Appendix 15d: Study characteristics – pharmacological and physical interventions

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| Anticonvulsants versus placebo                 |                                |                                                          |                              |                                        |
| KASPER2009                                     |                                |                                                          |                              |                                        |
| MONTGOMERY2006                                 |                                |                                                          |                              |                                        |

| Benzodiazepines versus azapirones              |                                |                                                          |                              |                                        |
| BOURIN1995                                     |                                |                                                          |                              |                                        |

| Benzodiazepines versus placebo                 |                                |                                                          |                              |                                        |
| ANDREATINI2002                                  |                                |                                                          |                              |                                        |
| ANSSEAU1991                                     |                                |                                                          |                              |                                        |
| FELTNER2003                                     |                                |                                                          |                              |                                        |
| FRESQUET2000                                    |                                |                                                          |                              |                                        |
| HACKETT2003                                     |                                |                                                          |                              |                                        |
| LYDIARD1997                                     |                                |                                                          |                              |                                        |
| MCLEOD1992                                     |                                |                                                          |                              |                                        |
| MOLLER2001                                     |                                |                                                          |                              |                                        |
| PANDE2003                                       |                                |                                                          |                              |                                        |
| PFIZER2008                                     |                                |                                                          |                              |                                        |
| RICKELS2000B                                   |                                |                                                          |                              |                                        |
| RICKELS2005                                    |                                |                                                          |                              |                                        |

| Benzodiazepines versus placebo                 |                                |                                                          |                              |                                        |
| ANDREATINI2002                                  |                                |                                                          |                              |                                        |
| ANSSEAU1991                                     |                                |                                                          |                              |                                        |
| FELTNER2003                                     |                                |                                                          |                              |                                        |
| FRESQUET2000                                    |                                |                                                          |                              |                                        |
| HACKETT2003                                     |                                |                                                          |                              |                                        |
| LYDIARD1997                                     |                                |                                                          |                              |                                        |
| MCLEOD1992                                     |                                |                                                          |                              |                                        |
| MOLLER2001                                     |                                |                                                          |                              |                                        |
| PANDE2003                                       |                                |                                                          |                              |                                        |
| PFIZER2008                                     |                                |                                                          |                              |                                        |
| RICKELS2000B                                   |                                |                                                          |                              |                                        |
| RICKELS2005                                    |                                |                                                          |                              |                                        |

| Buspirone versus placebo                        |                                |                                                          |                              |                                        |
| DAVIDSON1999                                    |                                |                                                          |                              |                                        |
| LADER1998                                       |                                |                                                          |                              |                                        |
| MAJERCSIK2003                                   |                                |                                                          |                              |                                        |
| POLLACK1997                                     |                                |                                                          |                              |                                        |
| SRAMEK1996                                      |                                |                                                          |                              |                                        |

| Duloxetine (SNRI) versus placebo                |                                |                                                          |                              |                                        |
| HARTFORD2007                                    |                                |                                                          |                              |                                        |
| KOPOLEN2007                                     |                                |                                                          |                              |                                        |
| NICOLINI2009                                    |                                |                                                          |                              |                                        |
| RYNN2008                                        |                                |                                                          |                              |                                        |

| Duloxetine (SNRI) versus placebo                |                                |                                                          |                              |                                        |
| HARTFORD2007                                    |                                |                                                          |                              |                                        |
| NICOLINI2009                                    |                                |                                                          |                              |                                        |

| Quetiapine versus placebo                       |                                |                                                          |                              |                                        |
| ASTRazeneca2007A                                |                                |                                                          |                              |                                        |
| ASTRazeneca2007B                                |                                |                                                          |                              |                                        |
| ASTRazeneca2007C                                |                                |                                                          |                              |                                        |
| ASTRazeneca2008                                 |                                |                                                          |                              |                                        |

| SSRI versus venlafaxine                         |                                |                                                          |                              |                                        |
| BOSE2008                                        |                                |                                                          |                              |                                        |

| SSRIs versus placebo                            |                                |                                                          |                              |                                        |
| ALLGULANDER2004                                  |                                |                                                          |                              |                                        |
| ASTRazeneca2007A                                |                                |                                                          |                              |                                        |
| ASTRazeneca2007B                                |                                |                                                          |                              |                                        |
| ASTRazeneca2007C                                |                                |                                                          |                              |                                        |
| ASTRazeneca2008                                 |                                |                                                          |                              |                                        |
| BALDWIN2006                                     |                                |                                                          |                              |                                        |
| BOSE2008                                        |                                |                                                          |                              |                                        |
| BRAWMAN-MINTZER2006                             |                                |                                                          |                              |                                        |
| DAVIDSON2004                                    |                                |                                                          |                              |                                        |
| GOODMAN2005                                    |                                |                                                          |                              |                                        |
| GSK2002                                         |                                |                                                          |                              |                                        |
| GSK2005                                         |                                |                                                          |                              |                                        |
| HEWETT2001                                     |                                |                                                          |                              |                                        |
| LENZE2005                                      |                                |                                                          |                              |                                        |
| LENZE2009                                      |                                |                                                          |                              |                                        |
| LENZE2009                                      |                                |                                                          |                              |                                        |
| PFIZER2008                                     |                                |                                                          |                              |                                        |
| POLLACK2001                                    |                                |                                                          |                              |                                        |
| RICKELS2003                                    |                                |                                                          |                              |                                        |

| SSRLs versus placebo                            |                                |                                                          |                              |                                        |
| ALLGULANDER2004                                  |                                |                                                          |                              |                                        |
| ASTRazeneca2007A                                |                                |                                                          |                              |                                        |
| ASTRazeneca2007B                                |                                |                                                          |                              |                                        |
| ASTRazeneca2007C                                |                                |                                                          |                              |                                        |
| ASTRazeneca2008                                 |                                |                                                          |                              |                                        |
| BALDWIN2006                                     |                                |                                                          |                              |                                        |
| BOSE2008                                        |                                |                                                          |                              |                                        |
| BRAWMAN-MINTZER2006                             |                                |                                                          |                              |                                        |
| DAVIDSON2004                                    |                                |                                                          |                              |                                        |
| GOODMAN2005                                    |                                |                                                          |                              |                                        |
| GSK2002                                         |                                |                                                          |                              |                                        |
| GSK2005                                         |                                |                                                          |                              |                                        |
| HEWETT2001                                     |                                |                                                          |                              |                                        |
| LENZE2005                                      |                                |                                                          |                              |                                        |
| LENZE2009                                      |                                |                                                          |                              |                                        |
| LENZE2009                                      |                                |                                                          |                              |                                        |
| PFIZER2008                                     |                                |                                                          |                              |                                        |
| POLLACK2001                                    |                                |                                                          |                              |                                        |
| RICKELS2003                                    |                                |                                                          |                              |                                        |
### Characteristics of Included Studies

<table>
<thead>
<tr>
<th>Study Type: RCT</th>
<th>Study Description: ITT: all eligible participants with at least one efficacy evaluation made whilst receiving study medication</th>
</tr>
</thead>
</table>
| **ALLGULANDER2001** | Type of Analysis: ITT/LOCF  
Blindness: Double blind  
Duration (days): Mean 188  
Setting: Belgium, Finland, France, Sweden, UK Outpatient (14 centres)  
Notes: RANDOMISATION: not reported. ALLOCATION CONCEALMENT: not addressed  
Info on Screening Process: 541 randomised, 529 met ITT criteria for inclusion |
| n= 529 | Age: Mean 45 Range 18-86  
Sex: 201 males 328 females  
Diagnosis:  
100% GAD by DSM-IV  
Exclusions: - DSM-IV diagnosis of GAD  
- HAM-A score < 20  
- HAM-A (anxious mood & tension items) < 2  
- MDD or other psychiatric disorder  
- Clinically important medical disease  
- Non-pharmacological drugs with psychotropic effects  
Notes: 74% had received prior treatment for anxiety (mostly benzodiazepines & antidepressants); 89% received non- 
anxiolytic concomitant therapy during the study (26 on beta- 
blockers, 52 zolpidem or chloral hydrate)  
Baseline: HAM-A baseline depression score (approximate): 26.48 (range 20 to 52). No significant differences between groups at baseline. Venlafaxine 37.5mg/d: 26.6 (range 20 to 44). Venlafaxine 75mg/d: 26.3 (range 20 to 43). Venlafaxine 150mg/d: 26.3 (17 to 38). Placebo: 26.7 (20 to 52). |
| **ALLGULANDER2004** | Type of Analysis: ITT/LOCF  
Blindness: Double blind  
Duration (days): Mean 84  
Setting: Australia, Canada, Denmark, Norway, Sweden |
| n= 373 | Age: Mean 41  
Sex: 167 males 206 females  
Diagnosis:  
100% GAD by DSM-IV  
Exclusions: - Less than 18 years of age  
- No DSM-IV primary diagnosis of GAD  
- HAM-A score < 18  
- HAM-A (anxious mood & tension items) < 2 |
Outpatient (21 centres)

Notes: RANDOMISATION: procedure not reported.
ALLOCATION CONCEALMENT: not addressed.
Info on Screening Process: 562 screened, 378 randomised, 5 did not receive study medication.

- No current use of medically accepted contraception in fertile women
- Other psychiatric diagnosis
- MADRS score > 15
- Concurrent psychotherpay for GAD
- Clinically significant acute/ unstable medical condition
- Treatment with any other psychotropic drug (other than infrequent use of chloral hydrate)
- Suicide risk
- Previous failure to respond to antidepressant drug treatment

Notes: 14% reported a previous diagnosis of depression. 30% reported previous treatment with psychotropic medication.
Baseline: HAM-A baseline depression score (approximately): 24.80 (4.75). Sertraline: 24.6 (4.6).
Placebo: 25.0 (4.9). No significant differences between groups at baseline.

Data Used

HAM-A
Leaving the study due to ineffectiveness
Leaving the study due to adverse events
Notes: TAKEN AT: baseline, end of treatment (4 weeks)
DROPOUTS: Diazepam: 1/12 (8.3%), Valepotriates: 2/12 (16.6%), Placebo: 2/12 (16.6%)

Group 1 N=12
Diazepam. Mean dose 6.5mg/day - Following a 2-week washout period, study drugs were administered in identical capsules containing 2.5mg. The capsules were administered three times a day with the lowest dose consisting of two placebo and one active capsules based on response. 4 weeks.

Group 2 N=12
Placebo - Following a 2-week washout period, study drugs were administered in identical capsules. The capsules were administered three times a day.

Group 3 N=12
Valepotriates. Mean dose 81.3mg/day - Following a 2-week washout period, study drugs were administered in identical capsules containing 50mg. The capsules were administered three times a day with the lowest dose consisting of two placebo and one active capsules based on response.

ANDREATIN2002

Study Type: RCT

Study Description: ITT using LOCF included all those who completed at least 1 week of treatment
Type of Analysis: ITT
Blindness: Double blind
Duration (days): Mean 28
Setting: Sao Paolo, BRAZIL
Notes: RANDOMISATION: used a computer programme

Info on Screening Process: 132 people were interviewed of whom 96 were excluded and 36 participated in the study. Participants were excluded due to the presence of another mental illness, refusal, marked reduction in HAM-A prior to study, use of other medications.

Data Used

STAI-trait
HAM-A
Notes: All participants were evaluated using the SCID-R
Baseline: HAM-A: Placebo: 25.2(7.5), Diazepam: 25.2(4.5), Valepotriates: 22.8(7.6)

Group 1 N=12
Diazepam. Mean dose 6.5mg/day - Following a 2-week washout period, study drugs were administered in identical capsules containing 2.5mg. The capsules were administered three times a day with the lowest dose consisting of two placebo and one active capsules based on response. 4 weeks.

Group 2 N=12
Placebo - Following a 2-week washout period, study drugs were administered in identical capsules. The capsules were administered three times a day.

Group 3 N=12
Valepotriates. Mean dose 81.3mg/day - Following a 2-week washout period, study drugs were administered in identical capsules containing 50mg. The capsules were administered three times a day with the lowest dose consisting of two placebo and one active capsules based on response.

ANSESSEU1991

Study Type: RCT

Study Description: 6 parallel groups. 1 week placebo run-in period following by 4 weeks of treatment.
Type of Analysis: ITT
Blindness: Double blind
Duration (days): Mean 28
Setting: Outpatients. France.
Notes: RANDOMISATION: no details provided.

Info on Screening Process: 341 entered: 325 went on to DB treatment phase (16 excluded - 9 did not fit inclusion criteria and 7 improved more than 25% on HAM-A scale during placebo week).

- No current use of medically accepted contraception in fertile women
- Other psychiatric diagnosis
- MADRS score > 15
- Concurrent psychotherpay for GAD
- Clinically significant acute/ unstable medical condition
- Treatment with any other psychotropic drug (other than infrequent use of chloral hydrate)
- Suicide risk
- Previous failure to respond to antidepressant drug treatment
Notes: Randomisation: no details provided.
Allocation concealment: not addressed.

Notes: Participants scored >20 on HAM-A and >9 on Covi Anxiety Scale.
Baseline: HAM-A at baseline: Suriclone 0.1 29.0 (5.6), Suriclone 0.2 28.6 (5.0), Suriclone 0.3 30.1 (5.2), Suriclone 0.5 26.2 (5.8), Valepotriates: 22.8(7.6).

Group 1 N=56
Suriclone. Mean dose 0.2mg/day - No details provided.

Group 2 N=57
Suriclone. Mean dose 0.1mg/day - No details provided.

Group 3 N=54
Diazepam. Mean dose 5mg/day - No details provided.

Group 4 N=57
Placebo - No details provided.

Group 5 N=58
Suriclone. Mean dose 0.3mg/day - No details provided.

Data Used

HAM-A
Adverse events
Leaving the study due to adverse events
Leaving the study early for any reason
Response (50% reduction in HAM-A score)
Notes: Assessments made at baseline and after 1, 2 and 4 weeks.

Group 1 N=56
Suriclone. Mean dose 0.2mg/day - No details provided.

Group 2 N=57
Suriclone. Mean dose 0.1mg/day - No details provided.

Group 3 N=54
Diazepam. Mean dose 5mg/day - No details provided.

Group 4 N=57
Placebo - No details provided.

Group 5 N=58
Suriclone. Mean dose 0.3mg/day - No details provided.

Data Used

HAM-A
Notes: TAKEN AT: 1, 2, 4, 6, 8, 12 weeks. DROP OUTS: 23%. CHANGE SCORES.
ASTRAZENECA2007A

Study Type: RCT
Blindness: Double blind
Duration (days): Mean 56
Setting: Europe, Argentina, Canada, Mexico, South Africa
Notes: Randomisation: no further details
Info on Screening Process: 1054 screened, 873 randomised

n= 873
Age: Mean 41
Sex: 306 males 567 females
Diagnosis: 100% GAD by DSM-IV
Exclusions: - <18 years >65 years
- HAM-A <20, and items 1 and 2 <2
- CGI <4
- MADRS >16

Data Used
Discontinuation adverse events (DAEs)
Leaving the study early for any reason
Remission (less than 7 on HAM-A)
Response (50% reduction in HAM-A score)

Data Not Used
HAM-A - no SD

Group 1 N= 218
Quetiapine. Mean dose 150mg

Group 2 N= 217
Placebo

Group 3 N= 217
Paroxetine. Mean dose 20mg

Group 4 N= 221
Quetiapine. Mean dose 50mg

Funding: Astra Zeneca

ASTRAZENECA2007B

Study Type: RCT
Blindness: Double blind
Duration (days): Mean 56
Setting: US
Notes: Randomisation: no further details
Info on Screening Process: 1344 screened, 854 randomised

n= 854
Age: Mean 38
Sex: no information
Diagnosis: 100% GAD by DSM-IV
Exclusions: - <18 years >65 years
- HAM-A <20, and items 1 and 2 <2
- CGI <4
- MADRS >16

Data Used
Leaving the study due to adverse events
Leaving the study early for any reason
Remission (less than 7 on HAM-A)
Response (50% reduction in HAM-A score)

Data Not Used
HAM-A - no SD

Group 1 N= 213
Escitalopram. Mean dose 10mg

Group 2 N= 207
Quetiapine. Mean dose 300mg

Group 3 N= 219
Quetiapine. Mean dose 150mg

Group 4 N= 215
Placebo

Funding: Astra Zeneca

ASTRAZENECA2007C

Study Type: RCT
Blindness: Double blind
Duration (days): Mean 56
Setting: US
Notes: Randomisation: no further details
Info on Screening Process: 1364 screened, 951 randomised

n= 951
Age: Mean 40
Sex: no information
Diagnosis: 100% GAD by DSM-IV
Exclusions: - <18 years >65 years
- HAM-A <20, and items 1 and 2 <2
- CGI <4
- MADRS >16

Data Used
Leaving the study due to adverse events
Leaving the study early for any reason
Remission (less than 7 on HAM-A)
Response (50% reduction in HAM-A score)

Data Not Used
HAM-A - no SDs

Group 1 N= 235
Placebo

Group 2 N= 234
Quetiapine. Mean dose 50mg

Group 3 N= 241
Quetiapine. Mean dose 300mg

Group 4 N= 241
Quetiapine. Mean dose 150mg

Funding: Astra Zeneca

ASTRAZENECA2008

Study Type: RCT
Blindness: Double blind
Duration (days): Mean 64
Setting: Estonia, Poland, Russia, Ukraine, United States
Notes: Randomisation: no further details
Info on Screening Process: 556 screened, 450 randomised

n= 556
Age: Mean 70 Range 65-87
Sex: 132 males 316 females
Diagnosis: 100% GAD by DSM-IV
Exclusions: - < 66 years of age
- HAM-A <20, and items 1 and 2 <2
- CGI <4
- MADRS >16

Data Used
Leaving the study due to adverse events
Leaving the study early for any reason
Remission (less than 7 on HAM-A)
Response (50% reduction in HAM-A score)

Data Not Used
HAM-A - no SDs

Group 1 N= 222
Quetiapine - Flexible dosing (50mg-300mg), periodic stepwise increases up to maximum of 300mg

Group 2 N= 216
Placebo

Funding: Astra Zeneca

Baseline: HAM-A: Quetiapine 25.2 (3.5) Placebo 25.1 (3.5)
**MADRS: Quetiapine 12.4 (2.6) Placebo 12.3 (2.3)**

**BALDWIN2006**

**Study Type:** RCT

**Study Description:** ITT: patients who took at least one dose of the study medication & at least one baseline efficacy assessment were included in the analysis

**Type of Analysis:** LOCF/ITT

**Blindness:** Double blind

**Duration (days):** Mean 84

**Setting:** UK

**Notes:** RANDOMISATION: computer-generated randomisation list. ALLOCATION CONCEALMENT: sealed opaque envelopes.

**Info on Screening Process:** Details not provided.

**Data Used**

- HAM-A
- Leaving the study due to inefficacy
- Leaving the study due to adverse events
- Leaving the study early for any reason
- DESS (modified)

**Data Not Used**

- Remission (less than 7 on HAM-A) - not extractable
- Response (50% reduction in HAM-A score)

**Notes:** TAKEN AT: 1,2,4,6,8,10,12,13,14 weeks.

**DROP OUTS:** 14% (98) MEAN CHANGE SCORES.

**n= 682**

**Group**

- Escitalopram. Mean dose 20 mg/ day - 1-week, single blind placebo lead-in period, 12 weeks of treatment with fixed doses. 2-week placebo wash-out period.
- Placebo - Identical appearance, taste and smell. Oral administration.

