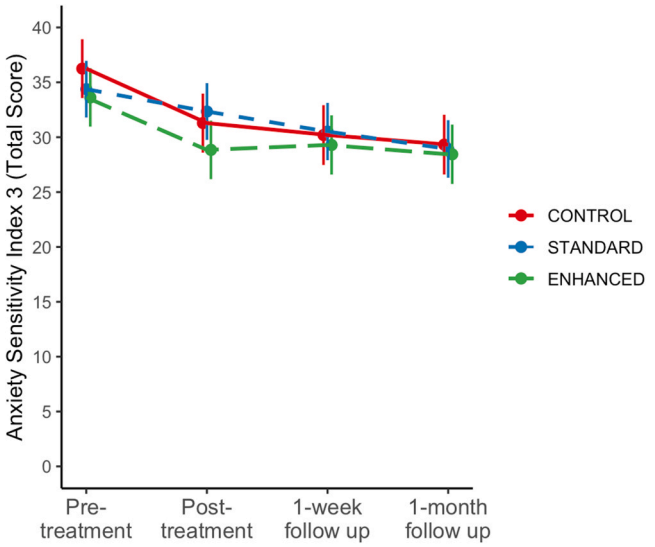

Fig. 2. Model estimated means and 95 % confidence intervals across phases of the study.

Aiming to extend research on exposure therapy in specific phobias (Wannemueller et al., 2017, 2018, 2020), single-session group exposure interventions for anxiety sensitivity were tested. It was hypothesized that exposure interventions would outperform stress management training and that an enhanced exposure condition with post-processing targeting the facilitation of safety learning would outperform a standard exposure condition without post-processing. Although all three interventions resulted in significant reductions in anxiety sensitivity, group differences were only observed at post-treatment where both ENHANCED and CONTROL were not significantly different from each other, and they each showed greater reductions compared to STANDARD.

It is only possible to speculate as to what explains the failure to demonstrate efficacy of single-session group exposure therapy for reducing anxiety sensitivity. Given the magnitude of change in anxiety sensitivity over the study period, it is plausible the intervention was underdosed. Recruitment for this study yielded a sample with a level of anxiety sensitivity (pre-treatment visit ASI $M = 33.98$, $SD = 12.02$) that is well above the clinical cut off of 25 (Allan et al., 2014). Indeed, post-treatment scores remained well above the entrance criteria, suggesting that the interventions were modestly effective overall. While the protocol involved supervised practice of three potent interoceptive exposure exercises (Antony et al., 2006), effective exposure therapy in persons with high anxiety sensitivity may simply require more practice within a session, across multiple sessions, or through self-guided homework assignments. Of note, intervention time did not emerge as a moderator of the efficacy of brief interventions for anxiety sensitivity in a recent meta analysis (Fitzgerald et al., 2021), but the analysis was underpowered and did not test whether the relation between intervention dose and efficacy depends on initial anxiety sensitivity severity. These observations highlight the need for dose-ranging studies in exposure therapy research.

Other possible explanations for the observed results warrant

consideration. For instance, unlike clinical or treatment-seeking populations, the student sample likely comprised individuals with varying levels of motivation to engage in the intervention and differing levels of perceived need for change. This variability may have diluted the efficacy of the exposure interventions. Also, it is possible that the psychoeducation provided in the CONTROL condition inadvertently enhanced participants' positive affective associations with arousal-related body sensations. This aligns with growing evidence suggesting that fostering positive affect during anxiety-related interventions can impact fear reduction (Craske et al., 2024; Taylor et al., 2023). For example, the focus on physiological responses in the CONTROL condition could have helped normalize and reframe participants' understanding of these sensations, indirectly promoting a sense of safety and reducing fear. It is also possible that the group format was less effective, particularly with the standardized video administration. Moreover, given that much of the study was conducted during or immediately after the COVID-19 epidemic, it is possible that the elevations in ASI were partially due to stress rather than "true" anxiety sensitivity, leading to less response to interoceptive exposure and greater response to relaxation. Future research could explore these possibilities further, particularly in relation to how variables like motivation, positive affect and psychoeducation interact to influence treatment outcomes in exposure therapy. This line of inquiry may benefit from also considering the potential moderating effects of individual differences including but not limited to sex, gender and age (Benito et al., 2024). The consortium aims to develop a comprehensive and standardized assessment of individual differences to facilitate future studies and meta-analyses of aggregate data.

4.2. Lessons Learned and Future Directions

To provide guidance for future investigations using a big-team science approach to studying psychological interventions, particularly within the Exposure Therapy Consortium, the following observations and recommendations are offered.

