NKR 58 PICO 3 skærmbaseret kognitiv adfærdsterapi ved angstlidelser

Review information

Authors

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Characteristics of studies

Characteristics of included studies

Andrews 2011

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Overall ● *mean age in years (SD)*:31.9 (7.8) ● *Number of females %*:40.5 % **Included criteria:** Patients were referred by their general practitioner to the Anxiety Disorders Clinic at St Vincent's Hospital, Sydney for possible treatment of an anxiety disorder. They were seen by a consultant psychiatrist and those meeting criteria for social phobia were offered treatment and then asked if they would participate in a trial in which they would have an even chance of being offered web-based treatment instead of the face to face treatment they and their referring doctor had expected. **Excluded criteria:** No information.
Interventions	**Intervention Characteristics** Intervention ● *Description*: Internet CBT: The iCBT programme was the Shyness programme reported as efficacious in previous RCTs for treating social phobia (Shyness 6) [9]. This treatment, delivered by computer, comprised six online lessons; a summary/homework assignment for each lesson; comments by participants on a forum moderated by the clinician (M.D.); access to supplementary materials; automatic emails and fortnightly short message service (SMS). Part of the content of each lesson was presented in the form of an illustrated story about a young man with social phobia who, with the help of a clinical psychologist, successfully gains mastery over his symptoms. Lessons 1 and 2 provided education about the symptoms and treatment of social phobia; Lesson 3 provided instructions on how to develop an exposure hierarchy and about practising graded exposure; Lessons 4 and 5 reinforced principles of graded exposure and demonstrated principles of cognitive restructuring; while Lesson 6 included information about relapse prevention. Participants were encouraged to complete the first four lessons within the first two weeks, in order to provide more opportunity to practise the graded exposure, cognitive skills and other coping techniques. All participants were asked to complete the six lessons within eight weeks of starting. Participants were telephoned or emailed each week by the clinician.

	● *Duration*: 7 weeks Control ● *Description*: Face-to-face CBT The format of the programme was a group setting with all participants meeting criteria for social phobia. Each group had a maximum of seven participants (not all of whom were research participants) who met weekly for seven weeks for 4 hours under the guidance of the same clinician (M.D.). The content of the programme outlined in a standard text. All particioants were given a copy of the programme to use in the sessions and to revise between sessio ● *Dose*: 7 weeks for 4 hours ● *Duration*: 7 weeks
Outcomes	*Grad af angst, Social Phobia Scale (SPS)* ● **Outcome type**: Continuous Outcome ● **Reporting**: Fully reported ● **Scale**: Social Phobia Scale (SPS) ● **Range**: 0-80 ● **Direction**: Lower is better ● **Data value**: Endpoint *Funktion, the World Health Organization Disability Assessment Schedule (WHODAS2)* ● **Outcome type**: Continuous Outcome ● **Reporting**: Fully reported ● **Scale**: Disability Assessment Schedule (WHODAS2) ● **Range**: 0-48 ● **Direction**: Lower is better ● **Data value**: Endpoint *Frafald, alle årsager* ● **Outcome type**: Dichotomous Outcome ● **Reporting**: Fully reported ● **Direction**: Lower is better ● **Data value**: Endpoint *Skadesvirkninger, totale antal personer med SAE + AE* ● **Outcome type**: Dichotomous Outcome ● **Reporting**: Fully reported ● **Direction**: Lower is better ● **Data value**: Endpoint
Identification	**Sponsorship source:** No information **Country:** Australia **Setting:** Outpatient clinic **Comments:** **Authors name:** Gavin Andrews

	Institution: Clinical Research Unit for Anxiety and Depression, School of Psychiatry **Email:** gavina@unsw.edu.au **Address:** Clinical Research Unit for Anxiety and Depression, School of Psychiatry, UNSW at St Vincent's Hospital, 390 Victoria St, Darlinghurst, Sydney, New South Wales 2010, Australia.
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The 37 patients accepted into the programme were randomized by NT via a true randomization process (www.random.org)"
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 professionals. Blinding not feasible.
Blinding of outcome assessment (detection bias)	High risk	Judgement Comment: No information of blinding of outcome assessors. Outcome measures were self-reported and participants and not blinded.
Incomplete outcome data (attrition bias)	High risk	Quote: "Post-treatment data was collected from 11/14 face-to-face CBT group participants and 14/21 iCBT group participants. In accordance with the intention-to-treat paradigm, the pre-treatment scores of the 10 participants who did not complete the post-treatment questionnaires were replicated as their post-treatment scores." Judgement Comment: Uensartet frafald i grupperne. 6/23 falder fra før interventions start i internet gruppen, 0/14 i face to face gruppen. intention to treat analyses inkluderer ikke alle randomiserede deltagere men kun, dem der starter behandling, dvs. 17/23 i internetgruppen og 14/14 i face to face gruppen. No sensitivity analysis of the drop outs. ITT analysis conducted with participants that started intervention but n=4 participants in the Internet group withdrew before and these are not included in analysis. Larger drop out in Internet group vs face to face group (9 vs 3).
Selective reporting (reporting bias)	High risk	Judgement Comment: protocol available. Three secondary outcomes are stated in the protocol, but not reported. One quality of life outcome is reported in the publication, but not mentioned in the protocol
Other bias	Low risk	Judgement Comment: The study appears to be free of other sources of bias

Bergstrom 2010

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Intervention ● *mean age in years (SD)*: 33.8 (9.7) ● *Number of females %*: 64% ● *years since onset mean (SD)*: 6.0 (9.3) Control

	● *mean age in years (SD)*: 34.6 (9.2) ● *Number of females %*: 59% ● *years since onset mean (SD)*: 7.3 (9.6) **Included criteria:** To be included in the study the patients had to meet the following criteria: 1. Fulfil DSM-IV criteria for panic disorder with or without agoraphobia (PD/A), 2. Have PD/Aas primary diagnosis, 3. Be above 18 years of age, 4. Not suffer from severe depression or suicidal ideation, 5. If taking prescribed drugs for panic disorder, having had a constant dosage for 2 months prior to commencing treatment in the study, 6. Not undergoing concurrent CBT. All patients were required to have regular daily Internet access as well as the possibility to print text materials used. **Excluded criteria:** See above
Interventions	**Intervention Characteristics** Intervention ● *Description*: Internet treatment. The treatment programme consisted of 10 self-help modules which were based on established CBT principles [31]: psychoeducation (module 1), cognitive restructuring (modules 2 and 3), interoceptive exposure (modules 4 and 5), exposure in-vivo (for agoraphobic situations;modules 6 to 9), and relapse prevention (module 10).In the Internet treatment the self-help programme was administered via web pages. The text modules consisted of information as well as exercises, to be performed in thepatient's every-day life. Each module ended with a number of questions to be answered by the patient through interactive forms (e.g. homework assignments). After reviewing these answers, the psychologist gave access tothe next module and provided feedback. At any moment the patient could post a message if he or she needed further help. Messages were answered within 24 hours on regular weekdays. No other contact than by e-mail between patient and psychologist took place during the treatment. The patient also had the opportunity to partic-ipate in an online discussion forum with other patients in treatment during the same time period. However, this was not mandatory. ● *Dose*: Booth the Internet and the group treatment were 10 weeks long(1 module/group session per week). ● *Duration*: 10 weeks Control ● *Description*: Group treatment. The group treatment was led by two clinical psychologists who presented the self-help programme mentioned above during weekly 2-hour sessions, with the support of printed handouts of the modules given to the patients.The homework assignments described above were addressed during the group sessions. The psychologists involved in the treatment were regular staff psychologistsnot specially trained for participation in the trial ● *Dose*: Both the Internet and the group treatment were 10 weeks long(1 module/group session per week). ● *Duration*: 10 weeks
Outcomes	*Grad af angst, Panic disorder severity scale (PDSS)* ● **Outcome type**: Continuous Outcome ● **Reporting**: Fully reported ● **Scale**: Panic disorder severity scale (PDSS) ● **Range**: 0-28 ● **Direction**: Lower is better ● **Data value**: Endpoint *Funktion, Shehan Disability Scale (SDS); subscale social* ● **Outcome type**: Continuous Outcome ● **Reporting**: Fully reported ● **Scale**: Shehan Disability Scale (SDS); subscale social

