

Appendix 15c: Study characteristics - high-intensity psychological interventions and combination therapies

In the treatment of GAD, what are the risks and benefits associated with high-intensity psychological interventions compared with other interventions (including treatment as usual)?.....2

In the treatment of GAD, what are the risks and benefits associated with combination therapies compared with other interventions (including treatment as usual)?.....20

Characteristics Table for The Clinical Question: In the treatment of GAD, what are the risks and benefits associated with the following high intensity psychological interventions compared with other interventions (including treatment as usual)?

Comparisons Included in this Clinical Question

Acceptance-based behavioural therapy versus waiting list control ROEMER2008	Affect-focused body psychotherapy vs TAU BERG2009	Analytic psychotherapy vs anxiety management DURHAM1994	Applied relaxation versus CT + applied relaxation BARLOW1992 BORKOVEC2002
Applied relaxation vs wait list control BARLOW1992 DUGAS2009A	Applied relaxation vs cognitive therapy ÖST2000	Applied relaxation vs worry exposure HOYER2009	Behaviour therapy versus WLC BUTLER1991
Brief dynamic therapy versus supportive therapy CRITS-CHRISTOPH2005	Brief versus standard CBT DURHAM2004	CBT versus applied relaxation DUGAS2009A	CBT versus other active psychological treatment ARNTZ2003 BORKOVEC1993 LEICHSENRING2009 STANLEY1996
CBT versus CBT + Interpersonal therapy REZVAN2008	CBT versus discussion group WETHERELL2003	CBT versus enhanced usual care STANLEY2009	CBT versus WLC DUGAS2009A LADOUCEUR2000 LINDEN2005 MOHLMAN2003A STANLEY2003B WETHERELL2003
Cognitive therapy vs Behaviour therapy BUTLER1991	CT + applied relaxation versus WLC BARLOW1992	CT versus analytic psychotherapy DURHAM1994	CT versus anxiety management DURHAM1994
CT versus CT + relaxation BARLOW1992 BORKOVEC2002	CT versus WLC BARLOW1992 BUTLER1991	Discussion group versus WLC WETHERELL2003	Group CBT versus WLC DUGAS2003
Integrative relaxation training vs WLC JANBOZORGI2009	Meta-cognitive therapy vs applied relaxation WELLS2010	Motivational interviewing + CBT versus CBT alone WESTRA2009	Motivational interviewing versus WLC WESTRA2009
Relaxation versus CT BARLOW1992 BORKOVEC2002			

Methods	Participants	Outcomes	Interventions	Notes
ARNTZ2003				
<p>Study Type: RCT</p> <p>Study Description: Comparison of cognitive therapy vs. applied relaxation for long term and immediate effects in sample of 45 GAD patients representative of population.</p> <p>Type of Analysis: Completer analysis</p> <p>Blindness: No mention</p> <p>Duration (days): Mean 84</p> <p>Followup: 6 months (extracted)</p> <p>Setting: Recruited from community mental health center: Maastricht, Netherlands</p> <p>Notes: RANDOMISATION: No details provided</p> <p>Info on Screening Process: 47 screened, 2 excluded because they received a primary diagnosis of personality disorder</p>	<p>n= 45</p> <p>Age: Mean 36 Range 20-60</p> <p>Sex: 15 males 30 females</p> <p>Diagnosis: 100% Generalised Anxiety Disorder (GAD) by DSM-III-R</p> <p>Exclusions: i) not having a primary diagnosis of GAD ii) not requesting treatment iii) younger than 17 or older than 70, iv) a depressive disorder preceding the current episode of GAD or requiring immediate treatment, v) receiving behaviour therapy for GAD, vi) evidence of organic mental disorder accounting for complaints, mental retardation, psychotic disorders, alcohol or drug dependence.</p> <p>Notes: 22.2% had a diagnosis of GAD alone, the others also had a secondary diagnosis (46.7%). Mean duration of GAD was 8.8 years (range = 1-35)</p> <p>Baseline: STAI-trait scale: CT = 57.5 (8.3), AR = 53.7 (10.2); AR group had lower education level (compared to CT)</p>	<p>Data Used</p> <p>STAI-trait</p> <p>Clinically significant change (>8 on STAI-T)</p> <p>Remission (STAI-T <45)</p> <p>Data Not Used</p> <p>Fear Questionnaire - no data</p> <p>SCL anxiety factor - no data</p> <p>Notes: Taken at baseline, 12 weeks, 1 and 6-month follow up. Follow-up data extracted at 6 months. DROP OUT: 5/25 CT (20%), 3/20 AR (15%). Therapist qualification: Trained specifically at workshops. Did not mention if they were clinical psychologists.</p>	<p>Group 1 N= 25</p> <p>Cognitive therapy. Mean dose 12 sessions - Self-monitored & challenged automatic thoughts and formulated rational thoughts in diaries, including behavioural experiments to test catastrophic beliefs. Did not involve exposure in-vivo nor relaxation training.</p> <p>Group 2 N= 20</p> <p>Applied relaxation. Mean dose 12 sessions - Learned to apply relaxation skills daily & in difficult situations, identified early signs of anxiety, to use skills to counter anxiety as early as possible. Instructed to practice at least twice a day. Graduated exposure to feared situations.</p>	<p>FUNDING: None declared, Quality assessed: selection bias-unclear; performance bias-unclear; attrition bias-low; detection bias-unclear. Additional booster sessions offered upon request from those with complex problems.</p>

Results from this paper:
AR and CBT are similarly effective.

BARLOW1992

<p>Study Type: RCT</p> <p>Study Description: Relaxation, CT or their combination were compared to WLC for those with GAD</p> <p>Type of Analysis: Completers</p> <p>Blindness: No mention</p> <p>Duration (days): Mean 105</p> <p>Followup: 24 months (not extractable)</p> <p>Setting: Phobia and Anxiety Disorder Clinic: New York (referred by health professionals, community agencies, or self-referred)</p> <p>Notes: RANDOMISATION: No details provided</p> <p>Info on Screening Process: No details provided</p>	<p>n= 65</p> <p>Age: Mean 40 Range 18-65</p> <p>Sex: no information</p> <p>Diagnosis: 100% Generalised Anxiety Disorder (GAD) by DSM-III-R</p> <p>Exclusions: a) had begun benzodiazepines or beta-blockers within previous 3 months or tricyclics of MAO inhibitors within the previous 6 months, b) subjects on medication or currently receiving alternative psychotherapy were included in the programme provided that they maintained their current medication regimen or psychotherapy contact at a constant level throughout c) outside the ages of 18-65, d) had been drug/alcohol dependent/misusers within past 6 months, e) were currently suicidal, or showed signs of psychosis or organic brain syndrome</p> <p>Notes: Only subjects meeting criteria for GAD as a principal diagnosis and for whom that diagnosis rated an ADIS-R clinical severity rating of 4 or more were included in study.</p> <p>Baseline: Those in the CT group scored significantly lower on BDI than WLC and combined CT and relaxation group.</p>	<p>Data Used</p> <p>STAI-trait</p> <p>HAM-A</p> <p>HDRS (Hamilton depression rating scale)</p> <p>ADIS-R (clinical severity)</p> <p>Fear Questionnaire</p> <p>Response (20% improvement on 3/4 outcome measures)</p> <p>Cognitive-Somatic Anxiety Questionnaire</p> <p>Beck Depression Inventory</p> <p>Notes: Taken at baseline, 15 weeks. DROP OUTS: WLC = 10/20 (50%), Relaxation = 6/16 (38 %), Cognitive therapy = 4/17, Combined = 1/12 (8%). Follow-up 6, 12, 24 - months (data not extractable).</p>	<p>Group 1 N= 12</p> <p>CBT. Mean dose 15 sessions (60 minutes each) - Involved training in both relaxation and cognitive restructuring. More emphasis was placed in earlier sessions on relaxation with gradually greater emphasis on cognitive restructuring and application to anxiety-provoking situations.</p> <p>Group 2 N= 16</p> <p>Applied relaxation. Mean dose 15 sessions (60 minutes each) - Focused attention onto particular muscle groups. Home practice was required twice per day. Required to apply skills to everyday anxiety provoking situations in a graduated manner based on an individualised, 10 item hierarchy.</p> <p>Group 3 N= 17</p> <p>Cognitive therapy. Mean dose 15 sessions (60 minutes each) - Involved 2 phases: exploration of the role of thoughts and their significance, and cognitive skills training in the form of an individualised, 10 item hierarchy.</p> <p>Group 4 N= 20</p> <p>Waiting-list control. Mean dose 15 - Required to self-monitor for 15 weeks following which they were to receive treatment. They were informed that help was available in event of a crisis but no other intervention took place.</p>	<p>FUNDING: National Institute of Mental Health, Quality assessed: Selection: unclear; Performance: unclear; Attrition: high; Detection: low. Delivered by doctoral students or psychologists.</p>
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Results from this paper:
Treatments effective against WLC.

But treatments do not differ between each other.
Note the higher drop out rate in Applied Relaxation. Author explained it is hard to retain participants by teaching them relaxation techniques.

