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)?

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

<table>
<thead>
<tr>
<th>Comparisons Included in this Clinical Question</th>
<th>Study References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Applied relaxation versus CT + applied relaxation</td>
<td>BARLOW1992, BORKOVEC2002</td>
</tr>
<tr>
<td>Applied relaxation vs wait list control</td>
<td>BARLOW1992, DUGAS2009A</td>
</tr>
<tr>
<td>Brief dynamic therapy versus supportive therapy</td>
<td>CRITS-CHRISTOPH2005</td>
</tr>
<tr>
<td>CBT versus WLC</td>
<td>DUGAS2009A, LADOUCER1999, LINDEN2005, MOHLMAN2003A,</td>
</tr>
<tr>
<td></td>
<td>STANLEY2003B, WETHERELL2003</td>
</tr>
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<td></td>
<td>BORKOVEC2002</td>
</tr>
<tr>
<td>Integrative relaxation training vs WLC</td>
<td>JANBOZORG12009, ROEMER2008, DURHAM1994, BORKOVEC2002</td>
</tr>
<tr>
<td>Relaxation versus CT</td>
<td>BARLOW1992, BORKOVEC2002</td>
</tr>
<tr>
<td></td>
<td>BORKOVEC2002</td>
</tr>
</tbody>
</table>
## ARNTZ2003

**Methods**
- Study Type: RCT
- Study Description: Comparison of cognitive therapy vs. applied relaxation for long term and immediate effects in sample of 45 GAD patients representative of population.
- Type of Analysis: Completer analysis
- Blindness: No mention

**Participants**
- n= 45
- Age: Mean 36 Range 20-60
- Sex: 15 males 30 females

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

**Exclusions:**
- i) 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.

**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)

**Baseline:**
- STAI-trait scale: CT = 57.5 (8.3), AR = 53.7 (10.2); AR group had lower education level (compared to CT)

**Interventions**
- 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.
- 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.

**Notes:**
- FUNDING: None declared.

## BARLOW1992

**Methods**
- Study Type: RCT
- Study Description: Relaxation, CT or their combination were compared to WLC for those with GAD
- Type of Analysis: Completers
- Blindness: No mention

**Participants**
- n= 65
- Age: Mean 40 Range 18-65
- Sex: no information

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

**Exclusions:**
- a) had begun benzodiazepines or beta-blockers within 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

**Baseline:**
- STAI-trait scale: CT = 57.5 (8.3), AR = 53.7 (10.2); AR group had lower education level (compared to CT)

**Interventions**
- **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.
- **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.

**Notes:**
- FUNDING: National Institute of Mental Health. Quality assessed: Selection; unclear; Performance: unclear; Attrition: high; Detection: low. Delivered by doctoral students or psychologists.

## 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  
*Study Description:* Explored the long-term effects of affect-focused body psychotherapy for patients with GAD.  
*Type of Analysis:* Intention to treat  
*Blindness:* Open  
*Followup:* 2 years (extracted)  
*Setting:* Recruited from 6 outpatient clinics: Sweden  
*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  

**Results from this paper:**  
No statistically significant difference between the two treatments.

**Data Used**

- **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.

**BORKOVEC1993**

*Study Type:* RCT  
*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  
*Type of Analysis:* Completers  
*Blindness:* No mention  
*Followup:* 6 & 12 - months (extracted)  
*Setting:* Recruited from agencies and advertisements: Pennsylvania, US.  
*Notes:* RANDOMISATION: Assignment to therapist was random within restrictions of availability and caseload.  
*Info on Screening Process:* 508 screened; 442 excluded for not meeting DSM-III-R criteria  

**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, GAD, and that reflective listening is just non-specific factor of treatment.

**Data Used**

- **Group 1**  
  - n= 69  
  - 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.

