NKR 58 PICO 7 Kropsterapi ved angstlidelser

Review information

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Characteristics of studies

Characteristics of included studies

Calbring 2003

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Intervention ● *Mean age, years (SD)*: 38.5 (11.0) ● *Female %*: 73% ● *Mean years since onset (SD)*: 11.9 (6.0) Control ● *Mean age, years (SD)*: 37.4 (6.1) ● *Female %*: 63% ● *Mean years since onset (SD)*: 8.8 (4.0) **Included criteria:** Participants were selected by an in-person Structured clinical interview for DSM-IV interview (SCID;First, Gibbon, Spitzer, & Williams, 1997). To be included in thestudy, participants had to meet the following criteria: fulfil the DSM-IV (AmericanPsychiatric Association, 1994) criteria for PD; PD duration of at least 1 year; agebetween 18 and 60 years; not suffering from any other psychiatric disorder inimmediate need of treatment; have a depression point total on the self-rated versionof the Montgomery(Asberg Depression Rating Scale (MADRS-SR;Svanborg & (Asberg, 1994) of less than 21 points and less than 4 points on the suicide question(Item 9); PD as the primary problem; at least one full-blown panic attack or onelimited symptom attack during the pre-treatment baseline (a limited symptom attackis an attack that meets all other criteria but has fewer than four somatic or cognitivesymptoms.); if on prescribed drugs for PD, (a) the dosage had to be constant for 3months before the start of the treatment, and (b) the patient had to agree to keep thedosage constant throughout the study; if in therapy, this had to have been ongoingfor more than 6 months and not be of CBT type; previous contact with a physician,psychologist, or other health professional as a consequence of panic attacks; noepilepsy, kidney problems, strokes, organic brain syndrome, emphysema, heartdisorders, or chronic high blood pressure. **Pretreatment:** The two groups did not differ significantly in any of the measurements at pre-treatment.
Interventions	**Intervention Characteristics** Intervention ● *Description:* Internet-administrated self-help programconsisting of Applied RelaxationIn the AR group. Ost's applied relaxation book(.Ost, 1997) was adapted for self-help use via the WWW. A compact Internet-administrated disc (CD) with three relaxation instructions was also sent to the participants. The treatment was divided into 9 modules: (1) psychoeducation, (2) rational, (3) progressive muscle relaxation: long version, (4)

	progressive muscle relaxation: short version, (5) conditioned relaxation, (6) differential relaxation, (7) quick relaxation, (8) applied relaxation, and (9) relapse prevention. Participants with a cellular phone (n=5) were sent short message service (SMS) reminders to relax about twice every weekday. ● *Dose*: The mean total time spent by the therapiston each participant was approximately 30 min, including administration, and responding to the e-mails. Most answers were fully standardized. Often only the participants name was altered in the greeting phrase of the e-mails. ● *Duration*: 9 modules (from may to december). Participants accessed to the first treatment module at the end of May 2001. They were expected to read the material and do the exercises described in the modules. No time limit was set for completing each module. An e-mail message to inquire howwork with the current module was progressing was sent out once in September 2001. Post-treatment assessment was conducted in December 2001. Each module ended with five to eight questions. Participants were asked to explain, in their own words, the most important sections of the module they had just completed. The questions were intended to encourage learning and to enable the research supervisors to assess whether the participants had assimilated the material, and finished their homework. Standardized feedback was given within 7 days of the participants sending their answers via e-mail. On the basis of these e-mails, an assessment was made of whether the participant was ready to continue, if so, the password to the next module was sent. If not, the participant received instructions on what needed to be completed before proceeding to the next step. Control ● *Description*: Internet-administrated self-help program consisting of CBT. The main treatment component in the CBT group was a self-help manual that was adapted for use via the WWW, and to be suitable for Swedish conditions. It consisted of 197 pages of text and exercises divided into 6 modules: (1) psychoeducation, (2) breathing retraining, (3) cognitive restructuring, (4) interoceptive exposure, (5) exposurein vivo, (6) relapse prevention and (7) assertiveness training (for details see Carlbringet al., 2001). ● *Dose*: The mean total time spent by the therapist on each participant was approximately 30 min, including administration, andresponding to the e-mails. Most answers were fully standardized. Often only the participants name was altered in the greeting phrase of the e-mails. ● *Duration*: 6 modules (from may to december). Participants accessed to the first treatment module at the end of May 2001. They were expected to read the material and do the exercises described in the modules. No time limit was set for completing each module. An e-mail message to inquire howwork with the current module was progressing was sent out once in September 2001. Post-treatment assessment was conducted in December 2001. Each module ended with five to eight questions. Participants were asked to explain, in their own words, the most important sections of the module they had just completed. The questions were intended to encourage learning and to enable the research supervisors to assess whether the participants had assimilated the material,and finished their homework. Standardized feedback was given within 7 days of the participants sending their answers via e-mail. On the basis of these e-mails, an assessment was made of whether the participant was ready to continue, if so, the password to the next module was sent. If not, the participant received instructions on what needed to be completed before proceeding to the next step.
Outcomes	*Grad af angst, Beck Anxiety Inventory (BAI), mean SD* ● **Outcome type**: Continuous Outcome ● **Reporting**: Fully reported ● **Scale**: Beck Anxiety inventory *(BAI)* ● **Range**: 0-63 ● **Direction**: Lower is better ● **Data value**: Endpoint *Livskvalitet, Quality of life inventory (QOLI), mean, SD* ● **Outcome type**: Continuous Outcome ● **Reporting**: Fully reported ● **Scale**: Quality of life inventory (QOLI) ● **Range**: 0-76 ● **Direction**: Lower is better ● **Data value**: Endpoint

	Grad af undgåelse, The Mobility Inventory for Agoraphobia (MI), mean, SD ● **Outcome type**: Continuous Outcome ● **Reporting**: Fully reported ● **Scale**: The Mobility Inventory for Agoraphobia (MI) ● **Range**: 1-125 ● **Direction**: Lower is better ● **Data value**: Endpoint *Frafald, alle årsager* ● **Outcome type**: Adverse Event ● **Reporting**: Fully reported ● **Direction**: Lower is better ● **Data value**: Endpoint
Identification	**Sponsorship source:** This study was sponsored by grants from the Swedish Foundation for Health Care Sciences and Allergy Research, the Boethius Foundation, the Swedish Council for Research in the Humanities and Social Sciences, and the Söderström-Köniska Foundation. **Country:** Sweden **Setting:** Internet-administrated self-help program **Authors name:** Per Calbring **Institution:** Department of Psychology, Uppsala University, Box 1225, Uppsala SE-751 42, Sweden **Email:** per.carlbring@psyk.uu.se
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement Comment: Insufficient information on sequence generation.
Allocation concealment (selection bias)	Unclear risk	Judgement Comment: Insufficient information on allocation concealment.
Blinding of participants and personnel (performance bias)	High risk	Judgement Comment: No information of blinding of participants, blinding not feasible. the intervention was an internet administered self help program. The participants were given standard feedback on questions at each module. No information of blinding of the personel which delivered the feedback. Blinding not feasible, and outcomes are self-reported.
Blinding of outcome assessment (detection bias)	High risk	Judgement Comment: Blinding not feasible, and outcomes are self-reported.
Incomplete outcome data (attrition bias)	Low risk	Quote: "the statistical analysis, preassessment data for applicants who were allocated to one of the two study groupings but who did not complete the treatment were brought forward and used as postassessment data (n=5). This was done on the basis of an intention-to-treat evaluation of the results, which is a more conservative approach compared to only including those who completed the treatment". Judgement Comment: 3 dropouts in th CBT group and 2 in the AR group. Intention to treat analysis.
Selective reporting (reporting bias)	Low risk	Quote: "The study protocol was approved by the ethics committee at Uppsala University." Judgement Comment: The protocol not available. The study seems to report on all the outcomes stated in the methods section.

Other bias	Low risk	Quote: "This study was sponsored by grants from the Swedish Foundation for Health Care Sciences and Allergy Research, the Böethius Foundation, the Swedish Council for Research in the Humanities and Social Sciences, and the S. oderstr. om-K. oniska Foundation. We thank Per Forslin and Carola Strandlund for the SCID-interviews." Judgement Comment: The study appears to be free from other sources of bias.

Clark 1994

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Overall ● *mean age, years (SD)*: 34.6 (9.2) ● *Number of females (%)*: 78% ● *Duration/mean years since onset (SD)*: 3.3 (range 0.5-15) **Included criteria:** a) DSM-III-R criteria for panic disorder with no, mild, or moderate agoraphobic avoidance. b) current episode duration at least 6 months. c) a least three panic attacks in the last three weeks. d) Consider panic their main problem. e) age 18 - 60 years. f) willing to accept random allocation. **Excluded criteria:** g) no depressive disorder, sever enough to require immediate psychiatric treatment. h) no cognitive therapy, applied relaxation or imipramine in the current episode. i) no evidence of organic mental disorder, schizophrenia, alcohol or drug dependence, cardiovascular disease, asthma, epilepsy, pregnancy or intention to become pregnant.
Interventions	**Intervention Characteristics** Intervention ● *Description*:Applied relaxation Kontrol ● *Description*: Cognitive therapy based on the cognitive theory of panic. Several cognitive and behavioral therapies were used to help patients identify and change misinterpretations of bodily sensations. Cognitive procedures included: identifying and challenging patients' evidence for their misinterpretations; substituting more realistic interpretations; and restructuring images. behavioral procedures included: inducing feared sensations (by hyperventilation, focusing attention on the body, or reading pairs of words representing feared sensations and catastrophes) in order to demonstrate possible causes of patients' symptoms; and stopping safety behaviors (such as holding unto solid objects when feeling dizzy) in order to help patient disconfirm their predictions about the consequence of their symptoms. Homework assignments also included keeping a daily record of negative thoughts and rational responses, and conducting behavioral experiments to test these thoughts. ● *Duration*: 6 months ● *Dose*: 12 weekly sessions in the first 3 months and up to 3 booster sessions in the next 3 months
Outcomes	*Grad af angst, HAM-A, mean, SD* ● **Outcome type**: ContinuousOutcome *Grad af undgåelse, social phobia scale, Mean, SD* ● **Outcome type**: ContinuousOutcome *Bedring, Free of panic attacks, percentages* ● **Outcome type**: DichotomousOutcome

Identification	**Sponsorship source:** Medical research council of the united kingdom **Country:** England **Setting:** Outpatient clinic **Authors name:** David M Clark **Institution:** Department of psychiatry, university of Oxford **Address:** Department of psychiatry, university of Oxford, Warneford hospital, Oxford OX3 7JX
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement Comment: No information of how the allocation sequence was geenrated
Allocation concealment (selection bias)	Unclear risk	Judgement Comment: no information of allocation concealment
Blinding of participants and personnel (performance bias)	High risk	Judgement Comment: No information of blinding of participants or health care providers, blinding of CBT not feasible
Blinding of outcome assessment (detection bias)	Low risk	Judgement Comment: Number of panic attacks were self-reported.HAM-A and FQ social phobia were clinician rated by blinded outcome assessors
Incomplete outcome data (attrition bias)	High risk	Judgement Comment: No diagram of participant flow. 72 were randomised. 16 in each group completed 3 month. Hereafter 12 patients from the waiting list were randomised to the three intervention groups. resulting in 20 in each group at 6 mionth follow up. No intention to treat analysis. Dropouts and refuseres after randomisation were replaced and not included in the analyses.
Selective reporting (reporting bias)	Low risk	Judgement Comment: No protocol available, the study reports on all the outcomes stated in the methods section
Other bias	Low risk	Judgement Comment: The study appears to be free of other sources of bias

Clark 2006

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Overall ● *Mean age, years (SD)*: 31.95 (8.58) ● *Mean years since onset (SD)*: 13.13.(11.15) **Included criteria:** Patients were given a written description of the trial and offered inclusion if they met the following criteria: (a) the patient met DSM-IV (American Psychiatric Association, 1994) criteria for social phobia; (b) the patient had experienced social phobia for a duration of at least 6 months; (c) social phobia was considered to be the patient's main problem; (d) the patient was 18-60 years old; (e) he or she did not meet DSM-IV IV criteria for alcohol or substance dependency; (f) he or she had no current or past psychosis; (g) the social phobia had not previously been treated with EXP or CBT; (h) the patient was on no psychotropic medication or had been on a stable dose for at least 2 months without symptomatic improvement and was willing to keep the dosage constant during the trial; and (i) he or she agreed not to start any additional treatment during the trial. With the exception of borderline personality disorder, Axis II personality disorders