BERG2009

Study Type: RCT n= 61
Study Description: Explored the long-term effects of affect-focused body psychotherapy for patients with GAD. Age: Mean 37 Range 21-55
Type of Analysis: Intention to treat Sex: 19 males 42 females
Blindness: Open Diagnosis:
Duration (days): Mean 365 100% Generalised Anxiety Disorder (GAD) by DSM-IV
Followup: 2 years (extracted) Exclusions: a) major depressive disorder and bipolar disorder according to DSM-IV; b) with or without severe suicidal risk; c) organic brain damage; d) psychotic syndrome; e) ongoing drug or alcohol misuse; f) current pregnancy
Setting: Recruited from 6 outpatient clinics: Sweden Notes: 49 (80%) patients met DSM-IV Axis 2 criteria for at least one personality disorder. Slightly more than 70% of patients were on medication.
Notes: RANDOMISATION: Random number table Baseline: No significant differences in baseline scores.
Info on Screening Process: 64 screened; 3 excluded due to not meeting inclusion criteria: GAD according to DSM-IV, aged 18-55 years and ability to speak Swedish

Data Used
SCL anxiety factor
SCL-90 General Severity index
Beck Anxiety Inventory
WHO (Ten) Well-being index
Notes: Taken at baseline, 1 and 2 years. Drop outs: 6/33 for ABP and 0/28 for TAU. Therapy delivered by physiotherapists.

Group 1 N= 28
Treatment as usual. Mean dose 52 weekly sessions - 11 patients given formal psychotherapy, 12 had regular but not frequent doctors visits and 5 had unsystematic treatment contacts.

Group 2 N= 33
Affect-focused body psychotherapy. Mean dose 33 weekly sessions - Integrated bodily techniques and the exploration of affects into psychodynamic frame of reference. Adhered to treatment manual throughout.

FUNDING: supported by grants from various institutions in Sweden, Quality Assessed: selection bias = unclear, performance bias = high, attrition bias = unclear, detection bias = unclear.

Results from this paper:

No statistically significant difference between the two treatments.

BORKOVEC1993

Study Type: RCT n= 66
Study Description: Non-directive, applied relaxation, & CBT therapies for GAD were compared at baseline, 10-14 days after 12th session and 6 & 12-month follow-up. Age: Mean 38
Type of Analysis: Completers Sex: 23 males 43 females
Blindness: No mention Diagnosis:
Duration (days): Mean 84 100% Generalised Anxiety Disorder (GAD) by DSM-III-R
Followup: 6 & 12 - months (extracted) Exclusions: 1) GAD not primary diagnosis; 2) panic disorder criteria met; 3) assessor severity was too mild (<4); 4) other psychosocial therapy ongoing; 4) reviewed methods of study previously; 5) medical conditions contributing to anxiety symptoms; 6) taking antidepressant medication; 7) presence of severe depression, substance misuse, psychosis, and organic brain syndrome.
Setting: Recruited from agencies and advertisements: Pennsylvania, US. Notes: Average duration of problem = 17.1 (17.2) years. 4 clients in each therapy condition were taking anti-anxiety drugs.
Notes: RANDOMISATION: Assignment to therapist was random within restrictions of availability and caseload. Baseline: HAM-A: ND = 19.7 (4.3), AR = 20.8 (4), CBT = 19.4 (5.4)
Info on Screening Process: 508 screened, 442 excluded for not meeting DSM-III-R criteria

Data Used
STAI-trait
Assessor Severity Scale
HDRS (Hamilton depression rating scale)
Penn State Worry Questionnaire
Responders (20% reduction in 75% of all scales)
Beck Depression Inventory
HARS (Hamilton anxiety rating scale)
Notes: Taken at: baseline, 10-14 days after session 12. DROP OUT: ND: 2/20, AR: 5/23, CBT: 4/23. Therapy delivered by two experienced & advanced clinical graduate students.

Group 1 N= 23
CBT. Mean dose 12 sessions (each 90 minutes) - All procedures equal to that of AR except that the extensive time spent in discussion of early cue detection and ways of relaxing in daily life was instead devoted to self-control desensitization. Only 10-15 minutes of cognitive therapy given per session.

Group 2 N= 23
Applied relaxation. Mean dose 12 sessions (each 90 minutes) - learned new coping technique for reducing anxiety. Guided by manual. Relaxation practice encouraged twice daily and daily diaries utilised to note early cues.

Group 3 N= 20
Non-directive therapy. Mean dose 12 sessions (each 90 minutes) - involved exploration of life experiences, changing anxious experience & increasing self-confidence, discovering new strengths through introspection & affective experience. Guided by manual, daily homework included.

FUNDING: supported in part by National Institute of Mental Health Research Grant. Quality assessed: Bias: Selection-Unclear; Performance-Unclear; Attrition-High; Detection-Low

Results from this paper:

CBT and AR are similarly effective. They are both superior to Non-Directive therapy.

Conclusions: Suggesting relaxation technique is the core component of treatment of GAD, and that reflective listening is just non-specific factor of treatment.

BORKOVEC2002

Study Type: RCT n= 69
Study Description: Comparison of applied relaxation with self-control desensitisation & cognitive therapy with a combination of these. Age: Mean 37
Sex: no information

Data Used
STAI-trait
Assessor Severity Scale

Group 1 N= 23
CBT. Mean dose 14 weekly sessions (90-120 minutes each) - A combination of previous 2 techniques, except that no

FUNDING: supported in part by NIMHRG. Quality assessed: Bias-Selection-unclear; performance-

methods for clients with GAD
 Type of Analysis: Intention to treat
 Blindness: Single blind
 Duration (days): Mean 98
 Followup: 6, 12, & 24 - months (all extracted)
 Setting: 9 referred by mental health practitioners, remaining responded to media advertisement: Pennsylvania, US
 Notes: RANDOMISATION: No details
 Info on Screening Process: 459 screened; 383 excluded by phone screening/diagnostic interviews for not meeting admission criteria

Diagnosis:
 100% Generalised Anxiety Disorder (GAD) by DSM-III-R
 Exclusions: Did not have a principal diagnosis of GAD; had Panic Disorder; had a low assessor severity rating (<4):had concurrent psychosocial therapy, history of receiving CBT methods in prior therapy, medical contributions to anxiety, on antidepressants, presence of severe depression, substance misuse, psychosis, and organic brain syndrome.
 Notes: duration of the GAD diagnosis averaged 12.81years (12.07). Only 2 clients (1 in applied relaxation, 1 in CBT) were taking psychotropic drugs for anxiety (agreed to maintain dosage & frequency during therapy)
 Baseline: Hamilton Anxiety: CT = 25.83 (7.73), AR= 25.04 (6.24), CBT = 23.21 (6.42)

Hospital Anxiety and Depression Scale (depression)
 HAM-A
 Penn State Worry Questionnaire
 Remission (not meeting diagnosis according to SCID
 Beck Depression Inventory
 Notes: Taken at baseline, 10-14 days after 14th session. DROP OUTS: 4/23 for applied relaxation, 2/23 for CT, 1/23 CBT. Delivered by doctoral therapists & advanced clinical graduate students.

supportive listening element was included & perspective shifts created during the CT portions of the session were used during self-control desensitisation rehearsals along with relaxation responses.
 unclear; attrition-low; detection-low

Group 2 N= 23

Cognitive therapy. Mean dose 14 weekly sessions (90-120 minutes each) - based on cognitive model of anxiety. Involved training in self-monitoring and early identification of cues. Homework emphasised frequent applications of alternative perspectives and behavioural tasks to test beliefs & predictions

Group 3 N= 23

Applied relaxation. Mean dose 14 weekly sessions (90-120 minutes each) - also involved self-control desensitisation, learning new coping techniques to reduce anxiety, self-monitoring, intervening with relaxation responses early, focusing attention on present moment, rehearsal of coping methods, relaxation training, homework

Results from this paper:
 No difference found between treatments. Effort to increase therapeutic effectiveness also not successful.

BUTLER1991

Study Type: RCT
 Study Description: Compared behavioural therapy & CBT to waiting list control for the treatment of a GAD.
 Type of Analysis: Completer
 Blindness: No mention
 Duration (days): Mean 56 Range 28-84
 Followup: 6 months (extracted)
 Setting: Referrals from psychiatric hospital sources & general practice; Oxford, UK
 Notes: RANDOMISATION: No details provided
 Info on Screening Process: 161 screened, 104 excluded due to insufficient severity or duration of anxiety (38); other psychiatric diagnosis (37) and failure to attend interview (23)

n= 57
 Age: Mean 35
 Sex: 8 males 49 females
 Diagnosis:
 100% Generalised Anxiety Disorder (GAD) by DSM-III-R
 Exclusions: a) patients who experienced panic attacks if they had a primary diagnosis of panic disorder or if their GAD centered around fear of another panic attack; b) met diagnostic criteria for phobic disorder or MDD; c) if they were taking antidepressant medication, or if they had received psychological treatment for anxiety within 2 years.
 Baseline: no significant differences between groups

Data Used
 STAI-trait
 HAM-A
 Beck Anxiety Inventory
 Beck Depression Inventory
 Remission (HAMA & BAI <10)
 Notes: Taken at baseline, 12 weeks & 6 months follow up; DROP OUT: CBT: none, WLC = NONE, BT = 3/19. Delivered by clinical psychologists. Note: Some indication CBT participants are more resistant to early relapse.

Group 1 N= 19

CBT. Mean dose 12 sessions over 3 months (60 minutes each) - Activity schedules and records of dysfunctional thoughts were used to identify anxious thoughts & develop skills needed to examine them and formulate alternatives.