**BORKOVEC2002**

*Study Type:* RCT  
*Study Description:* Comparison of applied relaxation with self-control desensitisation & cognitive therapy with a combination of these

**Data Used**

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

**FUNDING:** supported in part by National Institute of Mental Health Research Grant. Quality assessed: Bias-Selection-Unclear; Performance-Unclear; Attrition-High; Detection-Low
### 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  
**Followup:** 6 months (extracted)  
**Setting:** Referrals from psychiatric hospital sources & general practice; Oxford, UK  
**Notes:** RANDOMISATION: No details provided  

### Info on Screening Process:
- 459 screened; 383 admitted  
- 383 responding to media advertisement: Pennsylvania, US  
- 161 screened, 104 took antidepressant medication, or if they had received 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.  
- 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 12.81 years (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)  

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

### 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  
**Followup:** 6, 12, & 24 - months (all extracted)  
**Setting:** 5 referred by mental health practitioners, remaining responded to media advertisement: Pennsylvania, US  
**Notes:** RANDOMISATION: No details provided  

### Info on Screening Process:
- 383 excluded by phone screening/diagnostic interviews for not meeting admission criteria  
- 383 not meeting admission criteria  
- 31 interviews for not meeting admission criteria  
- 31 met admission criteria  

### Results from this paper:
- CBT significantly better than waiting list control  
- CBT significantly better than waiting list control  

### Data Used:
- Beck Depression Inventory  
- Beck Anxiety Inventory  
- STAI-trait  
- Hospital Anxiety and Depression Scale  
- Penn State Worry Questionnaire  
- DSM-III-R  
- DSM-IV  

### Data Not Used:
- Beck Depression Inventory  
- Beck Anxiety Inventory  
- STAI-trait  
- Hospital Anxiety and Depression Scale  
- Penn State Worry Questionnaire  
- DSM-III-R  
- DSM-IV  

### 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.  

### 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= 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  

### Funding:
- Funded in part by National Institute of Mental Health Grants (R21-MH56018 & P3D-MH45178).  

### Quality assessed:
- Bias: selection-unclear; performance-unclear; attrition-unclear; detection-low  

### Detection bias = unclear risk, attrition bias = low risk, performance bias = unclear risk
Diagnosis: N= 27

(2), or a medical problem required immediate
least 2 points less on Clinician’s Severity Rating
the severity of comorbid disorder was not at
diagnosed (5) or was not primary diagnosis (5),

Setting: Recruited from outpatient referral line,
adverts & professionals referrals: Pennsylvania
Notes: RANDOMISATION: No details provided
(note this is a pilot RCT)
Info on Screening Process: No details provided

Notes: Random allocation sequence used and
Setting: Referred by GPs, recruited from
advertisements in Canada
Type of Analysis: Intention to treat
Blindness: Single blind
Type of Analysis: Intention to treat
Age: Mean 39 Range 18-64
Sex: 15 males 37 females

Notes: Taken at 12 weeks, 6-,12- and 24-month
Pre and post (16 wks). No follow up. Delivered by
psychologists (with 5 year's experience) with

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

Results from this paper:
No statistically significant difference between the two treatments.

Results from this paper:
Effective against waiting list control and results maintained at 2 years (not extractable as WLC data not extractable)

Results from this paper:
Effective against waiting list control and results maintained at 2 years (not extractable as WLC data not extractable)

Results from this paper:
No statistically significant difference between the two treatments.

n = 52
Age: Mean 41
Sex: 15 males 37 females

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: 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)

n = 65
Age: Mean 39 Range 18-64
Sex: 22 males 43 females

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

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) & hypocondriasis (1), 55.4%

Notes: DROP OUTS: psychodynamic – 1/15,
Supportive therapy = 2/16. Outcomes taken at
pre and post (16 wks). No follow up. Delivered by
 phosph & 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.
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)

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
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
Type of Analysis: Completers
Blindness: No mention
Duration (days): Mean 98 Range 56-140
Followup: 6 & 12 months (extracted)
Setting: Referred outpatients by GPs & psychiatrists. Dundee, UK
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.