4.2.1. Commitment to an iterative approach to treatment development

Treatment development research on exposure therapy research has been largely a single-lab small-scale study enterprise (Smits et al., 2024). Often guided by theory and basic research, countless pilot studies have shown early positive findings supporting the efficacy of a procedural modification or augmentation strategy. Replication efforts have often failed (Sy et al., 2011) or, especially when testing using larger samples, yielded smaller effects (Mataix-Cols et al., 2017). This pattern is not unique to exposure therapy research (Kühberger et al., 2014; Turner et al., 2013; Vries et al., 2023). Coupled with the fact that there have likely been many (potentially false) negative findings that have led to the premature abandonment of treatment development (Czajkowski et al., 2015), it underscores the importance of establishing realistic goals and expectations at every phase of treatment development. When the aim is to develop and test brief interventions or optimization or augmentation strategies, it is reasonable to expect small (between-group) effect sizes. It is also important to consider the likelihood that efficacy varies as a function of dose parameters (Rosenfield et al., 2019) or individual difference factors. An effective treatment development process therefore requires a commitment to a series of studies that build progressively upon one another, with each phase designed to refine the intervention, determine the effective dose, optimize the study design, and address previous limitations - all elements of an iterative, and if needed, recursive, stage model (Onken et al., 2014). Specifically, early small-sample studies often serve primarily to assess feasibility - such as screening, recruitment, treatment fidelity and adherence (Leon et al., 2010). These studies can provide valuable insights that inform larger, adequately-powered efficacy studies, which in turn lay the foundation for subsequent research on dosing or personalized treatments.

4.2.2. Careful selection of research sites

The successful and timely implementation of a clinical trial requires research sites that have the necessary infrastructure (e.g., available staff, access to study population, facilities) to achieve the study aims (Warden et al., 2011). The current study used a number of strategies to make study initiation relatively "turn-key" - a detailed protocol with videos provided for key procedures to enhance cross-site transportability of interventions and research assistant duties, clear specification of the on site effort needed for study completion, a sharable REDCap library to aid uniform data collection, and a single-IRB approach to reduce administrative burden for study initiation. Despite these aids, sites differed widely in their ability to initiate study procedures in a timely way and achieve the expected sample size. Some of the difficulties of initiation of in person research during the post-COVID years led to the loss of firm rules for study initiation dates and would have resulted in a decrease overall sample size while achieving more uniform study conditions. Under more normal (non-crises) conditions, there may be merit to implementing the use of clear go/no go dates to terminate sites that are unlikely to initiate the study within a reasonable time frame.

4.3. Conclusions

This proof-of-principle study successfully demonstrated the feasibility of using a big-team science model to study exposure therapy. Despite variability in adherence to study timelines and sample sizes across sites, enrollment of 400 participants in an unfunded clinical trial is a notable achievement. The continued success of the Exposure Therapy Consortium will require a commitment to rigorous research site selection and an iterative approach to treatment development.

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Project administration. **Jill Newby:** Writing – review & editing, Resources. **Michael W. Otto:** Writing – original draft, Resources, Investigation, Funding acquisition. **Santiago Papini:** Writing – original draft, Methodology, Formal analysis, Data curation, Visualization. **E. Marie Parsons:** Writing – review & editing. **Andre Pittig:** Writing – review & editing, Investigation. **Roxana Pittig:** Writing – review & editing. **Winfried Rief:** Writing – review & editing, Resources, Investigation. **Svenja Schaumburg:** Writing – review & editing. **Kiara R. Timpano:** Writing – review & editing, Resources, Investigation. **Lena Waltemate:** Writing – review & editing. **Andre Wannemüller:** Writing – review & editing, Resources, Investigation. **Cornelia Weise:** Writing – review & editing.

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Data availability

Data will be made available on request.

References

Allan, N. P., Korte, K. J., Capron, D. W., Raines, A. M., & Schmidt, N. B. (2014). Factor mixture modeling of anxiety sensitivity: A three-class structure. *Psychological Assessment, 26*(4), 1184–1195. https://doi.org/10.1037/a0037436

Antony, M. M., Ledley, D. R., Liss, A., & Swinson, R. P. (2006). Responses to symptom induction exercises in panic disorder. *Behaviour Research and Therapy, 44*(1), 85–98. https://doi.org/10.1016/j.brat.2004.12.005

Bates, D., Mächler, M., Bolker, B., & Walker, S. (2015). Fitting Linear Mixed-Effects Models Using lme4. *Journal of Statistical Software, 67*, 1–48. https://doi.org/10.18637/jss.v067.i01