	were not a reason for exclusion. **Pretreatment:** There were no significant differences between the groups in comorbidity.
Interventions	**Intervention Characteristics** Intervention ● *Description*: Exposure and applied relaxation. EXP and AR was based on the EXP described by Butler (1985) and the AR training described by Öst (1987). Throughout treatment, therapy sessions included exposure exercises and relaxation training, each of which was also included in weekly homework assignments. Exposure was presented in the context of a habituation rationale. Hierarchies were con-structed, and patients were encouraged to progress up their hierarchy in arelatively rapid manner that also helped build their confidence. As advo-cated by Butler (1985), considerable attention was paid to in-situation (subtle) avoidance, with patients being encouraged to reverse in-situationavoidance and to enter situations they would normally avoid. In-session exposure focused on in vivo exercises, rather than role-plays with the therapist. Training in AR was presented as an anxiety management procedure. It was explained that strong physical reactions in feared situations are a major contributor to patients' social fears and that the training had been specifically developed to deal with these reactions. In the original AR protocol, exposure is not introduced until after the relaxation techniques have been fully mastered. We deviated from this practice by using exposure exercises throughout treatment. However, as advocated by Öst (1987), patients were instructed to refrain from using their newlyacquired relaxation techniques in phobic situations until they had com-pleted all the steps in the relaxation training program (around Session 10). ● *Dose*: In both CT and EXPAR, sessions typically lasted 90 min. Therelaxation training component of EXPAR took approximately 20 min. weekly sessions. Treatment consisted of to 14 weekly session and up to 3 booster sessions were given in the first 3 monthsof follow-up, after which no further treatment was offered. ● *Duration*: 14 weeks Control ● *Description:* Cognitive therapy (CT). CT was essentially the same as in Clark et al. (2003). A variety of procedures, which are described in a manual (Clark, 1997) and elsewhere (Clark, 2001; Wells, 1997, pp. 167-199), were used to reverse the maintaining factors identified in Clark and Wells's (1995) model of social phobia. This model provides a similar account of maintenance to that proposed by Rapee and Heimberg (1997). Although overlapping in some respects with other empirically validated CBT programs, CT has several distinctive features. These include the following: (a) the development of version of Clark & Wells (1995) model by using the patient's own thoughts, images, attentional strategies, safety behaviors, and symptoms;(b) experiential exercises in which self-focused attention and safety behaviors are systematically manipulated in order to demonstrate their adverse effects; (c) systematic training in externally focused attention with practice in nonsocial and social situations; (d) techniques for restructuring distorted self-imagery, including a specialized way of using video feedback (see Harvey, Clark, Ehlers, & Rapee, 2000); (e) surveys to collect data on other peoples beliefs about such issues as blushing and trembling; and (f) the structuring of planned confrontation with feared social situations as a behavioral experiment in which patients test pre-specified negative predictions while dropping their habitual safety behaviors and focusing externally. A habituation rationale was not used, and repeated exposure to the same situation was not encouraged. Unlike some CBT programs, patients were not encouraged to develop positive self-talk before or during social situations, and there was no formal social skills training. ● *Dose*: In both CT and EXPAR, sessions typically lasted 90 min. weekly sessions. Treatment consisted of up to 14 weekly session and up to 3 booster sessions were given in the first 3 months of follow-up, after which no further treatment was offered. ● *Duration*: 14 weeks
Outcomes	*Funktion, The Social Interaction Scale (SIAS), mean, SD* ● **Outcome type**: Continuous Outcome ● **Reporting**: Fully reported ● **Scale**: *The Social Interaction Scale (SIAS)* ● **Range**: 0-80 ● **Direction**: Lower is better ● **Data value**: Endpoint

	Grad af undgåelse, ADIS fear and avoidance, mean, SD ● **Outcome type**: Continuous Outcome ● **Reporting**: Fully reported ● **Scale**: *ADIS fear and avoidance* ● **Range**: No found. ● **Direction**: Lower is better ● **Data value**: Endpoint *Frafald, alle årsager* ● **Outcome type**: Adverse Event ● **Reporting**: Fully reported ● **Direction**: Lower is better ● **Data value**: Endpoint
Identification	**Country:** Engalnd **Setting:** Outpatient clinic **Authors name:** David M. Clark and Anke Ehlers **Institution:** King's College London **Email:** E-mail: d.clark@iop.kcl.ac.uk **Address:** David M.Clark, Department of Psychology (PO 77), Institute of Psychiatry, King's College London, De Crespigny Park, London SE5 8AF, United Kingdom
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement Comment: Insufficient information on sequence generation
Allocation concealment (selection bias)	Unclear risk	Judgement Comment: Insufficient information allocation concealment
Blinding of participants and personnel (performance bias)	High risk	Judgement Comment: No information of blinding of personel and participants. Blinding of participants not feasible.
Blinding of outcome assessment (detection bias)	High risk	Judgement Comment: Blinding is not feasible, and outcomes are self-reported
Incomplete outcome data (attrition bias)	Low risk	Quote: "Analyses were intention to treat with last available data point carried forward,"
Selective reporting (reporting bias)	Low risk	Quote: "There were no protocol violations. Therapist" Judgement Comment: No study protocol were available, but the study appears to be free from other sources of bias
Other bias	Low risk	Judgement Comment: The study appears to be free from other sources of bias

Dermyer 2009

Methods	**Study design:** Randomized controlled trial **Study grouping:** Crossover

Participants	**Baseline Characteristics** Intervention ● *Female %*: 15 (88.24%) Control 2 ● *Female %*: 13 (81.25%) Overall ● *Female %*: 28 (84.85%) **Included criteria:** To be included in the study, volunteers had to beadults over the age of 18. Volunteers also had to have aprior diagnosis of GAD made by a physician or mental healthpractitioner. Prospective participants were required toobtain a referral from a physician or mental healthpractitioner to participate in the study. Additionally, theparticipants were required to document general healthinformation to identify factors that may have confoundedthe analysis. Participants also needed to have the capacityand willingness to fill out psychological tests. **Excluded criteria:** Including reasons for exclusion: An initial screening took place using the Generalized Anxiety Disorder Questionnaire-IV (GADQ-IV; Appendix H) tosubstantiate GAD diagnoses made by a physician or mental health practitioner in regard to the participant referrals. If there were discrepancies between the referral and the diagnostic test score, the volunteer was excluded from the study. Four potential participants were excluded from this study for this reason. Volunteers also were excluded from the study if they had practiced yoga regularly (once a week) in the past 3 months. In this instance, no participants were excluded for this reason. Additionally, individuals diagnosed with a severe psychiatric illness were unable to participate. There were no such individualswho volunteered for this research study. **Pretreatment:** NI however, a t-test was conducted by the statistical consultant to confirm that the randomization process was effective and that both the experimental and wait-list control groups were equivalent at baseline.
Interventions	**Intervention Characteristics** Intervention ● *Description:* The Fu-ZEN D^{2TM} Yoga-Stretch Program Protocol: Participants in the experimental group received the Fu-ZEN D^{2TM} Yoga-Stretch Program intervention. during a 1-month period. Research participants receiving the mind-body intervention met three days a week (Sunday, Tuesday, and Thursday) for one month at the City of Marquette Arts and Culture Center in the Peter White Public Library. The researcher logged attendance. The participants practiced the Fu-ZEN D^{2TM} Yoga-Stretch Program for one hour, three days a week, at the same pre-set evening time. The researcher, who was also the originator of the program, led instruction of the exercises. The researcher has performed the Fu-ZEN D^{2TM} Yoga-Stretch Program twice a day, every day, for over 14 years, in addition to practicing other various forms of yoga. The focus of the Fu-ZEN D^{2TM} Yoga-Stretch Program is stretching, flexibility, strength, balance, breathing, mindfulness, non-sectarian spirituality, and relaxation. Each posture was held for a minimum of 30 seconds. Virtually every muscle in the body was targeted. The exercise sessions began and ended with warm-up and cooldown exercises. For cost efficiency, traditional yoga propssuch as blocks and belts were not used in this study. However, the absence of these props was not a deterrent to growth and progress in this program. The temperature of the room was kept at 70 degrees. ● *Dose*: One hour, three times per week ● *Duration*: 1 month. Control ● *Description*: During the initial month, participants in the wait-list control group went home and carried on normally with their lives. ● *Duration*: 1 month

Outcomes	*Grad af angst, The State-Trait Anxiety Inventory (STAI), subscale state, mean, SD* ● **Outcome type**: Continuous Outcome ● **Reporting**: Fully reported ● **Scale**: *The State-Trait Anxiety Inventory (STAI)* ● **Range**: 0-80 ● **Direction**: Lower is better ● **Data value**: Endpoint *Funktion, Penn State Worry Questionnaire (PSWQ), mean, SD* ● **Outcome type**: Continuous Outcome ● **Reporting**: Fully reported ● **Scale**: *Penn State Worry Questionnaire (PSWQ)* ● **Range**: 1-80 ● **Direction**: Lower is better ● **Data value**: Endpoint
Identification	**Sponsorship source:** No information. **Country:** USA **Setting:** Volunteer participants for this study were recruited via local newspaper, television, radio, e-mail, and poster advertising. Intervention setting was the City of Marquette Arts and Culture Center in the Peter White Public Library. **Authors name:** Heather L. Dermyer **Institution:** Saybrook Graduate School **Email:** hdermyer@earthlink.net **Address:** Saybrook Graduate School Alumni, 747 Front St.San Francisco, CA 94111
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Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "internal validity of the study. In this study, the research assistant used a table of random numbers to assign each participant to the experimental or wait-list control group. Random assignment is the best"
Allocation concealment (selection bias)	Unclear risk	Judgement Comment: Insufficient information on allocation concealment
Blinding of participants and personnel (performance bias)	High risk	Judgement Comment: Blinding of participants and personnel not feasible
Blinding of outcome assessment (detection bias)	High risk	Judgement Comment: Blinding not feasible and it was self-reported outcomes
Incomplete outcome data (attrition bias)	High risk	Judgement Comment: NI about the drop out participant's (n=5), neither which groups they where allocated to, nor handling of the data sample however, they state on p. 78: "It is important to note that the number of participants for this statistical test, in accordance with the ITT, was 38, not 33. This indicated the total number of individuals whostarted the research study (5 dropped out before the randomization and treatment and 5 dropped out during theprocess) and not exclusively those who completed the study."
Selective reporting (reporting bias)	High risk	Judgement Comment: No protocol and not possible to extract data on adverse events / drop outs from groups due to lack of reporting. However, stated primary and secondary outcomes are comprehensively reported.

Other bias	High risk	Quote: "the same pre-set evening time. Instruction of the exercises was led by the researcher, who was also the originator of the program. The researcher has performed the Fu-ZEN D^{2TM} Yoga-Stretch Program twice a day, every day, for over 14 years, in addition to practicing other various forms of yoga. Judgement Comment: NI about funding. The founder of Fu-ZEN D^{2TM} Yoga-Stretch Program is also the author and the yoga instructor in this study.

Dugas 2010

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Overall ● *Mean age, years (SD)*: 38.5 (12.0) ● *Female %*: 66.2% **Included criteria:** Inclusion criteria were: (a) a primary diagnosis of GAD with a Clinician's Severity Rating of at least 4/8 (moderate severity); (b) a differenceof at least 2 points on the Clinician's Severity Rating between GAD and all comorbid conditions; (c) between 18 and 64 years of age; (d) no change in medication type or dose during 4 to 12 weeks before assessment (4 weeks for benzodiazepines, 12 weeks for antidepressants and hypnotics); (e) willingness to keep medication stable during the treatment phase of the study (no change in medication type or increase in dose); (f) no evidence of suicidal intent; (g) no evidence of current substance abuse; and (h) no evidence of current or past schizophrenia, bipolar disorder, or organic mental disorder. **Pretreatment:** No between-group differences were found for demographic variables.
Interventions	**Intervention Characteristics** Intervention ● *Description*: Applied relaxation. Covered the following treatment phases. 1.Psychoeducation and tension awareness training (1 session). During the first phase of treatment, the therapist explained that the goal of AR was to learn to recognize muscle tension and to apply relaxation methods, thereby reducing overall levels of tension, anxiety, and worry. Patients also learned to monitor their levels of muscle tension on a daily basis. 2.Tension-release training (4 sessions). Patients learned to tense then relax different musclegroups (moving from 16 to 4 muscle groups) until full relaxation was achieved. 3. Relaxation by recall (2 sessions). Once the tension-relaxation procedure with 4 musclegroups had been mastered, patients learned to relax their muscles without tensing them first. 4.Relaxation by counting (1 session). At the end of sessions when patients had achieved full relaxation through recall alone, the therapist slowly counted from 1 to 10, asking patients to imagine their relaxation becoming even deeper. Once the patients had successfully integrated the counting into the recall procedure, they learned to relax by counting alone. 5. Conditioned relaxation (3 sessions): In this phase of treatment, patients learned to apply relaxation skills in everyday situations using a graded hierarchy. This enabled them toachieve relaxation in response to a self-produced cue (e.g., by counting to 10) in real-life stressful situations. For a detailed description, see Bernstein and Borkovec(1973) and Öst (1987). ● *Dose*: Consisted of 12 weekly 1-hour therapy sessions. ● *Duration*: 12 weeks. Control ● *Description*: CBT Cognitive-behavioral therapy. Covered the following treatment phases.1. Psychoeducation and worry awareness train-ing (1 session). The therapist first explained that the goal of CBT was to learn to recognizeand reduce worry, thereby decreasing overalllevels of worry, anxiety, and tension. Patients learned to monitor their worrying on a day-to-day basis, and to distinguish between worries about current problems (e.g., meeting dead-lines at work) and worries about hypothetical situations (e.g., being involved in an accident). 2.Uncertainty recognition and behavioral exposure (3 sessions). The therapist then helped patients to understand the role of intolerance of uncertainty in

	worry and anxiety, to realize that uncertainty-inducing situations are largely unavoidable, to recognize the various manifestations of intolerance of uncertainty, and to seek out and experience uncertainty-inducing situations. 3. Reevaluation of the usefulness of worry (1 session). In the next phase, patients learned to identify and reevaluate their positive beliefs abouts worry (e.g. "my worries prepare med for bad things that might happen") using strategies such as the lawyer-prosecutor role play. 4. Problem-solving training (3 sessions). Patients then learned to address worries about current problems by using a problem-solving procedure targeting problem orientation, problem definition and goal formulation, generation of alternative solutions, decision making, and solution implementation and verification (See D'Zurilla, 1986). 5. Imaginal exposure (3 sessions). Finally, patients learned to use imaginal exposure for worries about hypothetical situations. With the help of the therapist, patients developed a scenario describing their worst fear using the downward arrow technique, and recorded the scenario on a looped tape for repeated exposure. They then listened to the recording for 20 to 60 minutes (long enough to experience a decrease in anxiety) everyday and continued to "expose" themselves to the scenario until it no longer provoked anxiety (typically 10 to 15 exposure sessions). See Dugas and Robichaud (2007) for a detailed description of the CBT protocol. ● *Dose:* Consisted of 12weekly 1-hour sessions. ● *Duration*: 12 weeks. Control 2 ● *Description*: Waiting list
Outcomes	*Grad af angst, Clinician Severity Rating* (CSR):*, mean, SD* ● **Outcome type**: Continuous Outcome ● **Reporting**: Fully reported ● **Scale**: Clinician Severity Rating (CSR) ● **Range**: 0-72 ● **Direction**: Lower is better ● **Data value**: Endpoint *Funktion, Clinical Global Impression, Improvement scale (CGI-I)* ● **Outcome type**: Continuous Outcome ● **Scale**: *Clinical Global Impression, Improvement Scale (CGI-I)* ● **Range**: 1-49 ● **Direction**: Lower is better ● **Data value**: Endpoint *Frafald, alle årsager* ● **Outcome type**: Adverse Event ● **Reporting**: Fully reported ● **Direction**: Lower is better ● **Data value**: Endpoint
Identification	**Sponsorship source:** No information. **Country:** Canada **Setting:** Outpatient clinic **Authors name:** Michel J. Dugas **Institution:** Concordia University and Hôpital du Sacré-Cœur de Montréal **Email:** Michel.Dugas@concordia.ca **Address:** Michel J. Dugas, Ph.D., Department of Psychology, Concordia University, 7141 Sherbrooke Street West, Montreal, Quebec, Canada, H4B 1R6;