Group 2 N= 19

Waiting-list control. Mean dose 19 weeks

Group 3 N= 19

Behaviour therapy. Mean dose 12 sessions over 3 months (60 minutes each) - Involved reducing avoidance through graded exposure & building confidence through reengagement in pleasurable and rewarding activities

FUNDING: Medical Research Council of GB, Quality assessed: Bias: selection-unclear; performance-unclear;attrition-unclear;detection-low

Results from this paper:
 CBT significantly better than behavioural therapy
 CBT significantly better than waiting list control.
 Behavioural therapy marginally better than waiting list control.

CRITS-CHRISTOPH2005

Study Type: RCT
 Study Description: Compared the efficacy of brief dynamic therapy with supportive therapy on interpersonal outcomes for people diagnosed with GAD.
 Type of Analysis: ITT
 Blindness: No mention
 Duration (days): Mean 112

n= 31
 Age: Range 18-60
 Sex: no information
 Diagnosis:
 100% Generalised Anxiety Disorder (GAD) by DSM-IV
 Exclusions: Patients who had begun a psychotropic

Data Used
 Remission (less than 7 on HAM-A)
Data Not Used
 HAM-A - no data
 HDRS (Hamilton depression rating scale) - no data
 Penn State Worry Questionnaire - no data
 Beck Anxiety Inventory - no data
 Beck Depression Inventory - no data

Group 1 N= 16

Supportive therapy. Mean dose 16 weekly sessions - Conducted using the treatment manual for non-directive therapy. Based on person-centered therapy & is oriented toward creating an accepting, non-judgemental, & empathic environment. Direct suggestion or coping methods are forbidden.

Funding: Funded in part by National institute of Mental health Grants (R21-MH56018 & P30-MH45178). Quality assessed: Selection bias = unclear risk, Performance bias = unclear risk, attrition bias = low risk, detection bias = unclear risk

Setting: Recruited from outpatient referral line, adverts & professional referrals: Pennsylvania

Notes: RANDOMISATION: No details provided (note this is a pilot RCT)

Info on Screening Process: No details provided

medicine within the previous 3 months or who had an acute, unstable, or severe AXIS III medical disorder that might interfere with either the safe conduct of the study or the interpretation of the study results. Patients with any current or past history of bipolar disorder, schizophrenic disorders, or Cluster A personality disorders, and patients with any current or past history of seizure disorder (other than febrile seizure as an infant). Also, patients with a clinically significant organic pathology and patients who, in the previous 12 months, met criteria for alcohol or substance dependence or misuse, OCD, eating disorder, or BPD.

Baseline: No details provided

Notes: DROP OUTS: psychodynamic = 1/15, Supportive therapy = 2/16. Outcomes taken at pre and post (16 wks). No follow up. Delivered by PhD & Master & social worker therapists with a minimum of 10 years experience. Note only data from study 2 is relevant.

Group 2 N= 15

Short-term psychodynamic psychotherapy. Mean dose 16 weekly sessions - Manual based therapy with boosters. Main goal was to understand the anxiety symptoms of the patient in the context of interpersonal conflicts. Through uncovering the patients' relationship pattern, the conflicts are worked through.

Results from this paper:

No statistically significant difference between the two treatments.

DUGAS2003

Study Type: RCT

n= 52

Study Description: CBT in group format is compared to a wait-list control group over 14 sessions.

Age: Mean 41

Sex: 15 males 37 females

Type of Analysis: Intention to treat

Diagnosis:

100% Generalised Anxiety Disorder (GAD) by DSM-IV

Blindness: No mention

Duration (days): Mean 98

Followup: 2 years (not extractable)

Setting: Outpatients recruited from advertisements in Canada

Notes: RANDOMISATION: No details provided

Info on Screening Process: 170 screened, 118 excluded due to: not meeting GAD diagnostic criteria (19 had another disorder that was as severe as GAD; 14 had another primary disorder; and 7 had subclinical GAD), and 10 were unable to fit weekly sessions into their schedule

Exclusions: a) not given a primary diagnosis of GAD; b) change in medication type or dose during the 8 weeks before treatment; c) unwilling to keep medication stable while participating in study; d) evidence of suicidal intent; e) evidence of substance misuse; and f) evidence of current or past schizophrenia, bipolar disorder, or organic mental disorder.

Notes: Average duration of 16.9 years (SD = 15.2), 35 had one/more additional diagnoses, with a range of 1-5 comorbid disorders. 11 participants were taking anxiolytic or antidepressant medication.

Baseline: BAI; group CBT: 18.43 (10.71), wait-list control: 16.30 (9.34)

Data Used

Worry and Anxiety Questionnaire

ADIS-IV

Penn State Worry Questionnaire

Beck Anxiety Inventory

Beck Depression Inventory

Data Not Used

Response (40% reduction in HAM-A score) - not reportable

Notes: Outcomes taken at pre-wait list, pre-treatment, & post-treatment. DROP OUT: WLC = 2/27, CBT = 3/25. Delivered by licensed, trained CBT psychologists.

Group 1 N= 27

Waiting-list control. Mean dose 14 weeks - Telephoned every 3 weeks by clinician who had administered the ADIS-IV to monitor their state

Group 2 N= 25

CBT. Mean dose 14 weekly 2-hour sessions. - Group CBT (4-6 in each group) which involved 5 treatment components : treatment rationale, awareness, reevaluation, problem-solving, & cognitive exposure. Involved a session-by-session treatment manual.

FUNDING: Canadian Institutes of Health Research, Quality assessed: selection bias-unclear; performance bias-unclear; attrition bias-low; detection bias-low

Results from this paper:

Effective against waiting list control and results maintained at 2 years (not extractable as WLC data not extractable)

DUGAS2009A

Study Type: RCT

n= 65

Study Description: A randomized clinical trial of CBT & AR for adults with GAD.

Age: Mean 39 Range 18-64

Sex: 22 males 43 females

Type of Analysis: Intention to treat analysis

Diagnosis:

100% Generalised Anxiety Disorder (GAD) by DSM-IV

Blindness: Single blind

Duration (days): Mean 84

Followup: 6, 12 and 24 months (not reportable)

Setting: Referred by GPs, recruited from Anxiety Disorder Clinic. Montreal, Canada

Notes: Random allocation sequence used and allocation concealed.

Info on Screening Process: 83 patients screened. 14 excluded because GAD was not diagnosed (5) or was not primary diagnosis (5), the severity of comorbid disorder was not at least 2 points less on Clinician's Severity Rating (2), or a medical problem required immediate

Exclusions: GAD not primary disorder or severity of comorbid disorder is not at least 2 points less on Clinician's Severity Rating, not between age range of 18-64, change in medication type or dose during 4-12 weeks before assessment, unwilling to keep medication stable during treatment phase of study, evidence of suicidal intent or current substance misuse or current or past schizophrenia, bipolar disorder or organic mental disorder

Notes: Secondary conditions were panic disorder (27), specific phobia (13), social anxiety disorder (9), dysthymic disorder (8), MDD (5), OCD (3) & hypochondriasis (1). 55.4%

Data Used

Worry and Anxiety Questionnaire

WAQ- somatic subscale

Remission (Clinician severity rating of 3 or less

STAI-T

Clinician-rated GAD severity

Penn State Worry Questionnaire

Beck Depression Inventory

Notes: Taken at 12 weeks, 6-, 12- and 24-month follow-up. DROP OUTS: 2/23 for CBT, 5/22 for AR, no drop outs of WLC. Delivered by licensed, psychologists (with 5 year's experience) with extensive training in CBT.

Group 1 N= 22

Applied relaxation - 12 weekly 1-hour sessions with a clinical psychologist. Modules included psychoeducation, tension release, relaxation by recall & counting and conditioned relaxation.

Group 2 N= 20

Waiting-list control - Duration of wait list condition was 12 weeks. Participants were contacted by telephone every 3 weeks. Following this patients were randomly allocated to one of the two active treatment conditions: 33 (CBT) and 31 (AR) with 1 drop out.

Funding: Supported by a grant MOP-42454 from the Canadian Institutes of Health Research. Quality assesment completed: unclear risk of bias for selection, unclear risk of bias for performance, unclear risk of bias for attrition, low risk of detection bias.

attention

on anxiolytic or antidepressant medication & 43.1% had previously received CBT

Baseline: CSR: CBT 5.78 (1.04) AR 5.36 (1.26) WL 5.90 (1.25), PSWQ: CBT 61.65 (8.27) AR 58.01 (5.51) WL 57.34 (9.78), WAQ-Som: CBT 21.13 (4.07) AR 20.82 (5.48) WL 22.42 (3.17), STAI-T: CBT 53.04 (7.30) AR 52.23 (7.15) WL 52.06 (9.62), BDI-II: CBT 15.36 (8.20) AR 16.65 (9.27) WL 13.70 (7.72)

Group 3 N= 23

CBT - 12 weekly 1-hour sessions with a clinical psychologist. Included sessions on psychoeducation, uncertainty recognition, reevaluation of usefulness of worry, problem-solving training and imaginal exposure.

Results from this paper:

Cognitive Behavioural therapy statistically significantly better than waiting list control

Applied Relaxation was marginally better than waiting list control

Cognitive Behavioural therapy marginally better than Applied Relaxation. Only Cognitive Behavioural therapy led to continued improvement.