	● **Range**: 0-10 ● **Direction**: Lower is better ● **Data value**: Endpoint *Bedring, Response on the Panic disorder severity scale (PDSS), min 40% reduction* ● **Outcome type**: Dichotomous Outcome ● **Reporting**: Fully reported ● **Scale**: Response on the Panic disorder severity scale (PDSS) ● **Direction**: Higher is better ● **Data value**: Endpoint *Frafald, alle årsager* ● **Outcome type**: Dichotomous Outcome ● **Reporting**: Fully reported ● **Direction**: Lower is better ● **Data value**: Endpoint
Identification	**Sponsorship source:** The Stockholm County Council sponsored this study. **Country:** Sweden **Setting:** Outpatient clinic **Authors name:** jan.o.bergstrom **Institution:** Karolinska Institutet, Department of Clinical Neuroscience, Center for Psychiatry Research, Stockholm, Sweden **Email:** jan.o.bergstrom@ki.se
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The participants were divided into two groups, Internet- or group treatment, by an independent random-number procedure,"
Allocation concealment (selection bias)	Low risk	Quote: "The participants were divided into two groups, Internet- or group treatment, by an independent random-number procedure, where each patient was assigned to either treatment by the opening of sealed numbered envelopes."
Blinding of participants and personnel (performance bias)	High risk	Judgement Comment: No information of blinding of participants and health care professionals. Blinding not feasible.
Blinding of outcome assessment (detection bias)	Unclear risk	Quote: "All outcome measures have previously established adequate psychometric properties and were administered during the clinical interview by a psychiatrist at pre-and post-treatment, as well as after a 6-month follow-up period." Judgement Comment: Outcome measures were clinician rated and no information of blinding of outcome assessors.

Incomplete outcome data (attrition bias)	Unclear risk	Quote: "Nine participants dropped out after randomisation but before commencing treatment. Various reasons were given for not starting treatment, but all pertained to different life circumstances of the individual participants and not to randomisation status. These initial dropouts were excluded from the statistical analyses." Judgement Comment: Balanced drop outs in both groups (Internet 6 vs control 5)under the intervention, however, participants were only included in analysis if they commenced treatment. A total of 9 participants left the study after randomization but before treatment, 3 from internet and 6 from control group. Mixed effects model should accommodate missing data. 3/53 dropped out from the internet group and 6/60 from the face ro face group. Intention to treat analyses only included participants which commenced treatment
Selective reporting (reporting bias)	High risk	Judgement Comment: Protocol available at ClinicalTrials.gov NCT00845260. Reports on all the outcomes stated in the protocol, but definition of resonse at the PDSS not reported in the protocol
Other bias	Low risk	Judgement Comment: The study appears to be free of other sources of bias

Carlbring 2005

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Intervention ● *mean age in years (SD)*: 34.2 (6.0) ● *Number of females %*: 68% ● *years since onset mean (SD)*: 8.2 (7.2) Control ● *mean age in years (SD)*: 35.8 (9.3) ● *Number of females %*: 75% ● *years since onset mean (SD)*: 9.9 (11.1) **Included criteria:** To be included in the study, participants had to meet the following criteria: fulfil the DSM-IV(American Psychiatric Association, 1994) criteria for PD; PD duration of at least 1 year; age between 18 and 60 years; not suffering from any other psychiatric disorder in immediate need of treatment; have a depression point total on the MADRS-SR (Svanborg & Åsberg, 1994) of less than 21 points and less than 4 points on the suicide question (Item 9; ‘‘I often think it would be better to be dead, and though I don’t really want to commit suicide it does seem a possible solution’’; possible range 0–6 points); PD as the primary problem; if on prescribed drugs for PD:(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; if in therapy, this had to have been ongoing for more than 6 months and not be of CBT type; to rule out general medical conditions the participant must have had a previous contact with a physician, psychologist, or other health professional as a consequence of panic attacks; no epilepsy, kidney problems, strokes, organic brain syndrome, emphysema, or heart disorders. **Excluded criteria:** See above
Interventions	**Intervention Characteristics** Intervention ● *Description*: Internet-based (IT). Internet-based therapy In the IT group, each module was converted into web pages and was accessible via the WWW. Each module included information and exercises, and ended with 3–8 essay questions. Participants were asked to explain, in their own words, the most important sections of the module they had just completed, provide thought records and describe their experience with and results