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Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "The 65 participants who made up the final sample were randomly allocated to CBT (n = 23), AR (n = 22), or WL (n = 20). Allocation concealment and implementation were dealt with as follows: (1) the independent diagnostic assessments (MINI and ADIS-IV) were discussed during weekly team meetings; (2) a decision was reached to either include or exclude the patient; (3) when a patient was accepted into the study, the research coordinator applied a random allocation sequence; (4) following the meeting, the psychiatrist who administered the MINI contacted the patient to inform him/her of the team's decision (and of the result of randomization if the patient was accepted into the study)." Judgement Comment: Insufficient information on sequence generation.
Allocation concealment (selection bias)	Unclear risk	Quote: "The 65 participants who made up the final sample were randomly allocated to CBT (n = 23), AR (n = 22), or WL (n = 20). Allocation concealment and implementation were dealt with as follows: (1) the independent diagnostic assessments (MINI and ADIS-IV) were discussed during weekly team meetings; (2) a decision was reached to either include or exclude the patient; (3) when a patient was accepted into the study, the research coordinator applied a random allocation sequence; (4) following the meeting, the psychiatrist who administered the MINI contacted the patient to inform him/her of the team's decision (and of the result of randomization if the patient was accepted into the study). Judgement Comment: Insufficient information on allocation concealment
Blinding of participants and personnel (performance bias)	High risk	Judgement Comment: Blinding not feasible, and outcomes are selfreported. No blinding of personnel. The same therapist conducted both interventions.
Blinding of outcome assessment (detection bias)	High risk	Judgement Comment: Blinding not feasible, and outcomes are selfreported.
Incomplete outcome data (attrition bias)	Low risk	Quote: "Seven (7) participants did not complete the first 12 weeks of the study; 2 dropped out of CBT and 5 dropped out of AR (there were no dropouts in the WL condition). Missing posttest data were replaced with pretest scores. Thus, the data presented in Table 1 (and the pretest to posttest analyses) are based on the intent-to-treat sample." Quote: "Missing posttest data were replaced with pretest scores. Thus, the data presented in Table 1 (and the pretest to posttest analyses) are based on the intent-to-treat sample."
Selective reporting (reporting bias)	Low risk	Quote: "See Dugas and Robichaud (2007) for a detailed description of the CBT protocol." Judgement Comment: The study appears to report on all outcomes of interest
Other bias	Low risk	Judgement Comment: The study appears to be free from other sources of bias.

Irgens 2012

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Intervention ● *Mean age, years*: 36.6 ● *Female %*: 73.9 ● *Mean years since onset*: 20.7 Control ● *Mean age, years*: 37.4

	● *Female %*: 72.7 ● *Mean years since onset*: 16.2 Overall ● *Mean age, years*: 37 ● *Female %*: 73.3% ● *Mean years since onset*: 18 **Included criteria:** Inclusion criteria were the presence of anxiety disorders and willingness to be randomized. **Excluded criteria:** The only exclusion criterion was ongoing psychosis. **Pretreatment:** Relevant tests revealed no significant (P.05) differences between the two groups, though for personality disorder the P value was 0.051. 14/23 in the intervention group vs 7/22 in the control group had personality disorders
Interventions	**Intervention Characteristics** Intervention ● *Description*: Thought field therapy (TFT). TFT intervention. In ordinary TFT practice, patients are offered a treatment package of five hours of individual therapy. The patients in the current study received only two sessions of individual therapy, the first one lasting up to 50 minutes, the other up to 25 minutes. The reason for giving such a short treatment was that the TFT therapist did not have time for a full treatment package, because he practices in another part of the country.Clinical experience has shown that such a short treatment maybe sufficient. Additional sessions were provided by the first author, when judged as necessary. In the 12-month follow-up, 11 patients received no additional treatment by the first author, eight patients received one session, 14 patients received from two to five sessions, six patients received from six to 10 sessions, and six patients received from 11 to 23 additional sessions.The treatment was based on the TFT guidelines1 and was conducted by an experienced TFT therapist. The treatment ses-sions were observed by the first author in order to ensure that the treatment given was TFT and that the treatment was provided in accordance with the study protocol, but no treatment fidelity instrument was applied ● *Duration*: 2.5 month Control ● *Description*: Waiting list
Outcomes	*Funktion, Shehan Disability Scale (SDS), mean, SD* ● **Outcome type**: Continuous Outcome ● **Reporting**: Fully reported ● **Scale**: Shehan Disability Scale (SDS) ● **Range**: 0-30 ● **Direction**: Lower is better ● **Data value**: Endpoint *Frafald, alle årsager* ● **Outcome type**: Adverse Event ● **Reporting**: Fully reported ● **Direction**: Lower is better ● **Data value**: Endpoint *Frafald, adverse events* ● **Outcome type**: Adverse Event ● **Reporting**: Fully reported ● **Direction**: Lower is better ● **Data value**: Endpoint

	AE + SAE , antal personer, mean, SD ● **Outcome type**: Adverse Event ● **Reporting**: Fully reported ● **Direction**: Lower is better ● **Data value**: Endpoint
Identification	**Sponsorship source:** No information **Country:** Norway **Setting:** Outpatient clinic at psychiatric department at Sorlandet Hospital in Arendal **Authors name:** Audun Irgens, **Institution:** DPS Aust-Agder, Sorlandet sykehus, Arendal, Norway **Email:** audun.irgens@sshf.no **Address:** DPS Aust-Agder, Sorlandet sykehus,Box 783 Stoa, 4809 Arendal, Norway
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Patients were consecutively randomized based on a computer-generated list."
Allocation concealment (selection bias)	High risk	Quote: "The randomization procedure was not blinded. The whole procedure of inclusion, randomization, group-allocation and follow-up was performed by the principal investigator."
Blinding of participants and personnel (performance bias)	High risk	Judgement Comment: No information of blinding of health care providers, blinding of participants not feasible.
Blinding of outcome assessment (detection bias)	High risk	Quote: "Patients were consecutively randomized based on a computer-generated list. The randomiza- tion procedure was not blinded. The whole procedure of inclusion, randomization, group-allocation and follow-up was performed by the principal investigator." Judgement Comment: Blinding is not feasible, and outcomes are self-reported
Incomplete outcome data (attrition bias)	Low risk	Quote: "One patient in the immediate treatment group did not return after the first TFT treatment. Another patient in this group did not complete rating scales at the three- and 12- month follow-up. One patient in the group receiving TFT after the waiting period did not provide data at the 12 month follow- up. We used last observation carried forward for the missing data for these three patients (Figure 1)." Judgement Comment: Low number of dropouts. 2 in the TFT group and 1 in the waiting list group. Reasons for dropouts stated.
Selective reporting (reporting bias)	High risk	Quote: "Registration number NCT00202709, http://Clinical.Trials. gov." Judgement Comment: Specifick symptoms scales were planned according to the protocol and the methods section. Because of changes in the inclusion criteria these symptom scales were omitted.Davidson Trauma Scale, Liebowitz Social Anxiety Scale, Fear Questionnaire (FQ) were planned in the protocol but not reported in the trial.
Other bias	Low risk	Judgement Comment: The study appears to be free from other sources of bias

Janbozorgi 2009

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Overall ● *Mean age, years (SD)*:24.64(3.77) ● *Female %*:87.5 **Included criteria:** Patients with a principal DSM-IV (general anxiety disorders) diagnosis reffered to a counselling and psychotherapy center in Tehran by general practioners and mental health professionals from both government and private orginations as well as self-refferals were concidered for the study. There were a total of 64 refferels to the center during the study period. We decided to include only thosed aged 19-35 years becvause the majority of the refferels were in this age range. Four people were outside this age range and were excluded and 6 refused to take part in the study, leaving 54 eligible participants who signed the consent form. The Structured Clinical Interview was used as the basis for DSM-IV (SCID-IV) diagnosis. Whenever over 1 diagnosis ws identified, clinical interwiews was used clinical interview was used to de-termine the primary reason for the visit and the degree of interference in functioning, as recommended in DSM-IV. **Excluded criteria:** A principal diagnosis other than generalized anxiety disorder. Individuals were also excluded from the study if they were undergoing concurrent psychological treatment for anxiety disorder (2), had a current diagnosis of schizophrenia (1), an intellectual disability (1), or an organic mental disorder (1).
Interventions	**Intervention Characteristics** Intervention ● *Description*: The IRT programme is a structured programme attended by participants in groups of 10-15 persons. Participants were also given a weekly task. The interventions ap-plied during the treatment period included 12-weeks of IRT: a combination of pro-gressive relaxation training adapted from jacobsens's programme (cited in Berrenstein et al.) a lifestyle relaxation programme (including: organization of sleep time and limitation of daily sleep; healthy eating and drinking; exercise; increase in and devel-opment of awareness and consciousness; training in decision-making processes; leisure time management; and guidance for self-dialogue and spiritual exercises (religious meditation, prayer and mention or remembrance of God in daily activities). Each session lasted for about 1.5-2 hours and was diveded into 4 sections: review of homework, relaxation training, discussion of lifestyle and spiritual dimensions. Our integrative relaxation timetable for the 12 weeks is presented in Table 1 ● *Dose*: Each session lasted for about 1.5-2 hours and was diveded into 4 sections: review of homework, relaxation training, discussion of lifestyle and spiritual dimensions. Our integrative relaxation timetable for the 12 weeks is presented in Table 1.. ● *Duration*: 12 weeks Control 2 ● *Description*: No treatment ● *Dose*: ● *Duration*:
Outcomes	*Grad af angst, The State-Trait Anxiety Inventory (STAI), subscale state, mena, SD* ● **Outcome type**: Continuous Outcome ● **Reporting**: Fully reported ● **Scale**: The State-Trait Anxiety Inventory, subscale state ● **Range**: 0-80 ● **Direction**: Lower is better ● **Data value**: Endpoint

	Frafald, alle årsager ● **Outcome type**: Adverse Event ● **Reporting**: Fully reported ● **Direction**: Lower is better ● **Data value**: Endpoint
Identification	**Sponsorship source:** We would like to thank Professor Dadsetan for her comments on the earlier versions of the study and Thalieh Counselling Centre in Tehran for financing this research. **Country:** Iran **Setting:** a private psychotherapy centre **Authors name:** M. Janbozorgi **Institution:** Department of Psychiatry and Behavioural Science Research, Medical Science Centre, Shahid Beheshti University of Medical Science, Tehran, Islamic Republic of Iran **Email:** Correspondence to M. Janbozorgi: janbozorgi@sbmu.ac.ir
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement Comment: Insufficient information on sequence generation
Allocation concealment (selection bias)	Unclear risk	Judgement Comment: Insufficient information on allocation concealment
Blinding of participants and personnel (performance bias)	High risk	Judgement Comment: No information of blinding of health care providers and participants, blinding not feasible No information of blinding of health care providers and participants, blinding not feasible
Blinding of outcome assessment (detection bias)	High risk	Quote: "The STAI comprises separate self-report psychometric scales for measuring 2 distinct but related anxiety concepts" Judgement Comment: Outcomes of interest were self-reported. Blinding of participants not feasible
Incomplete outcome data (attrition bias)	High risk	Judgement Comment: No dropouts from the waiting list, 3/18 dropouts in the intervention group (lost to follow-up) No intention to treat analyses
Selective reporting (reporting bias)	High risk	Judgement Comment: No reference to study protocol, but appears to report on all outcomes, but the dropouts are not described in details
Other bias	Low risk	Quote: "We would like to thank Professor Dadsetan for her comments on the earlier versions of the study and Thalieh Counselling Centre in Tehran for financing this research." Judgement Comment: The study appears to be free from other sources of bias

Milrod 2016

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Intervention (Cornell) ● *Mean age, years (SD)*: 40.9 (14.3) ● *Female %*: 90%