DURHAM1994

Study Type: RCT

n= 110

Study Description: Tested whether CT was of comparable efficacy to psychodynamic psychotherapy & if 8-10 sessions of therapy is as effective as 16-20 sessions

Age: Mean 39 Range 18-65

Sex: 35 males 75 females

Type of Analysis: Completers

Diagnosis:

100% Generalised Anxiety Disorder (GAD) by DSM-III-R

Blindness: No mention

Duration (days): Mean 98 Range 56-140

Exclusions: Aged under 18 years or over 65, duration of less than 6 months, scored less than 6 on Leeds Anxiety Scale, primary diagnosis not GAD

Followup: 6 & 12 months (extracted)

Setting: Referred outpatients by GPs & psychiatrists. Dundee, UK

Baseline: No significant differences

Notes: RANDOMISATION: No details

Info on Screening Process: 178 screened, 68 excluded as; primary diagnosis other than GAD (22), failure to complete self-report (25), failure to attend interviews (8), unwilling to participate (5), receiving other treatment (2)

Data Used

STAI-trait
Remission (Jacobson criteria for normative funct)
Brief symptom inventory
Beck Anxiety Inventory
Beck Depression Inventory
HAM-A
Social Adjustment Scale

Data Not Used

Self-esteem scale - no data
Notes: DROP OUTS: AP (HIGH) = 5/20, AP (LOW) = 4/25, CT (HIGH) = 4/19, CT (LOW) = 0/21, AMT = 6/25. Follow-up data extractable at 6 months. Delivered by clinical psychologists, consultant psychotherapists & trainee psychiatrists.

Group 1 N= 19

High intensity CT. Mean dose 20 sessions - Main focus was on identifying anxious cognitions and thinking errors, and on learning to switch to more helpful thoughts and reactions to stressful situations and unpleasant bodily sensations

Group 2 N= 20

High intensity analytic psychotherapy. Mean dose 20 sessions - Consisted of 16-20 hour long sessions of analytic psychotherapy. Involved the exploration and understanding of the presenting symptom, attention paid to negative transference reaction to the pre-set termination.

Group 3 N= 25

Anxiety Management training. Mean dose 10 sessions - Taught coping skills, structured individual session, & given homework

Group 4 N= 25

Low intensity analytic psychotherapy. Mean dose 10 sessions - Consisted of 8-10 hours of therapy over 6 months (same as before only less intensive)

Group 5 N= 21

Low intensity CT. Mean dose 10 sessions - Same as before only less intensive

FUNDING: Scottish Hospital Endowments Research Trust, Quality Assessed: Bias: Selection-unclear; Performance-unclear; Attrition-High; Detection-Low

Results from this paper:

Cognitive Therapy was found to be significantly more effective than Analytic Psychotherapy.

Cognitive Therapy had similar effects as Anxiety Management training

There are no statistically significant difference between the high or low contact groups.

Cognitive Therapy has relatively more sustainable with regard to long term outcomes.

DURHAM2004

Study Type: RCT

n= 55

Study Description: Examined whether standard CBT in comparison to high intensity CBT improved outcome for those with poor prognosis

Age: Mean 39 Range 18-65

Sex: 27 males 28 females

Type of Analysis: Completers

Diagnosis:

100% Generalised Anxiety Disorder (GAD) by DSM-IV

Data Used

STAI-trait
Remission (Jacobson criteria for normative funct)
Brief symptom inventory
ADIS-IV (CGS)
HAM-A

Group 1 N= 18

Standard CBT. Mean dose 10 sessions (each 60 minutes) - All participants assigned to this group were given a poor prognosis.

FUNDING: Chief Scientist Office, Scottish Home and Health dept, Quality assessed: unclear risk of bias for performance, selection, detection & attrition.

Blindness: No mention

Duration (days): Mean 70 Range 35-105

Followup: 6 months (extracted)

Setting: referrals from clinical sources; Scotland

Notes: RANDOMISATION: No details provided

Info on Screening Process: 171 screened, 77 excluded as failed to attend interview (27), insufficient duration or severity of anxiety (24), primary AXIS I diagnosis other than GAD (25), and one patient too old

Exclusions: No primary diagnosis of GAD, clinical global severity rating of less than 4, aged below 18 or older than 65, unwilling to accept random allocation, receiving concurrent psychological intervention, CBT 2 years prior to referral, evidence of psychosis, substance misuse or a medical condition underlying anxiety

Baseline: Patients in standard tended to have scores indicating somewhat greater severity compared with intensive on some measures, but controlled for in analysis

Notes: DROP OUT: brief = 14/33, standard = 11/29, intensive = 14/32. Follow-up data extractable at 6 months. Delivered by clinical psychologist & clinical nurse specialists trained in CBT.

Group 2 N= 18

Intensive CBT. Mean dose 15 sessions (each 60 minutes) - More opportunity to focus on key issues. All participants assigned to this group were given a poor prognosis.

Group 3 N= 19

Brief CBT. Mean dose 5 sessions (each 60 minutes) - Broad CBT approach with least opportunity to focus on key issues. All participants assigned to this group were given a good prognosis.

Results from this paper:

Brief intervention was statistically significantly better than standard on clinician-rated anxiety, but not on self-rated scores.

Brief intervention slightly better than intensive therapy on clinician-rated anxiety, but not on self-rated scores.

No statistically significant difference between standard and intensive therapy (both poor prognosis).

Conclusions: This study may have implications for stepped-care model

HOYER2009

Study Type: RCT

n= 73

Study Description: Examined whether worry exposure alone is as efficacious as the empirically supported stand-alone treatment for GAD, applied relaxation over 15 sessions

Age: Mean 45 Range 18-70

Sex: 21 males 52 females

Type of Analysis: ITT analysis

Diagnosis:
100% Generalised Anxiety Disorder (GAD) by DSM-IV

Blindness: No mention

Duration (days): Mean 105

Followup: 6 & 12 months (extracted)

Setting: Outpatient psychotherapy unit: Germany

Notes: RANDOMISATION: Random number generator, randomisation not balanced, therefore resulting in unequal groups.

Info on Screening Process: 688 screened, 615 excluded for following reasons: a) no GAD diagnosis; b) intake assessment not completed; c) refused participation

Exclusions: a) no primary diagnosis of GAD as assessed by DSM-IV; b) younger than 18 and older than 80; c) serious physical impairment (axis III); d) any lifetime history of schizophrenia, bipolar disorder, seizure or organic brain syndrome, substance misuse or dependence within the past year, serious personality disorder, any concurrent psychotherapeutic intervention or benzodiazepine use.

Notes: 3 participants from worry exposure group and 5 in applied relaxation group were on antidepressant medication before onset of study and maintained a stable dosage throughout study

Baseline: HAM-A: WL = 23.33 (7.02), AR = 22.71 (7.16), WE = 21.6 (7.23)

Data Used

STAI-trait

HAM-A

HDRS (Hamilton depression rating scale)

Penn State Worry Questionnaire

Beck Depression Inventory

Response (50% reduction in HAM-A score)

Notes: Taken at baseline & 15 weeks. DROP OUT: AR = 4/18, WE = 7/24, WL = 1/31. Follow up data available for some but not all measures. Delivered by graduate clinical psychology students.

Group 1 N= 24

Worry exposure. Mean dose 15 weekly sessions - Manualised protocol addressing avoidance and reassurance behaviours with the aim of reduction. Homework involved practicing worry exposure alone.

Group 2 N= 18

Applied relaxation. Mean dose 15 weekly sessions - Manualised protocol with homework at end of each session. Involved psychoeducation, relaxation procedures and homework focused on learning relaxation skills & applying these whenever signs of arousal were noticed.

Group 3 N= 31

Waiting-list control. Mean dose 15 weeks - patients who completed waiting list condition were subsequently rerandomised to 1 of 2 active treatments.

FUNDING: German Research Council, Quality assessed: Bias: Selection-Low; Performance-Unclear; Attrition-Low; Detection-Low

Results from this paper:

Worry Exposure statistically significantly better than waiting list control, Applied Relaxation statistically significantly better than waiting list control.

No statistically significant difference between Applied Relaxation or waiting list control.

JANBOZORGI2009

Study Type: RCT

n= 35

Study Description: Examined the effects of integrative relaxation training (relaxation, lifestyle, & spirituality) on emotional stability for people with GAD.

Age: Mean 24 Range 19-35

Sex: 4 males 31 females

Type of Analysis: Completers

Diagnosis:
100% Generalised Anxiety Disorder (GAD) by DSM-IV

Blindness: No mention

Duration (days): Mean 84

Followup: No follow-up

Setting: Patients were referred from a counselling & psychotherapy centre; Iran.

Notes: RANDOMISATION: No information provided

Exclusions: a) undergoing concurrent psychological treatment for anxiety disorder (n = 2); b) had a current diagnosis of schizophrenia (n = 1); c) an intellectual disability (n = 1); d) an organic mental disorder (n = 1); e) not within the age range of 19-35 (n = 4), refused to take part in the study (n = 6), or a principal diagnosis other than GAD was indicated at assessment (n = 19)

Data Used

STAI-T

Notes: DROP OUTS: Treatment = 1/18, WLC = 2/17. Note STAI-T was the Iranian version of this measure

Group 1 N= 18

Integrative relaxation training. Mean dose 12 sessions (weekly & lasted 1.5-2 hours each) - Group programme consisting of a combination of progressive relaxation, lifestyle (e.g. sleep, eating, leisure time management and physical & spiritual exercise). Given a weekly task.

Group 2 N= 17

Waiting-list control. Mean dose 12 weeks - Completed the questionnaires but did not take part in the interventions.