	of their exposure exercises.The questions were intended to promote learning and to enable the research supervisors to assess whether the participants had assimilated the material, and completed their homework. Also, each module ended with an interactive multiple-choice quiz that the participants needed to get 100% correct in order to proceed. If they were unsuccessful they received immediate automatic feedback on what specific questions they failed and what the correct answer was, together with an explanation on why that was the correct response. Another thing that separated this Internet-based treatment from regular bibliotherapy was that in every module the participants were required to post at least one message in an online discussion group about a predetermined topic. As fellow participants were able to read and comment on each others messages a rather warm and supportive atmosphere developed. Feedback on the homework was usually given within 36 hours after sending their answers via e-mail. On the basis of these e-mails, a subjective assessment was made by the therapist 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 module. All contact was exclusively via e-mail.The participants were encouraged to come up with questions or reflections during treatment, and they were free to send an unlimited number of e-mails.The total number of reciprocal contacts (receive and send) ranged from 4 to 31 (M=15:4;SD=5.5). As the e-mail response to the participants often were very similar much text could be recycled.The mean total time spent on each participant was approximately 150 min, including administration, and responding to the e-mails. ● *Dose*: The treatment was manualized and divided into 10 modules: (1–2) psychoeducation andsocialization, (3) breathing retraining and hyperventilation test, (4–5) cognitive restructuring,(6–7) interoceptive exposure, (8–9) exposure in vivo, and finally (10) relapse prevention and as sertiveness training. Each module consisted of approximately 25 pages, and was in large partsimilar to the previously tested self-help material by ● *Duration*: 10 weeks Control ● *Description*: Live therapy (LIVE). Face to face cognitive behavioral therapy . Participants in the live therapy condition received 10 weekly individual sessions lasting 45–60 min. Between each session the participant was expected to do homework, which included reading a module handout identical to the text in the IT condition. Furthermore, each session was tape recorded and the participant was instructed to listen to it after the sessions to consolidate learning (Clark, 1989).The tapes were later used for adherence checks and supervision ● *Dose*: 10 weekly individual sessions lasting 45–60 min. ● *Duration*: 10 weeks.
Outcomes	*Grad af angst, Beck Anxiety Inventory (BAI)* ● **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)* ● **Outcome type**: Continuous Outcome ● **Reporting**: Fully reported ● **Scale**: quality of life inventory (QOLI) ● **Direction**: Higher is better ● **Data value**: Endpoint *Grad af undgåelse, mobility inventory (MI-A) - subscale avoidance when alone* ● **Outcome type**: Continuous Outcome

	● **Reporting**: Fully reported ● **Scale**: mobility inventory (MI-A) - subscale avoidance ● **Range**: 1-130 ● **Direction**: Lower is better ● **Data value**: Endpoint *Bedring, Free from panic disorder* ● **Outcome type**: Dichotomous Outcome ● **Reporting**: Fully reported ● **Scale**: Free from panic disorder ● **Direction**: Higher is better ● **Data value**: Endpoint *Frafald, alle årsager* ● **Outcome type**: Dichotomous Outcome ● **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 (Vårdal), the Boethius Foundation, the Swedish Council for Research in the Humanities and Social Sciences, and the Soderstro Koniska Foundation **Country:** Sweden **Setting:** Outpatient clinic and internet based **Authors name:** Per Carlbring **Institution:** Department of Psychology, Uppsala University, Box 1225, 751 42 Uppsala, Sweden **Email:** per.carlbring@psyk.uu.se
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Participants were divided into two groups, Live therapy (LIVE) or Internet-based (IT) by a true random-number-service (http://www.random.org)."
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 professionals. Blinding not feasible.
Blinding of outcome assessment (detection bias)	High risk	Judgement Comment: No information of blinding of outcome assessors. Outcome measures were self-reported and participants not blinded.

Incomplete outcome data (attrition bias)	Low risk	Quote: "After randomization, six people dropped out during the course of the study. There were three dropouts from the LIVE therapy group and three from the IT group. Lack of time was given as the main reason for discontinuing. However, in accordance with the intention to treat paradigm (e.g., Nich & Carroll, 2002; Newell, 1992) post- treatment data were collected from all dropouts. Six participants did not return their follow-up questionnaires, and their post-treatment scores were carried forward to the follow-up assessment point. Hence, all 49 participants that were randomized to one of the two conditions are included in the statistical analysis." Judgement Comment: Low number of dropouts, equal in numbers and reasons between the two groups. Intention to treat analyses was performed.
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

Hedman 2011

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Intervention ● *mean age in years (SD)*: 24.0 (37.5) ● *Number of females %*: 24 (37.5%) ● *years since onset mean (SD)*: 20 Control ● *mean age in years (SD)*: 21 (33.8) ● *Number of females %*: 21 (33.8%) ● *years since onset mean (SD)*: 22 **Included criteria:** To be eligible for inclusion potential participants had to meet the following criteria: (a) fulfill the DSM-IV [25] criteria of social anxiety disorder as assessed using the Structured Clinical Interview for DSM-IV axis I disorders (SCID-I) [26], (b) agree to undergo no other psychological treatment for the duration of the study, (c) have no history of CBT for the last four years, (d) have constant dosage two months prior to treatment of any prescribed medication for anxiety or depression and agree to keep dosage constant throughout the study, (e) have a primary diagnosis ofSAD as assessed by the interviewing psychiatrist (individuals with comorbid disorders according to the Mini International Neuro-psychiatric Interview (MINI) [27] were not excluded), (f) not currently meet the diagnostic criteria for substance abuse (g) have no history of psychosis or bipolar disorder, (h) not score.20 on the Montgomery Åsberg Depression Rating Scale-self report(MADRS-S) [28], (j) if criteria for major depression were met,have a score of less than 4 of 6 on the suicide ideation item of MADRS-S, and (k) not meet criteria for any personality disorders within cluster A (e.g. paranoid personality disorder) or B (e.g.antisocial personality disorder), which could interfere with the therapeutic process in group therapy **Excluded criteria:**See above
Interventions	**Intervention Characteristics** Intervention ● *Description*: Internet-based cognitive behavior therapy (ICBT).The ICBT employed in this study was based on the treatment developed by Andersson and coworkers, and has been validated by several randomized controlled trials [13,14,15]. The treatment followed a CBT-model, developed for individual therapy, that stresses the importance of avoidance and safety behaviors as well as misinterpretations of social events and internal focus as maintaining factors of SAD [48]. A vital part of the treatment was the gradual access to internet-based self-help text comprising

	15 text modules, each covering a specific theme (e.g., exposure or cognitive restructuring) completed with a homework component. The modules provided the participants with the same knowledge and tools as conventional individual CBT for SAD. The duration of ICBT was 15 weeks and throughout this period the patient had access to a therapist via an online secure messaging system. The role of the therapist was mainly to provide feedback regarding home work and to grant access to the treatment modules. However, the patient could contact the therapist at anytime and expect a reply within 24 hours during week days. Patients and therapists had no face-to-face or telephone contact during the treatment. The general instruction to the internet therapists was to have the ambition to restrict time spent on each patient to less than 10 minutes per week. This time frame was judged possible as most messages to patients are very brief entailing the core feed-back that the homework was successfully completed and the next treatment module is accessible. The therapists conducting ICBT were eight psychologists with one to four years of experience in delivering CBT via the internet. ● *Dose*: 15 modules with graduated access. ● *Duration*: 15 weeks Control ● *Description*: Cognitive behavioral group therapy (CBGT).This treatment comprised an initial individual session followed by 14 group sessions over 15 weeks. The individual session prepared the participant to begin group treatment sessions and included a rationale for group treatment. Each group session was 2.5 hours long, including a 15 minute break. Groups were lead by two therapists and had six to seven participants. The CBGT followed the protocol developed by Heimberg and Becker [46] with the addition of two group sessions. The first two group sessions (i.e.,Sessions 2–3) were aimed at teaching participants the role and components of anxiety and how to identify and challenge negative automatic thoughts. Sessions 4–14 focused primarily on individually tailored in-session exposure in combination with cognitive restructuring. Prior to exposure exercises, participants identified and disputed negative automatic thoughts, developed rational alternatives, and behavioral goals were set. Following the exposure exercises, additional cognitive restructuring was conducted and goal attainment was reviewed. Participants were also given homework to continue exposure exercises in the same fashion in their home environment. Session 14–15 were devoted to assessing the progress of the participant and setting goals for the future. A detailed plan was created for each participant to ensure that goals and methods to achieve them were clear. The therapists facilitating the CBGT sessions were six clinical psychologists with2 to15 years experience in treating patients with SAD using CBT. ● *Dose*: 14 group sessions over 15 weeks. ● *Duration*: 15 weeks.
Outcomes	*Grad af angst, Beck Anxiety Inventory (BAI)* ● **Outcome type**: Continuous Outcome ● **Reporting**: Fully reported ● **Scale**: Beck Anxiety Inventory (BAI) ● **Range**: 0-63 ● **Direction**: Lower is better ● **Data value**: Endpoint *Funktion, Global Assessment of Functioning Scale (GAF)* ● **Outcome type**: Continuous Outcome ● **Reporting**: Fully reported ● **Scale**: Global Assessment of Functioning Scale (GAF) ● **Range**: 1-100 ● **Direction**: Higher is better ● **Data value**: Endpoint