Benito, K., Pittig, A., Abramowitz, J., Arch, J. J., Chavira, D., de Kleine, R., De Nadai, A. S., Hermans, D., Hofmann, S. G., Hoyer, J., Huppert, J. D., Kircanski, K., McEvoy, P. M., Meyer, H., Monfils, M.-H., Papini, S., Rief, W., Rosenfield, D., Storch, E. A., … Smits, J. A. J. (2024). Mechanisms of Change in Exposure Therapy for Anxiety and Related Disorders: A Research Agenda. *Clinical Psychological Science*. , Article 21677026241240727. https://doi.org/10.1177/21677026241240727

Craske, M. G., Dunn, B. D., Meuret, A. E., Rizvi, S. J., & Taylor, C. T. (2024). Positive affect and reward processing in the treatment of depression, anxiety and trauma. *Nature Reviews Psychology, 3*(10), 665–685. https://doi.org/10.1038/s44159-024-00355-4

Czajkowski, S. M., Powell, L. H., Adler, N., Naar-King, S., Reynolds, K. D., Hunter, C. M., Laraia, B., Olster, D. H., Perna, F. M., Peterson, J. C., Epel, E., Boyington, J. E., & Charlson, M. E. (2015). From ideas to efficacy: The ORBIT model for developing behavioral treatments for chronic diseases. *Health Psychology, 34*(10), 971–982. https://doi.org/10.1037/hea0000161

Feaster, D. J., Mikulich-Gilbertson, S., & Brincks, A. M. (2011). Modeling site effects in the design and analysis of multisite trials. *The American Journal of Drug and Alcohol Abuse, 37*(5), 383. https://doi.org/10.3109/00952990.2011.600386

Fitzgerald, H. E., Hoyt, D. L., Kredlow, M. A., Smits, J. A. J., Schmidt, N. B., Edmondson, D., & Otto, M. W. (2021). Anxiety Sensitivity as a Malleable Mechanistic Target for Prevention Interventions: A Meta-Analysis of the Efficacy of Brief Treatment Interventions. *Clinical Psychology: A Publication of the Division of Clinical Psychology of the American Psychological Association, 28*(4), 323–337. https://doi.org/10.1037/cps0000038

Forscher, P., Wagenmakers, E., Coles, N., Silan, M., Dutra, N., Basnight-BrownH, D., & IJzerman, H. (2023). The Benefits, Barriers, and Risks of Big-Team Science. *Perspectives on Psychological Science: A Journal of the Association for Psychological Science, 18*(3). https://doi.org/10.1177/17456916221082970

Ginat-Frolich, R., Kara-Ivanov, A., Strauss, A. Y., Myers, A., & Huppert, J. D. (2023). Mechanisms underlying interoceptive exposure: Belief disconfirmation or extinction? A preliminary study. *Cognitive Behaviour Therapy, 52*(2), 132–145. https://doi.org/10.1080/16506073.2022.2109511

Harris, P. A., Taylor, R., Minor, B. L., Elliott, V., Fernandez, M., O'Neal, L., McLeod, L., Delacqua, G., Delacqua, F., Kirby, J., Duda, S. N., & REDCap Consortium. (2019). The REDCap consortium: Building an international community of software platform partners. *Journal of Biomedical Informatics, 95*, Article 103208. https://doi.org/10.1016/j.jbi.2019.103208

Harris, P. A., Taylor, R., Thielke, R., Payne, J., Gonzalez, N., & Conde, J. G. (2009). Research electronic data capture (REDCap)—A metadata-driven methodology and workflow process for providing translational research informatics support. *Journal of Biomedical Informatics, 42*(2), 377–381. https://doi.org/10.1016/j.jbi.2008.08.010

Kamphuis, J. H., & Telch, M. J. (2000). Effects of distraction and guided threat reappraisal on fear reduction during exposure-based treatments for specific fears. *Behaviour Research and Therapy, 38*(12), 1163–1181.

Kühberger, A., Fritz, A., & Scherndl, T. (2014). Publication Bias in Psychology: A Diagnosis Based on the Correlation between Effect Size and Sample Size. *PLOS ONE, 9*(9), Article e105825. https://doi.org/10.1371/journal.pone.0105825

Leon, A. C., Davis, L. L., & Kraemer, H. C. (2010). The Role and Interpretation of Pilot Studies in Clinical Research. *Journal of Psychiatric Research, 45*(5), 626. https://doi.org/10.1016/j.jpsychires.2010.10.008

Marsic, A., Broman-Fulks, J. J., & Berman, M. E. (2010). The Effects of Measurement Frequency and Timing on Anxiety Sensitivity Scores. *Cognitive Therapy and Research, 35*(5), 463–468. https://doi.org/10.1007/s10608-010-9321-3