**n= 133**

**Group**

- Escitalopram. Mean dose 5 mg/ day - 1-week, single blind placebo lead-in period, 12 weeks of treatment with fixed doses. 2-week placebo wash-out period.

**n= 134**

**Group**

- Paroxetine. Mean dose 20 mg/ day - 1-week, single blind placebo lead-in period, 12 weeks of treatment with fixed doses. 2-week placebo wash-out period.

**n= 140**

**Group**

- Escitalopram. Mean dose 10 mg/ day - 1-week, single blind placebo lead-in period, 12 weeks of treatment with fixed doses. 2-week placebo wash-out period.

**n= 136**

**Group**

- Placebo - Identical appearance, taste and smell. Oral administration.

**n= 139**

**Funding:** Pfizer. Quality assessed +.

**Data on Exclusions:**

- Age: Mean 41
- Sex: 244 males 438 females

**Diagnosis:**

100% GAD by DSM-IV-TR.

**Exclusions: - not primary diagnosis of GAD (DSM-IV-TR) - not between 18 and 65 - HAM-A score < 20 - HAM-A (anxious mood & tension items) < 2 - MADRS > 15 - Diagnosis: MDD, panic disorder, social anxiety, PTSD, bipolar, OCD, body dysmorphic disorder, substance misuse, personality disorder - suicide risk - receiving psychosocial interventions (i.e. CBT, ECT) - physical health problems (i.e. vascular) - concomitant medication (i.e. psychoactive substances, antidepressants, benzodiazepines, antipsychotics)

**Baseline:** HAM-A scores at baseline (approximate): 27.04 (4.46). No significant differences at baseline.

**BALL2005**

**Study Type:** RCT

**Type of Analysis:** ITT (LOCF)

**Blindness:** Double blind

**Duration (days):** Mean 56

**Setting:** US outpatients

**Notes:** Randomisation: no further details

**Info on Screening Process:** 61 participants; 6 failed study entry for medical or diagnostic reasons.

**Data Used**

- HAM-A
- CGI-I
- CGI (Response) - Not critical outcome
- CGI-I (Response) - Not critical outcome
- QoL

**Data Not Used**

- Remission (less than 7 on HAM-A) - not extractable
- CGI (Response) - Not critical outcome
- CGI-I (Response) - Not critical outcome

**Notes:** Response based on CGI score of 1 or 2.

**n= 55**

**Group**

- Sertraline - Starting dose 25mg could be increased up to maximum of 100mg
- Paroxetine - starting dose 10mg and then could be increased up to 40mg

**Funding:** Pfizer. Quality assessed +.

**Data on Exclusions:**

- Age: Mean 39
- Sex: 14 males 41 females

**Diagnosis:**

100% GAD by DSM-IV.

**Exclusions: - <18 years - HAM-A <18 - GAD not primary diagnosis - HDRS >20 - history of psychotic or bipolar illness**

**Baseline:** HAM-A: Paroxetine 20.8 (2.3) Sertraline 21.4 (3.4)

**BIELSKI2005**

**Study Type:** RCT

**Type of Analysis:** ITT (LOCF)

**Blindness:** Double blind

**Duration (days):** Mean 168

**Setting:** US, outpatients

**Notes:** Randomisation: no further details

**Info on Screening Process:** 81 participants; 6 failed study entry for medical or diagnostic reasons.

**Data Used**

- HAM-A
- CGI-I
- CGI (Response) - Not critical outcome
- QoL

**Data Not Used**

- Remission (less than 7 on HAM-A) - not extractable
- CGI (Response) - Not critical outcome
- CGI-I (Response) - Not critical outcome

**Notes:** Response based on CGI score of 1 or 2.

**n= 121**

**Group**

- Escitalopram - 10mg first 4 weeks, could then be increased to 20mg/day, then every 2 weeks could be increased by 10mg/day
- Paroxetine - starting dose 10mg and then could be increased up to 40mg

**Funding:** Forest Laboratories. Quality assessed +.

**Data on Exclusions:**

- Age: Mean 37
- Sex: 76 males 45 females

**Diagnosis:**

100% GAD by DSM-IV.

**Exclusions: - not 18-65 years - HAM-A <18 - HDRS >17 - Axis I psychiatric disorder - Psychosis**

**Baseline:** HAM-A: Escitalopram 23.7 (SE =0.5) Paroxetine 23.4 (SE = 0.4)

**Group**

- Escitalopram - 10mg first 4 weeks, could then be increased to 20mg/day, then every 2 weeks could be increased by 10mg/day
- Paroxetine - 20mg/day first 2 weeks, increased every 2 weeks by 10mg/day

**Received support from Lundbeck and sponsored by GlaxoSmithKline. Quality assessed: +.
BOSE2008
Study Type: RCT
Type of Analysis: ITT
Blindness: Double blind
Duration (days): Mean 56
Setting: Outpatients from 28 centres, US
Notes: RANDOMISATION: no further details
Info on Screening Process: 597 screened, 404 randomised, 7 dropped out before start of study

Group 1 N= 131
Escitalopram - starting dose of 10mg/day for first week, second week could be increased to 20mg/day

Group 2 N= 140
Placebo - No details given

Group 3 N= 133
Venlafaxine (extended release) - Starting dose of 75mg/day could be increased to maximum of 150mg/day on week 2, and up to 225mg/day in weeks 3-8.

Notes: Side effects reported if incidence over 10%.

HAM-A
Adverse events
Leaving the study due to adverse events
Leaving the study early for any reason
Remission (less than 7 on HAM-A)
Response (50% reduction in HAM-A score)
Notes: Side effects reported if incidence over 10%.

Data Used
HAM-A

Funded by Forest Laboratories. Quality assessed +.

BOURIN1995
Study Type: RCT
Study Description: Compared discontinuation following 8 weeks of treatment. Parallel groups.
Type of Analysis: Unclear
Blindness: Double blind
Duration (days): Mean 56
Notes: RANDOMISATION: allocation done before the study (30 ppts in each group).
Info on Screening Process: 60 participants assessed before and after washout period.

Group 1 N= 20
Lorazepam - 3 or 4mg/day. 1mg in 3-4 divided doses.

Group 2 N= 23
Buspirone - 15-20mg/day. 3-4 capsules of 5mg in 3-4 divided doses per day.

Notes: RANDOMISATION: computerised list
ALLOCATION CONCEALMENT: not addressed
Setting: US
Outpatient (9 centres)
Duration (days): Mean 70
Notes: RANDOMISATION: compared discontinuation
Info on Screening Process: Patients registered 428; 338 randomly assigned.

Group 1 N= 165
Sertraline. Mean dose 149.1mg/d - Did not include a placebo run-in phase. 10 weeks of treatment. 1 week taper period. Flexible dose. Week 1: 35mg/d. Weeks: 2,3,4,7 could be increased by 50mg increments. Maximum dose 200mg/d. Dosage reduction permitted.

Group 2 N= 163
Placebo

Notes: SIDE EFFECTS: 53.7% (sertraline group) and 51.2% (placebo group) received prior psychotropic medication. 17% reported previous history of depression.

HAM-A
Adverse events
Leaving the study due to inefficacy
Leaving the study due to adverse events
Leaving the study early for any reason
Response (50% reduction in HAM-A score)
Notes: TAKEN AT: 1,2,3,4,6,8,10, 11 weeks.
DROP OUTS: 26% CHANGE SCORES USED.

Data Used
HAM-A

Notes: Funding: no details provided. Quality assessed +.

BRAWMAN-MINTZER2006
Study Type: RCT
Study Description: ITT: all randomly assigned participants who had at least 1 post-baseline primary outcome measurement.
Type of Analysis: ITT
Blindness: Double blind
Duration (days): Mean 70
Setting: US
Outpatient (9 centres)
Notes: RANDOMISATION: computerised list
ALLOCATION CONCEALMENT: not addressed
Info on Screening Process: Patients registered 428; 338 randomly assigned.

Group 1 N= 165
Sertraline. Mean dose 149.1mg/d - Did not include a placebo run-in phase. 10 weeks of treatment. 1 week taper period. Flexible dose. Week 1: 35mg/d. Weeks: 2,3,4,7 could be increased by 50mg increments. Maximum dose 200mg/d. Dosage reduction permitted.

Group 2 N= 163
Placebo

Notes: Financial contributions from Eli Lilly. Quality assessed: +.

HAM-A
Leaving the study due to inefficacy
Leaving the study due to adverse events
Leaving the study early for any reason
Response (50% reduction in HAM-A score)
Notes: TAKEN AT: 1,2,3,4,6,8,10, 11 weeks.
DROP OUTS: 26% CHANGE SCORES USED.

Data Used
HAM-A

Funding: no details provided. Quality assessed +.

Notes: Funded by Forest Laboratories. Quality assessed +.

Data Used
HAM-A
Adverse events
Leaving the study due to adverse events
Leaving the study early for any reason
Remission (less than 7 on HAM-A)
Response (50% reduction in HAM-A score)
Notes: Side effects reported if incidence over 10%.
**DARCIS1995**

**Study Type:** RCT

**Study Description:** Participants were randomly allocated to either hydroxyzine or placebo for 4 weeks, followed by a treatment-free period of 1 week.

**Type of Analysis:** ITT (LOCF)

**Blindness:** Double blind

**Duration (days):** Mean 28

**Followup:** 1 week

**Setting:** No details provided.

**Notes:** RANDOMISATION: no details provided.

**Info on Screening Process:** 405 patients completed placebo run-in period & received study drug, 36 had no primary efficacy evaluations & 4 randomised at one site were excluded for administrative reasons.

**Notes:** RANDOMISATION: details not provided.

**Outpatient (17 centres)**

<table>
<thead>
<tr>
<th>Setting: US</th>
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<td>Outpatient: No details provided.</td>
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**Info on Screenmg Process:** 133 assessed but 9 were excluded. No details provided.

**Notes:** Randomisation procedure not reported.

**Notes:** No. of participants taking chloral hydrate: placebo 100%, hydroxyzine: 98%.

**Notes:** TAKEN AT: 1, 2, 3, 4, 6, 8 weeks & 4 to 10 days after drug taper. DROP OUTS: 27%.

**Notes:** Ppts were assessed at the start of the study, after 1 and 4 weeks of treatment, and one week after stopping therapy.

**Notes:** Ppts were assessed at the start of the study, after 1 and 4 weeks of treatment, and one week after stopping therapy.

**Notes:** No details provided. Quality assessed: +.

**Notes:** No. of participants taking chloral hydrate: placebo 100%, hydroxyzine: 98%.

**Notes:** TAKEN AT: 1, 2, 3, 4, 6, 8 weeks & 4 to 10 days after drug taper. DROP OUTS: 27%.

**Notes:** Ppts were assessed at the start of the study, after 1 and 4 weeks of treatment, and one week after stopping therapy.

**Notes:** No details provided. Quality assessed: +.

**Notes:** No. of participants taking chloral hydrate: placebo 100%, hydroxyzine: 98%.

**Notes:** TAKEN AT: 1, 2, 3, 4, 6, 8 weeks & 4 to 10 days after drug taper. DROP OUTS: 27%.

**Notes:** Ppts were assessed at the start of the study, after 1 and 4 weeks of treatment, and one week after stopping therapy.

**Baseline: HAM-A scores at baseline (approximately) total: 24.3 (3.00); sertraline: 24.5 (3.1); placebo: 24.1 (2.6). No significant differences at baseline.**

**Data Used**

**Adverse events**

Hospital Anxiety and Depression Scale (anxiety)

Leaving the study due to adverse events

Notes: Ppts were assessed at the start of the study, after 1 and 4 weeks of treatment, and one week after stopping therapy.

**Data Used**

**HAM-A**

Leaving the study due to adverse events

Compliance

Response (50% reduction in HAM-A score)

Notes: TAKEN AT: 1, 2, 3, 4, 6, 8 weeks & 4 to 10 days after drug taper. DROP OUTS: 27%.

**Notes:** Ppts were assessed at the start of the study, after 1 and 4 weeks of treatment, and one week after stopping therapy.

**Notes:** No details provided. Quality assessed: +.

**Notes:** No. of participants taking chloral hydrate: placebo 100%, hydroxyzine: 98%.

**Notes:** TAKEN AT: 1, 2, 3, 4, 6, 8 weeks & 4 to 10 days after drug taper. DROP OUTS: 27%.

**Notes:** Ppts were assessed at the start of the study, after 1 and 4 weeks of treatment, and one week after stopping therapy.

**Notes:** No details provided. Quality assessed: +.

**Notes:** No. of participants taking chloral hydrate: placebo 100%, hydroxyzine: 98%.

**Notes:** TAKEN AT: 1, 2, 3, 4, 6, 8 weeks & 4 to 10 days after drug taper. DROP OUTS: 27%.

**Notes:** Ppts were assessed at the start of the study, after 1 and 4 weeks of treatment, and one week after stopping therapy.

**Notes:** No details provided. Quality assessed: +.

**Notes:** No. of participants taking chloral hydrate: placebo 100%, hydroxyzine: 98%.

**Notes:** TAKEN AT: 1, 2, 3, 4, 6, 8 weeks & 4 to 10 days after drug taper. DROP OUTS: 27%.

**Notes:** Ppts were assessed at the start of the study, after 1 and 4 weeks of treatment, and one week after stopping therapy.

**Notes:** No details provided. Quality assessed: +.

**Notes:** No. of participants taking chloral hydrate: placebo 100%, hydroxyzine: 98%.

**Notes:** TAKEN AT: 1, 2, 3, 4, 6, 8 weeks & 4 to 10 days after drug taper. DROP OUTS: 27%.

**Notes:** Ppts were assessed at the start of the study, after 1 and 4 weeks of treatment, and one week after stopping therapy.

**Notes:** No details provided. Quality assessed: +.

**Notes:** No. of participants taking chloral hydrate: placebo 100%, hydroxyzine: 98%.

**Notes:** TAKEN AT: 1, 2, 3, 4, 6, 8 weeks & 4 to 10 days after drug taper. DROP OUTS: 27%.

**Notes:** Ppts were assessed at the start of the study, after 1 and 4 weeks of treatment, and one week after stopping therapy.

**Notes:** No details provided. Quality assessed: +.

**Notes:** No. of participants taking chloral hydrate: placebo 100%, hydroxyzine: 98%.

**Notes:** TAKEN AT: 1, 2, 3, 4, 6, 8 weeks & 4 to 10 days after drug taper. DROP OUTS: 27%.

**Notes:** Ppts were assessed at the start of the study, after 1 and 4 weeks of treatment, and one week after stopping therapy.

**Notes:** No details provided. Quality assessed: +.

**Notes:** No. of participants taking chloral hydrate: placebo 100%, hydroxyzine: 98%.

**Notes:** TAKEN AT: 1, 2, 3, 4, 6, 8 weeks & 4 to 10 days after drug taper. DROP OUTS: 27%.

**Notes:** Ppts were assessed at the start of the study, after 1 and 4 weeks of treatment, and one week after stopping therapy.

**Notes:** No details provided. Quality assessed: +.

**Notes:** No. of participants taking chloral hydrate: placebo 100%, hydroxyzine: 98%.

**Notes:** TAKEN AT: 1, 2, 3, 4, 6, 8 weeks & 4 to 10 days after drug taper. DROP OUTS: 27%.

**Notes:** Ppts were assessed at the start of the study, after 1 and 4 weeks of treatment, and one week after stopping therapy.

**Notes:** No details provided. Quality assessed: +.

**Notes:** No. of participants taking chloral hydrate: placebo 100%, hydroxyzine: 98%.

**Notes:** TAKEN AT: 1, 2, 3, 4, 6, 8 weeks & 4 to 10 days after drug taper. DROP OUTS: 27%.

**Notes:** Ppts were assessed at the start of the study, after 1 and 4 weeks of treatment, and one week after stopping therapy.