	● *Mean years since onset (SD)*: Control (Cornell) ● *Mean age, years (SD)*: 39.4 (14.0) ● *Female %*: 68% ● *Mean years since onset (SD)*: Control 2 (Cornell) ● *Mean age, years (SD)*: 44.0(12.5) ● *Female %*: 66% ● *Mean years since onset (SD)*: Intervention (Penn) ● *Mean age, years (SD)*: 31.0 (9.6) ● *Female %*: 74% ● *Mean years since onset (SD)*: Control (Penn) ● *Mean age, years (SD)*: 39.2 (11.4) ● *Female %*: 46% ● *Mean years since onset (SD)*: Control 2 (Penn) ● *Mean age, years (SD)*: 35.5 (13.9) ● *Female %*: 79% ● *Mean years since onset (SD)*: **Included criteria:** occurrence of more than one spontaneous weekly panic attack for the month before entry. Ongoing psychotherapy wa prohibited. Medications, permitted if stable for over 2 month at presentation, recorded, heæd constant and monitored. **Excluded criteria:** Active substance dependence (< 6 month's remission), history of psychosis or bipolar disorder, acute suicidality, and organic mental syndrome. **Pretreatment:**
Interventions	**Intervention Characteristics** Intervention ● *Description*: Applied relaxation (AR). Progressive muscle relaxation training involves focusing of attention onto particular muscle groups, tensing the muscle group for 5-10 seconds, attending to the sensations of tension, relaxing of the muscle group, attending to the difference betweeen the sensation of tension and relaxation and suggestions of deepening the relaxation. The number of muscle groups is gradually reduced from 16 to 4. Discrimination training, generalization, relaxation by recall, and cue-controlled relaxation (pairing the relaxed state with the word "relax") follow. Home practice is required twice a day. At session 11, patients are encouraged to begin applying relaxation skills whenever they notic etension in their bodies, and beginning at session 17 they are asked to deliberately enter mildly, then moderately anxiety. provoking situations for practice of their skills. ART involved no cognitive restructuring or interoceptive exposure ● *Dose*: 24 sessions ● *Duration*: 12 weeks Control ● *Description*: Cognitive behavioral therapy (CBT). CBT has the following features: education anxiety and panic, identification and correction of maladaptive thoughts about anxiety and panic, training in slow, diagphragmatic breating, and exposure to bodily sensations designed to mimic those experienced durring panic. in vivo exposure via homework assingments was introduces at session 17 for those patients with significant agoraphobic avoidance, whereas session 24 focused on review and relapse prevention

	● *Dose*: 24 sessions ● *Duration*: 12 weeks Control 2 ● *Description*: Panic focused psychodynamic psychotherapy (PFPP) ● *Dose*: ● *Duration*:
Outcomes	*Funktion, Shehan Disability Scale (SDS), mean, SD (data kunne ikke indgå i metaanalyser, men beskrives narrativt)* ● **Outcome type**: Continuous Outcome ● **Reporting**: Not fully reported ● **Scale**: *Shehan Disability Scale (SDS)* ● **Range**: 0-30 ● **Direction**: Lower is better ● **Data value**: Endpoint *Funktion, Panic Disorder Severity Scale (data kunne ikke indgå i metaanalyser, men beskrives narrativt)* ● **Outcome type**: Continuous Outcome ● **Reporting**: Not fully reported ● **Scale**: *Panic Disorder Severity Scale* ● **Range**: 0-30 ● **Direction**: Lower is better ● **Data value**: Endpoint *Frafald, alle årsager* ● **Outcome type**: Adverse Event ● **Reporting**: Fully reported ● **Direction**: Lower is better ● **Data value**: Endpoint *AE + SAE , antal personer, mean, SD* ● **Outcome type**: Adverse Event ● **Reporting**: Fully reported ● **Direction**: Lower is better ● **Data value**: Endpoint
Identification	**Sponsorship source:** Supported by the national institute of mental health and by a fund uín the New York Community **Country:** USA **Setting:** Outpatient Clinic **Authors name:** Barbara Milrod **Institution:** Well Cornell Medical College, Cornell Univsersity, New York
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement Comment: No information of how the allocation sequence was generated
Allocation concealment (selection bias)	Unclear risk	Judgement Comment: No information of allocation concealment
Blinding of participants and personnel (performance bias)	High risk	Judgement Comment: No information of blinding of participants or health care providers, blinding not feasible
Blinding of outcome assessment (detection bias)	Low risk	Judgement Comment: Outcome assessors blinded to treatment and therapist (p. 3)
Incomplete outcome data (attrition bias)	Low risk	Judgement Comment: Extensive reporting of reasons for drop out (<45% for all groups) and appropriate analysis conducted (including multiple imputation). High number of dropouts, but imputation via multilevel models
Selective reporting (reporting bias)	High risk	Judgement Comment: Protocol at clinicaltrials.gov. The study fails to report on all the outcomes stated in the protocol
Other bias	Low risk	Judgement Comment: Affiliations, author contributions, potential conflicts of interest, funding af role of sponsor extensively reported. No other sources of bias is suspected. The study appears to be free from other sources of bias

Ost 1993

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Intervention ● *Female, n (%)*: 10 (66.67%) Control ● *Female, n (%)*: 10 (66.67%) Control 2 ● *Female, n (%)*: 10 (66.67%) Overall ● *Age, mean, SD*: 37.42 (8.38) ● *Female, %*: 66.67% ● *Years since onset, mean, SD*: 9.0 (7.52) **Included criteria:** - DSM-III-R (APA, 1987) criteria for panic disorder with agoraphobia;- be between 20 and 60 yr of age; - have no other psychiatric complaint in need of immediate treatment;- have no psychotic or organic symptoms;- if any medication was used the intake was to be held constant during the study;- not to receive any other kind of psychiatric or psychological treatment except for any ongoing medication during the treatment; and- express a willingness to participate in the study for a period of 3 months. **Excluded criteria:** Reasons for exclusion:Those excluded were either not phobic enough, ie. they had only a mild avoidance (n = 11), had social phobia as their primary problem (n = 6), or primary depression, i.e. the onset of the first depressive episode was earlier than the onset of the panic disorder (n = 2). One patient dropped out after two sessions due to time scheduling difficulties and was replaced. **Pretreatment:** ANOVAs on the self-report and behavioral measures at the pre-treatment assessment yielded no significant differences between the groups on any measure.

Interventions	**Intervention Characteristics** Intervention ● *Description*: All patients had self-exposure instructions which emphasized the importance of regular and prolonged exposure to the phobic situations. Applied relaxafion (AR). During the first two sessions the treatment was described to the patient and a specific analysis concerning both anxiety-arousing aspects of the phobic situations and the patients psychological reactions was made. Early signs of arousal and anxiety, or the critical aspectsof the phobic situations, were specified and used as cues for relaxation. The relaxation trainingstarted with progressive relaxation with tension-release of the muscles (Session 3). The short version(release only) was introduced during Session 4, and conditioned relaxation during Session S, Thelatter was continued in Session 6, during which the patients also practised identifying early signs of anxiety. This was continued during Session 7 and here differential relaxation was introduced,which was continued during Session 8. In Session 9 the patients were taught rapid relaxation andpracticed applying their relaxation skills in stressful but nonphobic situations, while Sessions 10-11were used for application training in natural agoraphobic situations. The 12th session was used for summary and maintenance instructions. Homework assignments: At the end of each session homework instructions were given for:(1) recording time spent away from home, kind of transportation used to arrive at that destination, if on their own or accompanied and a rating of anxiety experienced on a O-IO scale;(2) practice in the respective treatment conditions. In the AR condition different relaxation taskswere to be practiced every day for about 15-20 min. The AR group was to self-observe and record early signs of anxiety to make them more awareof these signs to use in their coping response ● *Dose*: 60 minutes once per week ● *Duration*: 12 sessions over a 3-month period. Control ● *Description*: All patients had self-exposure instructions which emphasized the importance of regular and prolonged exposure to the phobic situations. Cognitiue treatment (CT). The treatment consisted of a combination of the Beck and Emery(1985) rationale for cognitive therapy in panic/agoraphobia, and the self-instruction training ofMeichenbaum (1977). It resembled, but cannot be considered equal to the cognitive therapydeveloped by Clark (1986) for panic disorder.During the first two sessions the treatment and its rationale was described to the patient and a specific analysis concerning both anxiety-arousing aspects of, and the patients cognitive reactions in the phobic situations was made. As a homework assignment the patient was instructed to record,in a specific dairy, negative thoughts while confronting phobic situations. Sessions 3 and 4 weredevoted to developing positive self-instructions and cognitive coping procedures. During session 5the self-instructions that the patient had found useful in natural phobic situations were summarizedon an index card that the patient could carry with him/her at all times and use in future phobicsituations. Sessions 6 and 7 were devoted to attribution training with the purpose of learning torecognize alternative explanations, besides anxiety, to various negative emotions. Sessions 8-10 consisted of continued cognitive reconstrucuring of imagery and attitudes to one's phobic problems. Session 11 sum,marized the treatment and session 12 was devoted to describing the maintenance programme. Homework assignments: At the end of each session homework instructions were given for:(1) recording time spent away from home, kind of transportation used to arrive at that destination, if on their own or accompanied and a rating of anxiety experienced on a O-IO scale;(2) practice in the respective treatment conditions. This was done every day if possible, or at times agreed upon until the next session. The CT-group recorded their negative thoughtsand the use of self-instructions and cognitive coping procedures when confronting phobicsituations. ● *Dose*: 60 minutes once per week ● *Duration*: 12 sessions over a 3-month period.
Outcomes	*Grad af angst, Agoraphobia Scale subscale anxiety, mean final, SD* ● **Outcome type**: Continuous Outcome ● **Reporting**: Fully reported ● **Scale**: Agoraphobia Scale subscale anxiety ● **Range**: 0-80 ● **Direction**: Lower is better ● **Data value**: Endpoint

	Grad af undgåelse, The Mobility Inventory for Agoraphobia (MI), mean, SD ● **Outcome type**: Continuous Outcome ● **Reporting**: Fully reported ● **Scale**: The Mobility Inventory for Agoraphobia (MI) ● **Range**: 1-125 ● **Direction**: Lower is better ● **Data value**: Endpoint *Frafald, alle årsager* ● **Outcome type**: Adverse Event ● **Reporting**: Fully reported ● **Direction**: Lower is better ● **Data value**: Endpoint *Frafald, adverse events* ● **Outcome type**: Adverse Event ● **Reporting**: Fully reported ● **Direction**: Lower is better ● **Data value**: Endpoint
Identification	**Sponsorship source:** This study was supported by Grant OS452 from the Swedish Medical Research Council. **Country:** Sweden **Setting:** Outpatients at the Ulleåker mental hospital, University of Uppsala. Interventions at the Hospital. **Authors name:** Lars-Göran Öst **Institution:** Department of Psychiatry, University of Uppsala. **Email:** ost@psychology.su.se **Address:** Department of Psychology, Stockholm University, S-106 91 Stockholm, Sweden.
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement Comment: Insufficient information on sequence generation
Allocation concealment (selection bias)	Unclear risk	Judgement Comment: Insufficient information on allocation concealment
Blinding of participants and personnel (performance bias)	High risk	Judgement Comment: Blinding not feasible, and outcomes are selfreported
Blinding of outcome assessment (detection bias)	High risk	Judgement Comment: Blinding not feasible, and outcomes are selfreported
Incomplete outcome data (attrition bias)	Low risk	Quote: " All patients in the AR- and CT-patients completed the study. At follow-up one patient (in the AR-group) had died, and one (AR-group) had moved and was unreachable by mail or telephone. Thus, follow-up assessment was done on 42 (93.3%) of the original patients." Judgement Comment: No information on handling of missing data or how the drop out (n=1) was replaced.
Selective reporting (reporting bias)	Low risk	Judgement Comment: There is no reference to study protocol, but appears to report on all outcomes of interest

Other bias	Low risk	Judgement Comment: The study appears to be free from other sources of bias

Ost 1995

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Overall ● *Age, mean, SD*: 32.6 (7.1) ● *Female, n (%)*: 26 (72%) ● *Years since onset, mean*: 7.0 (5.7) **Included criteria:** 1. DSM-III-R criteria for panic disorder with no or mild avoidance. 2. A duration of the panic disorder of at least 1 yr. 3. Be between 18 and 60 yr of age. 4. Having at least 3 panic attacks during the 3-wk baseline. 5. Not suffer from primary depression (i,e. onset before the start of the panic disorder). 6. Not suffer from any other psychiatric disorder in immediate need of treatment. 7. Panic disorder must be the patient's primary problem. 8. If on prescribed drugs for panic disorder: (a) the dosage had to be constant for 3 months before the start of the treatment; and (b) the patient had to agree to keep the dosage constant throughout the study. 9. Agreeing to take part in the study for 18 wk, including pre- and post-assessment, and l-yr follow-up, and be willing to accept random allocation. **Excluded criteria:** Reasons for exclusion. In order to recruit the 38 patients that started treatment 160 referred patients went through the screening-interview and 122 (76.3%) of them were excluded. In 44 cases it turned out that the patients did not have a panic disorder; 18 had social phobia, 10 generalized anxiety disorder, 8 major depression, 2 simple phobia, 2 hypochondriasis, 2 psychosis and 2 adjustment disorder. A total of 78 out of the 122 excluded patients fulfilled criteria for panic disorder but were still excluded due to the following reasons: severe agoraphobic avoidance 22, too low panic frequency (<3 attacks during the baseline) 14, too short duration (<1 yr) 12, only limited symptom attacks 11, recently started pharmacotherapy for panic disorder 10, the panic disorder was in remission 5, a concurrent somatic disorder 2, and time scheduling problems 2. Personality disorders were not a reason to exclude patients from the study. However, since no formal assessment of personality disorders was made we cannot say anything about the frequencies. **Pretreatment:** The AR-group had higher means on the Hamilton Anxiety Scale [28.2 vs 22.1; t(34) = 3.07, P < 0.01] and the Body Sensations Questionnaire [53.6 vs 43.4; t(34)= 2.78, P < 0.01].
Interventions	**Intervention Characteristics** Intervention ● *Description*: Applied relaxation (AR). During the first session the treatment was described to the patient and a specific analysis concerning both panic-eliciting situations and the patient's physiological reactions was made. Early signs of arousal and anxiety, or critical aspects of the panic situations, were specified and used as cues for relaxation. The relaxation training started with progressive relaxation with tension-release of the muscles (Sessions 2 and 3). The short version (release-only) was introduced during Session 4 and cue-controlled (conditioned) relaxation during Session 5. During Session 6 differential relaxation was introduced, and it was continued during Session 7. In Session 8 the patients were taught rapid relaxation and practised applying their relaxation skills in stressful but nonpanic situations, and this was continued during Session 9. Sessions 10-11 were used for application training in natural situations. Finally Session 12 was used for a review of the treatment and maintenance instructions. Between sessions the patients had homework assignments to carry out and record on specific forms. ● *Dose*: therapy sessions lasted 50-60 min and were scheduled once a week for a total of 12 sessions. ● *Duration*: 12 weeks Control ● *Description*: Cognitive Behavior Therapy (CBT). This method is based on the cognitive theory of panic (Beck et al., 1985; Clark, 1986) and makes use of both cognitive and behavioral techniques (Clark, 1989). The first step consists of identifying the misinterpretation of bodily sensations that is characteristic of the individual patient. The second step entails generating an alternative, non-catastrophic, interpretation of the sensations. In this phase it is important to use Socratic questioning in order for the patient him-/herself to come up with an alternative