	Livskvalitet, quality of life inventory (QOLI) ● **Outcome type**: Continuous Outcome ● **Reporting**: Fully reported ● **Scale**: quality of life inventory (QOLI) ● **Direction**: Higher is better ● **Data value**: Endpoint *Grad af undgåelse, Liebowitz Social Anxiety Scale (LSAS)* ● **Outcome type**: Continuous Outcome ● **Reporting**: Fully reported ● **Scale**: Liebowitz Social Anxiety Scale (LSAS) ● **Range**: 0-72 ● **Direction**: Lower is better ● **Data value**: Endpoint *Bedring, Resonders at LSAS, antal personer* ● **Outcome type**: Dichotomous Outcome ● **Reporting**: Fully reported ● **Scale**: LSAS ● **Direction**: Higher is better ● **Data value**: Endpoint *Frafald, alle årsager* ● **Outcome type**: Dichotomous Outcome ● **Reporting**: Fully reported ● **Direction**: Lower is better ● **Data value**: Endpoint
Identification	**Sponsorship source:** No information **Country:** Sweden **Setting:** Outpatient clinic **Authors name:** Erik Hedman **Institution:** Department of Clinical Neuroscience, Division of Psychiatry, Karolinska Institutet, Stockholm, Sweden **Email:** erik.hedman.2@ki.se
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The randomization procedure involved two external persons not involved in the study; one provided randomization data and the other monitored that no manipulation of treatment allocation was performed by the research group. A true random number service (http://www.random.org) was used to ensure randomization."
Allocation concealment (selection bias)	Low risk	Quote: "The random sequence was generated after inclusion of participants to ensure that assignment of intervention was concealed from assessing psychiatrists and researchers of the study. Participants were allocated to CBGT or ICBT in a 1:1 ratio using simple randomization with no restrictions or matching. To ensure the integrity of the blinding procedure, participants were instructed not to mention which treatment they had received during the post- treatment and follow-up interviews. After completing the interviews, the assessing psychiatrists guessed allocation status for each participant. There were no significant assiciotion between the assessors guess and actual treatment allocation". Quote: "The randomization procedure involved two external persons not involved in the study; one provided randomization data and the other monitored that no manipulation of treatment allocation was performed by the research group. A"
Blinding of participants and personnel (performance bias)	High risk	Judgement Comment: No information of blinding of participants and health care providers. Blinding not feasible.
Blinding of outcome assessment (detection bias)	Low risk	Quote: "As shown in Table 3, there was no significant association between assessors' guess and actual treatment allocation (x 2 = 0.27, df = 1, p = .61), indicating successful blinding." Quote: "Outcome assessors were blind to treatment status." Judgement Comment: Outcome measured were clinician rated, outcomes assessors were blinded.
Incomplete outcome data (attrition bias)	Low risk	Quote: "The main analyses were conducted in accordance to intention-to-treat principle, i.e. all available assessment data was analyzed in accordance to how participants were randomized. This meant that participants were encouraged to provide assessment data regardless of treatment adherence. On the CGI-I scale, missing values were replaced with ‘‘no change’’." Judgement Comment: Main analysis was Intention to treat where all randomised particiapnts were included (n=62 in control group, n=64 in intervention group).Level of attrition was similar in both groups for Completers analyses Dropouts are balanced in numbers and reasons across groups
Selective reporting (reporting bias)	Low risk	Judgement Comment: The protocol is available at ClinicalTrials.gov. All the outcomes of interest are stated in the protocol.
Other bias	Low risk	Judgement Comment: The study appears to be free of ohter sources of bias

Kiropoulos 2008

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Intervention ● *mean age in years (SD)*: ● *Number of females %*: 33 (71.7%) Control ● *mean age in years (SD)*: ● *Number of females %*: 29 (72.5%)

	Included criteria: Inclusion criteria for this study were that participants were Australian residents and living in Victoria, Australia and had a Diagnostic and Statistical Manual of Mental Disorders-IV (DSM-IV) primary diagnosis of PD (with or without agoraphobia) asassessed with the anxiety disorders interview schedule(ADIS-IV) (Brown, Di Nardo, & Barlow, 1994). PD (with or without agoraphobia) was considered to be the primary diagnosis when the severity was estimated tobe two points greater than any secondary diagnosis onthe clinician's nine-point severity rating scale in the ADIS-IV. **Excluded criteria:** Exclusion criteria were presence of a seizure disorder, stroke, schizophrenia, organic brain syndrome, heart condition, alcohol or drug dependency, personality disorder, or chronic hypertension. All participants were between the ages of 18 and 70 years. They agreed not to undertake any other type of therapy during the study. Those participants who were taking medication for anxiety or depression were accepted if they had been stabilised on their medication for at least 12 weeks but continued to experience panic symptoms and met a diagnosis of PD.
Interventions	**Intervention Characteristics** Intervention ● *Description*: Internet-based CBT progran Panic Online (PO) is a structured program comprised of an introductory module, four learning modules, and a relapse prevention module. PO included common treatment methods used in standard CBT for panic disorder (i.e., instructions for controlled breathing, cognitive restructuring, and interoceptive and situational exposure). In addition, participants had access to the stress and benzodiazepine reduction modules also housed in PO. Nine registered and one probationary psychologist (overall seven female and two male), all trained in CBT for PD, made contact via email with the PO treatment participants assigned to them and guided each participant through the internet-based program. All psychologists interacted with their participant via email, which allowed the psychologist to provide individualized support and feedback to the participant, according to the participants' individual needs. The PO program contained standardized instructions and information that did not vary according to participant input. Participants were instructed to read one specified module per week and to practice the described activities in this module. Therapists responded to participants' emails within 24 hours of receiving them. Therapists maintained a log of the time they spent on treatment for each PO participant including time spent reading emails, constructing return emails, and listing any deviation from treatment protocol such as having telephone contact with the participant. The majority of participants reported using the program at home. ● *Dose*: 6 modules and home practice. ● *Duration*: 12 weeks. Control ● *Description*: Face-to-face CBT therapy. The face-to-face CBT therapy condition included the assisted use of a manualized CBT program over a period of 12 weeks. Participants attended one hour weekly treatment sessions with their allocated psychologist in the Department of General Practice, Monash Universityor the Baker Heart Research Institute. During the first face-to-face therapy session, participants were given a copy of the manual ‘‘Mastery of Your Anxiety andPanic – Third Edition’’ (MAP-3;Barlow & Craske,2000) free of charge. This manual presents the rationale for the 12 week CBT treatment and focuses on teaching participants a variety of cognitive and behavioral strategies that include controlled breathing, cognitive restructuring, and interoceptive and situational exposure similar to that used in the PO condition in thisstudy. Both PO and face-to-face CBT treatment conditions provided the same type of CBT information although organized and presented differently. Participants in this condition had designated weekly reading and were instructed to work through this manual with the assistance of the treating psychologist. ● *Dose*: 1 hour weekly session in 12 weeks. ● *Duration*: 12 weeks.
Outcomes	*Grad af angst, Anxiety disorders interview schedule for DSM-IV (ADIS-IV)* ● **Outcome type**: Continuous Outcome ● **Scale**: Anxiety disorders interview schedule for DSM-IV ● **Range**: 0-8 ● **Direction**: Lower is better