**Notes:** No details provided. Quality assessed: +.

**Notes:** No. of participants taking chloral hydrate: placebo 100%, hydroxyzine: 98%.

**Notes:** TAKEN AT: 1, 2, 3, 4, 6, 8 weeks & 4 to 10 days after drug taper. DROP OUTS: 27%.

**Notes:** Ppts were assessed at the start of the study, after 1 and 4 weeks of treatment, and one week after stopping therapy.

**Notes:** No details provided. Quality assessed: +.
FELTNER2003

Study Type: RCT
Study Description: ITT included all randomised participants who received at least one dose of study medication
Type of Analysis: ITT
Blindness: Double blind
Duration (days): Mean 28
Setting: Four study centres, USA
Outpatients
Notes: RANDOMISATION: procedure not reported
Info on Screening Process: Not reported

Data Used
CGI-I
HAM-A
Adverse events
Serious adverse events
Leaving the study due to adverse events
Leaving the study early for any reason
Remission (less than 7 on HAM-A)
Response (50% reduction in HAM-A score)
Notes: TAKEN AT: Baseline and end of active treatment (4 weeks)
DROPOUTS: total drop outs not reported

Baseline: HAM-A scores at baseline (approximate): 23.40
Data Not Used

Baseline: HAM-A: Pregabalin (50mg) 24.9(3.9), Pregabalin (200mg) 25.4(4.6), Lorazepam 24.7(3.7), Placebo 24.8(4.1)

Notes: Participants with a dual comorbid psychiatric disorder were required to have GAD as a primary disorder as judged by the psychiatrist, considering relative severity and time of onset
Baseline: HAM-A: Pregabalin (50mg) 24.9(3.9), Pregabalin (200mg) 25.4(4.6), Lorazepam 24.7(3.7), Placebo 24.8(4.1)

Group 1 N= 68
Lorazepam. Mean dose 6mg - Fixed dose regimen with 2 mg TID. Study medication was titrated during days 1-6 of double-blind treatment.
Group 2 N= 70
Pregabalin. Mean dose 150mg - Fixed dose regimen with 50 mg TID. Study medication was titrated during days 1-6 of double-blind treatment.
Group 3 N= 66
Pregabalin. Mean dose 600mg - Fixed dose regimen with 200 mg TID. Study medication was titrated during days 1-6 of double-blind treatment.
Group 4 N= 67
Placebo

Data Not Used

Notes: 34% (placebo), 40% (escitalopram) received prior GAD pharmacotherapy, majority were nonresponders or intolerant to prior treatment
Baseline: HAM-A scores at baseline (approximate): 23.40

Notes: TAKEN AT: 1, 2, 4, 6 and 8 weeks. DROP OUTS: 4/158 (escitalopram), 4/157 (placebo).
CHANGE SCORES USED.

Baseline: HAM-A: Pregabalin (50mg) 24.9(3.9), Pregabalin (200mg) 25.4(4.6), Lorazepam 24.7(3.7), Placebo 24.8(4.1)

Notes: Participants with a dual comorbid psychiatric disorder were required to have GAD as a primary disorder as judged by the psychiatrist, considering relative severity and time of onset
Baseline: HAM-A: Pregabalin (50mg) 24.9(3.9), Pregabalin (200mg) 25.4(4.6), Lorazepam 24.7(3.7), Placebo 24.8(4.1)

FRESQUET2000

Study Type: RCT
Study Description: Phase II study. 1 week placebo lead-in. Received placebo, lesopitron or lorazepam twice daily for 6 weeks followed by 1 week taper period.
Type of Analysis: ITT
Blindness: Double blind
Duration (days): Mean 42
Notes: RANDOMISATION: no details provided.

Data Used
CGI-I
HAM-A
Adverse events
Leaving the study due to adverse events
Leaving the study early for any reason
Response (50% reduction in HAM-A score)
Data Not Used

Baseline: HAM-A: Pregabalin (50mg) 24.9(3.9), Pregabalin (200mg) 25.4(4.6), Lorazepam 24.7(3.7), Placebo 24.8(4.1)

Notes: TAKEN AT: Baseline and end of active treatment (4 weeks)
DROPOUTS: total drop outs not reported

Baseline: HAM-A: Pregabalin (50mg) 24.9(3.9), Pregabalin (200mg) 25.4(4.6), Lorazepam 24.7(3.7), Placebo 24.8(4.1)

Notes: Participants with a dual comorbid psychiatric disorder were required to have GAD as a primary disorder as judged by the psychiatrist, considering relative severity and time of onset
Baseline: HAM-A: Pregabalin (50mg) 24.9(3.9), Pregabalin (200mg) 25.4(4.6), Lorazepam 24.7(3.7), Placebo 24.8(4.1)

Notes: 34% (placebo), 40% (escitalopram) received prior GAD pharmacotherapy, majority were nonresponders or intolerant to prior treatment
Baseline: HAM-A scores at baseline (approximate): 23.40

Notes: TAKEN AT: 1, 2, 4, 6 and 8 weeks. DROP OUTS: 4/158 (escitalopram), 4/157 (placebo).
CHANGE SCORES USED.

Baseline: HAM-A: Pregabalin (50mg) 24.9(3.9), Pregabalin (200mg) 25.4(4.6), Lorazepam 24.7(3.7), Placebo 24.8(4.1)

Notes: Participants with a dual comorbid psychiatric disorder were required to have GAD as a primary disorder as judged by the psychiatrist, considering relative severity and time of onset
Baseline: HAM-A: Pregabalin (50mg) 24.9(3.9), Pregabalin (200mg) 25.4(4.6), Lorazepam 24.7(3.7), Placebo 24.8(4.1)
GELENBERG2000

Study Type:
RCT

Study Description: Pooled analysis from 3 RCTs. Single-blind placebo lead-in for 1 week followed by 8 weeks of double-blind treatment with escitalopram or placebo.

Type of Analysis: ITT (LOCF)
Blindness: Double blind
Duration (days): Mean 56

Setting: Multicentre: US.

Notes: RANDOMISATION: table of random numbers. ALLOCATION CONCEALMENT: not addressed

Info on Screening Process: 261 patients enrolled; 251 randomised, 10 LTFU, 127 placebo, 124 venlafaxine; 4 placebo, 9 venlafaxine no primary outcome measure (not included in ITT); 44 placebo, 60 venlafaxine completed trial

n= 238
Age: Mean 40
Sex: 98 males 140 females
Diagnosis: 100% GAD by DSM-IV
Exclusions: - less than 18 years
- MDD
- primary diagnosis not GAD (DSM-IV)
- HAM-A score < 18
- HAM-A (anxious mood & tension items) < 2
- Reduction of at least 20% in the HAMA total score between screening visit & baseline
- Lower scores on the Covl Anxiety scale than the Raskin Depression Scale
- Raskin Depression Scale score greater than 3 on any item
- History of previous psychotic illness, bipolar disorder, ASPD or severe Axis II disorder
- Previous treatment with venlafaxine
- Concomitant medication (i.e. antipsychotic drug, antidepressant, benzodiazepine) or ECT
- Women lactating, pregnant or of childbearing potential not using an acceptable form of contraception

Baseline: HAM-A at baseline. Placebo: 20.3 (1.7), Lesopitron: 21.7 (3.0) and Lorzepam: 21.5 (3.2).

Data Used
HAM-A
Leaving the study due to inefficacy
Leaving the study due to adverse events
Leaving the study early for any reason

Data Not Used
Response (40% reduction in HAM-A score) - does not meet criteria

Notes: TAKEN AT: 1, 2, 3, 4, 6, 8, 12, 16, 20, 24 28 weeks. DROP OUTS: 61% but adequately taken account of in ITT (LOCF).

GOODMAN2005

Study Type:
RCT

Study Description: Pooled analysis from 3 RCTs. Single-blind placebo lead-in for 1 week followed by 8 weeks of double-blind treatment with escitalopram or placebo.

Type of Analysis: ITT (LOCF)
Blindness: Double blind
Duration (days): Mean 56

Setting: Multicentre: US.

Notes: RANDOMISATION: no details given.

Info on Screening Process: No details given.

n= 656
Age: Mean 39
Sex: 377 males 479 females
Diagnosis: 100% GAD by DSM-IV
Exclusions: Score of >=17 on the HAMD or a lower score on the Covl Anxiety Scale than the Raskin Depression Scale. Patients with a principal diagnosis of any Axis I disorder other than GAD (including MDD) or who met DSM-IV criteria for bipolar disorder, schizophrenia or any psychotic disorder, OCD, mental retardation, or any pervasive developmental disorder or cognitive disorder. A history of psychotic features or disorder, or substance misuse or dependence within the past 6 months. Use of any of the following psychotropic medications prior to study entry: depot neuroleptics within 6 months, any antiepileptic, antidepressants or anxiolytic within 2 weeks (5 weeks for fluoxetine), or daily benzodiazepine therapy within 1 month. Use of concomitant treatment with any psychotropic drug (except zolpidem as needed for

Data Used
HAM-A

Data Not Used
Adverse events - not extractable for individual studies
Leaving the study due to adverse events - not extractable for individual studies
Leaving the study early for any reason - not extractable for individual studies
Remission (less than 7 on HAM-A) - Not extractable for individual studies

Notes: TAKEN AT: Baseline and endpoint DROP OUT:13% across both groups.

100% GAD by DSM-IV

Notes: Assessments conducted weekly.
sleep). Women who were pregnant or breastfeeding, or of child-bearing potential and not practising a medically reliable method of birth control. Notes: ONLY USING STUDY 1 & 2 (as study 3 is reported already in DAVIDSON2004)
Baseline: HAM-A baseline scores: Placebo 22 (0.2) and Escitalopram 23.0 (0.2). Baseline scores are based on the ITT population.

GSK2002
Study Type: RCT
Study Description: Parallel-group study. 1 week single-blind placebo run-in phase. Randomised to either paroxetine or placebo.
Type of Analysis: ITT (LOCF)
Blindness: Double blind
Duration (days): Mean 56
Setting: Multicentre (32 centres): USA.
Notes: RANDOMISATION: no details given.
Info on Screening Process: No details given.

n= 335
Age: Mean 39
Sex: 119 males 208 females
Diagnosis:
100% GAD by DSM-IV
Exclusions: Diagnosis of any current Axis I disorder or within the 6 months prior to screening, posed a current suicidal or homicidal risk in the investigator's judgement, had a score of >=18 on the MADRS at screening or at baseline, showed greater than a 20% reduction in the HAM-A total score from screening to baseline, had taken other psychotropic drugs that had not been discontinued within the minimum discontinuation period prior to screening, had received formal psychotherapy either concurrently or in the 12 weeks prior to screening.

Notes: Participants received medication for a maximum of 10 weeks, including a 1-week placebo run-in phase followed by an 8-week treatment phase and a double-blind taper phase of up to 1 week.
Baseline: HAM-A: Paroxetine 24.43 (3.71) and Placebo 24.83 (3.64).

GSK2005
Study Type: RCT
Study Description: Placebo run-in medication for 1 week followed by randomisation to paroxetine (20mg/day) or placebo.
Type of Analysis: LOCF method used.
Blindness: Double blind
Duration (days): Mean 56
Setting: Multicentre (58 centres): Japan.
Notes: RANDOMISATION: procedure not known.
Info on Screening Process: Not known.

n= 361
Age: Mean 40
Sex: 144 males 214 females
Diagnosis:
100% GAD by DSM-IV
Exclusions: Subjects with suspected history of psychiatric disorder other than GAD or with history or complications of such diseases, subjects who had taken MAOIs within 1 week prior to week 1 and subjects with history of complications that might affect the subjects' safety.

Notes: Subjects classed as non-responders at week 8 continued to receive paroxetine or placebo orally for a further 4 weeks in a flexible dosing schedule.
Baseline: Baseline statistics not provided.

HACKETT2003
Study Type: RCT
Study Description: Randomised, double-blind, placebo-controlled, parallel-group study. Followed by long-term phase study that is reported separately.
Type of Analysis: ITT (LOCF method)

n= 540
Age: Mean 44
Sex: 175 males 365 females
Diagnosis:
100% GAD by DSM-IV
Exclusions: - <18 years of age

Notes: Participants received medication for a maximum of 10 weeks, including a 1-week placebo run-in phase followed by an 8-week treatment phase and a double-blind taper phase of up to 1 week.
Baseline: Baseline statistics not provided.
HARTFORD2007

Study Type: RCT

Study Description: ITT analysis included all randomised participants with >=1 post-baseline analysis. Safety analysis included all randomised participants.

Type of Analysis: ITT

Blindness: Double blind

Duration (days): Mean 70

Setting: Outpatients. Multicentre 42 sites in the USA

Notes: RANDOMISATION: procedure not reported

Info on Screening Process: 707 people were evaluated of whom 220 failed to meet the inclusion criteria.

Exclusions:
- <18 years
- No primary DSM-IV diagnosis of GAD
- CGI-S <4
- HADS anxiety subscale <10
- Covi Anxiety score <9 or not greater and then Raskin depression total score.
- Medical illness that would contraindicate use of duloxetine
- Women of childbearing age not using adequate contraception
- Recent diagnosis of depression or substance misuse/dependence
- Past year history of panic disorder, PTSD or eating disorder
- Lifetime history of bipolar disorder, OCD or psychosis
- Lack of response of GAD to 2 prior adequate trials of antidepressants or benzodiazepine treatments
- Psychotherapy initiated 6 weeks prior to study enrollment
- Benzodiazepine use in the 2 weeks before visit 2
- Judged clinically to be a serious suicide risk
- Previous duloxetine treatment

Baseline: HAM-A: Dulox 25.6(5.8) Venl 24.9(5.4) Placebo 25.0(5.8)

Notes: Rating scales were administered at baseline, and again after 7, 14, 21, 28, 42 and 56 days.

Data Used
- CGI-I (Response)
- CGI-I (Adverse events)
- DSQ-SF (Hospital Anxiety and Depression Scale (anxiety))
- SHEE (Sheehan Disability Scale (SDS))
- Remission (less than 7 on HAM-A)

Groups:
- Group 1: N=164
  - Venlafaxine (extended release). Mean dose 183.82mg/d - Started at 37.5mg/d for week 1, increased to 75mg/d for week 2 onwards. Dose could be increased to 150mg/d for at least 1 week and then to 225mg/d based on efficacy and tolerability
- Group 2: N=161
  - Placebo

Notes: TAKEN AT: Baseline and endpoint

Dropout:
- Duloxetine: 67/162 (45.7%) DROPOUT: Duloxetine: 67/162 (45.7%), Venlafaxine 62/164 (37.8%), Placebo 62/161 (38.5%)
- Other Group 1 and 2

Drug company funded - Eli Lilly trial 7107

Quality assessed +.

Funding: GlaxoSmithKline.
concurrently or in the 12 weeks prior to screening.

Notes: Participant requiring more than one dose reduction were withdrawn from the study. Gradual reduction of medication during double-blind taper phase of >3 weeks for participants who completed treatment or withdrew prematurely at dose of 30mg/day or higher.

Baseline: HAM-A: Paroxetine 26.0 (0.4) and Placebo 25.9 (0.4).

KASPER2009

**Study Type:** RCT

**Study Description:** A 1 week open-label lead-in period, then randomised to 8 weeks of double-blind, parallel-group treatment.

**Blindness:** Double blind

**Duration (days):** Mean 56

**Setting:** 47 sites in Belgium, Canada, France, Ireland, Italy, Netherlands, Spain, Sweden

**Notes:** RANDOMISATION: computer generated randomisation list.

**Info on Screening Process:** 466 screened, 374 met eligibility criteria.

**Data Used**

- CGI-I
- HAM-A
- Adverse events
- Sheehan Disability Scale (SDS)
- Hospital Anxiety and Depression Scale (anxiety)
- EQ-5D
- Leaving the study due to adverse events
- Leaving the study early for any reason
- Response (50% reduction in HAM-A score)

**Group 1 N=121**

- Pregabalin - Starting dose of 150mg/day for first week, thereafter flexible from 300-600mg/day

**Group 2 N=125**

- Venlafaxine (extended release) - starting dose of 75mg/day for first week then flexible thereafter between 75-225mg/day

**Group 3 N=128**

- Placebo - No details given.

KOPONEN2007

**Study Type:** RCT

**Study Description:** ITT analysis included all randomised participants with >=1 post-baseline analysis. Safety analysis included all randomised participants.

**Type of Analysis:** ITT

**Blindness:** Double blind

**Duration (days):** Mean 63

**Setting:** Outpatient clinics.

**Multicentre - 7 countries**

**Notes:** RANDOMISATION: procedure not reported. Participants were stratified by baseline HAM-A score.

**Info on Screening Process:** 639 participants were screened for the study with 126 failing to meet the inclusion criteria.

**Data Used**

- Q-LES-Q-SF
- Response (50% reduction in HAM-A score)
- Remission (less than 7 on HAM-A)
- Leaving the study early for any reason
- PGI-I
- Leaving the study due to adverse events
- Significant improvement (30% reduction)
- EQ-5D
- CG-I
- Symptom Questionnaire-Somatic subscale (SQ-SS)
- Leaving the study due to inefficacy
- Serious adverse events
- Sheehan Disability Scale (SDS)
- Visual Analog Scale (VAS)
- HAM-A
- Discontinuation adverse events (DAEs)

**Notes:** TAKEN AT: baseline and endpoint

**DROP OUT:** Dul 60 33/168 (19.6%); Dul 120 46/170 (27.1%); Placebo 45/175 (25.7%)

LADER1998

**Study Type:** RCT

**Study Description:** Week 1 open-label, then randomised to 8 week double blind, parallel group treatment.

**Blindness:** Double blind

**Duration (days):** Mean 94

**Setting:** Outpatient clinics.

**Multicentre - 7 countries**

**Notes:** RANDOMISATION: computer generated randomisation list.

**Info on Screening Process:** 466 screened, 374 met eligibility criteria.

**Diagnosis:**

- Age: Mean 41
- Sex: 146 males  228 females
- Exclusions:
  - <18 years or >65 years
  - HAM-A <20
  - HAM-A psychic and somatic factors <10
  - bipolar disorder, schizophrenia, psychosis
  - MDD, dysthymia, OCD, PTSD, eating disorder, substance misuse or dependence
  - pregnant

Baseline: HAM-A: Placebo 26.8 (SE=0.8) Venlafaxine 27.4 (SE=0.4) Pregabalin 27.6 (SE=0.4)

**Group 1 N=175**

- Placebo

**Group 2 N=168**

- Duloxetine. Mean dose 60mg/d - Participants were started with 60mg/d, if there were tolerability concerns this was lowered to 30mg/d with all participants having their doses gradually increased to their randomised dose within the first 2 study weeks.