Mataix-Cols, D., Fernández de la Cruz, L., Monzani, B., Rosenfield, D., Andersson, E., Pérez-Vigil, A., Frumento, P., de Kleine, R. A., Difede, J., Dunlop, B. W., Farrell, L. J., Geller, D., Gerardi, M., Guastella, A. J., Hofmann, S. G., Hendriks, G.-J., Kushner, M. G., Lee, F. S., Lenze, E. J., & Thuras, P. (2017). D-Cycloserine Augmentation of Exposure-Based Cognitive Behavior Therapy for Anxiety, Obsessive-Compulsive, and Posttraumatic Stress Disorders: A Systematic Review and Meta-analysis of Individual Participant Data. *JAMA Psychiatry, 74*(5), 501–510. https://doi.org/10.1001/jamapsychiatry.2016.3955

Onken, L. S., Carroll, K. M., Shoham, V., Cuthbert, B. N., & Riddle, M. (2014). Reenvisioning Clinical Science: Unifying the Discipline to Improve the Public Health. *Clinical Psychological Science: A Journal of the Association for Psychological Science, 2*(1), 22–34. https://doi.org/10.1177/2167702613497932

Pittig, A., Heinig, I., Goerigk, S., Richter, J., Hollandt, M., Lueken, U., Pauli, P., Deckert, J., Kircher, T., Straube, B., Neudeck, P., Koelkebeck, K., Dannlowski, U., Arolt, V., Fydrich, T., Fehm, L., Ströhle, A., Totzeck, C., Margraf, J., & Wittchen, H.-U. (2023). Change of Threat Expectancy as Mechanism of Exposure-Based Psychotherapy for Anxiety Disorders: Evidence From 8,484 Exposure Exercises of 605 Patients. *Clinical Psychological Science, 11*(2), 199–217. https://doi.org/10.1177/21677026221101379

R Core Team. (2023). A Language and Environment for Statistical Computing [Computer software]. R Foundation for Statistical Computing. ⟨https://www.R-project.org/⟩.

Reiss, S., Peterson, R. A., Gursky, D. M., & McNally, R. J. (1986). Anxiety sensitivity, anxiety frequency and the prediction of fearfulness. *Behaviour Research and Therapy, 24*(1), 1–8.

Rosenfield, D., Smits, J. A. J., Hofmann, S. G., Mataix-Cols, D., de la Cruz, L. F., Andersson, E., Rück, C., Monzani, B., Pérez-Vigil, A., Frumento, P., Davis, M., de Kleine, R. A., Difede, J., Dunlop, B. W., Farrell, L. J., Geller, D., Gerardi, M., Guastella, A. J., Hendriks, G.-J., & Otto, M. W. (2019). Changes in Dosing and Dose Timing of D-Cycloserine Explain Its Apparent Declining Efficacy for Augmenting Exposure Therapy for Anxiety-related Disorders: An Individual Participant-data Meta-analysis. *Journal of Anxiety Disorders*. , Article 102149. https://doi.org/10.1016/j.janxdis.2019.102149

Schielzeth, H., Dingemanse, N. J., Nakagawa, S., Westneat, D. F., Allegue, H., Teplitsky, C., Réale, D., Dochtermann, N. A., Garamszegi, L. Z., & Araya-Ajoy, Y. G. (2020). Robustness of linear mixed-effects models to violations of distributional assumptions. *Methods in Ecology and Evolution, 11*(9), 1141–1152. https://doi.org/10.1111/2041-210X.13434

Schmidt, N. B., Zvolensky, M. J., & Maner, J. K. (2006). Anxiety sensitivity: Prospective prediction of panic attacks and Axis I pathology. *J Psychiatr Res, 40*, 691–699.

Sloan, T., & Telch, M. J. (2002). The effects of safety-seeking behavior and guided threat reappraisal on fear reduction during exposure: An experimental investigation. *Behaviour Research and Therapy, 40*(3), 235–251. https://doi.org/10.1016/S0005-7967(01)00007-9

Smits, J. A. J., Abramowitz, J. S., Arch, J. J., Papini, S., Anderson, R. A., Dixon, L. J., Graham, B. M., Hofmann, S. G., Hoyer, J., Huppert, J. D., Jacquart, J., Johnson, D., McEvoy, P. M., McKay, D., Newby, J., Otto, M. W., Pittig, A., Rief, W., Rosenfield, D., & Exposure Therapy Consortium. (2024). Improving Exposure Therapy: Rationale and Design of an International Consortium. *The Psychiatric Clinics of North America, 47*(2), 433–444. https://doi.org/10.1016/j.psc.2024.02.008

Smits, J. A. J., Berry, A. C., Tart, C. D., & Powers, M. B. (2008). The efficacy of cognitive-behavioral interventions for reducing anxiety sensitivity: A meta-analytic review. *Behaviour Research and Therapy*.