DURHAM2004

Study Type: RCT
Study Description: Examined whether standard CBT in comparison to high intensity CBT improved outcome for those with poor prognosis
Type of Analysis: Completers

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

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

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: Bias: Selection-unclear; Performance-unclear; Attrition-High; Detection-Low
**HOYER2009**

| Study Type: RCT |
| Study Description: Examined whether worry exposure alone is as efficacious as the empirically supported stand-alone treatment for GAD; applied relaxation over 15 sessions |
| Type of Analysis: ITT analysis |
| 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 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. |

**Data Used**

| STAI-trait |
| HAM-A |
| HDRS (Hamilton depression rating scale) |
| Penn State Worry Questionnaire |

**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.

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

**JANBOZORGI2009**

| Study Type: RCT |
| Study Description: Examined the effects of integrative relaxation training (relaxation, lifestyle, & spirituality) on emotional stability for people with GAD. |
| Type of Analysis: Completers |
| Duration (days): Mean 84 |
| Followup: No follow-up |
| Setting: Patients were referred from a counselling & psychotherapy centre; Iran. |
| Notes: RANDOMISATION: No information provided |

**Data Used**

| STAI-T |

**Results from this paper:**

Worry Exposure statistically significantly better than standard on clinician-rated anxiety, but not on self-rated scores.

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

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)

Results from this paper:
CBT statistically significantly better than WLC
Results maintained at 6, 12-months follow up (but not meta-analysable)

LEICHSERING2009

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.

Baseline: No baseline statistics provided for STAI-T

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 forward)

Note: 72 % had comorbid mental disorders.
Baseline: HAM-A: CBT = 25.90 (5.83), Short-term psychodynamic therapy = 25 (4.18)

Results from this paper:
CBT statistically significantly better than WLC
Results maintained at 6, 12-months follow up (but not meta-analysable)

Data Used
HAM-A
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

Data Not Used
STAI-trait

FUNDING: Medical Research Council of Canada. Quality assessed: bias: selection-unclear; performance-unclear; attrition-low; detection-unclear
MOHLMAN2003A

Study Type: RCT

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

Type of Analysis:Completers

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

Exclusions: Did not meet criteria for GAD, duration of less than 1 year, outside age range of 18-60, had a primary 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

Results from this paper:
Statistically significant difference in favour of CBT which was sustained at follow-up.

OST2000

Study Type: RCT

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

Type of Analysis:Completers

Blindness: No mention

Duration (days): Mean 84

Followup: 1 year (extracted)

Setting: Recruited by media: Sweden

Notes: RANDOMISATION: no details provided

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

Results from this paper:
CBT only marginal effective against WLC.might be due to the lack of statistical power
Results from this paper:
No statistical significance between CBT or AR.

**REZVAN2008**

Study Type: RCT

<table>
<thead>
<tr>
<th>Study Description: Compared the effectiveness of CBT with the combination of CBT &amp; interpersonal therapy on decreasing the excessiveness of pathological worry in GAD.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blindness: Open</td>
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<tr>
<td>Duration (days): Mean 56</td>
</tr>
<tr>
<td>Followup: 1 year (extracted)</td>
</tr>
<tr>
<td>Setting: Self-recruited from university counselling centre, Iran.</td>
</tr>
<tr>
<td>Notes: RANDOMISATION: No details provided</td>
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</table>

<table>
<thead>
<tr>
<th>Group</th>
<th>N= 12</th>
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</thead>
<tbody>
<tr>
<td>Waiting-list control. Mean dose 8 weeks</td>
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</tbody>
</table>

**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.

**Baseline: All conditions scored similarly on PSWQ and Oxford Happiness Scale.**

Results from this paper:
CBT statistically significantly better than WLC.
But no statistically significant difference between CBT and CBT+IPT

**ROEMER2008**

Study Type: RCT

<table>
<thead>
<tr>
<th>Study Description: Examined the efficacy of an acceptance-based behaviour therapy aimed at increasing acceptance of internal experiences for those with GAD.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of Analysis: ITT</td>
</tr>
<tr>
<td>Blindness: Unclear</td>
</tr>
<tr>
<td>Duration (days): Mean 98</td>
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<tr>
<td>Followup: 9 months (not reportable)</td>
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<tr>
<td>Setting: Unknown, Boston, US</td>
</tr>
<tr>
<td>Notes: RANDOMISATION: coin flip, randomised block fashion</td>
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</table>

<table>
<thead>
<tr>
<th>Group</th>
<th>N= 16</th>
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<tbody>
<tr>
<td>Waiting-list control. Mean dose 16 weeks</td>
<td></td>
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</tbody>
</table>

**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. DROPOUT: 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.

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 non-directive, 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

**Diagnosis:**

- N= 20
- N= 26
- N= 41
- N= 64

**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

**Data Used**

- 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.