	explanation. The final step consists of testing the validity of these alternative hypotheses, which is done both with discussions to challenge the patient's evidence for their beliefs, and with behavioral experiments by inducing the very sensations that the patient misinterprets and prevent them from carry out safety behaviors. In this way the patients will gain factual knowledge concerning the feared consequences of their panic symptoms and eventually change their catastrophic misinterpretations. Between sessions the patients had homework assignments to carry out and record on specific forms. ● *Dose*: therapy sessions lasted 50-60 min and were scheduled once a week for a total of 12 sessions. ● *Duration*: 12 weeks
Outcomes	*Grad af angst, HAM-A, mean final, SD* ● **Outcome type**: Continuous Outcome ● **Reporting**: Fully reported ● **Scale**: HAM-A ● **Range**: 0-56 ● **Direction**: Lower is better ● **Data value**: Endpoint *Funktion,* Panic attack scale subscale distress/disability ● **Outcome type**: Continuous Outcome ● **Reporting**: Not fully reported ● **Scale**: Panic attack scale subscale distress/disability ● **Range**: 0-63 ● **Direction**: lower is better ● **Data value**: Endpoint *Frafald, alle årsager* ● **Outcome type**: Adverse Event ● **Reporting**: Fully reported ● **Direction**: Lower is better ● **Data value**: Endpoint
Identification	**Sponsorship source:** Supported by Grant 87/151 from the Bank of Sweden Tercentenary Foundation. **Country:** Sweden **Setting:** Recruited through referrals from psychiatrists in the Uppsala county and through advertisements in local newspapers. Interventions delivered in clinic. **Comments:** **Authors name:** LARS-GÖRAN ÖST **Institution:** Department of Psychology, Stockholm University **Email:** ost@psychology.su.se **Address:** Stockholm University, S-l06 91 Stockholm, Sweden
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement Comment: Insufficient information on sequence generation
Allocation concealment (selection bias)	Unclear risk	Judgement Comment: Insufficient information on allocation concealment
Blinding of participants and personnel (performance bias)	High risk	Judgement Comment: Blinding not feasible and outcome is self-reported
Blinding of outcome assessment (detection bias)	High risk	Quote: "Post-treatment assessment. Immediately after the last session the patient once more filled in the questionnaires, and went through a brief interview in which a shortened version of the ADIS-R (mainly including the Hamilton scales) was used." Judgement Comment: Blinding not feasible and outcome is self-reported
Incomplete outcome data (attrition bias)	Low risk	Quote: "Two patients, both in the AR-group, dropped out at an early stage of treatment due to scheduling difficulties."
Selective reporting (reporting bias)	Low risk	Judgement Comment: Insufficient information on study protocol, buta appears to report on all outcomes of interest
Other bias	Low risk	Judgement Comment: The study appears to be free from other sources of bias

Ost 2000

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** ● Not reported. **Included criteria:** 1. DSM-III-R (APA, 1987) criteria for generalized anxiety disorder. 2. A duration of the disorder of at least 1 year. 3. Be between 18±60 yr of age. 4. Not suffer from primary depression (i.e. onset before the start of the GAD). 5. Not suffer from any other psychiatric disorder in more need of treatment. 6. Generalized anxiety disorder must be the patient's primary problem. 7. If on prescribed drugs for anxiety disorder, (a) the dosage had to be constant for 3 months before the start of the treatment and (b) the patient had to agree to keep the dosage constant throughout the study. 8. Agreeing to take part in the study for 18 weeks, including pre- and post-assessment and 1 year follow-up and be willing to accept random allocation. **Excluded criteria:** Reasons for exclusion:In order to recruit the 36 patients that started treatment 68 patients went through the screening-interview and 24 (35%) of them were excluded, since they did not have GAD as their primary diagnosis. Ten had panic disorder, four social phobia, three obsessive-compulsive disorder, two major depression and one each had bipolar disorder, alcoholism and hypochondriasis, while two subjects did not fulfill any DSM-III-R diagnosis. Six of the 24 excluded patients fulfilled GAD-criteria as a secondary diagnosis. Personality disorders were not a reason to exclude patients from the study. However, since no formal assessment ofpersonality disorders was made we cannot say anything about the frequencies. Besides the 36 patients who started treatment another eight subjects fulfilled the inclusion criteria but did not start treatment for various reasons; two started to take anxiolytic drugs while waiting for the first session, two became too depressed to participate in the treatment, two lived too far from Uppsala to come once a week for therapy and two did dot show up after the screening-interview. **Pretreatment:**
Interventions	**Intervention Characteristics** Intervention ● *Description*: During the first session the treatment was described to the patient and a specific analysis concerning both anxiety and worry eliciting situations and the patient's physiological reactions was made. Early signs of arousal and anxiety, or worry were specified and used as cues for relaxation. The relaxation training started with progressive relaxation with tension-release of the muscles (session 2 and 3). The short version (release only) was introduced during session 4 and cue-controlled (conditioned) relaxation during session 5. During session 6

	differential relaxation was introduced and it was continued during session 7. In session 8 the patients were taught rapid relaxation and practiced applying their relaxation skills in stressful but not anxious situations and this was continued during session 9. Sessions 10±11 were used for application training in natural situations. Finally, session 12 was used for a review of the treatment and maintenance instructions. The reader is referred to Öst (1987) for a detaileddescription of AR. ● *Dose*: 12 sessions (one per week) of 50-60 minutes. ● *Duration*: 12 weeks Control ● *Description*: This treatment is based on the cognitive theory of generalized anxiety (Beck, Emery &Greenberg, 1985) and specifically the manual for CT developed by Borkovec and Costello(1993). According to the latter manual the treatment involves the following steps: (1) Identifying the anxiety associated thoughts, beliefs etc., (2) Discussing the causal role of these, (3) Getting the patient to question the thoughts and beliefs and search for evidence for andagainst, (4) Helping the patient to develop alternative assumptions that are less, or not at allanxiety-arousing, (5) Testing these alternatives through behavioral experiments and home workassignments and (6) Teaching the above skills in such a way that they can be used as coping techniques in everyday life. The above steps were used in a flexible way guided by the needs ofthe individual patients and it is not possible to say how they were employed across the 12 sessions. ● *Dose*: 12 sessions (one per week) of 50-60 minutes. ● *Duration*: 12 weeks
Outcomes	*Grad af angst, HAM-A, mean final, SD* ● **Outcome type**: ContinuousOutcome ● **Reporting**: Fully reported ● **Scale**: HAM-A ● **Range**: 0-56 ● **Direction**: Lower is better ● **Data value**: Endpoint *Funktion, Penn State Worry Questionnaire (PSWQ), mean, SD* ● **Outcome type**: Continuous Outcome ● **Reporting**: Fully reported ● **Scale**: *Penn State Worry Questionnaire (PSWQ)* ● **Range**: 1-80 ● **Direction**: Lower is better ● **Data value**: Endpoint *Funktion, Severity rating, observer* ● **Outcome type**: Continuous Outcome ● **Reporting**: Fully reported ● **Scale**: *Severity rating, observer* ● **Range**: 1-8 ● **Direction**: Lower is better ● **Data value**: Endpoint *Frafald, alle årsager* ● **Outcome type**: Adverse Event ● **Reporting**: Fully reported ● **Direction**: Lower is better ● **Data value**: Endpoint

Identification	**Sponsorship source:** Supported by grant 9527 from the Swedish Medical Research Council and grant F207/93 from the Swedish Council for Research in the Humanities and Social Sciences. **Country:** Sweden **Setting:** The patients were recruited through referrals from general practitioners and advertisements in the local newspaper. Treatments (AR and CT) conducted in clinic. **Comments:** **Authors name:** Lars-Göran Öst **Institution:** Department of Psychology, Stockholm University **Email:** ost@psychology.su.se **Address:** Stockholm University, 106 91 Stockholm, Sweden
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "The patients were randomly assigned to two treatments," Judgement Comment: No info on randomization method Insufficient information on sequence generation
Allocation concealment (selection bias)	Unclear risk	Judgement Comment: Insufficient information on allocation concealment
Blinding of participants and personnel (performance bias)	High risk	Judgement Comment: Not feasible to blind the groups, and it it likely that the knowledge of group allocation will influence outcome
Blinding of outcome assessment (detection bias)	High risk	Judgement Comment: No info about blinding of individual assessors (relevant for HAM-A).All other outcomes are self-reported.
Incomplete outcome data (attrition bias)	Low risk	Quote: "Three patients, 2 in the AR-group (12%) and 1 in the CT-group (5%) dropped out at an early stage of treatment. The dropouts did not differ significantly from the completers on any demographic or pre-treatment measures." Judgement Comment: Sparse information about number of participants allocated to each group.
Selective reporting (reporting bias)	Low risk	Judgement Comment: No pre-specified protocol however, comprehensive reporting of outcome results specified in methods.
Other bias	Low risk	Judgement Comment: The study appears to be free from other sources of bias

Song 2014

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Intervention ● *Mean age, years (SD)*: 65.3 (7.1) Control ● *Mean age, years (SD)*: 66.1 (8.3) **Included criteria:** The patients suffered from anxiety disorder at the ages of 60-75 years old. Thepatients meet the diagnostic criteria for anxietydisorder in Chinese Classification and Diagnostic Criteria of Mental Disorders (The third version) (CCMD-3) and their Hamilton Anxiety Scale (HAM-A) evaluation scores.

	Excluded criteria: Exclude and merge these patients who suffer from other mental disorders, severe organic diseases and severe somatic diseases. **Pretreatment:** No significant baseline differences
Interventions	**Intervention Characteristics** Intervention ● *Description*: Tai Chi and Paroxetine. The experimental group: the therapy combining the oral drug with Tai Chi exercise. The patients in the experimental group are same with those in the control group and they are treated by the drugs, besides they do Tai Chi exercise for 35 minutes respectively at morning and at evening. Each exercise is divided into two parts. The first part is preparation for exercise: Chen Style Tai Chi-activity of all joints in the whole body. This part focuses on the stretching exer-cise and practice for all joints from top to bot-tom and from hand to foot; the second part is 18 essences of Chen Style Tai Chi. These 18 essences are the core of Chen Style Tai Chi and it integrates 18 postures required by the modern fitness training. The entire postures integrate motion and quietness and it is easy for the old people to learn and practice. ● *Dose*: Tai Chi exercise for 35 minutes respectively at morning and at evening. Paroxetine two times pr. day 10mg/time ● *Duration*: 45 days Control ● *Description*: Paroxetine. The control group: it is only treated by oral drug. Drug name: Paroxetine (Produced by Tianjin TSKF Pharmaceutical Company Limited, the trade name "Seroxat". ● Dose: Paroxetine two times pr. day 10mg/time. ● *Duration*: 45 days
Outcomes	*Grad af angst, H*AM-A, mean SD ● **Outcome type**: Continuous Outcome ● **Reporting**: Fully reported ● **Scale**: HAM-A ● **Range**: 0-56 ● **Direction**: Lower is better ● **Data value**: Endpoint *Funktion, Adopt Generic Quality of Life Inventory-74 (GQOLI-74)- subscale psychological functioning, mean, SD* ● **Outcome type**: Continuous Outcome ● **Reporting**: Fully reported ● **Scale**: Adopt Generic Quality of Life Inventory-74 ● **Range**: 0-70 ● **Direction**: Higher is better ● **Data value**: Endpoint *Livskvalitet, Adopt Generic Quality of Life Inventory-74 (GQOLI-74)- subscale general life quality, mean, SD* ● **Outcome type**: Continuous Outcome ● **Reporting**: Fully reported ● **Scale**: GQOLI-74 subscale general life quality ● **Range**: 0-7 ● **Direction**: Higher is better ● **Data value**: Endpoint

Identification	**Sponsorship source:** No information **Country:** China **Setting:** The Henan Province Second Charity Hospital and the hospital of Henan Polytechnic University (Psychological Counseling Center) **Authors name:** Qing-Hua Song **Institution:** The Center of Physical Health, Henan Polytechnic University, Jiaozuo 454000, Henan Province, P. R. China **Email:** sqh@hpu.edu.cn **Address:** Qing-Hua Song or Rong-Mei Xu, Health Center of Physical Education Institute of Henan Polytechnic University, Shiji Road No. 2001, Jiaozuo 454000, Henan Province, China.
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement Comment: No information of how the allocation sequence was generated
Allocation concealment (selection bias)	Unclear risk	Judgement Comment: No information of allocation concealment
Blinding of participants and personnel (performance bias)	High risk	Judgement Comment: No information of blinding of participants and health care providers. Blinding of the intervention (Tai Chi) Not feasible. No information of placebo drug.
Blinding of outcome assessment (detection bias)	Unclear risk	Quote: "HAMA evaluation includes 14 items and each item score is 0-4 in 5 grades. It is checked by a professional asses- sor and the patients are evaluated for their severity of anxiety symptoms by the means of chat and observation." Judgement Comment: No informaiton of blinding of outcome assessors. Outcomes are asssessed by observers not self-reported.
Incomplete outcome data (attrition bias)	Low risk	Judgement Comment: No information of dropouts. Assume no dropouts. 16 participants in each group. 16 in each group is analyses Likely no missing outcome data.
Selective reporting (reporting bias)	Low risk	Judgement Comment: No protocol available. Reports on all the outcomes stated in the method section
Other bias	Unclear risk	Judgement Comment: The study appears to bee frem from other sources of bias No information about funding.