**Group 3 N=170**

- Duloxetine. Mean dose 120mg/d - Participants were started with 60mg/d, if there were tolerability concerns this was lowered to 30mg/d with all participants having their doses gradually increased to their randomised dose within the first 2 study weeks.
Study Type: RCT
Study Description: 1-week single-blind placebo run-in then 4-week DB treatment with either hydroxyzine, buspirone or placebo followed by 1 week placebo administration.
Type of Analysis: ITT (LOCF)
Blindness: Double blind
Duration (days): Mean 28
Setting: Multicentre (62 centres): France (48 centres) and UK (14 centres). Patients seen by primary care doctors.
Notes: RANDOMISATION: no details provided.
Info on Screening Process: Excluded anyone who responded in placebo period or showed positive for benzodiazepines at entry. 266 recruited: 20 failed to meet inclusion criteria.

LENOSXHIT2003
Study Type: RCT
Blindness: Double blind
Duration (days): Mean 168
Setting: 31 Primary care centres, UK
Notes: RANDOMISATION: method not reported
Setting: Recruited from adverts and in a primary care centre, US
Notes: RANDOMISATION: method not reported
Info on Screening Process: 791 screened, 47 consented to participate. Of these 10 refused randomisation, 1 spontaneous improvement, 1 did not meet diagnostic criteria, 1 had MDD.

LENZ2005
Study Type: RCT
Blindness: Double blind
Duration (days): Mean 56
Setting: Recruited from adverts and in a primary care centre, US
Notes: RANDOMISATION: method not reported
Info on Screening Process: 791 screened, 47 consented to participate. Of these 10 refused randomisation, 1 spontaneous improvement, 1 did not meet diagnostic criteria, 1 had MDD.

LENZ2009
Study Type: RCT
Study Description: ITT: all participants who dropped out or were considered non-responders were included except for 2

n=244
Age: Mean 41 Range 30-42
Sex: 73 males 171 females
Diagnosis:
100% GAD by DSM-IV
Exclusions:
- Depressive disorders according to DSM-IV criteria. Pregnancy or inadequate contraceptive precautions, major depressive disorder, alcohol misuse, organic or psychotic disorders, undergoing long-term psychotherapy or intake of psychotropic medication during the previous 4 weeks.
- Participants had HAM-A score >20. Low levels of depressive symptoms allowed.
- Baseline: HAM-A at baseline. Hydroxyzine: 26.6 (4.3), Buspirone: 26.7 (4.1) and Placebo: 26.2 (4.2).

Funding: UCB, S.A. Quality assessed +.
Data Used
- CGI-I
- HAM-A

Adverse events
Hospital Anxiety and Depression Scale (anxiety)
Leaving the study early for any reason
Response (50% reduction in HAM-A score)
Notes: Assessments carried out weekly.

Group 1 N= 81
Hydroxyzine. Mean dose 50mg/day - 12.5mg morning and midday, 25mg evening.
Group 2 N= 81
Placebo. Mean dose 3 capsules/day - 3 capsules throughout the day.
Group 3 N= 82
Buspirone. Mean dose 20mg/day - 5mg morning and midday, 10mg evening.

n=177
Age: Mean 72
Sex: 58 males 119 females
Diagnosis:
100% GAD by DSM-IV
Exclusions:
- Current MDD
- Dementia
- Psychosis
- Unstable medical illness
- Substance misuse
Notes: 2 people in each group did not have GAD. 8 people in Citalopram group and 4 people in placebo group received lorazepam.
Baseline: HAM-A: Citalopram 21.4 (4.8) Placebo 23.1 (3.8)
HDRS: Citalopram 11.3 (2.1) Placebo 12.4 (3.8)

Funding: Wyeth. Quality assessed -.
Data Used
- HAM-A
- CGI (Response)
- Adverse events

Group 1 N= 122
Placebo
Group 2 N= 122
Venlafaxine (extended release) - Starting dose 75mg, could be increased to 150mg after 2 weeks. At end of 24 weeks patients on 150mg were reduced to 75mg and then the second week all patients received placebo.

n=34
Age: Mean 69
Sex: 13 males 21 females
Diagnosis:
90% GAD by DSM-IV
Exclusions:
- Current MDD
- Dementia
- Psychosis
- Unstable medical illness
- Substance misuse
Notes: 2 people in each group did not have GAD.
8 people in Citalopram group and 4 people in placebo group received lorazepam.
Baseline: HAM-A: Citalopram 21.4 (4.8) Placebo 23.1 (3.8)
HDRS: Citalopram 11.3 (2.1) Placebo 12.4 (3.8)

Funding: Forest Pharmaceuticals. Quality assessed +.

LENZ2009
Study Type: RCT
Study Description: ITT: all participants who dropped out or were considered non-responders were included except for 2

n=177
Age: Mean 72
Sex: 58 males 119 females
Diagnosis:
100% GAD by DSM-IV
Exclusions:
- Current MDD
- Dementia
- Psychosis
- Unstable medical illness
- Substance misuse
Notes: 2 people in each group did not have GAD.
8 people in Citalopram group and 4 people in placebo group received lorazepam.
Baseline: HAM-A: Citalopram 21.4 (4.8) Placebo 23.1 (3.8)
HDRS: Citalopram 11.3 (2.1) Placebo 12.4 (3.8)

Funding: National Institute of Health grant, drugs provided by Forest Laboratories. Quality assessed +.
participants who did not receive medication

Type of Analysis: ITT
Blindness: Double blind
Duration (days): Mean 84

Setting: USA
Notes: Randomisation: permuted block, 1:1 randomised list generated by study statistician
Info on Screening Process: 550 screened, 293 excluded, 257 consented to further assessment, 179 randomised, 2 did not receive medication

Diagnosis:
14% Major depressive disorder by DSM-IV
100% GAD by DSM-IV

Exclusions: - Less than 60 years of age
- Without a principal diagnosis of GAD
- Less than 17 on the HAM-A
- Bipolar disorder, dementia
- Increased suicide risk
- Medical instability
- Ongoing psychotherapy
- Current antidepressant or anxiolytic use (except for benzodiazepines up to 2 mg/day equivalent of lorazepam)

Notes: 17.1% (escitalopram), 13.2% (placebo) were on benzodiazepines. 12.1% of escitalopram and 15.2% of placebo groups had MDD diagnosis.
Baseline: HAM-A baseline depression score (approximate): 23.00 (2.30). No significant differences between groups at baseline.

Data Used
- CGI-I
- HAM-A
- Adverse events

Notes: Assessed weekly.

LLORCA2002

Study Type: RCT
Study Description: Parallel-group. 2 weeks single-blind run-in placebo, 12 weeks DB treatment and 4 weeks SB run-out placebo.
Type of Analysis: ITT
Blindness: Double blind
Duration (days): Mean 84

Notes: RANDOMISATION: no details provided.
Info on Screening Process: 369 entered recruitment period. 334 entered DB treatment.

n= 334
Age: Mean 43
Sex: 106 males 228 females

Diagnosis:
100% GAD by DSM-IV

Exclusions: Pregnant, breastfeeding, absence of a contraception method for women, known alcohol or drug dependence, major depressive episode within the preceding 6 months or >=7 on Raskin Severity of Depression and Mania scale, psychotic or delusional disorders within the preceding 3 years, concomitant chronic diseases, closed-angle glaucoma or prostatic adenoma, intolerance or allergy to hydroxyzine, bromazepam, lactose or cellulose, inability to use self-assessment scales, treatment with antipsychotics, neuroleptics, morphine or derivatives, hydroxyzine or bromazepam within the preceding 4 weeks, treatment with benzodiazepines >2 days per week during the previous 30 days or benzodiazepine intake during the previous 2 weeks, CNS active treatment within the last week preceding inclusion, need for psychotherapy.

Notes: GPs were trained to diagnose GAD. Participants not diagnosed by psychiatrists. Pts scored >=20 on HAM-A.

Data Used
- CGI-I
- HAM-A
- Adverse events

Notes: Remission (less than 7 on HAM-A): 14% (escitalopram), 10% (placebo).
Response (50% reduction in HAM-A score): 18.5% (escitalopram), 18.4% (placebo)

Data Used
- CGI-I
- HAM-A
- Adverse events

Notes: Assessed weekly.

LYDIARD1997

Study Type: RCT
Study Description: 4 weeks treatment with either abecarnil, alprazolam or placebo followed by 1-2 week taper.
Type of Analysis: ITT (LOCF)
Blindness: Double blind
Duration (days): Mean 28

Setting: Multicentre: outpatients, USA.
Notes: RANDOMISATION: no details provided.
Info on Screening Process: No details provided.

n= 192
Age: Mean 42
Sex: 89 males 103 females

Diagnosis:
100% GAD by DSM-III-R

Exclusions: No psychotherapeutic medication for at least 1 week and for at least 1 month for therapeutic doses of neuroleptics or antidepressants. History of psychosis, mania, current major depression, substance misuse, or other Axis I disorders likely to interfere with objectives of study. Any

Data Used
- CGI-I
- HAM-A
- Adverse events

Notes: Assessed weekly.

Group 1 N= 116
Bromazepam. Mean dose 6mg/day - 1.5mg in the morning and at noon and 3mg in the evening.

Group 2 N= 113
Placebo - Oral capsules divided into 3 daily doses.

Group 3 N= 105
Hydroxyzine. Mean dose 50mg/day - 50mg/day. 12.5mg in the morning and at noon and 25mg in th evening.

Funding: UCB-Pharma.
Quality assessed: +.

14
investigational drug taken within 30 days preceding study admission. Women of childbearing potential who were not using medically accepted birth-control methods or who were planning on becoming pregnant. Pregnant women.

Notes: Flexible dosage schedules used. Patients who discontinued for reasons unrelated to medication before completing 2 weeks of treatment were replaced. Participants had HAM-A score >=18 and Cov>Raskin score.


Data Used

HAM-A

Notes: randomisation: no further details

**MAJERCSIK2003**

Study Type: RCT

Blindness: Double blind

Duration (days): Mean 42

Setting: Hungary

Notes: randomisation: no further details

**MCLEOD1992**

Study Type: RCT

Blindness: Double blind

Duration (days): Mean 42

Setting: US volunteers recruited through adverts in local newspapers.

Notes: RANDOMISATION: no further details. Assignments were made so that the groups were matched according to gender.

**MOLLER2001**

Study Type: RCT

Study Description: ITT using LOCF. 307/313 participants were included in the ITT analysis

Type of Analysis: ITT

Blindness: Double blind

Duration (days): Mean 28

Setting: Multicentre, GERMANY. Outpatients

Notes: RANDOMISATION: procedure not

Group 1 N= 33

Buspirone - 30mg/day for 6 weeks

Group 2 N= 19

Placebo - 3 tablets a day

Group 2 N= 14

Imipramine. Mean dose 92.6mg - Starting dose 25mg but could be adjusted according to clinical need. Range 1-12 capsules.

Group 2 N= 14

Alprazolam. Mean dose 2.3mg - Starting dose of 0.5mg but could be adjusted according to clinical need.

Group 3 N= 14

Placebo - Took 1 capsule three times a day unless they developed excessive side effects.

Notes: Funded by NIH grant. Quality assessed -.

The study included a 7-day placebo washout period, followed by 4 weeks of active treatment. Active treatment was followed by tapering with placebo.

n= 52

Age: Mean 81

Sex: all males

Diagnosis: 100% GAD by DSM-IV

Exclusions: HAM-A <15
- anxiolytic medication in previous 6 months

Baseline: HAM-A Buspirone 19.45 (SE=0.46) Placebo 21.48 (SE=0.47)

**Data Used**

HAM-A

Blood pressure

Group 1 N= 33

Buspirone - 30mg/day for 6 weeks

Group 2 N= 19

Placebo - 3 tablets a day

n= 42

Age: Mean 41

Sex: 15 males 27 females

Diagnosis: 100% GAD by DSM-IV

Exclusions: - history of panic attacks, psychosis or substance misuse and could not have taken any medications that affect the autonomic or central nervous systems for at least 2 weeks prior to entry into the study

Notes: Participants were seen weekly for medication pick-up and supportive therapy, in which they discussed how they were coming along and received a sympathetic and understanding response from a therapist.

Baseline: HAM-A: Placebo 25.1 (2.0) Imipramine 25.3 (4.0) Alprazolam 28.1 (4.3)

**Data Used**

HAM-A

Blood pressure

2

Group 2 N= 14

Alprazolam. Mean dose 2mg/day - Medication was prepared in identical capsules containing 0.5mg. Day 0 of the 2 evening capsules was active, day 1, 2 of the evening capsules active, day 2 morning capsules were also active. By Day 3 the final dose of 2mg was given.

n= 313

Age: Mean 48

Sex: 104 males 209 females

Diagnosis: 100% GAD by ICD-10

Exclusions: - No ICD-10 diagnosis of GAD
- HAM-A <17 and HRSD >20
- Ages <18 or >65 years
- Significant other psychiatric disorders such as panic

Data Not Used

Leaving the study due to adverse events - not extractable

Leaving the study early for any reason - data not extractable

**Data Used**

Plasma concentrations

HAM-A

Adverse events
**MONTGOMERY2006**

**Study Type:** RCT  
**Study Description:** ITT: all randomised patients who received at least 1 dose of study drug. LOCf used on all primary and secondary outcome measures.  
**Type of Analysis:** ITT  
**Blindness:** Double blind  
**Duration (days):** Mean 42  
**Follow-up:** None  
**Setting:** Multicentre (76): Austria, Belgium, Germany, the Netherlands and the United Kingdom. Outpatients attending primary care or psychiatric practices.  
**Notes:** Randomisation procedure not reported. Parallel-group design.  

Info on Screening Process: 543 participants entered baseline phase; 421 were randomised and received study medication. Reasons for exclusion: did not meet entry criteria, lost to follow-up, withdrew consent, other/administrative and randomised but did not take study medication.

**Notes:** Participants were diagnosed using the Mini-International Neuropsychiatric Interview (MINI).

Baseline: Pregabalin 400mg/day (N=97, 23%), Pregabalin 600mg/day (N=110, 26%), Venlafaxine (N=113, 27%) and Placebo (N=101, 24%). HAM-A baseline: Pregabalin 400mg/day 26.3 (4.4), Pregabalin 600mg/day 25.4 (4.6), Venlafaxine 26.0 (4.6) and Placebo 27.4 (5.5). TOTAL: 26.6 (4.8). HRSD baseline: Pregabalin 400mg/day 12.2 (3.6), Pregabalin 600mg/day 12.2 (4.0), Venlafaxine 12.0 (3.4) and Placebo 12.8 (4.9). TOTAL: 12.3 (4.0).

**Data Used**  
**CGI-I**  
**HAM-A**  
**Adverse events**  
**SCL anxiety factor**

- *Placebo responders (defined as those showing a decrease >6 points during the washout period)*
- *Notes: ~66% of participants had concomitant diseases*
- *Baseline: No relevant differences at baseline*
- *HAM-A: Opipramol 27.7(7.4), Alprazolam: 29.7(7.6), Placebo: 29.3(7.0)*

**MONTGOMERY2008**

**Study Type:** RCT  
**Study Description:** Parallel group study, 1-week drug-free period then 8-week double-blind study, followed by a 1-5 day taper with a final follow-up visit at 1 week.  
**Type of Analysis:** ITT (LOCf)  
**Blindness:** Double blind  
**Duration (days):** Mean 56  
**Setting:** Outpatients. Multicentre study: 13 in the

**Study Description:** Parallel-group design.

- *Setting: Outpatients. Multicentre study: 13 in the
- *Duration (days): Mean 56
- *Blindness: Double blind
- *Type of Analysis: ITT (LOCF)
- *Study Type: RCT
- *Notes: ~66% of participants had concomitant diseases
- *Baseline: No relevant differences at baseline
- *HAM-A: Opipramol 27.7(7.4), Alprazolam: 29.7(7.6), Placebo: 29.3(7.0)*

**Data Used**  
**CGI-I**  
**HAM-A**  
**Adverse events**  
**SCL anxiety factor**

- *Notes: TAKEN AT: baseline and end of treatment (end of active treatment)*
- *DROPOUTS: Opipramol 8/101 (8%), Alprazolam 13/105 (12%), Placebo 18/107 (17%)*
- *Group 3 N=101 Opipramol. Mean dose 200mg/day - Medication was prepared in identical capsules containing 50mg. Day 0 1 of the 2 evening capsules was active, day 1, 2 of the evening capsules active, day 2 morning capsules were also active. By Day 3 the final dose of 200mg was given.*

**Funding:** Pfizer, Inc. Quality assessed: +.
US and 69 in Europe.

Notes: RANDOMISATION: were randomised 2:1 pregabalin: placebo.

Info on Screening Process: 366 people screened. 68 did not meet entry criteria, 16 withdrew consent and 11 did not enter for other reasons.