**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

**Data Used**

- n= 134
- Age: Mean 70 Range 60-100
- Sex: 29 males 105 females
- Diagnosis: 100% Generalised Anxiety Disorder (GAD) by DSM-IV

**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).

**Results from this paper:**

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
**WESTRA2009**

**Study Type:** RCT

**Study Description:** Examined whether adding motivational interviewing as a pre-treatment to CBT would improve outcomes

**Type of Analysis:** ITT

**Blindness:** Single blind

**Duration (days):** Mean 42

**Followup:** 6 months (extractable)

**Setting:** Participants were recruited from blocks of 10 to receive CBT or TAU, random number generator

**Notes:** RANDOMISATION: 1: 1 ratio within blocks of 10 to receive CBT or TAU, random number generator

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 would improve outcomes

**Data Used**

- ADIS-IV
- Sheehan Disability Scale (SDS)
- Penn State Worry Questionnaire (PSWQ)
- CGI
- Meta-cognition Questionnaire
- Depression Anxiety Stress Scales

**Data Not Used**

- Clinical significant change - Not standardised

**Group 1 N=44**

**Group 2 N=70**

CBT. Mean dose 10 sessions - included education and awareness, motivational interviewing, relaxation training, cognitive therapy, exposure, problem-solving skills training and behavioural sleep management.

**FUNDING:** None declared.

**Quality assessed:** Selection = low risk, performance bias = unclear risk, attrition bias = low risk, detection bias = unclear risk.

---

**RESULTS2010**

**Study Type:** RCT

**Study Description:** Compared meta-cognitive therapy to applied relaxation in 20 outpatients with GAD.

**Type of Analysis:** Comparator

**Blindness:** No mention

**Duration (days):** Mean 84

**Followup:** 6 & 12 months' follow-up (extractable)

**Setting:** Outpatients; UK. Recruitment: drawn from 2 clinical psychology NHS waiting lists comprised of individuals referred mostly by GPs or psychiatrists.

**Notes:** RANDOMISATION: Individuals unrelated to the trial were asked to draw sealed envelopes from a box.

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

**Data Used**

- STAI-T
- Remission- SCID (free of GAD)
- Beck Anxiety Inventory
- Beck Depression Inventory
- Meta-cognition Questionnaire

**Data Not Used**

- Meta-cognition Questionnaire
- Penn State Worry Questionnaire
- SIGH-A (anxiety) severity rating of less than 4 on the ADIS-IV

**Group 1 N=10**

**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.

**FUNDING:** None declared.

**Quality assessed:** Selection = low risk, performance bias = unclear risk, attrition bias = low risk, detection bias = unclear risk.

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**RESULTS2010**

**Study Type:** RCT

**Study Description:** Examined whether adding motivational interviewing as a pre-treatment to CBT would improve outcomes

**Type of Analysis:** ITT

**Blindness:** Single blind

**Duration (days):** Mean 42

**Followup:** 6 months (extractable)

**Setting:** Participants were recruited from

<table>
<thead>
<tr>
<th>n= 20</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age: Mean 49 Range 25-78</td>
</tr>
<tr>
<td>Sex: 8 males 12 females</td>
</tr>
<tr>
<td>Diagnosis: 100% Generalised Anxiety Disorder (GAD) by DSM-IV-TR</td>
</tr>
<tr>
<td>Exclusions: a) did not have excessive worry, difficulty controlling worry, a minimum of 2 worry topics or were not troubled by excessive &amp; 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 &amp; spoken English; were younger than 18; had previous CBT treatment for GAD; or evidence of a psychotic or organic illness</td>
</tr>
</tbody>
</table>

**Baseline: PSWQ: CBT = 53.3 (10.57), TAU = 57.6 (10.91)**

**Followup at 15 months. Delivered by 5 therapists (3 had a MSc, 1 predoctoral, 1 post-bachelor) with 2-5 years of experience).**