Zullino 2015

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Intervention ● *Age, mean, SD*: 45.6 (11.3) ● *Female, n (%)*: 13 (46.4%) Control ● *Age, mean, SD*: 44.9 (8) ● *Female, n (%)*: 11 (36.7%) **Included criteria:** Patients had to be between 18 and 65 years old, capable of informed consent, meet the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) criteria for a diagnosis of GAD, have a score of at least 20 on the HAM-A, and have a negative serum pregnancy testat screening (for women of childbearing potential).

	Excluded criteria: Exclusion criteria included intolerance to venlafaxine; history or presence of clinically significant hepatic, cardiovascular, renal, or other serious medical disease that might compromise patient safety; history or presence of bipolar disorder, schizophrenia, or other psychotic disorder; alcohol or drug dependence other than nicotine; current mental disorder due to a general medical condition; and women who were breast feeding, pregnant, or sexually active and not using a method of birth control.Further exclusion criteria included use of venlafaxine or a monoamine oxidase inhibitor(MAOI) within 30 days of inclusion, an antidepressant other than an MAOI within 7 daysof inclusion, or any psychotropic treatment of more than three consecutive days within the 7 days preceding randomization. Treatment with beta blockers was not allowed at inclusion or during the study. Furthermore, the introduction of, or change in, cognitive behavioral therapy or any other psychotherapy within 3 months preceding randomization was also an exclusion criterion. **Pretreatment:** No significant baseline differences were found between treatment groups.
Interventions	**Intervention Characteristics** Intervention ● *Description*: Applied relaxation. Patients recieving applied relaxation attended 8 weekly individual 45 minutes sessions. Between sessions, the homework assingments was for patients to practice relaxation for 30 minutes per day with the help of tape-recorded versions of relaxation exercises. Applied relaxation sessions were given by a cognitive-behavioral psychotherapist. ● *Dose*: 8 weekly individual 45 minutes sessions. ● *Duration*: 8 weeks Control ● *Description*: Venlafaxine ● *Dose*: 75mg/day for one week. thereafter the dose was increased to 150 mg/day in the absence of intolerable side effects. After 2 weeks the dose was increased to 300mg/day (based on tolerability) for patients who did not achieve remmision (HAM-A < 8) ● *Duration*: 8 weeks
Outcomes	*Grad af angst, HAM-A, mean final, SD* ● **Outcome type**: Continuous Outcome ● **Reporting**: Fully reported ● **Scale**: HAM-A ● **Range**: 0-56 ● **Direction**: Lower is better ● **Data value**: Endpoint *Funktion, Penn State Worry Questionnaire (PSWQ), mean, SD* ● **Outcome type**: Continuous Outcome ● **Reporting**: Fully reported ● **Scale**: Penn State Worry Questionnaire (PSWQ) ● **Range**: 0-80 ● **Direction**: Lower is better ● **Data value**: Endpoint *Frafald, alle årsager* ● **Outcome type**: AdverseEvent ● **Reporting**: Fully reported ● **Direction**: Lower is better ● **Data value**: Endpoint

Identification	**Sponsorship source:** The study was supported by an unrestricted Grant from Wyeth Pharmaceuticals, Switzerland. The authors reported no other conflicts of interest in relation with the present work. **Country:** Switzerland **Setting:** Patients were recruited through referrals from regional clinics and from psychiatrists and general practitioners in private practice, as well as through advertising in local newspapers. NI on intervention setting, probably research laboratory. **Authors name:** Y. Khazaal **Institution:** Department of Mental Health and Psychiatry, Geneva University Hospitals and Geneva University **Email:** yasser.khazaal@hcuge.ch **Address:** Grand Pre´70C, 1206 Geneva, Switzerland
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "This was a randomized, comparative, partial crossover study. Following screening and written informed consent, patients were randomly assigned to one of the following treatment groups: 8 weeks of venlafaxine ER treatment, or 8 weeks of weekly applied relaxation treatment (Phase I)." Judgement Comment: Insufficient information on sequence generation
Allocation concealment (selection bias)	Unclear risk	Quote: "No baseline differences were found between treatment groups" Judgement Comment: Insufficient information on allocation concealment
Blinding of participants and personnel (performance bias)	High risk	Judgement Comment: Blinding not feasible, and outcomes are selfreported
Blinding of outcome assessment (detection bias)	High risk	Judgement Comment: Blinding not feasible, and outcomes are selfreported
Incomplete outcome data (attrition bias)	Low risk	Quote: "the dropout rates were 10 % in the venlafaxine ER group and 25 % in the applied relaxation group, with no statistically significant difference between groups (v 2 = 2.3, df = 1, P = 0.1). Patients who dropped out did not differ significantly from the others on any measure." Quote: "Intent-to-treat analyses were performed for the above outcomes and led to similar conclusions." Judgement Comment: Patients who dropped out did not differ significantly from the others on any measure.
Selective reporting (reporting bias)	High risk	Quote: "Adverse events and concomitant treatments were recorded at each visit." Judgement Comment: No protocol however, stated that they wanted to measure adverse events but this is not reported.
Other bias	Low risk	Quote: "Acknowledgments The study was supported by an unrestricted Grant from Wyeth Pharmaceuticals, Switzerland. The authors reported no other conflicts of interest in relation with the present work."

Footnotes

Characteristics of excluded studies

Annapoorna 2011

Reason for exclusion	only a abstract

Arntz 2003

Reason for exclusion	Wrong patient population

Borkovec 1993

Reason for exclusion	Wrong comparator

Borkovec 2002

Reason for exclusion	Wrong comparator

Bowden 2011

Reason for exclusion	Wrong patient population

Bowden 2011a

Reason for exclusion	Wrong patient population

Breitholtz 2000

Reason for exclusion	Dublet, study already identified and included from systematic review

Chen 2017

Reason for exclusion	Wrong comparator

Conrad 2008

Reason for exclusion	Wrong outcomes

Falsafi 2016

Reason for exclusion	Wrong patient population

Gaudlitz 2015

Reason for exclusion	Wrong comparator

Gupta 2013

Reason for exclusion	Wrong comparator

Hayes Skelton 2013

Reason for exclusion	Wrong comparator

Jacob 2012

Reason for exclusion	Wrong comparator

Kohli 2000

Reason for exclusion	Only an abstract without data

Kurebayashi 2016

Reason for exclusion	Wrong patient population

Mander 2019

Reason for exclusion	Wrong patient population

Martinsen 1989

Reason for exclusion	Wrong comparator

Merom 2008

Reason for exclusion	Wrong comparator

Meuret 2010

Reason for exclusion	Wrong outcomes

Newman 2017

Reason for exclusion	Wrong intervention

Newman 2018

Reason for exclusion	Wrong intervention

Newman 2019

Reason for exclusion	Wrong intervention

Phongsavan 2008

Reason for exclusion	Wrong outcomes

Richeson 2010

Reason for exclusion	Wrong patient population

Sherman 2010

Reason for exclusion	Wrong comparator

Smits 2008

Reason for exclusion	Wrong patient population

Welford 2010

Reason for exclusion	Wrong comparator

Wells 2017

Reason for exclusion	Wrong comparator

Wollburg 2011

Reason for exclusion	Wrong outcomes

Footnotes

Characteristics of studies awaiting classification

Footnotes

Characteristics of ongoing studies

Footnotes

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Wollburg 2011

Wollburg, Eileen; Roth, Walton T.; Kim, Sunyoung. Effects of breathing training on voluntary hypo- and hyperventilation in patients with panic disorder and episodic anxiety.. Applied Psychophysiology & Biofeedback 2011;36(2):81-91. [DOI:]

Data and analyses

1 Kropsterapi vs active control

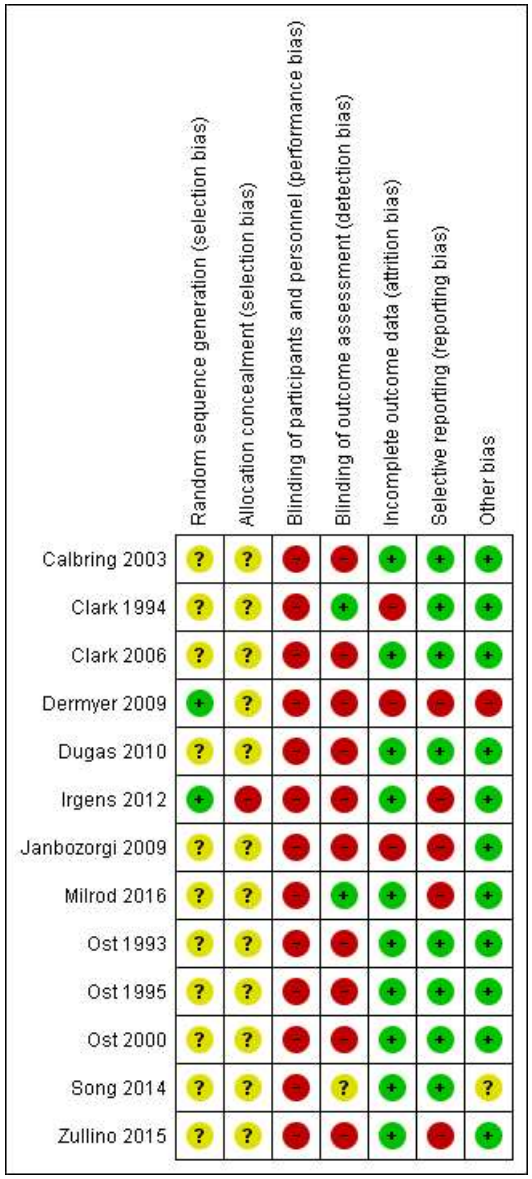
Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
1.1 Grad af angst (severity of anxiety)	7	264	Std. Mean Difference (IV, Random, 95% CI)	0.06 [-0.24, 0.37]
1.2 Funktionsniveau (function)	4	178	Std. Mean Difference (IV, Random, 95% CI)	0.45 [0.07, 0.84]
1.3 Livskvalitet (quality of life)	1	22	Mean Difference (IV, Fixed, 95% CI)	0.40 [-0.69, 1.49]
1.4 Grad af undgåelse (avoidance)	4	134	Std. Mean Difference (IV, Random, 95% CI)	0.12 [-0.50, 0.75]
1.5 Frafald, alle årsager (dropouts, all causes)	8	391	Risk Ratio (M-H, Random, 95% CI)	1.78 [1.16, 2.74]
1.6 Antal personer med skadesvirkninger (SAE og AE) Numbers vith adverse events	2	150	Risk Ratio (M-H, Random, 95% CI)	6.23 [0.67, 57.99]
1.7 Bedring (response)	4	238	Risk Ratio (M-H, Random, 95% CI)	0.69 [0.54, 0.88]

2 Kropsterapi vs no treatment

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
2.1 Grad af angst (anxiety severity)	4	139	Std. Mean Difference (IV, Random, 95% CI)	-1.32 [-1.88, -0.77]
2.2 Funktion (function)	5	193	Std. Mean Difference (IV, Random, 95% CI)	-0.83 [-1.18, -0.49]
2.3 Livskvalitet (quality of life)	1	32	Mean Difference (IV, Fixed, 95% CI)	3.80 [-0.80, 8.40]
2.4 Grad af undgåelse (avoidance)	1	41	Mean Difference (IV, Fixed, 95% CI)	-1.53 [-2.24, -0.82]
2.5 Frafald, alle årsager (dropouts, all causes)	4	166	Risk Ratio (M-H, Random, 95% CI)	2.92 [0.68, 12.53]
2.8 Bedring (response) Risk diff analyse	1	41	Risk Difference (M-H, Fixed, 95% CI)	0.38 [0.17, 0.59]
2.9 Bedring (response) relative risk analyse	1	41	Risk Ratio (M-H, Fixed, 95% CI)	16.23 [1.00, 263.88]

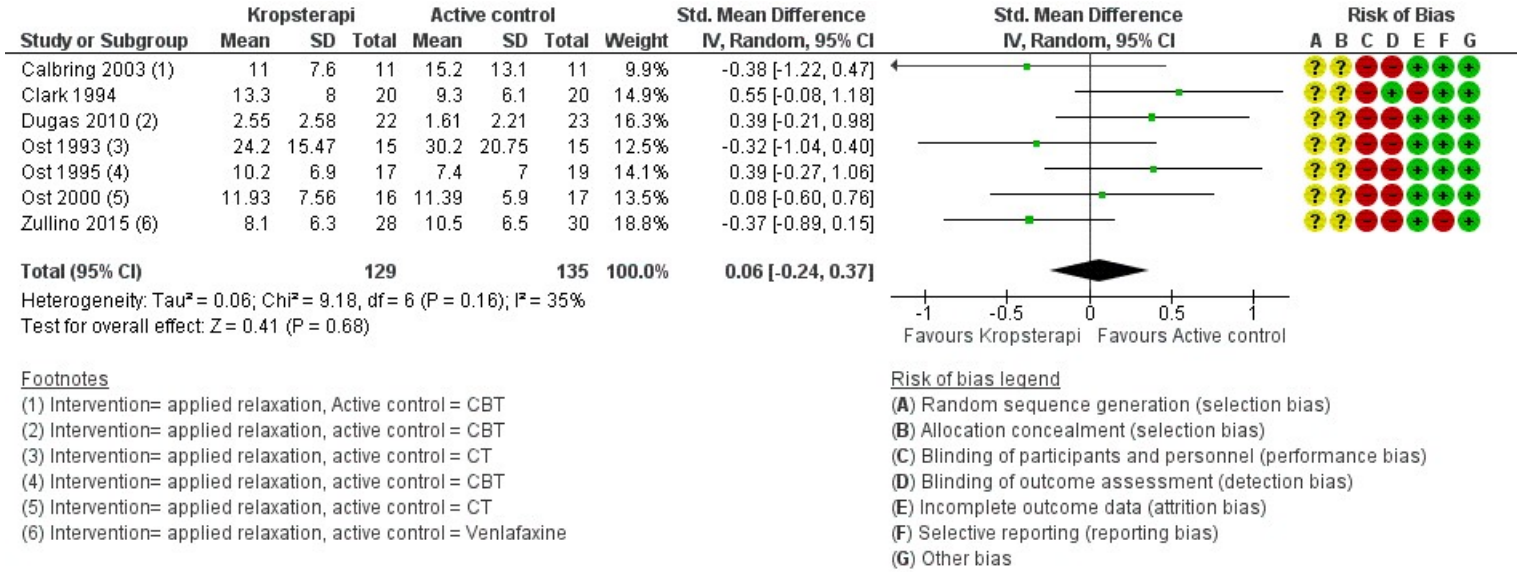
Figures

Figure 1


Random sequence generation (selection bias)
Allocation concealment (selection bias)
Blinding of participants and personnel (performance bias)
Blinding of outcome assessment (detection bias)
Incomplete outcome data (attrition bias)
Selective reporting (reporting bias)
Other bias
Calbring 2003
Clark 1994
Clark 2006
Dermyer 2009
Dugas 2010
Irgens 2012
Janbozorgi 2009
Milrod 2016
Ost 1993
Ost 1995
Ost 2000
Song 2014
Zullino 2015