**NICOLINI2009**

Study Type: RCT

Type of Analysis: ITT (LOCF)

Blindness: Double blind

Duration (days): Mean 70

Setting: Australia, Argentina, Belgium, Canada, Mexico, Russia, Taiwan, UK

Outpatients

Notes: RANDOMISATION: computer-generated ALLOCATION CONCEALMENT: interactive voice response system

Info on Screening Process: Patients entered (N=771); did not meet criteria/consent (N=190); patients randomised (N=581); did not meet criteria/concent (N=190); patients completed trial (N=396)

**NIMATOUDIS2004**

Study Type: RCT

Study Description: Venlafaxine vs. Placebo for 8 weeks. 1-week placebo run-in phase.

Type of Analysis: ITT (LOCF)

Blindness: Double blind

Duration (days): Mean 56

Followup: 4-10 days


Notes: RANDOMISATION: no details provided.

Info on Screening Process: Removed anyone with <12. Recent history or current diagnosis of drug or alcohol dependence and/or misuse in the past 6 months, positive urine drug screen, any clinically significant acute or unstable medical condition or clinically significant ECG or laboratory abnormalities, alanine/aspartate aminotransferase levels >3 times the upper limit of normal or creatinine clearance rates, concurrent psychotherapy for generalised anxiety disorder unless in stable treatment >3 months, concomitant treatment with psychotropic medication during the study and for at least 2 weeks prior to the screening visit, current suicide risk based on the clinical judgement of the investigator, depressive symptoms predominating over anxiety symptoms.

Notes: Diagnosis based on MINI interview, HAM-A score >20 and MMSE score >24. Monitored adherence by counts of returned medication and ppts were counselled if they were found to be non-adherent.

Baseline: HAM-A at baseline. Pregabalin: 27 (4.8) and Placebo: 26 (4.1).

**Data Used**

**CGI**

**HAM-A**

Sheehan Disability Scale (SDS)

Hospital Anxiety and Depression Scale (anxiety)

Leaving the study due to inefficacy

Leaving the study due to adverse events

PGI-I

Leaving the study early for any reason

Remission (less than 7 on HAM-A)

Response (50% reduction in HAM-A score)

Notes: DROP OUTS: 21/84 (25%) - DUL 20mg; 49/158 (31%) - DUL 60-120 mg; 47/122 (39%) - VENLAFAXINE; 68/170 (40%) - PLACEBO.

Notes: Duration of GAD M (S.D.) = 4.37 (8.19) years

Baseline: BASELINE HAM-A scores = 27.4 (total); 27.33 (7.33) (placebo); 27.65 (7.99) - DUL 20mg; 27.74 (7.32) - DUL 60-120mg), 27.36 (7.57) - VEN 75-125mg)

**Notes**: Funding: possibly Wyeth. Quality assessed: -

**Group 1**

N= 169

Venlafaxine (extended release). Mean dose 151.3mg/day - 75 - 225 mg/day; flexible dosing of an increase of 75mg/day. Dose increase required if CGI-I score > 4 after 3 weeks. Dose could be decreased no more than twice. Dose stabilised after 6 weeks.

**Group 2**

N= 84

Duloxetine 20mg. Mean dose 20mg/day - Once daily fixed dose of 20mg. Those who required dose increase received additional placebo capsules.

**Group 3**

N= 170

Placebo

**Group 4**

N= 158

Duloxetine. Mean dose 90mg/day - 60-120 mg/day flexible dosing of an increase of 30mg/day. Dose increase required if CGI-I score > 4 after 3 weeks. Dose could be decreased no more than twice. Dose stabilised after 6 weeks.

**Data Used**

**CGI**

**HAM-A**

Adverse events

Leaving the study early for any reason

Remission (less than 7 on HAM-A)

Response (50% reduction in HAM-A score)

Notes: Trial report collected (R7106). Quality assessed: +

**Group 1**

N= 24

Venlafaxine (extended release). Mean dose 75mg/day - Participants with a less than 30% decrease in their HAM-A total score at the end of 2 weeks compared with the end of the pre-study period doubled their dose for the rest of the treatment period (150mg/day).

**Group 2**

N= 22

Placebo - No details provided.
with a 20%+ decrease in HAM-A score during pre-study period.

**PANDE2003**

**Study Type:** RCT

**Study Description:** 1 week placebo lead-in followed by 4 weeks of treatment and then a 1-week dose taper.

**Type of Analysis:** ITT (LOCF method)

**Blindness:** Double blind

**Duration (days):** Mean 28

**Setting:** Outpatients. Multicentre: USA (Seattle, Portland, Lansing, Los Angeles and Durham).

**Notes:** RANDOMISATION: no details provided.

**Info on Screening Process:** Recruited via clinic referrals or from advertisements. 361 screened; 84 excluded because didn’t meet inclusion criteria (N=31), experienced an adverse event (N=1) or because of other administrative reasons (N=52).

**Data Used**

- HAM-A
- CGI-I
- Adverse events

**Data Not Used**

- Discontinuation adverse events (DAEs) - not extractable

**Group 1** N= 69

Placebo - Day 1 received 1/6 of dose, which was increased daily until targeted dose was reached.

**Group 2** N= 70

Lorazepam. Mean dose 6mg/day - 2mg three times a day. Day 1 received 1/6 of dose, which was increased daily until targeted dose was reached.

**Group 3** N= 68

Pregabalin. Mean dose 150mg/day - 50mg three times a day. Day 1 received 1/6 of dose, which was increased daily until targeted dose was reached.

**Group 4** N= 66

Pregabalin. Mean dose 600mg/day - 200mg three times a day. Day 1 received 1/6 of dose, which was increased daily until targeted dose was reached.

**Notes:**
- Pts had HAM-A baseline score >=18 and Covi Anxiety score >=8.
- Baseline: HAM-A at baseline. Venlafaxine: 27.1 (4.8) and Placebo: 28.5 (6.4)

**PFIZER2005**

**Study Type:** RCT

**Blindness:** Double blind

**Duration (days):** Mean 28

**Follow-up:** No Info

**Setting:** No Info

**Notes:** No Info

**Info on Screening Process:** No Info

**Data Used**

- HAM-A
- CGI-I

**Data Not Used**

- Discontinuation adverse events (DAEs) - not extractable

**Group 1** N= 67

Placebo - Day 1 received 1/6 of dose, which was increased daily until targeted dose was reached.

**Group 2** N= 64

Lorazepam. Mean dose 6mg/day - 2mg three times a day. Day 1 received 1/6 of dose, which was increased daily until targeted dose was reached.

**Group 3** N= 69

Pregabalin. Mean dose 150mg/day - 50mg three times a day. Day 1 received 1/6 of dose, which was increased daily until targeted dose was reached.

**Group 4** N= 66

Pregabalin. Mean dose 600mg/day - 200mg three times a day. Day 1 received 1/6 of dose, which was increased daily until targeted dose was reached.

**Notes:**
- Pts had HAM-A baseline score >=18 and Covi Anxiety score >=8.
- Baseline: HAM-A at baseline. Venlafaxine: 27.1 (4.8) and Placebo: 28.5 (6.4)

**PFIZER2008**

**Study Type:** RCT

**Type of Analysis:** ITT

**Blindness:** Double blind

**Duration (days):** Mean 28

**Notes:**

- Exclusions: Any axis I disorder except dysthymia, simple phobia, social phobia, somatisation disorder, or a history of MDD. Patients at suicide risk. No psychotropic medications for 2 weeks before enrollment. Score >=2 on HRSD item 3.
- Notes: Administered Mini International Neuropsychiatric Interview. Divergent findings between clinical interview and MINI were resolved by judgement of principal investigator. Had to have Covi Anxiety Scale >=9 and Raskin Depression Scale score <=7.
- HAM-A >20.
- Notes: Administered Mini International Neuropsychiatric Interview. Divergent findings between clinical interview and MINI were resolved by judgement of principal investigator. Had to have Covi Anxiety Scale >=9 and Raskin Depression Scale score <=7.

**Data Used**

- HAM-A total score

**Data Not Used**

- Discontinuation adverse events (DAEs) - not extractable

**Group 1** N= 56

Paroxetine. Mean dose 20mg - Capsules for oral administration. 20mg daily for 28 days
Exclusions: Pregnant and lactating females. No primary diagnosis of GAD. HAM-A <20. Covi Anxiety Scale total score <9. Raskin Depression Scale total score >7. Subjects who had past or current DSM-IV Axis I diagnosis or receiving daily benzodiazepines 3 months prior to screening.

Baseline: HAMA Placebo 24.0 (4.9) Paroxetine 23.5 (3.3) Lorazepam 24.2 (3.6)

POHL2005
Study Type: RCT
Study Description: Comparison of the efficacy and tolerability of BID versus TID dosing of pregabalin. 1-week drug-free screening phase followed by 6 weeks DB treatment.
Type of Analysis: ITT (LOCF)
Blindness: Double blind
Duration (days): Mean 42
Setting: 19 centres: USA. Participants recruited via clinic referrals and adverts in the local media.
Notes: RANDOMISATION: randomised in a 1:1:1:1 fashion.
Info on Screening Process: 605 screened: 174 did not meet entry criteria, 22 were lost to follow-up, 36 withdrew consent, 3 were randomised but did not take study medication and 29 were lost for other or administrative reasons.

n= 464
Age: Mean 39
Sex: 181 males 277 females
Diagnosis: 100% GAD by DSM-III-R

Exclusions: Current diagnosis of or a history of bipolar illness, organic mental syndromes, schizophrenia or other psychotic disorders, or seizure disorders.

Notes: Participants scored >=20 on the HAM-A, >=9 on Covi Anxiety Scale and >=7 on the Raskin Depression Scale. Diagnosis made via MINI.
Baseline: HAMA Placebo 24.0 (4.9) Paroxetine 23.5 (3.3) Lorazepam 24.2 (3.6)

Data Used

HAM-A
CGI (Response)
Adverse events
Leaving the study due to adverse events
Leaving the study early for any reason
Remission (less than 7 on HAM-A)
Response (50% reduction in HAM-A score)
Notes: Participants were assessed at baseline and study weeks 1, 2, 3, 4 and 6.

Group 1 N= 89
Pregabalin. Mean dose 400mg/day - Treatment was initiated at 200mg/day and titrated to 400mg/day on day 4.

Group 2 N= 86
Placebo

Group 3 N= 88
Pregabalin. Mean dose 450mg/day - Treatment was initiated at 300mg/day and titrated to 450mg/day on day 4.

Group 4 N= 78
Pregabalin. Mean dose 200mg/day - Treatment was initiated at 200mg/day and participants were maintained on this dosage.

Data Used

Group 1 N= 115
Buspirone - Started at 15-45mg/day. Increased in first 2 weeks up to 15mg three times a day by day 15. Kept fixed thereafter.

Group 2 N= 116
Abecarnil - Started at 3-9mg/day. Increased during first 2 weeks up to 3mg three times a day by day 15. Kept fixed after day 15.

Group 3 N= 112
Placebo - No details.

Group 4 N= 115
Abecarnil - Started at 7.5-22.5mg/day. Increased during first 2 weeks to be given maximum of 7.5mg three times a day by day 15. Kept fixed after day 15.

Data Used

Group 1 N= 163
Placebo

Funding: Pfizer, Inc. Quality assessed: +.

Funding: GSK. Quality assessed +.


Funding: GSK. Quality assessed +.
Baseline assessment, 7 withdrew before start of treatment

- HAM-A items 1 and 2 <2
- diagnosis of any other Axis I disorder
- MADRS >17
- substance misuse or dependence
- women of child bearing potential not using reliable contraception

Baseline: HAM-A: Placebo 24.1(0.30) Paroxetine 24.2(0.30)

Notes: Study consisted of 6 weeks' double-blind treatment followed by an optional maintenance period for a total of 24 weeks were withdrawn. After 2 weeks could be increased depending on response within range of 3-7 capsules per day.

Data Used
HAM-A

Leaving the study due to inefficacy
Leaving the study due to adverse events
Leaving the study early for any reason

Notes: Response was based on CGI score 1 or 2

Group 2 N=161
Paroxetine - 10mg/day first week, 20mg/day second week, those who could not tolerate the medication during first 2 weeks were withdrawn. After 2 weeks could be increased every week by 10mg/day up to 50mg/day.

Group 1 N=92
Venlafaxine (extended release), Mean dose 75mg/d - 8-week intervention. Fixed doses. Week 1 to 8: 75mg/d. One pill in the morning.

Group 2 N=90
Venlafaxine (extended release), Mean dose 225mg/d - 8-week intervention. Fixed doses. Week 1: 75mg/d. Week 2: 150mg/d. Week 3 to 8: 225mg/d.

Group 3 N=91
Venlafaxine (extended release), Mean dose 150mg/d - 8-week intervention. Fixed doses. Week 1: 75mg/d. Week 2 to 8: 150mg/d.

Group 4 N=97
Placebo - No information given.

Paroxetine: 24.0 (4.1). Venlafaxine 225mg/d: 23.6 (3.7). Placebo: 24.1 (4.2).

Baseline: HAM-A baseline depression score (approximate): 24.23 (4.10). No significant differences between groups at baseline. Venlafaxine 75mg/d: 24.7 (4.4). Venlafaxine 150mg/d: 24.5 (4.1).Venlafaxine 225mg/d: 23.6 (3.7). Placebo: 24.1 (4.2).

Funding: Wyeth-Ayerst Laboratories. Quality assessed: 

Week 1: 75mg/d. Week 2: 150mg/d. Week 3 to 8: 225mg/d.

Quality assessment score =

Drug company sponsored: Schering AG, Berlin and

Notes: Randomisation: not reported.

Allocation concealment: not addressed

Notes: Randomisation: procedure not reported

Info on screening process: 370 completed placebo run-in period & received study drug, 21 of these were excluded as they had no primary outcome.

Notes: Study consisted of 6 weeks' double-blind treatment followed by an optional maintenance period for a total of 24 weeks were withdrawn. After 2 weeks could be increased depending on response within range of 3-7 capsules per day.

Data Used
HAM-A

Leaving the study due to inefficacy
Leaving the study due to adverse events
Leaving the study early for any reason

Notes: Response was based on CGI score 1 or 2

Group 2 N=161
Paroxetine - 10mg/day first week, 20mg/day second week, those who could not tolerate the medication during first 2 weeks were withdrawn. After 2 weeks could be increased every week by 10mg/day up to 50mg/day.

Group 1 N=92
Venlafaxine (extended release), Mean dose 75mg/d - 8-week intervention. Fixed doses. Week 1 to 8: 75mg/d. One pill in the morning.

Group 2 N=90
Venlafaxine (extended release), Mean dose 225mg/d - 8-week intervention. Fixed doses. Week 1: 75mg/d. Week 2: 150mg/d. Week 3 to 8: 225mg/d.

Group 3 N=91
Venlafaxine (extended release), Mean dose 150mg/d - 8-week intervention. Fixed doses. Week 1: 75mg/d. Week 2 to 8: 150mg/d.

Group 4 N=97
Placebo - No information given.

Paroxetine: 24.0 (4.1). Venlafaxine 225mg/d: 23.6 (3.7). Placebo: 24.1 (4.2).

Baseline: HAM-A baseline depression score (approximate): 24.23 (4.10). No significant differences between groups at baseline. Venlafaxine 75mg/d: 24.7 (4.4). Venlafaxine 150mg/d: 24.5 (4.1). Venlafaxine 225mg/d: 23.6 (3.7). Placebo: 24.1 (4.2).

Funding: Wyeth-Ayerst Laboratories. Quality assessed: 

Week 1: 75mg/d. Week 2: 150mg/d. Week 3 to 8: 225mg/d.

Quality assessment score =

Drug company sponsored: Schering AG, Berlin and

Notes: Randomisation: not reported.

Allocation concealment: not addressed

Notes: Randomisation: procedure not reported

Info on screening process: 370 completed placebo run-in period & received study drug, 21 of these were excluded as they had no primary outcome.

Notes: Study consisted of 6 weeks' double-blind treatment followed by an optional maintenance period for a total of 24 weeks were withdrawn. After 2 weeks could be increased depending on response within range of 3-7 capsules per day.

Data Used
HAM-A

Leaving the study due to inefficacy
Leaving the study due to adverse events
Leaving the study early for any reason

Notes: Response was based on CGI score 1 or 2

Group 2 N=161
Paroxetine - 10mg/day first week, 20mg/day second week, those who could not tolerate the medication during first 2 weeks were withdrawn. After 2 weeks could be increased every week by 10mg/day up to 50mg/day.

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Group 4 N=97
Placebo - No information given.

Paroxetine: 24.0 (4.1). Venlafaxine 225mg/d: 23.6 (3.7). Placebo: 24.1 (4.2).

Baseline: HAM-A baseline depression score (approximate): 24.23 (4.10). No significant differences between groups at baseline. Venlafaxine 75mg/d: 24.7 (4.4). Venlafaxine 150mg/d: 24.5 (4.1). Venlafaxine 225mg/d: 23.6 (3.7). Placebo: 24.1 (4.2).

Funding: Wyeth-Ayerst Laboratories. Quality assessed: 

Week 1: 75mg/d. Week 2: 150mg/d. Week 3 to 8: 225mg/d.

Quality assessment score =

Drug company sponsored: Schering AG, Berlin and

Notes: Randomisation: not reported.

Allocation concealment: not addressed

Notes: Randomisation: procedure not reported

Info on screening process: 370 completed placebo run-in period & received study drug, 21 of these were excluded as they had no primary outcome.
Data Used
HAM-A
Adverse events
Leaving the study due to adverse events
Leaving the study early for any reason
Remission (less than 7 on HAM-A)
Data Not Used
Response (50% reduction in HAM-A score) - not extractable
Notes: Response based on CGI score of 1 or 2.