**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.
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.

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: Complete cases

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 as did not meet inclusion criteria (n = 315) or refused to participate (n = 248)

Baseline: GAD severity rating: CBT n=26 (4.9 (0.3)), 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 DSM-IV)
- 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 OUTS: MI + CBT = 6/44 (2 primary diagnosis shifted to MDD), CBT = 6/46 (2 primary diagnosis misdiagnosed), DG = 6/46 (2 primary diagnosis misdiagnosed), CBT = 6/46 (2 primary diagnosis misdiagnosed), WLC = same as CBT group.

Results from this paper:
There was no statistically significant difference found 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: 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

<table>
<thead>
<tr>
<th>Reference ID</th>
<th>Reason for Exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>BAKHSHANI2007</td>
<td>Participants aged under 18</td>
</tr>
<tr>
<td>BARLOW1984</td>
<td>50% of sample had anxiety disorders other than GAD as a primary diagnosis</td>
</tr>
<tr>
<td>Reference</td>
<td>Description</td>
</tr>
<tr>
<td>-------------------------</td>
<td>-----------------------------------------------------------------------------</td>
</tr>
<tr>
<td>BARROWCLOUGH2001</td>
<td>81% of the sample had anxiety disorders other than GAD as a primary diagnosis</td>
</tr>
<tr>
<td>BLOWERS1987</td>
<td>DSM-III criteria</td>
</tr>
<tr>
<td>BOND2002A</td>
<td>Combination therapy</td>
</tr>
<tr>
<td>BONNE2003</td>
<td>Not a psychological intervention</td>
</tr>
<tr>
<td>BORKOVEC1987</td>
<td>DSM-III used</td>
</tr>
<tr>
<td>BORKOVEC1988</td>
<td>40% of sample had anxiety disorders other than GAD as a primary diagnosis</td>
</tr>
<tr>
<td>BOYER2004</td>
<td>Pharmacological study</td>
</tr>
<tr>
<td>BUTLER1987</td>
<td>Diagnostic criteria</td>
</tr>
<tr>
<td>BUTLER1988</td>
<td>Comorbidity and diagnostic criteria</td>
</tr>
<tr>
<td>CONRAD2008</td>
<td>Outcome measures not valid</td>
</tr>
<tr>
<td>DEN-BOER2007</td>
<td>GAD not primary diagnosis (only 6% had GAD)</td>
</tr>
<tr>
<td>DURHAM1987</td>
<td>Aged under 18</td>
</tr>
<tr>
<td>EVANS2008</td>
<td>Not RCT</td>
</tr>
<tr>
<td>FAVA2005</td>
<td>n &lt; 10 in each group</td>
</tr>
<tr>
<td>FEDERICA2010</td>
<td>n = 4 in each group</td>
</tr>
<tr>
<td>GARCIA2004</td>
<td>Not GAD specific: related to all anxiety disorders</td>
</tr>
<tr>
<td>GATH1986</td>
<td>Not given a primary diagnosis of GAD</td>
</tr>
<tr>
<td>GOSSELIN2006</td>
<td>Outside the scope: discontinuation of medication with psychological treatment</td>
</tr>
<tr>
<td>JANNOUN1982</td>
<td>Diagnostic criteria</td>
</tr>
<tr>
<td>KIM2006A</td>
<td>Pharmacological data</td>
</tr>
<tr>
<td>KITCHINER2006</td>
<td>&lt;80% of sample had anxiety disorders other than GAD as primary diagnosis</td>
</tr>
<tr>
<td>LAVALLEE1993</td>
<td>DSM-III diagnosis</td>
</tr>
<tr>
<td>LINDEN2002</td>
<td>In German</td>
</tr>
<tr>
<td>LINDSAY1987B</td>
<td>DSM-III diagnosis</td>
</tr>
<tr>
<td>MOHLMAN2003B</td>
<td>N&lt;10</td>
</tr>
<tr>
<td>NEWMAN2008</td>
<td>Non-RCT</td>
</tr>
<tr>
<td>NORTON2005</td>
<td>57% of sample had anxiety disorders other than GAD as primary diagnosis</td>
</tr>
<tr>
<td>RUINI2006</td>
<td>Outcome measures not viable. Also in Italian.</td>
</tr>
<tr>
<td>STANLEY2003A</td>
<td>Only 6 participants in each condition</td>
</tr>
<tr>
<td>SVARTBERG</td>
<td>85% of sample had anxiety disorders other than GAD as a primary diagnosis</td>
</tr>
<tr>
<td>VAN-BOEIJEN2005</td>
<td>GAD not primary diagnosis</td>
</tr>
<tr>
<td>WELLS2006</td>
<td>Non-RCT</td>
</tr>
<tr>
<td>WHITE1992</td>
<td>Non-RCT</td>
</tr>
<tr>
<td>WOODWARD1980</td>
<td>DSM-III diagnosis</td>
</tr>
<tr>
<td>YONG2009</td>
<td>Non-RCT</td>
</tr>
</tbody>
</table>