Quality assessed: selection = unclear risk of bias, performance = high risk of bias, attrition = unclear risk of bias, detection = unclear risk of bias. FUNDING: Funded by the Thaleh Counselling Centre in Tehran.

excluded met one or more of the exclusion criteria below.

Baseline: No baseline statistics provided for STAI-T

LADOUCEUR2000

Study Type: RCT

Study Description: Examined the efficacy of CBT for GAD compared with a delayed treatment control condition.

Type of Analysis: ITT

Blindness: Open

Duration (days): Mean 112

Followup: 1 year (not reportable)

Setting: Outpatients self-recruited, Canada

Notes: RANDOMISATION: no details provided

Info on Screening Process: 99 screened; 73 excluded due to following reasons: a) clearly did not have GAD b) would not benefit from treatment being offered, c) GAD not the most severe psychological disorder.

n= 26

Age: Mean 40

Sex: 6 males 20 females

Diagnosis:

100% Generalised Anxiety Disorder (GAD) by DSM-IV

Exclusions: a) no primary diagnosis of GAD, b) change in medication type or dose during the 8 weeks before treatment, c) unwilling to keep medication status stable while participating in study, d) evidence of suicidal intent, e) evidence of current substance misuse, and f) evidence of current or past schizophrenia, bipolar disorder, or organic mental disorder

Notes: 9 participants were taking medication and mean duration of GAD of 15.6 years (13.3)

Baseline: BAI: CBT = 16.54 (10.53), WL = 14.33 (5.85)

Data Used

Worry and Anxiety Questionnaire

ADIS-IV

Penn State Worry Questionnaire

Beck Anxiety Inventory

Beck Depression Inventory

Data Not Used

Response (40% reduction in HAM-A score) - not reported separately for each group

Notes: Taken at: Baseline & 16 weeks. DROP OUT: none. Therapy was delivered by licensed psychologists.

Group 1 N= 14

CBT. Mean dose 16 sessions (each 60 minutes) - Treatment consisted a) rationale, b) awareness training, c) correction of erroneous beliefs, d) problem-orientation training, and cognitive exposure.

Group 2 N= 12

Waiting-list control. Mean dose 16 weeks - Treatment began after 16 weeks of their initial assessment. Telephoned once a month to monitor their state and provide a minimal amount of support.

FUNDING: Medical Research Council of Canada. Quality assessed: bias: selection-unclear; performance-unclear; attrition-low; detection-unclear

Results from this paper:

CBT statistically significantly better than WLC

Results maintained at 6, 12-months follow up (but not meta-analysable)

LEICHSENRING2009

Study Type: RCT

Study Description: Compared short-term psychodynamic psychotherapy and CBT with regard to treatment outcome in GAD.

Type of Analysis: ITT

Blindness: Open

Duration (days): Mean 210

Followup: 6 months (extracted)

Setting: Recruited by referrals in private practice & advertisements: Germany

Notes: RANDOMISATION: No details

Info on Screening Process: 231 screened, 174 excluded as did not meet inclusion criteria and/or met exclusion criteria

n= 57

Age: Mean 42 Range 18-65

Sex: 11 males 46 females

Diagnosis:

100% Generalised Anxiety Disorder (GAD) by DSM-IV

Exclusions: a) younger than 18 or older than 65; b) no primary diagnosis of GAD; c) any acute, unstable, or severe axis III medical disorder that might interfere with the successful completion of treatment; d) any current or past history of schizophrenic disorder, bipolar disorder, or cluster A or B axis II disorder; e) any current or past neurological disorder; f) alcohol or substance dependence or misuse, eating disorder, or major depression in the previous 12 months, and g) current concomitant psychotherapeutic or psychopharmacological treatment.

Notes: 72 % had comorbid mental disorders.

Baseline: HAM-A: CBT= 25.90 (5.83), Short-term psychodynamic therapy = 25 (4.18)

Data Used

STAI-trait

Hospital Anxiety and Depression Scale (anxiety)

Penn State Worry Questionnaire

Beck Anxiety Inventory

Beck Depression Inventory

HAM-A

Notes: Taken at baseline, 30 weeks and 6-month follow up. DROP OUTS: CBT=2/29, Psychodynamic therapy = 3/28. Therapy delivered by licensed psychotherapists (both>15 years experience).

Group 1 N= 29

CBT. Mean dose 30 - Included up to 30 (50 minute) sessions carried out accord. to treatment manualisation. Included relaxation training, problem solving, planning of recreational activities and homework.

Group 2 N= 28

Short-term psychodynamic psychotherapy. Mean dose 30 - Based on supportive-expressive therapy. Focused on the core conflictual relationship theme associated with the symptoms of GAD. Emphasis was put on a positive therapeutic allegiance

FUNDING: LE 1250/1-1/1-2. Quality assessed: Selection-unclear; Performance-unclear; Attrition-low; Detection-low

Results from this paper:

No statistically significant differences between treatments for primary outcome measures.

But CBT is superior than psychodynamic on secondary outcomes (depression, worry)

LINDEN2005

Study Type: RCT

Study Description: A controlled clinical trial was done to evaluate the efficacy of CBT treatment in outpatients with GAD who treated by a therapist.

Type of Analysis: ITT (Last observation carried

n= 72

Age: Mean 43 Range 18-65

Sex: 12 males 60 females

Diagnosis:

100% Generalised Anxiety Disorder (GAD) by DSM-IV

Data Used

HAM-A

STAI-S

Remission (NIMH-CGI "Not ill at all")

Group 1 N= 36

CBT. Mean dose 20 sessions over 35 weeks (50 minutes each) - CBT (A): Given immediate CBT treatment

Group 2 N= 36

Waiting-list control. Mean dose 14.5

FUNDING: Yes. Quality assessed: Bias: Selection-unclear; Performance-unclear; Attrition-Low; Detection-Unclear

forward)

Blindness: No mention

Duration (days): Mean 175

Followup: 8 months (not reportable)

Setting: Recruited from GPs and anxiety call centre, Germany

Notes: RANDOMISATION: simple

Info on Screening Process: 576 screened, 504 excluded as did not meet criteria

Exclusions: had psychiatric comorbidity, a score of less than 18 on HAM-A, serious somatic illness, younger than 18 or older than 65, intake of sedatives during last 3 months, psychotropic treatment for the duration of the therapy, other psychotherapy during last 2 years or insufficient language competency.

Baseline: No significant differences

Notes: Taken at baseline, 25 weeks and 8 month follow-up, DROP OUT: CBT = 5/36 (13.9%), WLC = 4/36 (11.1%). Therapy delivered by professionals in private practice for 11 years.

Results from this paper:

Statistically significant difference in favour of CBT which was sustained at follow-up.

MOHLMAN2003A

Study Type: RCT

n= 27

Study Description: Examined the efficacy of CBT in comparison with waiting list in late-life GAD.

Age: Mean 66 Range 60-74

Sex: 8 males 19 females

Type of Analysis: Completers

Diagnosis:

100% Generalised Anxiety Disorder (GAD) by DSM-IV

Blindness: Open

Duration (days): Mean 91

Followup: 6 months (not reportable)

Setting: Recruited via radio and print advertisements: New York, US

Notes: RANDOMISATION: no details provided

Info on Screening Process: 81 screened, 54 excluded as did not meet DSM-IV criteria for principal diagnosis of GAD.

Exclusions: a) current use of anti-anxiety medications; b) active suicidality over previous 6 month; c) acute current MDD episode; d) lifetime psychotic symptoms; e) organic brain disease; f) current use of medications that can cause anxiety-like symptoms; g) raw scores of 131 or below on the Dementia Rating Scale.

Notes: Those who reported frequent, uncontrollable worries and other GAD symptoms were scheduled for a comprehensive consultation

Baseline: There was a significant difference between groups on gender composition, with a higher proportion of women in the CBT group (86 vs. 54%). Comorbid psychiatric problems: WLC = 1.08 (1.04), CBT = 0.67 (0.71)

Data Used

Free of comorbid psychiatric diagnosis

Clinician-rated GAD severity

Remission- SCID (free of GAD)

SCL anxiety factor

Trait worry (PSWQ + STAI-TRAIT)

Responders (20% reduction in 75% of all scales)

SCL-90 General Severity index

Beck Anxiety Inventory

Beck Depression Inventory

Notes: Taken at baseline, 13-week and 6-month follow-up. DROP OUT: CBT = 3/14, WLC = 3/13. Therapy delivered by doctoral clinicians with CBT training.

Group 1 N= 13

Waiting-list control. Mean dose 13 weeks - contacted every month by phone. Any participants who experienced a worsening of symptoms was referred to a clinic in the community for immediate treatment (n= 1). All invited to begin CBT after waiting period.

Group 2 N= 14

CBT. Mean dose 13 sessions (each 50 minutes) - consisted of psychoeducation about GAD and mood, muscle relaxation, cognitive restructuring, worry prevention, problem-solving, daily exercises, homework etc

FUNDING: Supported in part by National Institute of Mental Health grant MH01397 & R01MH53582, Q.A.: Bias: Selection-Unclear; Performance-Unclear; Attrition-High; Detection-Unclear

Results from this paper:

CBT only marginal effective against WLC.might be due to the lack of statistical power

ÖST2000

Study Type: RCT

n= 36

Study Description: Investigates the efficacy of applied relaxation and CT in the treatment of GAD.