Smits, J. A. J., Julian, K., Rosenfield, D., & Powers, M. B. (2012). Threat reappraisal as a mediator of symptom change in cognitive-behavioral treatment of anxiety disorders: A systematic review. *Journal of Consulting and Clinical Psychology, 80*, 624–635. https://doi.org/10.1037/a0028957

Smits, J. A. J., Otto, M. W., Powers, M. B., & Baird, S. O. (2018). Anxiety sensitivity as a transdiagnostic treatment target. In J. A. J. Smits, M. W. Otto, M. B. Powers, & S. O. Baird (Eds.), *The clinician's guide to anxiety sensitivity treatment and assessment* (1 edition). Academic Press.

Sy, J. T., Dixon, L. J., Lickel, J. J., Nelson, E. A., & Deacon, B. J. (2011). Failure to replicate the deleterious effects of safety behaviors in exposure therapy. *Behaviour Research and Therapy, 49*(5), 305–314. https://doi.org/10.1016/j.brat.2011.02.005

Taylor, C. T., Rosenfield, D., Dowd, S. M., Dutcher, C. D., Hofmann, S. G., Otto, M. W., Pollack, M. H., & Smits, J. A. J. (2023). What good are positive emotions for treatment? A replication test of whether trait positive emotionality predicts response to exposure therapy for social anxiety disorder. *Behaviour Research and Therapy, 171*, Article 104436. https://doi.org/10.1016/j.brat.2023.104436

Taylor, S., Zvolensky, M. J., Cox, B. J., Deacon, B. J., Heimberg, R. G., Ledley, D. R., Abramowitz, J. S., Holaway, R. M., Sandin, B., Stewart, S. H., Coles, M., Eng, W., Daly, E. S., Arrindell, W. A., Bouvard, M., & Cardenas, S. J. (2007). Robust dimensions of anxiety sensitivity: Development and initial validation of the Anxiety Sensitivity Index-3. *Psychological Assessment, 19*(2), 176–188.

Turner, R. M., Bird, S. M., & Higgins, J. P. T. (2013). The impact of study size on meta-analyses: Examination of underpowered studies in Cochrane reviews. *PloS One, 8*(3), Article e59202. https://doi.org/10.1371/journal.pone.0059202

Vries, Y. A. de, Schoevers, R. A., Higgins, J. P. T., Munafò, M. R., & Bastiaansen, J. A. (2023). Statistical power in clinical trials of interventions for mood, anxiety, and psychotic disorders. *Psychological Medicine, 53*(10), 4499–4506. https://doi.org/10.1017/S0033291722001362

Wannemueller, A., Fasbender, A., Kampmann, Z., Weiser, K., Schaumburg, S., Velten, J., & Margraf, J. (2018). Large-Group One-Session Treatment: A Feasibility Study of Exposure Combined With Applied Tension or Diaphragmatic Breathing in Highly Blood-Injury-Injection Fearful Individuals. *Frontiers in Psychology, 9*, 1534. https://doi.org/10.3389/fpsyg.2018.01534

Wannemueller, A., Jöhren, H.-P., Borgstädt, A., Bosch, J., Meyers, M., Völse, M., Scholten, S., & Margraf, J. (2017). Large Group Exposure Treatment: A Feasibility Study of Exposure Combined with Diaphragmatic Breathing in Highly Dental Fearful Individuals. *Frontiers in Psychology, 7*, 2007. https://doi.org/10.3389/fpsyg.2016.02007

Wannemueller, A., Schaumburg, S., Tavenrath, S., Bellmann, A., Ebel, K., Teismann, T., Friedrich, S., & Margraf, J. (2020). Large-group one-session treatment: Feasibility and efficacy in 138 individuals with phobic fear of flying. *Behaviour Research and Therapy, 135*, Article 103735. https://doi.org/10.1016/j.brat.2020.103735

Warden, D., Trivedi, M. H., Greer, T. L., Nunes, E., Grannemann, B. D., Horigian, V. E., Somoza, E., Ring, K., Kyle, T., & Szapocznik, J. (2011). Rationale and Methods for Site Selection for a Trial Using a Novel Intervention to Treat Stimulant Abuse. *Contemporary Clinical Trials, 33*(1), 29. https://doi.org/10.1016/j.cct.2011.08.011