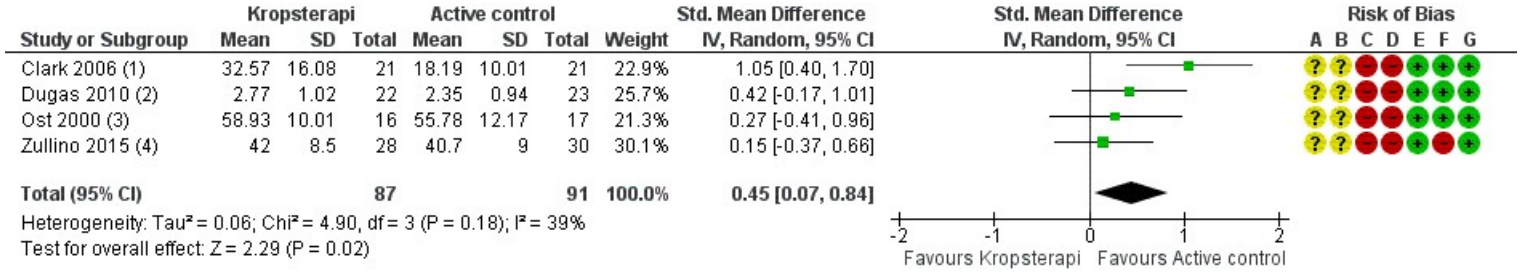
Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

Figure 2 (Analysis 1.1)



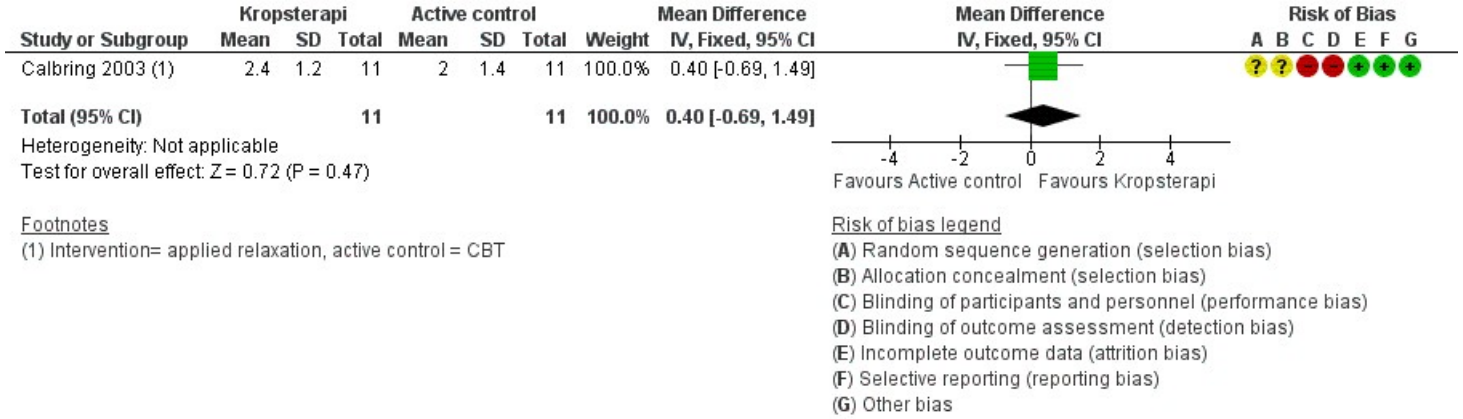
Forest plot of comparison: 1 Kropsterapi vs active control, outcome: 1.1 Grad af angst (severity of anxiety).

Figure 3 (Analysis 1.2)



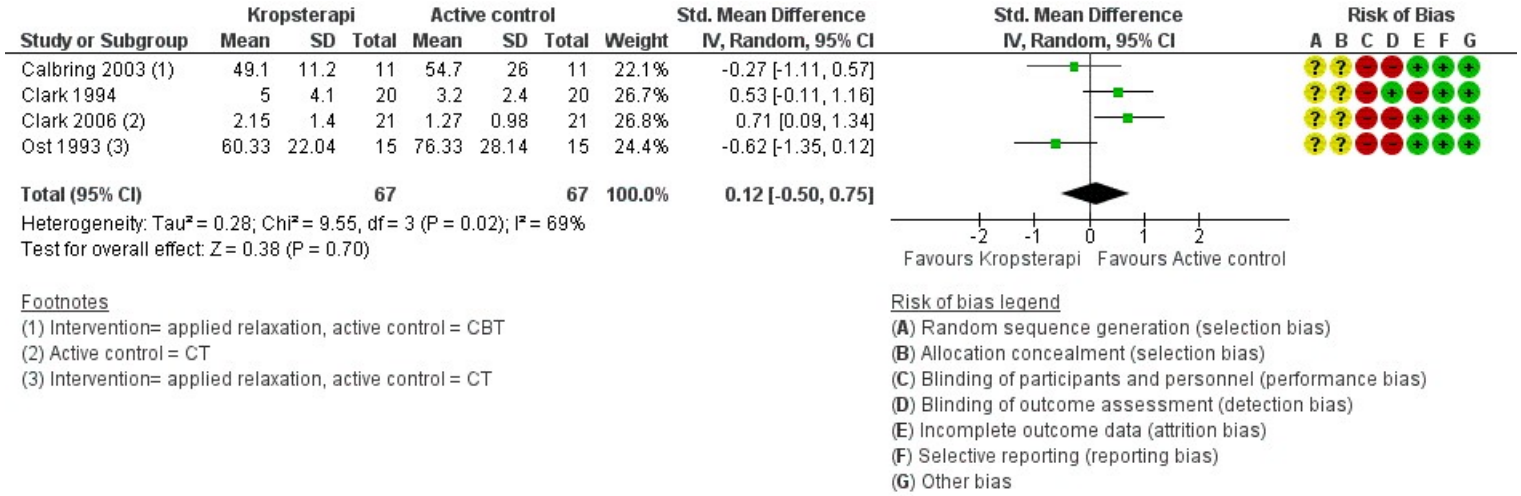
Forest plot of comparison: 1 Kropsterapi vs active control, outcome: 1.2 Funktionsniveau (function).

Figure 4 (Analysis 1.3)



Forest plot of comparison: 1 Kropsterapi vs active control, outcome: 1.3 Livskvalitet (quality of life).

Figure 5 (Analysis 1.4)

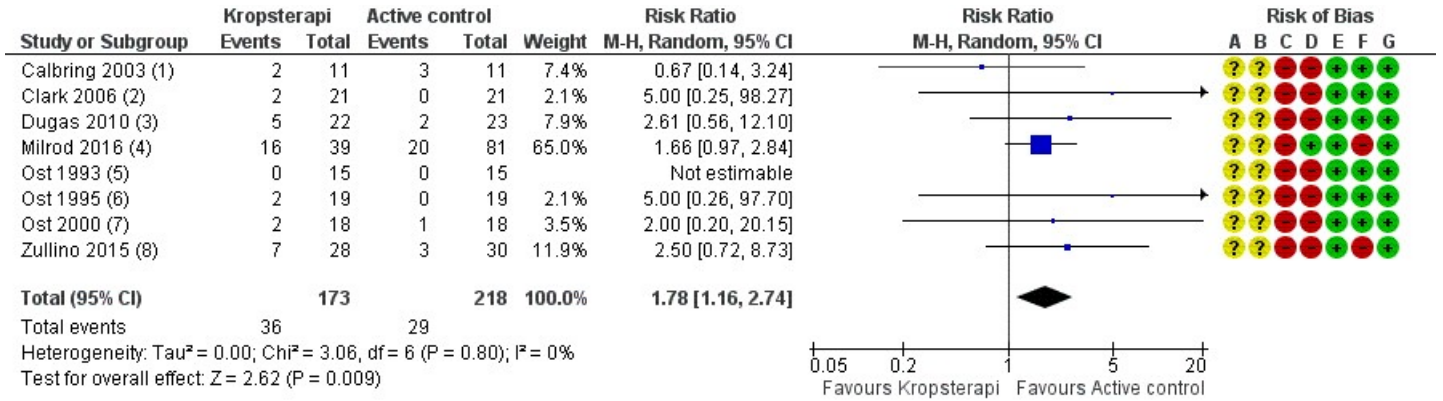


Footnotes
(1) Intervention= applied relaxation, active control = CBT
(2) Active control = CT
(3) Intervention= applied relaxation, active control = CT

Risk of bias legend
(**A**) Random sequence generation (selection bias)
(**B**) Allocation concealment (selection bias)
(**C**) Blinding of participants and personnel (performance bias)
(**D**) Blinding of outcome assessment (detection bias)
(**E**) Incomplete outcome data (attrition bias)
(**F**) Selective reporting (reporting bias)
(**G**) Other bias

Forest plot of comparison: 1 Kropsterapi vs active control, outcome: 1.4 Grad af undgåelse (avoidance).

Figure 6 (Analysis 1.5)

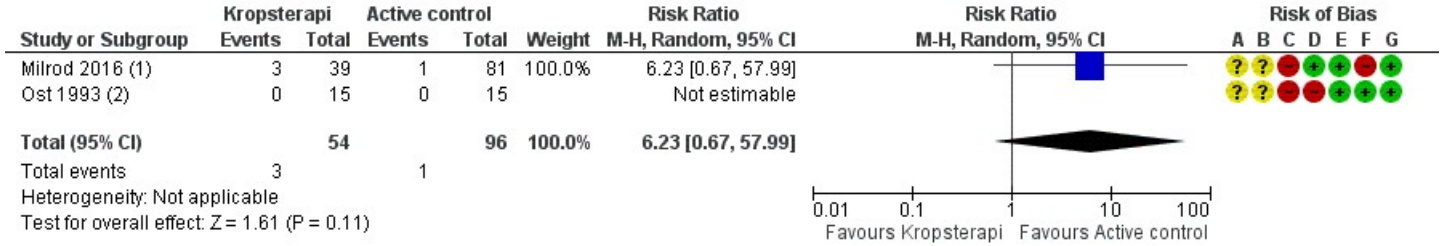


Footnotes
(1) Intervention= applied relaxation, active control = CBT
(2) Active control = CT
(3) Intervention= applied relaxation, active control = CBT
(4) Active control = CBT
(5) Intervention= applied relaxation, active control = CT
(6) Intervention= applied relaxation, active control = CBT
(7) Intervention= applied relaxation, active control = CT
(8) Intervention= applied relaxation, active control = Venlafaxine

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Forest plot of comparison: 1 Kropsterapi vs active control, outcome: 1.5 Frafald, alle årsager (dropouts, all causes).

Figure 7 (Analysis 1.6)

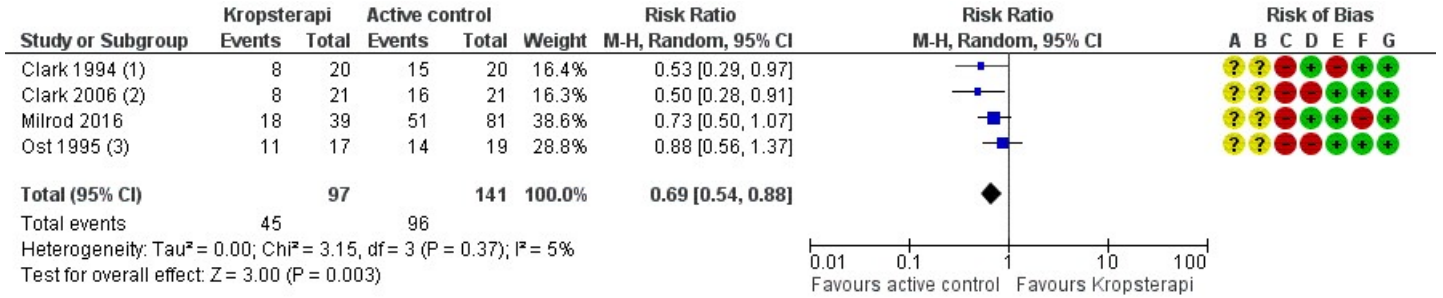


Footnotes
(1) Active control = CBT
(2) Intervention= applied relaxation, active control = CT

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Forest plot of comparison: 1 Kropsterapi vs active control, outcome: 1.6 Antal personer med skadesvirkninger (SAE og AE) Numbers vith adverse events.