Age: Mean 40 Range 22-60

Sex: 10 males 26 females

Type of Analysis: Completers

Diagnosis:

100% Generalised Anxiety Disorder (GAD) by DSM-IV

Blindness: No mention

Duration (days): Mean 84

Followup: 1 year (extracted)

Setting: Recruited by media: Sweden

Notes: RANDOMISATION: no details provided

Info on Screening Process: 68 screened, 32 excluded since did not have GAD as primary diagnosis or began drugs while waiting for first session, becoming too depressed to take part, lived too far away.

Exclusions: Did not meet criteria for GAD, duration of less than 1 year, outside age range of 18-60, had a primary diagnosis of depression, had other psychiatric illness in need of treatment, GAD not primary disorder, if on prescribed drugs for GAD dosage was not kept constant over 3 months before commencement of treatment or unwilling to keep constant for duration of study, unwilling to take part for whole duration of study.

Baseline: No significant differences

Data Used

Assessor Severity Scale

HAM-A

HDRS (Hamilton depression rating scale)

STAI-T

STAI-S

Penn State Worry Questionnaire

Cognitive-Somatic Anxiety Questionnaire

Beck Anxiety Inventory

Beck Depression Inventory

Response-Clinical improvement (HAM-A+/- 2SD)

Group 1 N= 16

Applied relaxation. Mean dose 12 - Progressive relaxation with tension release of muscles

Group 2 N= 20

Cognitive therapy. Mean dose 12 - Manualised therapy involving 6 steps across six sessions

FUNDING: Swedish Medical Research Council, Quality assessed: low- unknown risk of bias

Notes: Taken at baseline, 12 weeks and 1 year follow-up. DROP-OUT: AR= 2/16 (12%), CT = 1/20 (5%). Therapy delivered by therapists with more than 8 years' experience. Bias: Selection-unclear; Performance-unclear; Attrition-unclear; Detection-low

Results from this paper:

No statistical significance between CBT or AR.

REZVAN2008

Study Type: RCT n= 36
 Study Description: Compared the effectiveness of CBT with the combination of CBT & interpersonal therapy on decreasing the excessiveness of pathological worry in GAD.
 Blindness: Open
 Duration (days): Mean 56
 Followup: 1 year (extracted)
 Setting: Self-recruited from university counselling centre, Iran.
 Notes: RANDOMISATION: No details provided
 Info on Screening Process: 120 people screened; 84 excluded due to not meeting the cut-off of the GAD-Q, did not meet criteria according to DSM-IV, GAD less severe than other comorbid diagnoses

Age: Mean 20
 Sex: all females
 Diagnosis:
 100% Generalised Anxiety Disorder (GAD) by DSM-IV
 Exclusions: a) did not meet cut off score of GAD-Q (5.7); b) did not meet GAD criteria after a diagnostic interview using DSM-IV; c) GAD not as severe as other comorbid diagnoses.
 Baseline: All conditions scored similarly on PSWQ and Oxford Happiness Scale.

Data Used

Penn State Worry Questionnaire
 Oxford Happiness Scale
 Notes: Taken at baseline, 8-week and 1-year follow-up. Did not report if any drop outs. No remission/response data. Follow-up data extracted at 1 year. No mention of therapist competence.

Group 1 N= 12

Waiting-list control. Mean dose 8 weeks

Group 2 N= 12

CBT + Interpersonal therapy. Mean dose 8 sessions (each 90 minutes) - In addition to the interventions that CBT group received, some more instructions and techniques were applied in CBT & IPT group

Group 3 N= 12

CBT. Mean dose 8 sessions (each 90 minutes) - 8 sessions of CBT. Included stimulus control methods, breathing and relaxation techniques, desensitisation and applied relaxation.

FUNDING:none declared, Quality Assessed: Selection-unclear; Performance-unclear; Attrition-unclear; Detection-unclear

Results from this paper:

CBT statistically significantly better than WLC.

But no statistically significant difference between CBT and CBT+IPT

ROEMER2008

Study Type: RCT n= 31
 Study Description: Examined the efficacy of an acceptance-based behaviour therapy aimed at increasing acceptance of internal experiences for those with GAD.
 Type of Analysis: ITT
 Blindness: Unclear
 Duration (days): Mean 98
 Followup: 9 months (not reportable)
 Setting: Unknown, Boston, US
 Notes: RANDOMISATION: coin flip, randomised block fashion
 Info on Screening Process: 36 screened; 5 excluded (3 declined, 1 missed informed consent meeting, 1 away during study period)

Age: Mean 34 Range 18-
 Sex: 9 males 22 females
 Diagnosis:
 100% Generalised Anxiety Disorder (GAD) by DSM-IV
 Exclusions: a) no primary diagnosis of GAD; b) reported current suicidal intent; c) met criteria for current bipolar disorder, substance dependence, or psychotic disorders; d) less than 18 years old
 Notes: a full 6 months of GAD symptoms without MDD was not required for inclusion.
 Baseline: Conditions did not differ significantly on demographic variables. BDI: Treatment = 17.53 (1.94), control = 19.69 (1.83), QOLI: Treatment = 0.83 (0.62), Control = 0.27 (0.48).

Data Used

ADIS-IV
 Penn State Worry Questionnaire
 Remission (not meeting diagnosis according to SCID
 Response (20% improvement on 3/4 outcome measures)
 Beck Depression Inventory
 QoL
 Depression Anxiety Stress Scales
 Notes: Taken at baseline, 14-week and 3 & 9-month follow-up. DROP OUT: Treatment grp = 2/15, WLC = 4/16. Follow-up data was not extractable as did not report for each group separately. Therapy delivered by doctoral students.

Group 1 N= 16

Waiting-list control. Mean dose 16 weeks - Completed a post-assessment at least 14 weeks after their informed consent meeting and were offered the full treatment, after which they were assessed

Group 2 N= 15

Acceptance-based behaviour therapy. Mean dose 16 sessions (each 60-90 minutes) - Taught a variety of mindfulness practices and were encouraged to engage in both formal and informal mindfulness practice every day.

FUNDING: National Institute of Mental Health Grant No. MH63208, Quality assessed: Bias: Selection-Low; Performance-Unclear; Attrition-Low; Detection-unclear

Results from this paper: Statistically significant difference in favour of acceptance-based behaviour therapy

STANLEY1996

Study Type: RCT

Study Description: Compared the efficacy of CBT and nondirective, supportive psychotherapy for older adults with GAD

Type of Analysis: Completers

Blindness: No mention

Duration (days): Mean 98

Followup: 1 & 6 months (extracted)

Setting: Recruited via community programmes for older adults, church groups and media: Texas

Notes: RANDOMISATION: No details

Info on Screening Process: 17% of potential participants excluded due to the use of psychotropic medicine

n= 48

Age: Mean 68 Range 55-81

Sex: 14 males 34 females

Diagnosis:
100% Generalised Anxiety Disorder (GAD) by DSM-III-R

Exclusions: Primary diagnosis of an alternate AXIS I disorder, current involvement in psychotherapy, serious medical conditions, alcohol or substance misuse within the previous 6 months, psychotic symptoms, or evidence of cognitive impairment according to a score of 22/lower on Mini-Mental State Exam

Baseline: No significant differences

Data Used

HAM-A
HDRS (Hamilton depression rating scale)
STAI-T
Clinician-rated GAD severity
Fear Questionnaire
Response (20% improvement on 3/4 outcome measures)
Beck Depression Inventory

Notes: Taken at baseline, 14 weeks and 6 months. DROP OUTS: SP = 7/20, CBT = 8/26. Follow-up data extracted at 6 months. Therapy delivered by therapists with 2 years' CBT experience, the other experienced in non-directive approach.

Group 1 N= 20

Non-directive therapy. Mean dose 14 sessions (each 90 minutes) - Focused on nondirective group discussion of anxiety symptoms and experiences

Group 2 N= 26

CBT. Mean dose 14 sessions (each 90 minutes) - Included 3 major components: progressive deep muscle relaxation (sessions 1-5), CT (sessions 6-10), and exposure treatment (session 11-14).

FUNDING: Texas Higher Education Coordinating Board, Quality assessed: Selection-unclear; Performance-unclear; Attrition-unclear; Detection-high

Results from this paper:

No statistically significant difference between CBT and NDT for older adults

STANLEY2003B

Study Type: RCT

Study Description: Addressed the efficacy of CBT, relative to WLC in sample of 85 older adults with GAD

Type of Analysis: Completer

Blindness: No mention

Duration (days): Mean 105

Followup: 3, 6, & 12 months (not reportable)

Setting: Recruited primarily via media, Texas, US

Notes: RANDOMISATION: No details

Info on Screening Process: Not stated how many screened or excluded: included only if principal or co-principal diagnosis was GAD with at least a moderate level of severity

n= 80

Age: Mean 66 Range 60-100

Sex: 20 males 60 females

Diagnosis:
100% Generalised Anxiety Disorder (GAD) by DSM-IV

Exclusions: Current involvement in psychotherapy, alcohol or substance misuse within the previous year, serious medical conditions that may have accounted for anxiety symptoms or may have interfered with treatment, psychotic symptoms and evidence of cognitive impairment. Also excluded if principal or co-principal diagnosis was not GAD with less than a moderate level of severity or if they failed to discontinue anti-anxiety or antidepressant medication at least 2 weeks prior to initial screening.

Baseline: Groups differed only with regard to gender, with more men and fewer women assigned to WLC than CBT.