	● **Data value**: Endpoint Funktion, World Health Organisations Quality of Life – bref (QOL) subdomain social ● **Outcome type**: Continuous Outcome ● **Reporting**: Fully reported ● **Scale**: QOL - subdomain social ● **Range**: 0-100 ● **Direction**: Higher is better ● **Data value**: Endpoint Livskvalitet, World Health Organisations Quality of Life – bref (QOL) subdomain psychological ● **Outcome type**: Continuous Outcome ● **Reporting**: Fully reported ● **Scale**: QOL - subdomain psychological ● **Range**: 0-100 ● **Direction**: Higher is better ● **Data value**: Endpoint *Frafald, alle årsager* ● **Outcome type**: Dichotomous Outcome ● **Reporting**: Fully reported ● **Direction**: Lower is better ● **Data value**: Endpoint
Identification	**Sponsorship source:** Funding for this research project was provided by aNational Health and Medical Research Council projectgrant. Funding for the original development of the POinternet-based therapy program used in this study wasgranted to the original Chief Investigator, the late Professor Jeffrey Richards by the Australian Rotary Health Research Fund. **Country:** Australien **Setting:** outpatient clinic **Authors name:** Litza A. Kiropoulos **Institution:** Department of General Practice, School of Primary Health Care, Monash University, Building 1,270 Ferntree Gully Road, Notting Hill, Victoria 3168, Australia **Email:** litza.kiropoulos@med.monash.edu.au **Address:** Department of General Practice, School of Primary Health Care, Monash University, Building 1,270 Ferntree Gully Road, Notting Hill, Victoria 3168, Australia
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "they were randomly allocated using a random numbers table to either the PO or face-to-face CBT treatment condition."
Allocation concealment (selection bias)	Unclear risk	Judgement Comment: No information of allocation concealment. It is stated that the personnel conducting screening assessment were different from the ones providing treatment, but it is unclear of the screening assessors where also the ones performing the randomisation.
Blinding of participants and personnel (performance bias)	High risk	Judgement Comment: No information of blinding of participants and health care professionals. Blinding not feasible.
Blinding of outcome assessment (detection bias)	High risk	Judgement Comment: No information of blinding of outcome assessors. Outcome measures for function and quality of life were self-reported and patients were not blinded. ADIS were clinician rated
Incomplete outcome data (attrition bias)	Low risk	Quote: "A Fisher's exact test revealed no difference in attrition rates between the two treatment conditions, x 2 (1, N = 86) = .44, p > .05. Reasons for non-completion of either treatment included participants not being con- tactable, changing their mind about taking part in the study, because they could no longer commit to the 12- week treatment program or because they no longer had access to the internet." Judgement Comment: No real intention to treat analyses for function and quality of life.missing data for 6/46 in the internet group and 4/40 in the face to face group Attrition rates were low and no real difference between groups (2/40 in control group and 5/46 in intervention group). Reasons for attrition are unlikely to affect outcome.
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.

Footnotes

Characteristics of excluded studies

Andersson 2006

Reason for exclusion	Wrong comparator

Andersson 2009

Reason for exclusion	Wrong patient population

Andersson 2013

Reason for exclusion	Wrong patient population

Botella 2010

Reason for exclusion	Wrong comparator

Haug 2015

Reason for exclusion	Wrong intervention

Nordgreen 2016

Reason for exclusion	Wrong intervention

Tillfors 2008

Reason for exclusion	Wrong comparator

Footnotes

Characteristics of studies awaiting classification

Footnotes

Characteristics of ongoing studies

Footnotes

References to studies

Included studies

Andrews 2011

Andrews, G.; Davies, M.; Titov, N.. Effectiveness randomized controlled trial of face to face versus Internet cognitive behaviour therapy for social phobia. The Australian and New Zealand Journal of Psychiatry 2011;45(4):337-340. [DOI: 10.3109/00048674.2010.538840 [doi]]

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Bergstrom, J.; Andersson, G.; Ljotsson, B.; Ruck, C.; Andreewitch, S.; Karlsson, A.; Carlbring, P.; Andersson, E.; Lindefors, N.. Internet-versus group-administered cognitive behaviour therapy for panic disorder in a psychiatric setting: a randomised trial. BMC psychiatry 2010;10(Journal Article):54-244X-10-54. [DOI: 10.1186/1471-244X-10-54 [doi]]

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Carlbring, P.; Nilsson-Ihrfelt, E.; Waara, J.; Kollenstam, C.; Buhrman, M.; Kaldo, V.; Soderberg, M.; Ekselius, L.; Andersson, G.. Treatment of panic disorder: live therapy vs. self-help via the Internet. Behaviour research and therapy 2005;43(10):1321-1333. [DOI: S0005-7967(04)00237-2 [pii]]

Hedman 2011

Hedman, E.; Andersson, G.; Ljotsson, B.; Andersson, E.; Ruck, C.; Mortberg, E.; Lindefors, N.. Internet-based cognitive behavior therapy vs. cognitive behavioral group therapy for social anxiety disorder: a randomized controlled non-inferiority trial. PloS one 2011;6(3):e18001. [DOI: 10.1371/journal.pone.0018001 [doi]]