Figure 8 (Analysis 1.7)

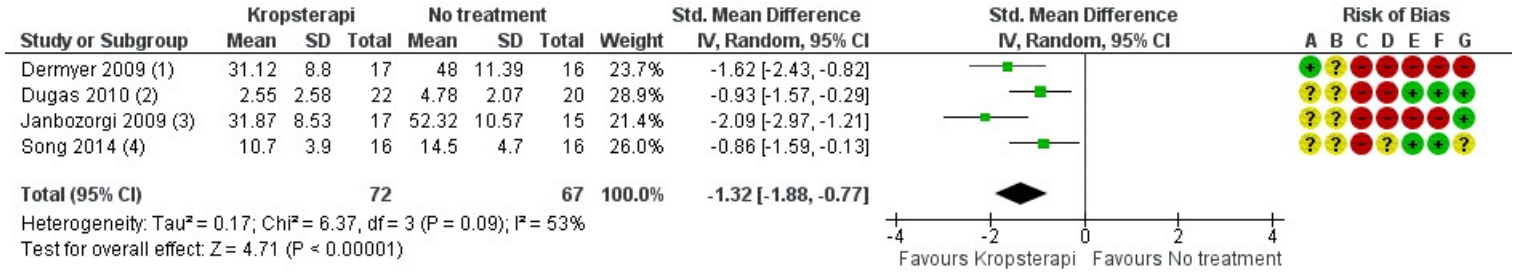


Footnotes
(1) Active control = CT
(2) Active control = CT
(3) Active control = CBT

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Forest plot of comparison: 1 Kropsterapi vs active control, outcome: 1.7 Bedring (response).

Figure 9 (Analysis 2.1)

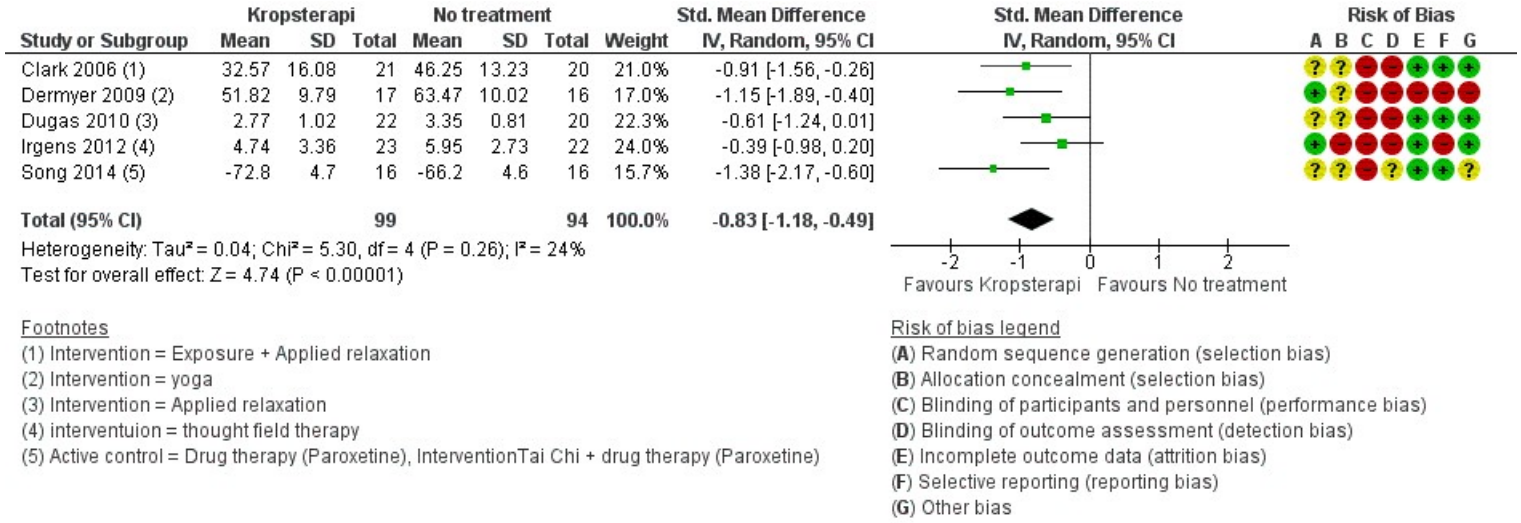


Footnotes
(1) Intervention = yoga
(2) Intervention = applied relaxation
(3) Intervention = integrative relaxation training
(4) Active control = Drug therapy (Paroxetine), InterventionTai Chi + drug therapy (Paroxetine)

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Forest plot of comparison: 2 Kropsterapi vs no treatment, outcome: 2.1 Grad af angst (anxiety severity).

Figure 10 (Analysis 2.2)

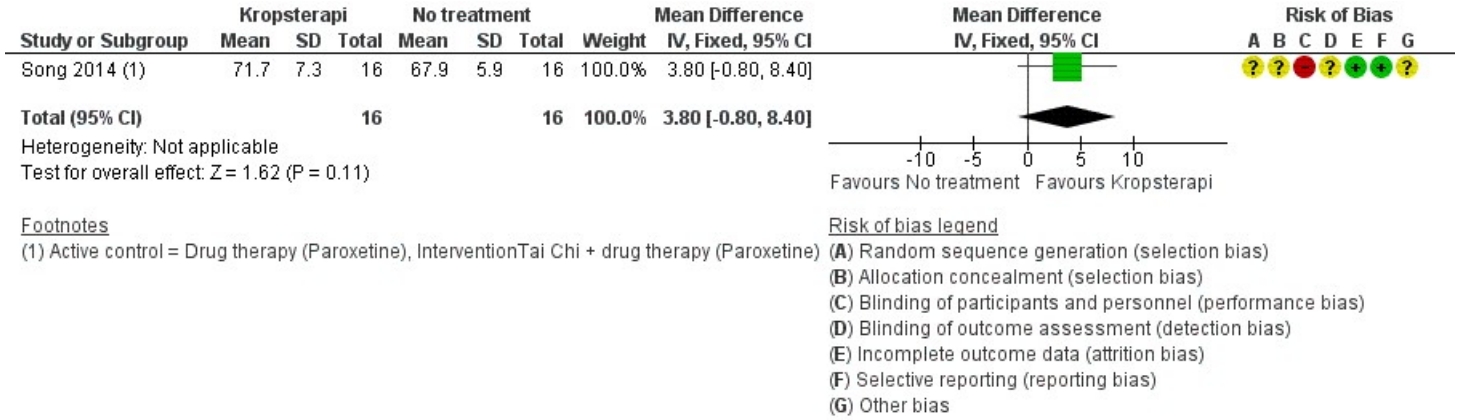


Footnotes
(1) Intervention = Exposure + Applied relaxation
(2) Intervention = yoga
(3) Intervention = Applied relaxation
(4) interventuion = thought field therapy
(5) Active control = Drug therapy (Paroxetine), InterventionTai Chi + drug therapy (Paroxetine)

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

Forest plot of comparison: 2 Kropsterapi vs no treatment, outcome: 2.2 Funktion (function).

Figure 11 (Analysis 2.3)

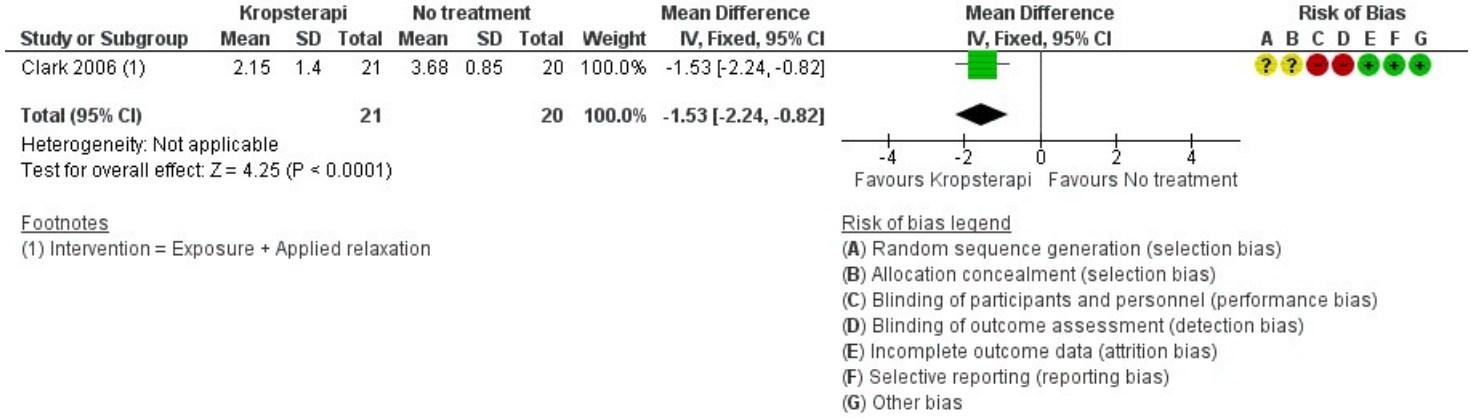


Footnotes
(1) Active control = Drug therapy (Paroxetine), InterventionTai Chi + drug therapy (Paroxetine)

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

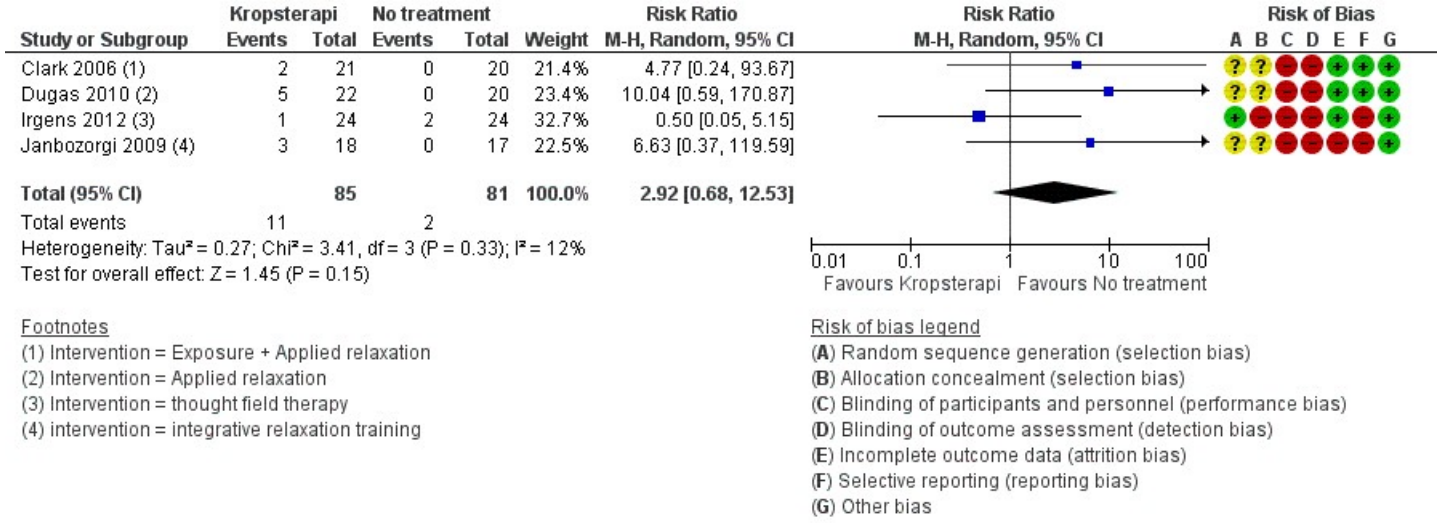
Forest plot of comparison: 2 Kropsterapi vs no treatment, outcome: 2.3 Livskvalitet (quality of life).

Figure 12 (Analysis 2.4)



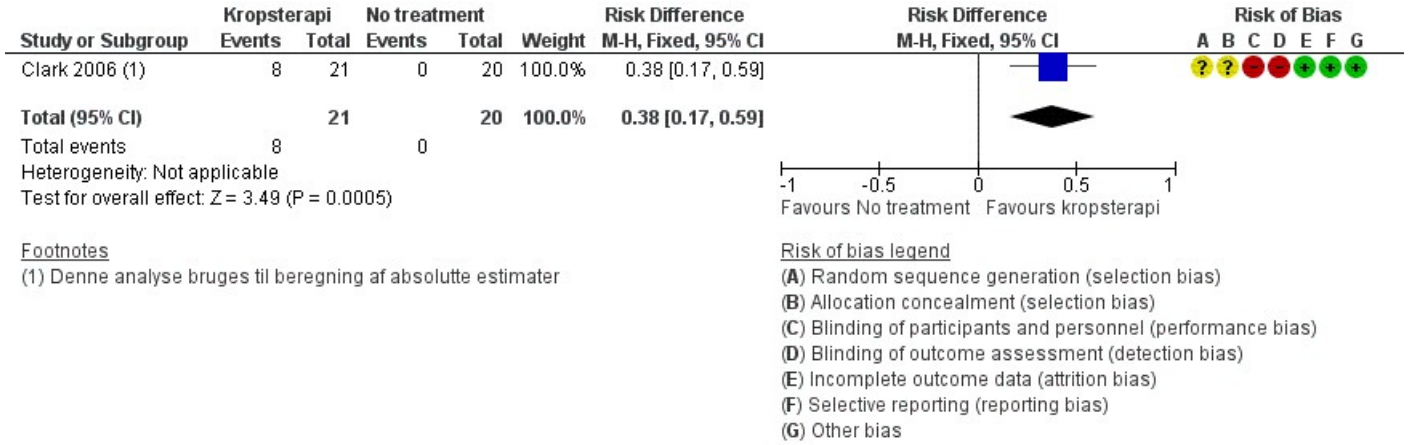
Forest plot of comparison: 2 Kropsterapi vs no treatment, outcome: 2.4 Grad af undgåelse (avoidance).

Figure 13 (Analysis 2.5)



Forest plot of comparison: 2 Kropsterapi vs no treatment, outcome: 2.5 Frafald, alle årsager (dropouts, all causes).

Figure 15 (Analysis 2.8)



Forest plot of comparison: 2 Kropsterapi vs no treatment, outcome: 2.8 Bedring (response) Risk diff analyse.