Data Used

HAM-A
HDRS (Hamilton depression rating scale)
STAI-T
Clinician-rated GAD severity
Penn State Worry Questionnaire
Remission (not meeting diagnosis according to SCID
Response (20% improvement on 3/4 outcome measures)
Beck Depression Inventory
QoL

Notes: Taken at baseline, 15-week and 3-, 6 & 12- month follow-up (however follow-up not extractable as not given for each group separately). Drop outs (not extractable but 14 in total). Delivered by post-doctoral psychologists, & advanced psychology graduates.

Group 1 N= 41

Waiting-list control. Mean dose 15 weeks - Involved weekly telephone calls to assess symptom severity, to determine the potential need for immediate care and to maintain low attrition rates. Minimum support provided, but no active intervention was administered.

Group 2 N= 39

CBT. Mean dose 15 sessions (each 90 minutes) - Adapted and standardised for use with the elderly in an earlier treatment study. Included education and awareness training, deep muscle relaxation, cognitive therapy and graduated exposure. Homework assignments were completed on a weekly basis.

FUNDING: Supported by a grant by National Institute of Mental Health, Quality assessed: Selection-unclear; Performance-unclear; Attrition-unclear; Detection-low

Results from this paper:

CBT statistically significantly better than WLC. Effects maintained over 1 year follow up

STANLEY2009

Study Type: RCT

Study Description: Examined the impact of CBT relative to enhanced usual care in older adults with GAD in primary care.

Type of Analysis: Completers

n= 134

Age: Mean 70 Range 60-100

Sex: 29 males 105 females

Diagnosis:
100% Generalised Anxiety Disorder (GAD) by

Data Used

SF-12 (MCS)
BDI-II
Penn State Worry Questionnaire
Generalized anxiety disorder severity scale

Group 1 N= 64

Treatment as usual. Mean dose 6 sessions - Enhanced usual care: telephoned biweekly during first 3 months to provide support and ensure patient safety. Calls lasted 15 minutes.

FUNDING: supported by National Institute of Health, Quality assessed: Selection-unclear; Performance-unclear; Attrition-unclear; Detection-low

Blindness: Open	DSM-IV	SIGH-A (anxiety)	Group 2 N= 70
Duration (days): Mean 92		Response (2 point change on GAD severity scale)	CBT. Mean dose 10 sessions - included education and awareness, motivational interviewing, relaxation training, cognitive therapy, exposure, problem-solving skills training and behavioural sleep management.
Followup: 6, 9, 12, &15 months (extracted)	Exclusions: No principal or co-principal diagnosis of GAD, Mini-Mental State exam score of less than 24, active substance misuse, psychosis, or bipolar disorder, or if younger than 60.	SF-12 (PCS)- Quality of life	
Setting: Primary care: Texas, US.		Notes: Taken at baseline, 3, 6, 9, 12-month follow up. DROP OUTS: CBT = 4/70, TAU = 14/64. Extracted follow-up at 15 months. Delivered by 5 therapists (3 had a MSc, 1 predoctoral, 1 post-bachelor) with 2-5 years of experience).	
Notes: RANDOMISATION: 1: 1 ratio within blocks of 10 to receive CBT or TAU, random number generator	Baseline: PSWQ: CBT = 53.3 (10.57), TAU = 57.6 (10.91)		
Info on Screening Process: 968 screened, 834 excluded due to following reasons: could not be contacted, reported no anxiety, ineligible, negative responses to screening questions on the primary care evaluation of mental disorders, lack of interest, logistic problems			

Results from this paper:
 CBT was statistically significantly better than enhanced usual care on depression, worry outcomes but not on clinician rated anxiety outcome

WELLS2010

Study Type: RCT	n= 20	Data Used	Group 1 N= 10	FUNDING: none declared. Quality assessed: Selection bias = low risk, performance bias = unclear risk, attrition bias = low risk, detection bias = unclear risk.
Study Description: Compared meta-cognitive therapy to applied relaxation in 20 outpatients with GAD.	Age: Mean 49 Range 25-78	STAI-T	Meta-cognitive therapy. Mean dose 8-12 weekly sessions - The therapist focused on beliefs about the uncontrollability of worry & used verbal strategies & behavioural experiments to begin to weaken these beliefs. Patients were instructed in the use of detached-mindfulness in response to intrusive thoughts.	
Type of Analysis: Completor	Sex: 8 males 12 females	Remission- SCID (free of GAD)		
Blindness: No mention	Diagnosis:	Penn State Worry Questionnaire	Group 2 N= 10	Applied relaxation. Mean dose 8-12 weekly sessions - Apply a relaxation response that could reduce anxious bodily symptoms & worry. 6 stages of relaxation: progressive, release-only, cue-controlled, differential, rapid & application training. Frequent practice was emphasised.
Duration (days): Mean 84	100% Generalised Anxiety Disorder (GAD) by DSM-IV-TR	Beck Anxiety Inventory		
Followup: 6 & 12 months' follow-up (both extractable)	Exclusions: a) did not have excessive worry, difficulty controlling worry, a minimum of 2 worry topics or were not troubled by excessive & uncontrollable worries more days than not; b) did not have a DSM-IV diagnosis of GAD; were not medication free or stable on medication for at least 12 weeks; suffered from alcohol or substance misuse; were not willing to accept random allocation; not fluent in written & spoken English; were younger than 18; had previous CBT treatment for GAD; or evidence of a psychotic or organic illness	Beck Depression Inventory		
Setting: Outpatients; UK. Recruitment: drawn from 2 clinical psychology NHS waiting lists comprised of individuals referred mostly by GPs or psychiatrists.	Notes: The duration of GAD ranged from 6 months to lifelong. The majority of cases (60%) reported a duration of greater than 5 years. 65% had an additional diagnosis.	Meta-cognition Questionnaire		
Notes: RANDOMISATION: Individuals unrelated to the trial were asked to draw sealed envelopes from a box.	Baseline: 2 patients were from an older age grp (76 & 78) & were yoked at randomisation. There were equal proportions of men & women in each group. MCQ-Neg was higher in the AR group (53.9 (4.2) vs. 45.7 (10.4)). Although the other measures were non-significant, examination of means show that AR group had higher scores on all measures suggesting they may be more severe.	Notes: Assessed before treatment, post-treatment (12 weeks), 6 & 12-month follow-up. DROP OUTS: MCT = 0/10, AR = 1/10 at 6-month follow up. RCI = reliable change index (Jacobson criteria)		
Info on Screening Process: 61 patients were identified & mailed the questionnaire & based on responses 33 were invited to the screening interview. 24 patients attended & were found to meet the inclusion criteria. Of these 24, 4 were excluded (medical diagnosis/regime & withdrew).				

Results from this paper:
 At post-treatment and at both follow-up points meta-cognitive therapy was superior to applied relaxation. Anxiety, depression and remission outcomes were significantly better for meta-cognitive therapy.

WESTRA2009

Study Type: RCT	n= 76	Data Used	Group 1 N= 44	FUNDING: National Institute of Mental Health R34-MH072615 and a New Investigator award from the Canadian Institute of Health Research. Quality assessed: Unclear risk of bias for selection, performance & attrition. Low risk of bias for detection.
Study Description: Examined whether adding motivational interviewing as a pre-treatment to CBT would improve outcomes	Age: Mean 42 Range 16-	ADIS-IV	Motivational interviewing + CBT. Mean dose MI = 4 weeks, CBT = 8 weeks - Received 4 individual 50-minute weekly MI sessions which followed the principles of Miller (2002) but with a focus on ambivalence and motivation to change worry & related problems. This was followed by 8 weeks of CBT (described above).	
Type of Analysis: ITT	Sex: 25 males 51 females	Sheehan Disability Scale (SDS)		
Blindness: Single blind	Diagnosis:	Penn State Worry Questionnaire		
Duration (days): Mean 42 Range 28-56	100% Generalised Anxiety Disorder (GAD) by DSM-IV	CGI		
Followup: 6 months (extractable)	Exclusions: A) did not meet the DMS-IV criteria for GAD; B) were not at least 16 years of age; C) received a GAD severity rating of less than 4 on the ADIS-IV	Meta-cognition Questionnaire		
Setting: Participants were recruited from		Depression Anxiety Stress Scales		
		Data Not Used		
		Clinical significant change - Not standardised		

community advertisements in Toronto which targeted those who worried excessively. No payment given.

Notes: RANDOMISATION: were randomly assigned to treatment condition by the research co-ordinator using a random numbers table.

Info on Screening Process: 650 screened, 543 excluded as did not meet inclusion criteria (n = 315) or refused to participate (n = 248)

Baseline: Baseline ADIS score:
MI-CBT 6.03 (0.97)
CBT 6.03 (0.75)

Notes: DROP OUTS: MI + CBT = 6/44 (2 misdiagnosed), CBT = 6/46 (2 primary diagnosis shifted to MDD), WLC = same as CBT group.

Group 2 N= 46

CBT. Mean dose 6 weekly 2-hour sessions, followed by 2 1-hr sessions - Received CBT only (no pre-treatment of MI provided). Followed manual developed by Borkovec and colleagues involving self-monitoring, applied relaxation, cognitive therapy, & exposure to worry. Total of 14 hours of CBT provided.

Group 3 N= 46

Waiting-list control. Mean dose 4 weeks - The CBT-only group were put on a waiting list for 4 weeks whilst awaiting CBT treatment and thus acted as a waiting list control comparison

Results from this paper:

There was no statistically significant difference found between participants who received 4 weeks of motivational interviewing and those who did not on any outcome measures.