**References of Included Studies**

ARNTZ2003 (Published Data Only)


MOHLMAN2003A (Published Data Only)

ÖST2000 (Published Data Only)

REZVAN2008 (Published Data Only)

ROEMER2008 (Published Data Only)

REZVAN2008 (Published Data Only)

STANLEY1996 (Published Data Only)

STANLEY2001B (Published Data Only)

STANLEY2003B (Published Data Only)

STANLEY2009 (Published Data Only)

WELLS2010 (Published Data Only)

WESTRA2009 (Published Data Only)

WETHERELL2003 (Published Data Only)

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BAKSHANII2007 (Published Data Only)

BARLOW1984 (Published Data Only)

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BORKOVEC1988 (Published Data Only)

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BUTLER1988 (Published Data Only)

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DEN-BOER2007 (Published Data Only)

DURHAM1987 (Published Data Only)

EVANS2008 (Published Data Only)

FAVA2005 (Published Data Only)

FEDERICA2010 (Unpublished Data Only)

GARCIA2004 (Published Data Only)

GATH1986 (Published Data Only)

GOSSELIN2006 (Published Data Only)

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WHITE1992 (Published Data Only)

WOODWARD1980 (Published Data Only)

YONG2009 (Published Data Only)

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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

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buspirone + anxiety management training vs. buspirone + non-directive therapy</td>
<td>BOND2002B</td>
</tr>
<tr>
<td>Buspirone + anxiety management training vs. placebo + anxiety management training</td>
<td>BOND2002B</td>
</tr>
<tr>
<td>Buspirone + non-directive therapy vs. placebo + anxiety management training</td>
<td>BOND2002B</td>
</tr>
<tr>
<td>Placebo + anxiety management training vs. placebo + non-directive therapy</td>
<td>BOND2002B</td>
</tr>
</tbody>
</table>

### Characteristics of Included Studies

#### BOND2002B

- **Methods**
  - Study Type: RCT
  - Study Description: Examined the effectiveness of a short course of psychological therapy (AMT or non-directive therapy) combined with buspirone or placebo.
  - Type of Analysis: Completers
  - Followup: no mention
  - Setting: Recruited patients from anxiety disorders clinic at Maudsley Hospital, London, UK

- **Participants**
  - n= 60
  - Age: Mean 34  Range 18-65
  - Sex: 17 males  27 females
  - Diagnosis:
    - DSM-III-R
  - 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

- **Outcomes**
  - Data Used
    - Hospital Anxiety and Depression Scale (depression)
    - HAM-A
    - Hospital Anxiety and Depression Scale (anxiety)
  - Notes: Outcomes are based on completer analysis. In total, 16 dropped out, no details for each group. Taken at baseline, 4 & 8 weeks.

- **Interventions**
  - Group 1 N= 14
    - 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.

- **Notes**
  - 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
  - Setting: Recruited patients from anxiety disorders clinic at Maudsley Hospital, London, UK
  - Diagnosis: 100% Generalised Anxiety Disorder (GAD) by DSM-III-R

### References of Included Studies

**BOND2002B**