Data Used
CGI-I
Ham-A
Adverse events
Leaving the study due to adverse events
Leaving the study early for any reason
Remission (less than 7 on HAM-A)

Notes: Diagnosis was based on structured Mini-International Neuropsychiatric Interview. Had HAM-A scores >9 and Covi Anxiety Scale scores >9.

Baseline: HAM-A: Placebo 24.4 (3.7) 20mg Parox 24.1 (3.6) 40mg Parox 23.8 (3.4)

Baseline: HAM-A at baseline: Pregabalin 300: 25.0 (SE 3.6) 40mg Parox 23.8 (3.4)

Weeks. During the maintenance period, participants continued to receive double-blind treatment.

Baseline: HAM-A: Placebo 24.4 (3.7) 20mg Parox 24.1 (3.6) 40mg Parox 23.8 (3.4)

Baseline: HAM-A at baseline: Pregabalin 300: 25.0 (SE 3.6) 40mg Parox 23.8 (3.4)

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Characteristics of Excluded Studies

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<tr>
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<tr>
<td>ANSSEAU1985</td>
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</table>

**RYNN2008**

**Study Type:** RCT

**Study Description:** ITT included all randomised participants with at least one post-baseline evaluation. Safety analysis included all randomised participants.

**Type of Analysis:** Double Blind

**Duration (days):** Mean 70

**Setting:** Outpatients, Multicentre trail across USA

**Notes:** RANDOMISATION: procedure not reported

Info on Screening Process: 515 patients were evaluated, 168 failed to meet the inclusion criteria

- **n= 327**
  - Age: Mean 42
  - Sex: 125 males 202 females
  - Diagnosis: 100% GAD by DSM-IV
  - Exclusions: <18 years - No primary DSM-IV diagnosis of GAD - CGI-S > 4 - HADS anxiety subscale > 10 - Covi Anxiety score < 9 or not greater and then Raskin depression total score.

  - Medical illness that would contraindicate use of duloxetine
  - Women of childbearing age not using adequate contraception
  - Recent diagnosis of depression or substance misuse/dependence
  - Past year history of panic disorder, PTSD or eating disorder
  - Lifetime history of psychotic, bipolar, OCD or psychosis
  - Lack of response of GAD to 2 prior adequate trials of antidepressants or benzodiazepine treatments
  - Psychotherapy initiated 6 weeks prior to study enrollment

  **Baseline:** HAM-A: Duloxetine 22.6(7.4) Placebo 23.5(7.9)

**Data Used**
- PAS-Q-LES-Q-SF
- Remission (less than 7 on HAM-A)
- Leaving the study due to adverse events
- Significant improvement (30% reduction)
- EQ-5D
- CGI-I
- Leaving the study due to inefficacy
- Serious adverse events
- Ongoing assessment due to adverse events (DAEs)

**Notes:** TAKEN AT: Baseline and endpoint

**DROP OUT:** Duloxetine: 75/168 (44.6%), Placebo 50/159 (31.4%)

**Group 1 N= 168**
- Duloxetine. Mean dose 101.94mg/d - Participants were started with 60mg/d, if there were tolerability concerns this was lowered to 30mg/d. By week 2 all patients were required to take a minimum of 60mg/d. Patient doses were progressively titrated if the CGI rating was >=3 up to max of 120mg

**Group 2 N= 159**
- Placebo

**SRAMEK1996**

**Study Type:** RCT

**Study Description:** Placebo for 7-10 days. Randomised to receive either buspirone or placebo for 6 weeks.

**Type of Analysis:** LOCF method (completed >= 2 weeks treatment)

**Blindness:** Double blind

**Duration (days):** Mean 42

**Setting:** Multicentre: USA

**Notes:** RANDOMISATION: no details provided.

Info on Screening Process: 222 patients entered study: 60 dropped out. 34 didn't meet study inclusion criteria.

- **n= 162**
  - Age: Mean 38
  - Sex: 72 males 90 females
  - Diagnosis: 100% GAD by DSM-III-R

**Exclusions:** Pregnant or lactating, DSM-III-R diagnosis of MDD, a concurrent DSM-III-R Axis I disorder, a history of two or more panic attacks within 4 weeks of the beginning of screening, score of 3 or more on the suicide item of the HRSD scale, used benzodiazepines for 14 days or more in the last 2 months or an investigational drug within the past month, received ECT within the last 3 months or treatment with other psychotropics in the previous month. Clinically significant and/or uncontrolled medical conditions, positive urine drug screen, current or recent history of drug or alcohol misuse.

**Notes:** HAM-A score >=18, score of 2 or 3 on the 'depressed mood' item of the HAM-A scale, score of >=2 on the 'anxious mood' and 'tension' items on the HAM-A. HRSD score between 12 and 15. Covi > Raskin.

**Baseline:** HAM-A at baseline. Buspirone: 24.9 (4.2) and Placebo: 25.6 (4.4)

**Data Used**
- CGI-I
- HAM-A

**Adverse events**

**Notes:** Assessed weekly.

**Group 1 N= 82**
- Placebo - No details.

**Group 2 N= 80**
- Buspirone - Titrated from an initial dosage of 5mg t.i.d. to 10 mg t.i.d. over first week. Dosage increased by 5mg/day every 2-3 days. After 2 weeks of maintenance at 10mg t.i.d., those who didn't show an improvement were titrated to 15mg t.i.d. over next 7 days.

**Funding:** Bristol-Myers Squibb Pharmaceutical Research Institute. Quality assessed: +.
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<td>BOND2002</td>
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FRESQUET2000 (Published Data Only)

GELENBERG2000 (Published Data Only)

GOODMAN2005 (Published Data Only)

GSK2002 (Unpublished Data Only)

GSK2005 (Unpublished Data Only)

HACKETT2003 (Published Data Only)

HARTFORD2007 (Published Data Only)

HEWETT2001 (Unpublished Data Only)

KASPER2009 (Published Data Only)

KOPONEN2007 (Published Data Only)

LADER1998 (Published Data Only)

LENOXSMITH2003 (Published Data Only)

LENZE2005 (Published Data Only)

LENZE2009 (Published Data Only)

LLORCA2002 (Published Data Only)

LYDIARD1997 (Published Data Only)


References of Excluded Studies


BUCHSBAUM1987 (Published Data Only)

BYSTRITSKY1991 (Published Data Only)

CASTILLO1988 (Published Data Only)

CEPHALON2006A (Unpublished Data Only)

CEULEMANS1985 (Published Data Only)

COHN1986B (Published Data Only)

CUTLER1994 (Published Data Only)

ENKELMANN1991 (Published Data Only)

FEIGHNER1982 (Published Data Only)

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GINSBERG2005 (Published Data Only)


NAUKKARINEN2005 (Published Data Only)

PANGALILARATU1988 (Published Data Only)

PEET1986 (Published Data Only)

PETRACCA1990 (Published Data Only)

POMARA2005 (Published Data Only)

POURMOTABBED1996 (Published Data Only)

POWER1985 (Published Data Only)

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POWER1990A (Published Data Only)


RAMCHANDRAN1990 (Published Data Only)

RAPAPORT2006 (Published Data Only)

REALINI1990 (Published Data Only)

RICKELS1972 (Published Data Only)

RICKELS1993 (Published Data Only)

RICKELS1997 (Published Data Only)
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ROLLAND2002

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SACCHETTI1995

SHAH1990

SHAH1991

SCHMIDT2004

SPRALIN2003

SRAMEK1996A

STRAND1990

TSUKAMOTO2004

WILCOX1994

WINGERSON1992

WURTHMAN2006

WURTHMAN2006
Characteristics Table for The Clinical Question: In the treatment of generalised anxiety disorder what treatment dose improves outcome?

### Comparisons Included in this Clinical Question

<table>
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### Characteristics of Included Studies

**ALLGULANDER2001**

- **Study Type:** RCT
- **Study Description:** ITT: all eligible participants with at least one efficacy evaluation made whilst receiving study medication
- **Type of Analysis:** ITT/LOCF
- **Blinding:** Double blind
- **Duration (days):** Mean 168
- **Setting:** Belgium, Finland, France, Sweden, UK
- **Outpatients:** (14 centres)
- **Notes:** RANDOMISATION: not reported.

#### Study Description: ITT

- All eligible patients with at least one baseline efficacy assessment were included in the analysis.
- **Allocation Concealment:** Sealed opaque envelopes.
- **Info on Screening Process:** 541 randomised, 529 met ITT criteria for inclusion.

#### Data Used

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| Notes | **Funding:** Wyeth-Ayerst Research. Quality assessed: +.

#### Data Not Used

- **Response (50% reduction in HAM-A score) - not extractable**
- **Outcome:** Leaving the study due to ineffectiveness

#### Interventions

- **Data Used:** HAM-A
- **Outcome:** Leaving the study due to ineffectiveness
- **Outcome:** Leaving the study due to adverse events
- **Outcome:** Leaving the study early for any reason

#### Notes

- **Diagnosis:** 100% GAD by DSM-IV
- **Exclusions:** - DSM-IV diagnosis of GAD - HAM-A score < 20 - HAM-A (anxious mood & tension items) < 2 - MDD or other psychiatric disorder

**Baldwin2006**

- **Study Type:** RCT
- **Study Description:** ITT: patients who took at least one dose of the study medication & at least one baseline efficacy assessment were included in the analysis
- **Type of Analysis:** LOCF/ITT
- **Blinding:** Double blind
- **Duration (days):** Mean 84
- **Setting:** UK

#### Study Description: ITT

- All eligible patients with at least one baseline efficacy assessment were included in the analysis.
- **Allocation Concealment:** Sealed opaque envelopes.
- **Info on Screening Process:** Details not provided.

#### Data Used

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| Notes | Received support from Lundbeck and sponsored by GlaxoSmithKline. Quality assessed: +.

#### Data Not Used

- **Response (50% reduction in HAM-A score) - not extractable**
- **Outcome:** Leaving the study due to ineffectiveness
- **Outcome:** Leaving the study due to adverse events
- **Outcome:** Leaving the study early for any reason

#### Interventions

- **Data Used:** HAM-A
- **Outcome:** Leaving the study due to ineffectiveness
- **Outcome:** Leaving the study due to adverse events
- **Outcome:** Leaving the study early for any reason

#### Notes

- **Diagnosis:** 100% GAD by DSM-IV-TR
- **Exclusions:** - not primary diagnosis of GAD (DSM-IV-TR) - not between 18 and 65 - HAM-A score < 20 - HAM-A (anxious mood & tension items) < 2 - MADRS >15 - Diagnosis of: MDD, panic disorder, social anxiety, PTSD, bipolar, OCD, body dysmorphic disorder, substance misuse, personality disorder

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**Characteristics of Included Studies**

<table>
<thead>
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<th>Participants</th>
<th>Outcomes</th>
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<td>Blinding: Double blind</td>
<td>Exclusions: - DSM-IV diagnosis of GAD - HAM-A score &lt; 20 - HAM-A (anxious mood &amp; tension items) &lt; 2 - MDD or other psychiatric disorder - Clinically important medical disease - Non-pharmacological drugs with psychotropic effects</td>
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<tr>
<td>Duration (days): Mean 168</td>
<td>Notes: 74% had received prior treatment for anxiety (mostly benzodiazepines &amp; antidepressants); 85% received non-anxiolytic concomitant therapy during the study (26 on beta-blockers, 52 zolpidem or chloral hydrate)</td>
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<td>Setting: Belgium, Finland, France, Sweden, UK</td>
<td>Baseline: HAM-A baseline depression score (approximate): 26.48 (range 20 to 52). No significant differences between groups at baseline. Venlafaxine 37.5mg/d: 26.6 (range 20 to 43). Venlafaxine 150mg/d: 26.3 (17 to 38). Placebo: 26.7 (20 to 52)</td>
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**Baldwin2006**

- **Study Type:** RCT
- **Study Description:** ITT: patients who took at least one dose of the study medication & at least one baseline efficacy assessment were included in the analysis
- **Type of Analysis:** LOCF/ITT
- **Blinding:** Double blind
- **Duration (days):** Mean 84
- **Setting:** UK

#### Study Description: ITT

- All eligible patients with at least one baseline efficacy assessment were included in the analysis.
- **Allocation Concealment:** Sealed opaque envelopes.
- **Info on Screening Process:** Details not provided.

#### Data Used

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</table>

#### Data Not Used

- **Response (50% reduction in HAM-A score) - not extractable**
- **Outcome:** Leaving the study due to ineffectiveness
- **Outcome:** Leaving the study due to adverse events
- **Outcome:** Leaving the study early for any reason

#### Interventions

- **Data Used:** HAM-A
- **Outcome:** Leaving the study due to ineffectiveness
- **Outcome:** Leaving the study due to adverse events
- **Outcome:** Leaving the study early for any reason

#### Notes

- **Diagnosis:** 100% GAD by DSM-IV-TR
- **Exclusions:** - not primary diagnosis of GAD (DSM-IV-TR) - not between 18 and 65 - HAM-A score < 20 - HAM-A (anxious mood & tension items) < 2 - MADRS >15 - Diagnosis of: MDD, panic disorder, social anxiety, PTSD, bipolar, OCD, body dysmorphic disorder, substance misuse, personality disorder

---
<table>
<thead>
<tr>
<th>Study Type: RCT</th>
<th>Study Type: RCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study Description: ITT: all eligible participants with at least one efficacy evaluation made whilst receiving study medication</td>
<td>Study Description: ITT: all included randomised participants who received at least one dose of study medication</td>
</tr>
<tr>
<td>Type of Analysis: ITT/LOCF</td>
<td>Type of Analysis: ITT</td>
</tr>
<tr>
<td>Blindness: Double blind</td>
<td>Blindness: Double blind</td>
</tr>
<tr>
<td>Duration (days): Mean 56</td>
<td>Duration (days): Mean 28</td>
</tr>
<tr>
<td>Setting: US Outpatient (17 centres)</td>
<td>Setting: Four study centres, USA Outpatients</td>
</tr>
<tr>
<td>Notes: RANDOMISATION: details not provided.</td>
<td>Notes: RANDOMISATION: procedure not reported</td>
</tr>
</tbody>
</table>

**Abbreviations:**
- **ITT**: Intention to Treat
- **LOCF**: Last Observation Carried Forward
- **DSM-IV**: Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition

### DAVIDSON1999

<table>
<thead>
<tr>
<th>n = 365</th>
<th>n = 365</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age: Mean 38</td>
<td>Age: Mean 38</td>
</tr>
<tr>
<td>Sex: 224 males 141 females</td>
<td>Sex: 128 males 143 females</td>
</tr>
<tr>
<td>Diagnosis: 100% GAD by DSM-IV</td>
<td>Diagnosis: 100% GAD by DSM-IV</td>
</tr>
<tr>
<td>Exclusions: - Not 18 years or older</td>
<td>Exclusions: - Not 18 years or older</td>
</tr>
<tr>
<td>- Primary diagnosis not GAD (DSM-IV)</td>
<td>- Primary diagnosis not GAD (DSM-IV)</td>
</tr>
<tr>
<td>- HAM-A score &lt; 18</td>
<td>- HAM-A score &lt; 18</td>
</tr>
<tr>
<td>- HAM-A (anxious mood &amp; tension items) &lt; 2</td>
<td>- HAM-A (anxious mood &amp; tension items) &lt; 2</td>
</tr>
<tr>
<td>- Raskin depression score &gt; 9 or &gt; Covi anxiety score or any item &gt; 3</td>
<td>- Raskin depression score &gt; 9 or &gt; Covi anxiety score or any item &gt; 3</td>
</tr>
<tr>
<td>- Presence of clinically significant psychiatric disorder other than GAD</td>
<td>- Presence of clinically significant psychiatric disorder other than GAD</td>
</tr>
<tr>
<td>- Use of other pharmacology except for chloral hydrate</td>
<td>- Use of other pharmacology except for chloral hydrate</td>
</tr>
<tr>
<td>Notes: No. of participants taking chloral hydrate: placebo (N=7), venlafaxine 75mg/d (N = 2), venlafaxine, 150mg/d, buspirone (N=2)</td>
<td>Notes: No. of participants taking chloral hydrate: placebo (N=7), venlafaxine 75mg/d (N = 2), venlafaxine, 150mg/d, buspirone (N=2)</td>
</tr>
<tr>
<td>Baseline: HAM-A scores at baseline (approximate) total: 23.55 (4.23); venlafaxine 75mg/d: 23.7 (4.1), 150 mg/d: 23.0 (4.0); buspirone: 23.8 (4.6); placebo: 23.7 (4.2). No significant differences at baseline.</td>
<td>Baseline: HAM-A scores at baseline (approximate) total: 23.55 (4.23); venlafaxine 75mg/d: 23.7 (4.1), 150 mg/d: 23.0 (4.0); buspirone: 23.8 (4.6); placebo: 23.7 (4.2). No significant differences at baseline.</td>
</tr>
</tbody>
</table>

### FEITNER2003

<table>
<thead>
<tr>
<th>n = 271</th>
<th>n = 271</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age: Mean 38 Range 18-74</td>
<td>Age: Mean 38 Range 18-74</td>
</tr>
<tr>
<td>Sex: 128 males 143 females</td>
<td>Sex: 128 males 143 females</td>
</tr>
<tr>
<td>Diagnosis: 100% GAD by DSM-IV</td>
<td>Diagnosis: 100% GAD by DSM-IV</td>
</tr>
<tr>
<td>Exclusions: - Did not meet DSM-IV criteria for GAD, or GAD not the primary diagnosis in the case of comorbidity and GAD &gt;20</td>
<td>Exclusions: - Did not meet DSM-IV criteria for GAD, or GAD not the primary diagnosis in the case of comorbidity and GAD &gt;20</td>
</tr>
<tr>
<td>- Aged &lt;18 years</td>
<td>- Aged &lt;18 years</td>
</tr>
<tr>
<td>- Had another other Axis I disorder except dysthymia, simple phobia, social phobia, somatisation disorder or a history of MDD</td>
<td>- Had another other Axis I disorder except dysthymia, simple phobia, social phobia, somatisation disorder or a history of MDD</td>
</tr>
<tr>
<td>- Current MDD</td>
<td>- Current MDD</td>
</tr>
<tr>
<td>- Severe personality disorder, drug or alcohol misuse / dependence (active within 6 months of study)</td>
<td>- Severe personality disorder, drug or alcohol misuse / dependence (active within 6 months of study)</td>
</tr>
<tr>
<td>- Suicide risk</td>
<td>- Suicide risk</td>
</tr>
<tr>
<td>- Covi anxiety scale &lt;9</td>
<td>- Covi anxiety scale &lt;9</td>
</tr>
<tr>
<td>- Raskin depression &gt; 7</td>
<td>- Raskin depression &gt; 7</td>
</tr>
<tr>
<td>Notes: Participants with a dual comorbid psychiatric disorder were required to have GAD as a primary disorder as judged by the psychiatrist, considering relative severity and time of onset</td>
<td>Notes: Participants with a dual comorbid psychiatric disorder were required to have GAD as a primary disorder as judged by the psychiatrist, considering relative severity and time of onset</td>
</tr>
<tr>
<td>Baseline: HAM-A: Pregabalin (50mg) 24.3(3.9); Pregabalin (200mg) 25.4(4.6); Lorazepam 24.7(3.7). Placebo 24.8(4.1)</td>
<td>Baseline: HAM-A: Pregabalin (50mg) 24.3(3.9); Pregabalin (200mg) 25.4(4.6); Lorazepam 24.7(3.7). Placebo 24.8(4.1)</td>
</tr>
</tbody>
</table>
### HACKETT2003

**Study Type:** RCT

**Study Description:** Randomised, double-blind, placebo-controlled, parallel-group study. Followed by long-term phase study that is reported separately.