There was no statistical significant difference between the MI plus CBT group and CBT-only group on anxiety and depression outcomes at post-treatment, 6 months or 12 months' follow-up. The only statistically significant finding was in improvement of worry score at post-treatment favouring the MI plus CBT group.

Conclusions: As these findings are based on a single study, it is difficult to conclude the effect of motivational interviewing as a pre-treatment to CBT.

WETHERELL2003

Study Type: RCT
Study Description: Examined the effectiveness of CBT, discussion groups or a waiting period for older adults with GAD.

Type of Analysis: Completers

Blindness: No mention

Duration (days): Mean 84

Followup: 6 months (not reportable)

Setting: Recruited through hospital-affiliated health education programmes, senior centres, and the media: California, US (advertised as Worry reduction class)

Notes: RANDOMISATION: No details

Info on Screening Process: 498 screened, 423 excluded due to refusing to provide baseline data or not meeting diagnostic criteria

n= 75

Age: Mean 67 Range 55-100

Sex: 15 males 60 females

Diagnosis:
100% Generalised Anxiety Disorder (GAD) by DSM-IV

Exclusions: a) primary diagnosis other than GAD; b) aged under 55; c) history of mania or psychosis, cognitive impairment; d) current participation in psychotherapy, alcohol or other substance misuse within 6 months; e) commencement of psychotropic medication within 2 months, and lack of a recent medical check-up to rule out alternative causes of anxiety symptoms.

Notes: Individuals with disorders that mimic anxiety were also included, provided that they were under the care of a physician and disorder was medically controlled. Average duration: 29.4 (28.7)

Baseline: GAD severity rating: CBT =4.9 (0.8), DG = 5.1 (1.1), WL = 5.1 (0.9)

Data Used

HDRS (Hamilton depression rating scale)

ADIS-IV

Penn State Worry Questionnaire

Remission (not meeting diagnosis according to SCID

Beck Anxiety Inventory

Beck Depression Inventory

QoL

HAM-A

Data Not Used

Response (20% improvement on 3/4 outcome measures) - no data

High end state functioning - no data

Notes: Taken at baseline, 12-week and 6-month follow-up. DROP OUT: CBT = 8/26, DG = 8/26, WL = 2/23. (medication, therapist, comorbidity->attrition bias). Therapy delivered by advanced doctoral students in clinical psychology.

Group 1 N= 23

Waiting-list control. Mean dose 12

Group 2 N= 26

CBT. Mean dose 12 sessions - Met for 90 minutes weekly in groups of 4-6 adults with a leader. Consisted of relaxation training, cognitive restructuring, and worry exposure based on a manual. Also incorporated 30 minutes per day homework exercises.

Group 3 N= 26

Discussion group. Mean dose 12 sessions - Designed to be comparable to CBT in level of structure, with participants required to adhere to an agenda during sessions and with homework assignments of similar duration. Series of 12 discussions focused on topics known to be worry-provoking.

FUNDING: National Institute for Mental Health Grant, Quality Assessed: Selection B-unclear; Performance B-unclear; Attrition B-high; Detection B-Low

Results from this paper:

Moderate to large effect on anxiety, depression, worry
Improved remission & response rates compared to WLC
No difference between CBT and discussion group.

Conclusions: Note the high attrition bias (those with history of psychotropic medication, those NOT taught by principal investigator had a higher attrition rate)

Characteristics of Excluded Studies

Reference ID	Reason for Exclusion
BAKSHANI2007	Participants aged under 18
BARLOW1984	50% of sample had anxiety disorders other than GAD as a primary diagnosis

BARROWCLOUGH2001	81% of the sample had anxiety disorders other than GAD as a primary diagnosis
BLOWERS1987	DSM-III criteria
BOND2002A	Combination therapy
BONNE2003	Not a psychological intervention
BORKOVEC1987	DSM-III used
BORKOVEC1988	40% of sample had anxiety disorders other than GAD as a primary diagnosis
BOYER2004	Pharmacological study
BUTLER1987	Diagnostic criteria
BUTLER1988	Comorbidity and diagnostic criteria
CONRAD2008	Outcome measures not valid
DEN-BOER2007	GAD not primary diagnosis (only 6% had GAD)
DURHAM1987	Aged under 18
EVANS2008	Not RCT
FAVA2005	n < 10 in each group
FEDERICA2010	n = 4 in each group
GARCIA2004	Not GAD specific: related to all anxiety disorders
GATHI1986	Not given a primary diagnosis of GAD
GOSSELIN2006	Outside the scope: discontinuation of medication with psychological treatment
JANNOUN1982	Diagnostic criteria
KIM2006A	Pharmacological data
KITCHINER2006	<80% of sample had anxiety disorders other than GAD as primary diagnosis
LAVALLEE1993	DSM-III diagnosis
LINDEN2002	In german
LINDSAY1987B	DSM-III diagnosis
MOHLMAN2003B	N<10
NEWMAN2008	Non-RCT
NORTON2005	57% of sample had anxiety disorders other than GAD as primary diagnosis
RUINI2006	Outcome measures not viable. Also in Italian.
STANLEY2003A	Only 6 participants in each condition
SVARTBERG	85% of sample had anxiety disorders other than GAD as a primary diagnosis
VAN-BOEIJEN2005	GAD not primary diagnosis
WELLS2006	Non-RCT
WHITE1992	Non-RCT
WOODWARD1980	DSM-III diagnosis
YONG2009	Non-RCT

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Characteristics Table for The Clinical Question: In the treatment of GAD, what are the risks and benefits associated with the following combination therapies compared with other interventions (including treatment as usual)?

Comparisons Included in this Clinical Question

Buspirone + anxiety management training vs. buspirone + non-directive therapy
BOND2002B

Buspirone + anxiety management training vs. placebo + anxiety management training
BOND2002B

Buspirone + anxiety management training vs. placebo + non directive therapy
BOND2002B

Buspirone + non-directive therapy vs. placebo + anxiety management training
BOND2002B

Buspirone + non-directive therapy vs. placebo + non-directive therapy
BOND2002B

Placebo + anxiety management training vs. placebo + non directive therapy
BOND2002B

Characteristics of Included Studies

Methods	Participants	Outcomes	Interventions	Notes
<p>BOND2002B</p> <p>Study Type: RCT</p> <p>Study Description: Examined the effectiveness of a short course of psychological therapy (AMT or non-directive therapy) combined with buspirone or placebo.</p> <p>Type of Analysis: Completers</p> <p>Blindness: No mention</p> <p>Duration (days): Mean 7</p> <p>Followup: no mention</p> <p>Setting: Recruited patients from anxiety disorders clinic at Maudsley Hospital, London, UK</p> <p>Notes: RANDOMISATION: no details</p> <p>Info on Screening Process: No details</p>	<p>n= 60</p> <p>Age: Mean 34 Range 18-65</p> <p>Sex: 17 males 27 females</p> <p>Diagnosis: 100% Generalised Anxiety Disorder (GAD) by DSM-III-R</p> <p>Exclusions: Any other current psychiatric comorbidity as a primary diagnosis, the use of any psychotropic drug in the past 6 weeks, or benzodiazepines in the past 6 months</p> <p>Baseline: HADS-anxiety: BUS + AMT = 28.8 (4.8), BUS + NDT = 29 (4.5), PL + AMT = 27.7 (4.3), PL + NDT = 28.1 (2.7)</p>	<p>Data Used</p> <p>Hospital Anxiety and Depression Scale (depression)</p> <p>HAM-A</p> <p>Hospital Anxiety and Depression Scale (anxiety)</p> <p>Notes: Outcomes are based on completer analysis. In total, 16 dropped out, no details for each group. Taken at baseline, 4 & 8 weeks.</p>	<p>Group 1 N= 14</p> <p>Placebo + non-directive therapy. Mean dose 7 sessions (45 minutes) - Placebo given at flexible dosage starting at 3 capsules a day in first week. NDT allowed clients to talk freely with feelings acknowledged, reflecting back content, adopting a non-judgmental stance.</p> <p>Group 2 N= 12</p> <p>Placebo + AMT. Mean dose 7 sessions (45 minutes) - Placebo given at flexible dosage starting at 3 capsules a day in first week. AMT was designed to be educational & interactive therapy.</p> <p>Group 3 N= 7</p> <p>Buspirone + non-directive therapy. Mean dose 5mg + 7 sessions (45 minutes) - Buspirone (5mg) given in flexible dosage starting at three capsules a day in first week. NDT allowed clients to talk freely with feelings acknowledged, reflecting back content, adopting a non-judgmental stance.</p> <p>Group 4 N= 11</p> <p>Buspirone + AMT. Mean dose 5 mg + 7 sessions (45 minutes) - Buspirone (5mg) was given in flexible dosage, starting at 3 capsules a day during 1st week but allowing for an increase of up to 6 capsules thereafter. AMT was designed to be educational & interactive therapy.</p>	<p>Funding = supported by the UK medical research council. Quality assessed: Selection bias: unclear risk of bias, performance bias: high risk, attrition bias: unclear risk, detection bias: low risk</p>

References of Included Studies

BOND2002B (Published Data Only)

Bond, A.J., Wingrove, J., Curran, H.V., et al. (2002) Treatment of generalised anxiety disorder with a short course of psychological therapy, combined with buspirone or placebo. Journal of Affective Disorders, 72, 267-271.