Kiropoulos 2008

Kiropoulos, L. A.; Klein, B.; Austin, D. W.; Gilson, K.; Pier, C.; Mitchell, J.; Ciechomski, L.. Is internet-based CBT for panic disorder and agoraphobia as effective as face-to-face CBT? Journal of anxiety disorders 2008;22(8):1273-1284. [DOI: 10.1016/j.janxdis.2008.01.008 [doi]]

Excluded studies

Andersson 2006

Andersson, G.; Carlbring, P.; Holmstrom, A.; Sparthan, E.; Furmark, T.; Nilsson-Ihrfelt, E.; Buhrman, M.; Ekselius, L.. Internet-based self-help with therapist feedback and in vivo group exposure for social phobia: a randomized controlled trial. Journal of consulting and clinical psychology 2006;74(4):677-686. [DOI: 2006-09621-005 [pii]]

Andersson 2009

Andersson, G.; Waara, J.; Jonsson, U.; Malmaeus, F.; Carlbring, P.; Ost, L. G.. Internet-based self-help versus one-session exposure in the treatment of spider phobia: a randomized controlled trial. Cognitive behaviour therapy 2009;38(2):114-120. [DOI: 10.1080/16506070902931326 [doi]]

Andersson 2013

Andersson, G.; Waara, J.; Jonsson, U.; Malmaeus, F.; Carlbring, P.; Ost, L. G.. Internet-based exposure treatment versus one-session exposure treatment of snake phobia: a randomized controlled trial. Cognitive behaviour therapy 2013;42(4):284-291. [DOI: 10.1080/16506073.2013.844202 [doi]]

Botella 2010

Botella, C.; Gallego, M. J.; Garcia-Palacios, A.; Guillen, V.; Banos, R. M.; Quero, S.; Alcaniz, M.. An Internet-based self-help treatment for fear of public speaking: a controlled trial. Cyberpsychology, behavior and social networking 2010;13(4):407-421. [DOI: 10.1089/cyber.2009.0224 [doi]]

Haug 2015

Haug, T.; Nordgreen, T.; Ost, L. G.; Kvale, G.; Tangen, T.; Andersson, G.; Carlbring, P.; Heiervang, E. R.; Havik, O. E.. Stepped care versus face-to-face cognitive behavior therapy for panic disorder and social anxiety disorder: Predictors and moderators of outcome. Behaviour research and therapy 2015;71(Journal Article):76-89. [DOI: 10.1016/j.brat.2015.06.002 [doi]]

Nordgreen 2016

Nordgreen, T.; Haug, T.; Ost, L. G.; Andersson, G.; Carlbring, P.; Kvale, G.; Tangen, T.; Heiervang, E.; Havik, O. E.. Stepped Care Versus Direct Face-to-Face Cognitive Behavior Therapy for Social Anxiety Disorder and Panic Disorder: A Randomized Effectiveness Trial. Behavior therapy 2016;47(2):166-183. [DOI: 10.1016/j.beth.2015.10.004 [doi]]

Tillfors 2008

Tillfors, M.; Carlbring, P.; Furmark, T.; Lewenhaupt, S.; Spak, M.; Eriksson, A.; Westling, B. E.; Andersson, G.. Treating university students with social phobia and public speaking fears: Internet delivered self-help with or without live group exposure sessions. Depression and anxiety 2008;25(8):708-717. [DOI: 10.1002/da.20416 [doi]]