**Type of Analysis:** ITT (LOCF method)

**Blindness:** Double blind

**Duration (days):** Mean 56

**Setting:** Outpatients. Multicentre: France.

**Notes:** RANDOMISATION: no further details

**Info on Screening Process:** 564 entered study, 16 did not receive any medication before dropping out

<table>
<thead>
<tr>
<th>Study Parameter</th>
<th>Data Used</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>Group 4</th>
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<tbody>
<tr>
<td><strong>n</strong></td>
<td>540</td>
<td>179</td>
<td>191</td>
<td>97</td>
<td>89</td>
</tr>
<tr>
<td><strong>Age:</strong> Mean</td>
<td>44</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Sex:</strong></td>
<td>175 males 365 females</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Diagnosis:</strong></td>
<td>100% GAD by DSM-IV</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Exclusions:</strong></td>
<td>&lt;18 years of age</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Duration:</strong></td>
<td>Mean 42</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Baseline:</strong></td>
<td>HAM-A = 27.6 Venlafaxine 75mg = 27.9 Venlafaxine 150mg = 27.9 Diazepam = 28.4. Doesn't report SDs or SEs.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### KOPONEN2007

**Study Type:** RCT

**Study Description:** ITT analysis included all randomised participants with >=1 post-baseline analysis. Safety analysis included all randomised participants

**Type of Analysis:** ITT

**Blindness:** Double blind

**Duration (days):** Mean 63

**Setting:** Outpatients. Multicentre - 7 countries

**Notes:** RANDOMISATION: procedure not reported. Participants were stratified by baseline HAM-A score.

**Info on Screening Process:** 639 participants were screened for the study with 126 failing to meet the inclusion criteria.

<table>
<thead>
<tr>
<th>Study Parameter</th>
<th>Data Used</th>
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<th>Group 2</th>
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<td>513</td>
<td>175</td>
<td>168</td>
<td>170</td>
<td>89</td>
</tr>
<tr>
<td><strong>Age:</strong> Mean</td>
<td>44</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Sex:</strong></td>
<td>165 males 348 females</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Diagnosis:</strong></td>
<td>100% GAD by DSM-IV</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Exclusions:</strong></td>
<td>&lt;18 years of age</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Duration:</strong></td>
<td>Mean 63</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Baseline:</strong></td>
<td>HAM-A (total) DUL (60mg) 25.0(7.1); DUL (120mg) 25.2(7.3); Placebo 25.8(7.6)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### MONTGOMERY2006

**Study Type:** RCT

**Study Description:** ITT: all randomised patients who received at least 1 dose of study drug. LOCF used on all primary and secondary outcome measures.

**Type of Analysis:** ITT

**Blindness:** Double blind

**Duration (days):** Mean 42

**Followup:** None

**Setting:** Multicentre (76): Austria, Belgium, Germany, the Netherlands and the United Kingdom

<table>
<thead>
<tr>
<th>Study Parameter</th>
<th>Data Used</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>Group 4</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>n</strong></td>
<td>421</td>
<td>97</td>
<td>113</td>
<td>101</td>
<td></td>
</tr>
<tr>
<td><strong>Age:</strong> Mean</td>
<td>44</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Sex:</strong></td>
<td>160 males 261 females</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Diagnosis:</strong></td>
<td>100% GAD by DSM-IV</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Exclusions:</strong></td>
<td>Diagnosis of any other current Axis 1 disorders except depression not otherwise specified, dysthymia, simple phobia or somatisation disorder. Additional exclusion criteria: clinically relevant hematologic, autoimmune, endocrine, cardiovascular, renal, hepatic, gastrointestinal, or neurologic disorders; a history of seizure disorder; a history of alcohol or drug misuse/dependence - past year history of panic disorder, PTSD or eating disorder - lifetime history of bipolar disorder, OCD or psychosis - current or past use of antidepressants or benzodiazepine treatments - lifetime history of bipolar disorder, OCD or psychosis - recent diagnosis of depression or substance misuse/dependence - lack of response to GAD to 2 prior adequate trials of antidepressants or benzodiazapine treatments - psychotherapy initiated 6 weeks prior to study enrollment</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Baseline:</strong></td>
<td>HAM-A: Placebo =27.6 Venlafaxine 75mg = 27.9 Venlafaxine 150mg = 27.9 Diazepam = 28.4. Doesn't report SDs or SEs.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Drugs: DULoxetine; Venlafaxine; Placebo

**Data Used:**
- **CGI-I**
- **HAM-A**
- **Q-LES-Q-SF**
- **CGI-I**
- **Q-LES-Q-SF**
- **CGI-I**
- **Q-LES-Q-SF**
- **CGI-I**
- **Q-LES-Q-SF**
- **CGI-I**
- **Q-LES-Q-SF**

**Group 1**
- **N:** 179
- **Venlafaxine (extended release).**
- **Mean dose:** 150mg - 150mg/day.

**Group 2**
- **N:** 191
- **Venlafaxine (extended release).**
- **Mean dose:** 75mg - 75mg/day.

**Group 3**
- **N:** 97
- **Placebo** - No details given.

**Group 4**
- **N:** 89
- **Diazepam.**
- **Mean dose:** 15mg/d - 15mg/day.

**Data Used:**
- **CGI-I**
- **HAM-A**
- **Q-LES-Q-SF**
- **CGI-I**
- **Q-LES-Q-SF**
- **CGI-I**
- **Q-LES-Q-SF**
- **CGI-I**
- **Q-LES-Q-SF**

**Data Not Used:**
- **CGI-I**
- **HAM-A**
- **Q-LES-Q-SF**
- **CGI-I**
- **Q-LES-Q-SF**
- **CGI-I**
- **Q-LES-Q-SF**

**Drug company funded - Eli Lilly study F1J-MC-HMBR (NCT001129824) - trial report collected**

All participants underwent a single-blind placebo lead-in week, 9-week acute phase and a 2-week discontinuation tapering phase. Quality assessment score = + / ++
Diagnosis:
- N= 84
- N= 169
- N= 69
- N= 158
- N= 110
- N= 170

Type of Analysis: ITT (LOCF method)

followed by 4 weeks of treatment and then a 1-week taper.

Study Description: 1 week placebo lead-in phase; 421 were randomised and received study medication. Reasons for exclusion: did not meet entry criteria, lost to follow-up, withdrew consent, other/administrative and randomised but did not take study medication.

Notes: Randomisation procedure not reported. Parallel-group design.

Info on Screening Process: 543 participants entered baseline phase; 421 were randomised and received study medication. Reasons for exclusion: did not meet entry criteria, lost to follow-up, withdrew consent, other/administrative and randomised but did not take study medication.

Type of Analysis: ITT (LOCF method)

Setting: Australia, Argentina, Belgium, Canada, Mexico, Russia, Taiwan, UK

Outpatients

Notes: RANDOMISATION: computer-generated ALLOCATION CONCEALMENT: interactive voice response system

Info on Screening Process: Patients entered voice response system ALLOCATION CONCEALMENT: interactive

Notes: Dropped from study early for any reason

Nicolin2009

Study Type: RCT

Type of Analysis: ITT (LOCF)

Blindness: Double blind

Duration (days): Mean 70

Setting: Australia, Argentina, Belgium, Canada, Mexico, Russia, Taiwan, UK

Outpatients

Notes: RANDOMISATION: computer-generated ALLOCATION CONCEALMENT: interactive voice response system

Info on Screening Process: Patients entered voice response system ALLOCATION CONCEALMENT: interactive

Notes: Dropped from study early for any reason

Pandé2003

Study Type: RCT

Study Description: 1 week placebo lead-in followed by 4 weeks of treatment and then a 1-week dose taper.

Type of Analysis: ITT (LOCF method)
### PFIZER2005

- **Study Type**: RCT
- **Blindness**: Double blind
- **Duration (days)**: Mean 28
- **Followup**: No Info
- **Setting**: No Info
- **Notes**: No Info

#### Info on Screening Process: No Info

#### Data Used

<table>
<thead>
<tr>
<th>Data Used</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>Group 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>HAM-A</td>
<td>Placebo</td>
<td>Lorazepam, Mean dose 6mg</td>
<td>Placebo</td>
<td>Lorazepam, Mean dose 6mg</td>
</tr>
<tr>
<td>Placebo</td>
<td>23.9</td>
<td>22.90 (3.88)</td>
<td>23.9</td>
<td>23.85 (3.24)</td>
</tr>
<tr>
<td>Pregabalin 150mg</td>
<td>25.5</td>
<td>Pregabalin 600mg, Mean dose 2mg</td>
<td>25.5</td>
<td>Pregabalin 600mg, Mean dose 2mg</td>
</tr>
<tr>
<td>Pregabalin 600mg</td>
<td>24.4</td>
<td>Lorazepam, Mean dose 6mg</td>
<td>24.4</td>
<td>Lorazepam, Mean dose 6mg</td>
</tr>
</tbody>
</table>

#### Funding: Pfizer

### POHL2005

- **Study Type**: RCT
- **Study Description**: Comparison of the efficacy and tolerability of BID versus TID dosing of pregabalin. 1-week drug-free screening phase followed by 6 weeks of DB treatment.
- **Type of Analysis**: ITT (LOCF)
- **Blindness**: Double blind
- **Duration (days)**: Mean 42
- **Setting**: 19 centres: USA. Participants recruited via clinic referrals and adverts in the local media.
- **Notes**: RANDOMISATION: randomised in a 1:1:1:1 fashion.

#### Info on Screening Process: 605 screened; 174 did not meet entry criteria, 22 were lost to follow-up, 36 withdrew consent, 3 were randomised but did not take study medication and 29 were lost to follow-up for other or administrative reasons.

#### Data Used

<table>
<thead>
<tr>
<th>Data Used</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>Group 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>CGI-I</td>
<td>Placebo</td>
<td>Lorazepam, Mean dose 6mg</td>
<td>Placebo</td>
<td>Lorazepam, Mean dose 6mg</td>
</tr>
<tr>
<td>Placebo</td>
<td>50.0</td>
<td>50.0</td>
<td>50.0</td>
<td>50.0</td>
</tr>
<tr>
<td>Pregabalin 150mg</td>
<td>50.0</td>
<td>Lorazepam, Mean dose 6mg</td>
<td>50.0</td>
<td>Lorazepam, Mean dose 6mg</td>
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<tr>
<td>Pregabalin 600mg</td>
<td>50.0</td>
<td>Lorazepam, Mean dose 6mg</td>
<td>50.0</td>
<td>Lorazepam, Mean dose 6mg</td>
</tr>
</tbody>
</table>

#### Funding: Pfizer, Inc. Quality assessed: +.

### RICKELS2000A

- **Study Type**: RCT
- **Study Description**: ITT: all eligible participants with at least one efficacy evaluation made whilst receiving study medication.
- **Type of Analysis**: ITT/LOCF

#### Info on Screening Process: Recruited via clinic referrals or from advertisements. 361 screened; 64 excluded because didn’t meet inclusion criteria (N=31), experienced an adverse event (N=1) or because of other administrative reasons (N=52).

#### Data Used

<table>
<thead>
<tr>
<th>Data Used</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>Group 4</th>
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</thead>
<tbody>
<tr>
<td>HAM-A</td>
<td>Placebo</td>
<td>Lorazepam, Mean dose 6mg</td>
<td>Placebo</td>
<td>Lorazepam, Mean dose 6mg</td>
</tr>
<tr>
<td>Placebo</td>
<td>23.9</td>
<td>24.3</td>
<td>23.9</td>
<td>24.3</td>
</tr>
<tr>
<td>Pregabalin 150mg</td>
<td>25.5</td>
<td>Lorazepam, Mean dose 6mg</td>
<td>25.5</td>
<td>Lorazepam, Mean dose 6mg</td>
</tr>
<tr>
<td>Pregabalin 600mg</td>
<td>24.4</td>
<td>Lorazepam, Mean dose 6mg</td>
<td>24.4</td>
<td>Lorazepam, Mean dose 6mg</td>
</tr>
</tbody>
</table>

#### Funding: Wyeth-Ayerst Laboratories. Quality assessed: -.
**RICKELS2003**

**Study Type:** RCT

Blindness: Double blind
Duration (days): Mean 56

Setting: Outpatients, 50 sites in US and Canada

Notes: RANDOMISATION: no further details

Info on Screening Process: 661 eligible, 35 lost to follow-up, 10 adverse events, 6 protocol violations, 44 for other reasons

Data Used
- HAM-A
- Adverse events
- Leaving the study due to adverse events
- Leaving the study early for any reason
- Remission (less than 7 on HAM-A)
- Response (50% reduction in HAM-A score) - not extractable

Data Not Used
- CGI-I
- HAM-A

**Exclusions:**
- <18 years
- HAM-A >20
- HAM-A items 1 and 2 <2
- other non-psychiatric condition including MDD
- using other psychoactive drugs

Baseline: HAM-A placebo depression score (approximate): 24.23 (4.10). No significant differences between groups at baseline.

Venlafaxine 75mg/d: 24.7 (4.4). Venlafaxine 150mg/d: 24.5 (4.1). Venlafaxine 225mg/d: 23.6 (3.7).

Placebo: 24.1 (4.2).

**Group 1 N=180**
Placebo - No details given.

**Group 2 N=197**
Paroxetine. Mean dose 40mg - Starting dose 10mg/day, increased 10mg/day each week until reach 40mg

**Group 3 N=188**
Placebo, Mean dose 20mg - Starting dose 10mg, followed by 20mg at week 2

**Funding:** GSK. Quality assessed -.

---

**RICKELS2005**

**Study Type:** RCT

Study Description: 1-week drug-free screening period before 4 weeks of double-blind treatment. This was followed by a 1-week taper period and then 1-week drug-free.

Type of Analysis: ITT (LOCF method)

Blindness: Double blind
Duration (days): Mean 28

Setting: Recruited via clinic referrals and from advertisements in the local media. Outpatients. Multicentre: USA.

Notes: RANDOMISATION: participants were randomised in blocks of 10. No further details.


Data Used
- CGI-I
- HAM-A
- Adverse events
- Leaving the study due to adverse events
- Leaving the study early for any reason
- Remission (less than 7 on HAM-A)
- Response (50% reduction in HAM-A score) - not extractable

Data Not Used
- PLACEBO

Baseline: HAM-A: Placebo 24.4 (3.7) 20mg Parox 24.1 (3.6) 40mg Parox 23.8 (3.4)

**Group 1 N=91**
Placebo - Three treatments a day.

**Group 2 N=91**
Pregabalin. Mean dose 300mg/day - Pregabalin was initiated at 300mg/day and kept constant throughout the study. Three treatments a day.

**Group 3 N=89**
Pregabalin. Mean dose 600mg/day - Pregabalin was initiated at 300mg/day and then titrated to 600mg/day on day 4. Dosage was titrated to 600mg/day on day 7. Three treatments a day.

**Group 4 N=90**
Pregabalin. Mean dose 450mg/day - Pregabalin was initiated at 300mg/day and then titrated to 450mg/day on day 4. Three treatments a day.

**Funding:** Pfizer, Inc. Quality assessed +.

---

Blindness: Double blind
Duration (days): Mean 56

Setting: US

Outpatient (15 centres)

Notes: RANDOMISATION: not reported. ALLOCATION CONCEALMENT: not addressed


Notes: RANDOMISATION: participants were randomised in blocks of 10. No further details.

Setting: Recruited via clinic referrals and from advertisements in the local media. Outpatients.

Type of Analysis: ITT (LOCF method)

Notes: RESPONSE BASED ON CGI SCORE OF 1 OR 2.