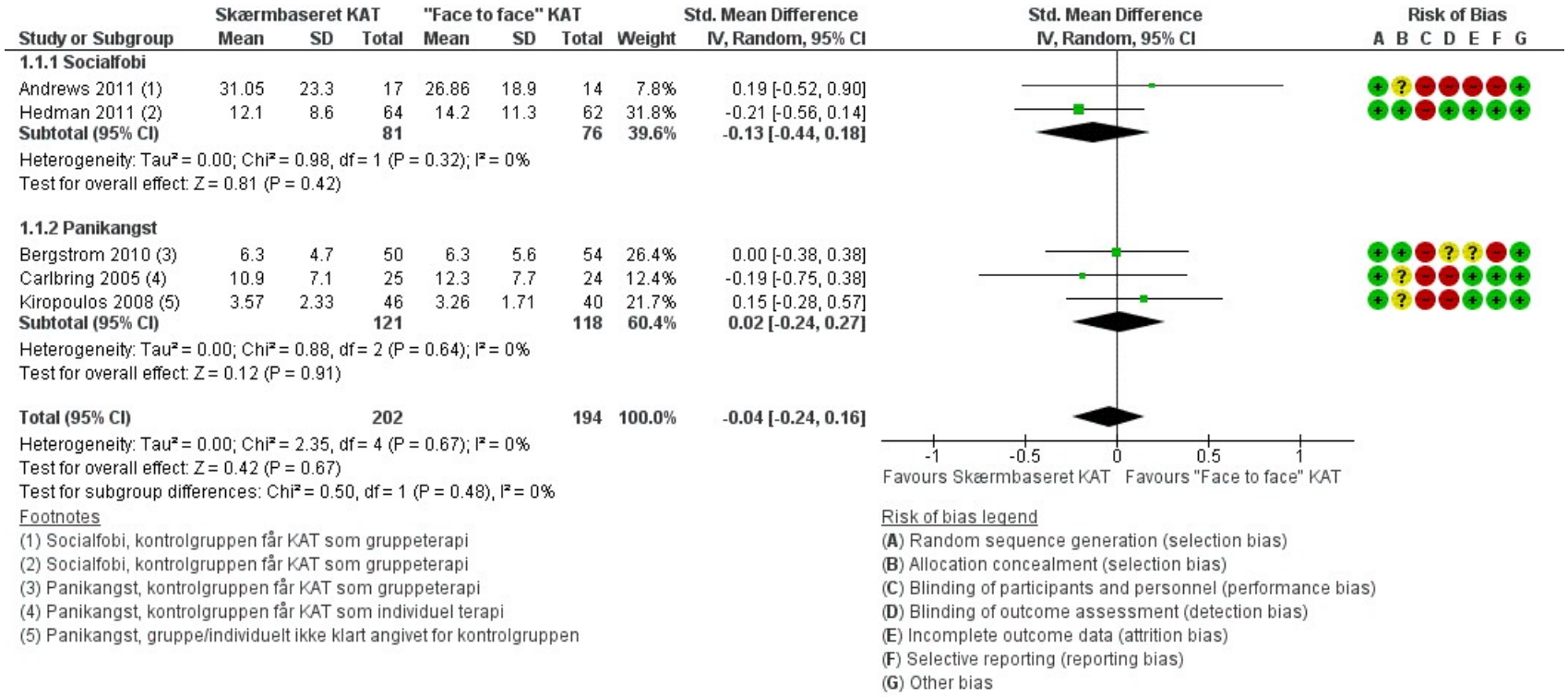
Data and analyses

1 Skærmbaseret KAT vs "Face to face" KAT

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
1.1 Grad af angst (severity of anxiety)	5	396	Std. Mean Difference (IV, Random, 95% CI)	-0.04 [-0.24, 0.16]
1.1.1 Socialfobi	2	157	Std. Mean Difference (IV, Random, 95% CI)	-0.13 [-0.44, 0.18]
1.1.2 Panikangst	3	239	Std. Mean Difference (IV, Random, 95% CI)	0.02 [-0.24, 0.27]
1.2 Funktion (function)	4	337	Std. Mean Difference (IV, Random, 95% CI)	-0.18 [-0.40, 0.03]
1.2.1 Socialfobi	2	157	Std. Mean Difference (IV, Random, 95% CI)	-0.24 [-0.55, 0.08]
1.2.2 Panikangst	2	180	Std. Mean Difference (IV, Random, 95% CI)	-0.13 [-0.42, 0.16]
1.3 Livskvalitet (quality of life)	3	251	Std. Mean Difference (IV, Random, 95% CI)	0.20 [-0.05, 0.45]
1.4 Grad af undgåelse (avoidance)	2	175	Std. Mean Difference (IV, Random, 95% CI)	-0.36 [-0.66, -0.06]
1.5 Bedring (response)	3	279	Risk Ratio (IV, Random, 95% CI)	1.11 [0.93, 1.32]
1.6 Frafald, alle årsager (dropouts all cauces)	5	411	Risk Ratio (IV, Random, 95% CI)	1.14 [0.71, 1.82]
1.7 Skadesvirkninger (Serious adverse events and adverse events) , totale antal personer med SAE + AE	1	37	Risk Difference (IV, Fixed, 95% CI)	0.00 [-0.11, 0.11]

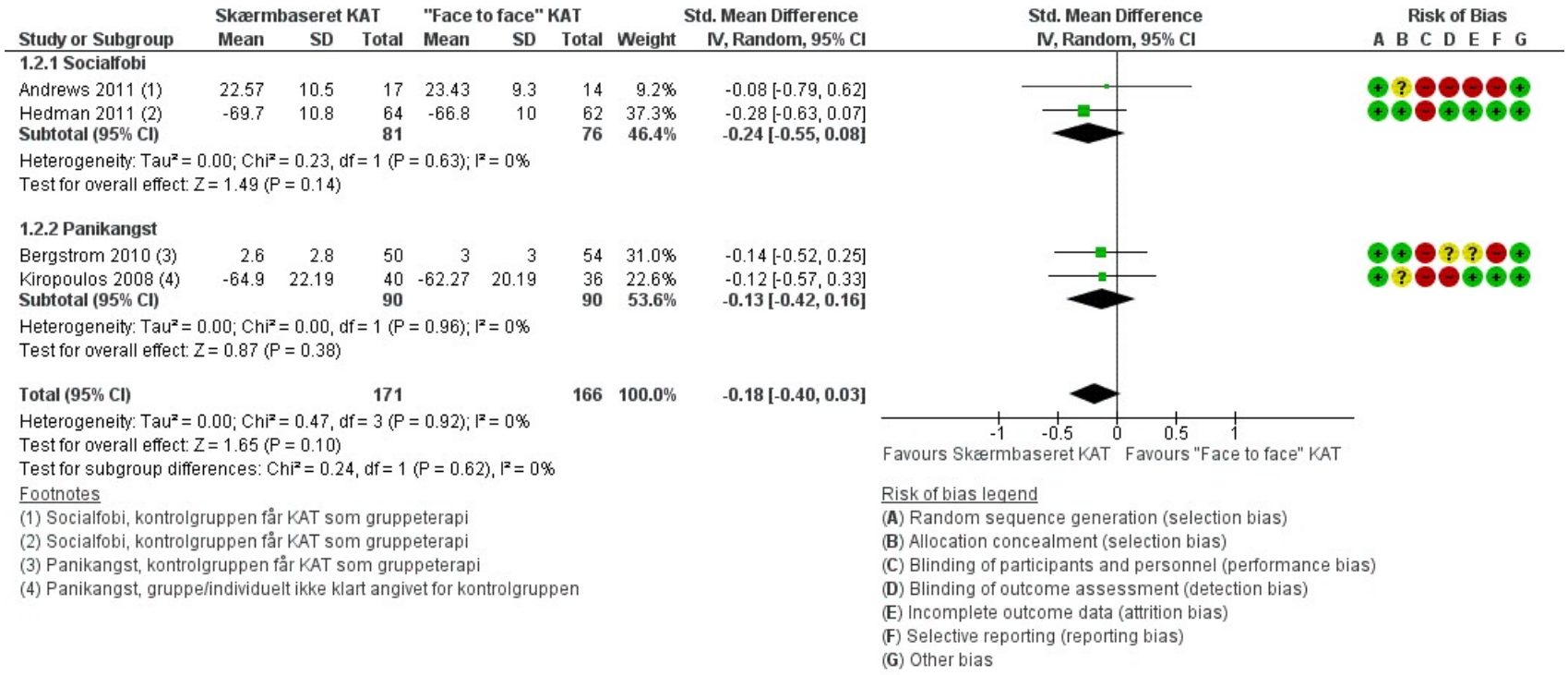
Figures

Figure 1 (Analysis 1.1)



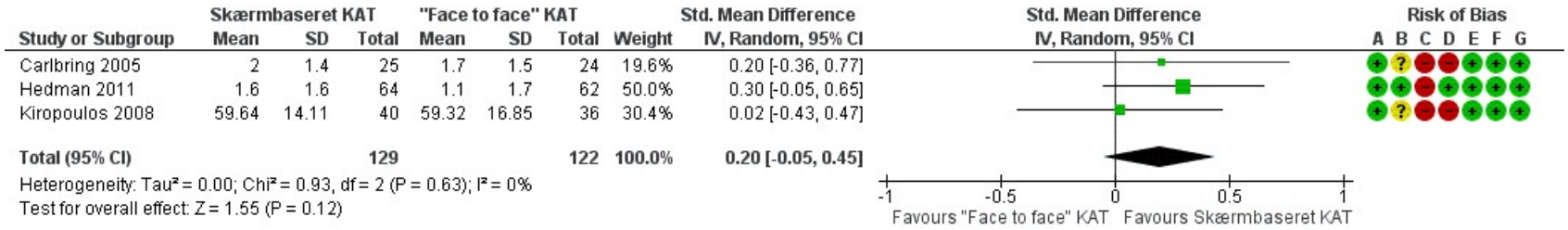
Forest plot of comparison: 1 Intervention vs Control, outcome: 1.1 Grad af angst (severity of anxiety).

Figure 2 (Analysis 1.2)



Forest plot of comparison: 1 Intervention vs Control, outcome: 1.2 Funktion (function).

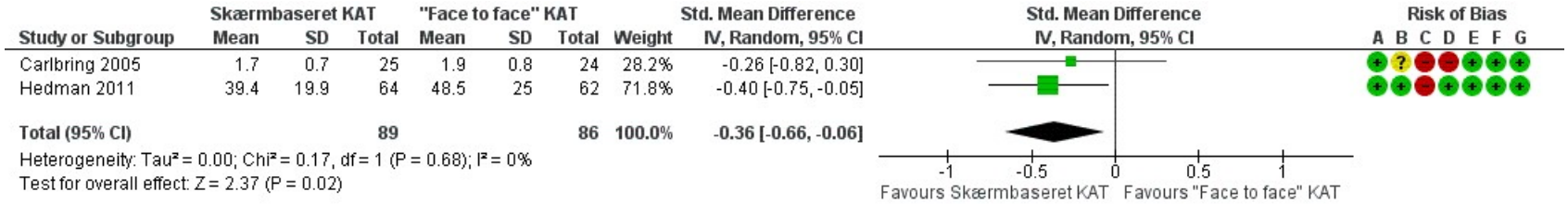
Figure 3 (Analysis 1.3)



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 Intervention vs Control, outcome: 1.3 Livskvalitet (quality of life).

Figure 4 (Analysis 1.4)



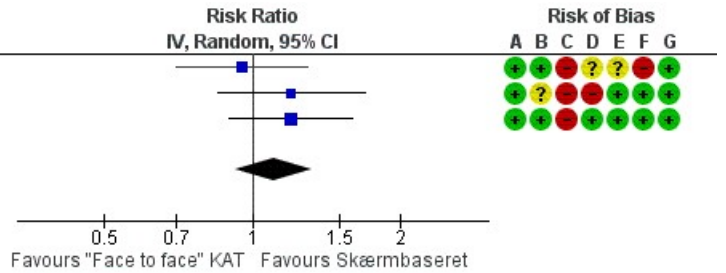
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting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

Forest plot of comparison: 1 Intervention vs Control, outcome: 1.4 Grad af undgåelse (avoidance).

Figure 5 (Analysis 1.5)

Study or Subgroup	Favours Skærmbaseret KAT Events	Total	"Face to face" KAT Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Bergstrom 2010	30	50	34	54	34.3%	0.95 [0.70, 1.29]
Carlbring 2005	20	25	16	24	27.0%	1.20 [0.85, 1.69]
Hedman 2011 (1)	42	64	34	62	38.7%	1.20 [0.90, 1.59]
Total (95% CI)		**139**		**140**	**100.0%**	**1.11 [0.93, 1.32]**
Total events	92		84			

Heterogeneity: Tau² = 0.00; Chi² = 1.42, df = 2 (P = 0.49); I² = 0%
Test for overall effect: Z = 1.12 (P = 0.26)



Footnotes
(1) Responders på CGI (much improved eller very much improved)

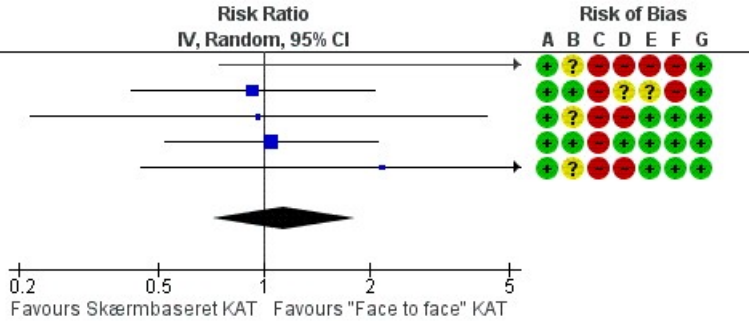
Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting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

Forest plot of comparison: 1 Skærmbaseret KAT vs "Face to face" KAT, outcome: 1.5 Bedring (response).

Figure 6 (Analysis 1.6)

Study or Subgroup	Skærmbaseret KAT Events	Total	"Face to face" KAT Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Andrews 2011	9	23	0	14	2.9%	11.88 [0.74, 189.45]
Bergstrom 2010	9	53	11	60	34.3%	0.93 [0.42, 2.06]
Carlbring 2005	3	25	3	24	9.8%	0.96 [0.21, 4.30]
Hedman 2011	13	64	12	62	44.4%	1.05 [0.52, 2.12]
Kiropoulos 2008	5	46	2	40	8.7%	2.17 [0.45, 10.60]
Total (95% CI)		**211**		**200**	**100.0%**	**1.14 [0.71, 1.82]**
Total events	39		28			

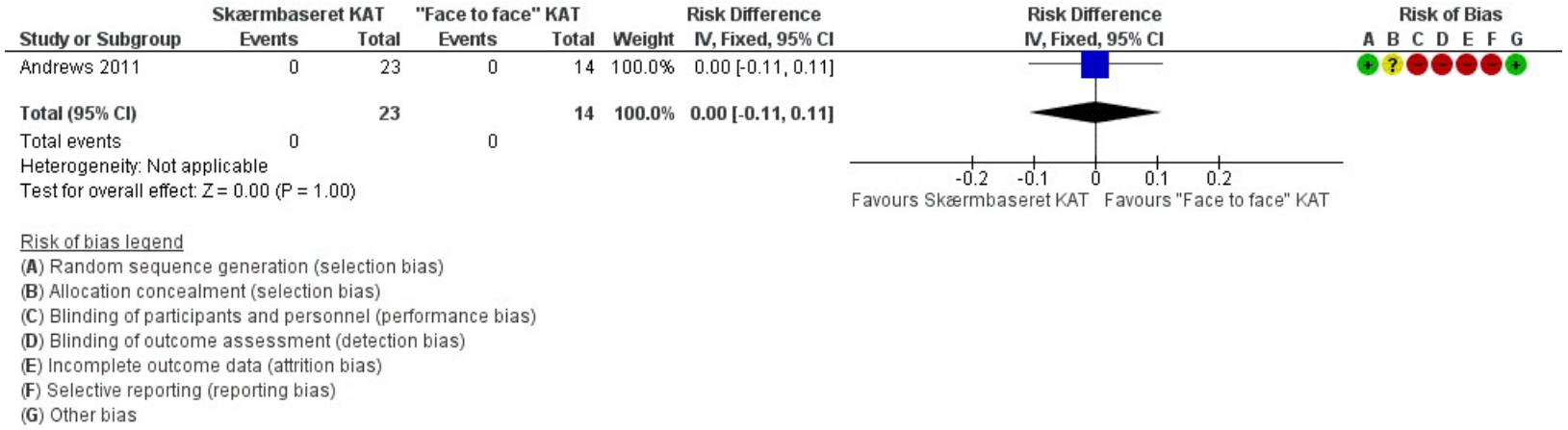
Heterogeneity: Tau² = 0.00; Chi² = 3.75, df = 4 (P = 0.44); I² = 0%
Test for overall effect: Z = 0.54 (P = 0.59)



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 Intervention vs Control, outcome: 1.6 Frafald, alle årsager (dropouts all cauces).

Figure 7 (Analysis 1.7)



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 Intervention vs Control, outcome: 1.7 Skadesvirkninger (Serious adverse events and adverse events) , totale antal personer med SAE + AE.