Diagnosis: 100% GAD by DSM-IV

Exclusions: Raskin Depression Scale score >7, being a fertile woman having a positive pregnancy test result, not using a medically accepted contraceptive or currently nursing, a current or past history of bipolar, schizophrenic, schizoaffective, psychotic or factitious disorder and dementia, current but not lifetime MDD, social anxiety disorder, panic disorder with or without agoraphobia, OCD, post-traumatic or acute stress disorders, and eating disorders at the diagnostic threshold but not subthreshold level and alcohol or other substance dependence and/or misuse, positive urine drug screen result, any clinically significant acute or unstable medical condition or clinically significant ECG result or laboratory abnormalities, concurrent psychotherapy for GAD, unless undergoing stable treatment for longer than 3 months, concomitant treatment with psychotropic medication during the study and for at least 2 weeks before the screening visit. current or
<table>
<thead>
<tr>
<th>References of Included Studies</th>
<th>Group</th>
<th>N=93</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Characteristics of Excluded Studies</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reference ID</td>
<td>Reason for Exclusion</td>
<td></td>
</tr>
<tr>
<td>BORISON1990</td>
<td>N&lt;10 in each treatment arm</td>
<td></td>
</tr>
</tbody>
</table>

**References of Included Studies**

**ALLGULANDER2001** (Published Data Only)

**BALDWIN2006** (Published Data Only)

**DAVIDSON1999** (Published Data Only)

**FELTNER2003** (Published Data Only)

**HACKETT2003** (Published Data Only)

**KOPONEN2007** (Published Data Only)

**MONTGOMERY2006** (Published Data Only)

**NICOLINI2009** (Published Data Only)

**PANDE2003** (Published Data Only)

**PFIZER2005** (Unpublished Data Only)

**POHL2005** (Published Data Only)


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### Comparisons Included in this Clinical Question

<table>
<thead>
<tr>
<th>Anxiolytic &amp; risperidone vs anxiolytic &amp; placebo</th>
<th>Fluoxetine &amp; olanzapine vs fluoxetine &amp; placebo</th>
<th>Risperidone augmentation vs placebo augmentation</th>
<th>Ziprasidone augmentation vs placebo augmentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>BRAWMAN-MINTZER2005</td>
<td>POLLACK2006</td>
<td>PANDINA2007</td>
<td>LOHOFF2010</td>
</tr>
</tbody>
</table>

### Characteristics of Included Studies

#### BRAWMAN-MINTZER2005

- **Methods**
  - Study Type: RCT
  - Study Description: Participants who continued to experience GAD despite anxiolytic treatment given placebo or risperidone at doses of 0.5 to 1.5mg/day.
  - Type of Analysis: ITT (LOCF method)
  - Blindness: Double blind
  - Duration (days): Mean 35
  - Setting: Outpatients: US.

- **Participants**
  - n= 40
  - Age: Mean 50
  - Sex: 7 males 33 females
  - Diagnosis: 100% GAD by DSM-IV
  - Exclusions: Diagnosis of MDD within 1 month of study entry and subjects with substance-use disorders within 6 months of study entry. Subjects with current or past history of bipolar or any psychotic disorder.

- **Outcomes**
  - Data Used: CGI-I, HAM-A
  - Adverse events
  - Hospital Anxiety and Depression Scale (anxiety)
  - Leaving the study due to adverse events
  - Leaving the study early for any reason

- **Interventions**
  - Group 1: N= 20
    - Placebo - No details provided.
  - Group 2: N= 19
    - Other active treatments - Risperidone. Increased weekly from 0.5mg/day to 1.5mg/day according to tolerability and clinical response.

- **Notes**
  - Randomisation: no details given.
  - Info on Screening Process: No details provided.
  - Setting: Outpatients: US.
  - Duration (days): Mean 35
  - Blindness: Double blind
  - Study Type: RCT
  - Study Description: Participants who continued to experience GAD despite anxiolytic treatment given placebo or risperidone at doses of 0.5 to 1.5mg/day.
  - Type of Analysis: ITT (LOCF method)
  - Blindness: Double blind
  - Duration (days): Mean 35
  - Setting: Outpatients: US.
  - Notes: Randomisation: no details given.
  - Info on Screening Process: No details provided.

#### LOHOFF2010

- **Methods**
  - Study Type: RCT
  - Study Description: Assesses the efficacy, safety and tolerability of ziprasidone in adults with treatment resistant GAD
  - Type of Analysis: LOCF
  - Blindness: Double blind
  - Duration (days): Mean 56
  - Setting: Subjects recruited from the University of Pennsylvania Mood and Anxiety Disorders Section.

- **Participants**
  - n= 62
  - Age: Mean 50
  - Sex: 7 males 33 females
  - Diagnosis: GAD by DSM-IV
  - Exclusions: <16 on HAM-A, <4 on CGI-S. History of mania, bipolar disorder, schizophrenia or other psychotic disorder or diagnosis that may affect clinical assessment. Clinically significant abnormalities on physical examination or unstable medical conditions. Females who are pregnant, breast feeding.

- **Outcomes**
  - Data Used: CGI-I, HAM-A
  - Adverse events
  - Hospital Anxiety and Depression Scale (anxiety)
  - Leaving the study due to adverse events
  - Leaving the study early for any reason

- **Interventions**
  - Group 1: N= 41
    - Ziprasidone. Mean dose 20mg - Flexible dose strategy. Daily dose increased in weekly increments by 20mg/d up to 80mg/d
  - Group 2: N= 21
    - Placebo - Identical placebo capsules

- **Notes**
  - Randomisation: An independent Duration (days): Mean 35
  - Blindness: Double blind
  - Study Type: RCT
  - Study Description: Participants who continued to experience GAD despite anxiolytic treatment given placebo or risperidone at doses of 0.5 to 1.5mg/day.
  - Type of Analysis: ITT (LOCF method)
  - Blindness: Double blind
  - Duration (days): Mean 35
  - Setting: Outpatients: US.
  - Notes: Randomisation: no details given.
  - Info on Screening Process: No details provided.
  - Setting: Outpatients: US.
  - Duration (days): Mean 35
  - Blindness: Double blind
  - Study Type: RCT
  - Study Description: Assesses the efficacy, safety and tolerability of ziprasidone in adults with treatment resistant GAD
  - Type of Analysis: LOCF
  - Blindness: Double blind
  - Duration (days): Mean 56
  - Setting: Subjects recruited from the University of Pennsylvania Mood and Anxiety Disorders Section.

#### PANDINA2007

- **Methods**
  - Study Type: RCT
  - Study Description: Adjunctive risperidone in the treatment of GAD
  - Type of Analysis: ITT
  - Blindness: Double blind
  - Duration (days): Mean 28

- **Participants**
  - n= 390
  - Age: Mean 44 Range 18-65
  - Sex: 114 males 276 females
  - Diagnosis: 100% GAD by DSM-IV
  - Exclusions: Females with known or suspected pregnancy, serious suicide risk or serious medical/neurological illness,

- **Outcomes**
  - Data Used: Q-LES-Q, HAM-A
  - Remission (less than 7 on HAM-A)
  - Response (50% reduction in HAM-A score)

- **Interventions**
  - Group 1: N= 196
    - Risperidone. Mean dose 1mg - 0.25mg day 1-3, 0.5mg day 4-15, 1.0 mg day 16-28. On day 29 of the 6-week study, dose could increase to 2mg per day for patients considered to have insufficient response, (reduced to 1mg per day if intolerant).

- **Notes**
  - Randomisation: An independent Duration (days): Mean 35
  - Blindness: Double blind
  - Study Type: RCT
  - Study Description: Participants who continued to experience GAD despite anxiolytic treatment given placebo or risperidone at doses of 0.5 to 1.5mg/day.
  - Type of Analysis: ITT (LOCF method)
  - Blindness: Double blind
  - Duration (days): Mean 35
  - Setting: Outpatients: US.
  - Notes: Randomisation: no details given.
  - Info on Screening Process: No details provided.
  - Setting: Outpatients: US.
  - Duration (days): Mean 35
  - Blindness: Double blind
  - Study Type: RCT
  - Study Description: Assesses the efficacy, safety and tolerability of ziprasidone in adults with treatment resistant GAD
  - Type of Analysis: LOCF
  - Blindness: Double blind
  - Duration (days): Mean 56
  - Setting: Subjects recruited from the University of Pennsylvania Mood and Anxiety Disorders Section.
  - Notes: Randomisation: An independent Duration (days): Mean 35
  - Blindness: Double blind
  - Study Type: RCT
  - Study Description: Adjunctive risperidone in the treatment of GAD
  - Type of Analysis: ITT
  - Blindness: Double blind
  - Duration (days): Mean 28
  - Notes: Randomisation: An independent Duration (days): Mean 35
  - Blindness: Double blind
  - Study Type: RCT
  - Study Description: Participants who continued to experience GAD despite anxiolytic treatment given placebo or risperidone at doses of 0.5 to 1.5mg/day.
  - Type of Analysis: ITT (LOCF method)
  - Blindness: Double blind
  - Duration (days): Mean 35
  - Setting: Outpatients: US.
  - Notes: Randomisation: no details given.
  - Info on Screening Process: No details provided.
  - Setting: Outpatients: US.
<table>
<thead>
<tr>
<th>Reference ID</th>
<th>Reason for Exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>FAVA2009</td>
<td>Primary outcome insomnia not anxiety</td>
</tr>
<tr>
<td>SIMON2008</td>
<td>Outside scope of guideline</td>
</tr>
</tbody>
</table>

### References of Included Studies

**BRAWMAN-MINTZER2005** (Published Data Only)

**LOHOFF2010** (Published Data Only)

**PANDINA2007** (Unpublished Data Only)

**POLLACK2006** (Published Data Only)

### References of Excluded Studies

**FAVA2009** (Published Data Only)

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Characteristics Table for The Clinical Question: In the treatment of GAD what pharmacological strategies are effective in preventing relapse (including maintenance treatment)?

Comparisons Included in this Clinical Question

<table>
<thead>
<tr>
<th>Treatments</th>
<th>Studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duloxetine (SNRI) vs placebo</td>
<td>DAVIDSON2008</td>
</tr>
<tr>
<td>Duloxetine (SNRI) vs venlafaxine (SNRI)</td>
<td>DAVIDSON2008</td>
</tr>
<tr>
<td>Escitalopram vs placebo</td>
<td>ALLGULANDER2006</td>
</tr>
<tr>
<td>Pregabalin vs placebo</td>
<td>FELTNER2008</td>
</tr>
<tr>
<td>SSRI vs placebo</td>
<td>STOCCHI2003</td>
</tr>
<tr>
<td>Venlafaxine (SNRI) vs placebo</td>
<td>DAVIDSON2008</td>
</tr>
</tbody>
</table>

Characteristics of Included Studies

<table>
<thead>
<tr>
<th>ALLGULANDER2006</th>
<th>DAVIDSON2008</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Methods</strong></td>
<td></td>
</tr>
<tr>
<td>Study Type: RCT</td>
<td></td>
</tr>
<tr>
<td>Study Description: 491 participants received open-label escitalopram for 12 weeks. 376 responded and were randomized to DB treatment with escitalopram or placebo.</td>
<td></td>
</tr>
<tr>
<td>Type of Analysis: ITT</td>
<td></td>
</tr>
<tr>
<td>Blindness: Double blind</td>
<td></td>
</tr>
<tr>
<td>Duration (days): Mean 532</td>
<td></td>
</tr>
<tr>
<td>Notes: RANDOMISATION: randomised in a 1:1 fashion using computer generated randomisation list. Info on Screening Process: 424 completed open-label phase. 49 dropped out before DB phase: 8 due to adverse events, 28 due to lack of efficacy, 3 withdrew consent, 5 did not comply and 5 for other reasons.</td>
<td></td>
</tr>
<tr>
<td><strong>Participants</strong></td>
<td></td>
</tr>
<tr>
<td>n= 375</td>
<td></td>
</tr>
<tr>
<td>Age: Mean 41 Range 18-65</td>
<td></td>
</tr>
<tr>
<td>Sex: 255 males 120 females</td>
<td></td>
</tr>
<tr>
<td>Diagnosis: 100% GAD by DSM-IV-TR</td>
<td></td>
</tr>
<tr>
<td>Exclusions: Major depressive disorder, panic disorder, social anxiety disorder, PTSD, bipolar disorder, OCD, eating disorders, substance use disorder and any current or past psychotic disorder. Body dysmorphic disorder or any personality disorder. At risk of suicide or had made a suicide attempt within the past year. Unstable serious somatic illness and/or serious sequelae of liver or renal insufficiency. Pregnant or breastfeeding women. Notes: Treatment continued for 24-76 weeks until the patient relapsed or was withdrawn for other reasons. Relapse was defined as HAM-A total score &gt;15. Was a 1-week screening period before open-label phase. Baseline. HAM-A at baseline. Escitalopram: 5.7 (3.9) and Placebo: 5.0 (3.1).</td>
<td></td>
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<tr>
<td><strong>Outcomes</strong></td>
<td></td>
</tr>
<tr>
<td>Data Used</td>
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<tr>
<td>CGH</td>
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<tr>
<td>HAM-A</td>
<td></td>
</tr>
<tr>
<td>Adverse events</td>
<td></td>
</tr>
<tr>
<td>Sheehan Disability Scale (SDS)</td>
<td></td>
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<tr>
<td>Hospital Anxiety and Depression Scale (anxiety)</td>
<td></td>
</tr>
<tr>
<td>Leaving the study due to adverse events</td>
<td></td>
</tr>
<tr>
<td>Leaving the study early for any reason</td>
<td></td>
</tr>
<tr>
<td>Notes: Assessed at 1, 2 and 4 weeks and then every 4 weeks until last dose of DB treatment.</td>
<td></td>
</tr>
<tr>
<td><strong>Interventions</strong></td>
<td></td>
</tr>
<tr>
<td>Group 1 N= 187</td>
<td></td>
</tr>
<tr>
<td>Placebo - No details provided.</td>
<td></td>
</tr>
<tr>
<td>Group 2 N= 186</td>
<td></td>
</tr>
<tr>
<td>Escitalopram. Mean dose 20mg/day - 20mg/day.</td>
<td></td>
</tr>
<tr>
<td><strong>Notes</strong></td>
<td></td>
</tr>
<tr>
<td>Participants who completed DB phase entered a 2-week taper period where the escitalopram group received escitalopram 10mg/day for a week and placebo for 2nd week. Placebo participants continued on placebo. Quality assessed: +. Funding: H. Lundbeck A/S.</td>
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<tr>
<td><strong>Characteristics</strong></td>
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<tr>
<td>Diagnosis: T100% GAD by DSM-IV-TR</td>
<td></td>
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<tr>
<td>Age: Mean 41 Range 18-65</td>
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<tr>
<td>Sex: 255 males 120 females</td>
<td></td>
</tr>
<tr>
<td>Exclusions: Major depressive disorder, panic disorder, social anxiety disorder, PTSD, bipolar disorder, OCD, eating disorders, substance use disorder and any current or past psychotic disorder. Body dysmorphic disorder or any personality disorder. At risk of suicide or had made a suicide attempt within the past year. Unstable serious somatic illness and/or serious sequelae of liver or renal insufficiency. Pregnant or breastfeeding women. Notes: Treatment continued for 24-76 weeks until the patient relapsed or was withdrawn for other reasons. Relapse was defined as HAM-A total score &gt;=15. Was a 1-week screening period before open-label phase. Baseline. HAM-A at baseline. Escitalopram: 5.7 (3.9) and Placebo: 5.0 (3.1).</td>
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<tr>
<td><strong>Participants</strong></td>
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<tr>
<td>n= 429</td>
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<td>Age:</td>
<td></td>
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<tr>
<td>Sex:</td>
<td></td>
</tr>
<tr>
<td>Diagnosis:</td>
<td></td>
</tr>
<tr>
<td>Exclusions: Patients who did not complete open label &amp; met response criteria</td>
<td></td>
</tr>
<tr>
<td>Exclusion criteria for open label trial:</td>
<td></td>
</tr>
<tr>
<td>&lt;18 years</td>
<td></td>
</tr>
<tr>
<td>- No primary DSM-IV diagnosis of GAD</td>
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</tr>
<tr>
<td>- CGI-S &gt;4</td>
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</tr>
<tr>
<td>- HADS anxiety subscale &lt;=10</td>
<td></td>
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<tr>
<td>- Covi Anxiety score &lt;9 or not greater and then Raskin depression total score. Raskin depression scale item rated &gt;3</td>
<td></td>
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<tr>
<td>Medical illness that would contraindicate use of duloxetine</td>
<td></td>
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<tr>
<td>women of childbearing age not using adequate contraception</td>
<td></td>
</tr>
<tr>
<td>recent diagnosis of depression or substance misuse/dependence</td>
<td></td>
</tr>
<tr>
<td><strong>Outcomes</strong></td>
<td></td>
</tr>
<tr>
<td>Data Used</td>
<td></td>
</tr>
<tr>
<td>Beck scale for suicide ideation</td>
<td></td>
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<tr>
<td>HAM-A</td>
<td></td>
</tr>
<tr>
<td>Relapse</td>
<td></td>
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<tr>
<td>Sheehan Disability Scale (SDS)</td>
<td></td>
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<tr>
<td>Hospital Anxiety and Depression Scale (anxiety)</td>
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<tr>
<td>Q-LES-Q-SF</td>
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<tr>
<td>EQ-5D</td>
<td></td>
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<tr>
<td>Leaving the study due to adverse events</td>
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</tr>
<tr>
<td>Notes: Relapse = (a) increase in CGI-S 2+ points to score 4+ while meeting criteria for GAD (MINI) or (b) discontinuation due to lack of efficacy. DROP OUTS: 49/216 (23%) - duloxetine; 97/213 (46%) - placebo.</td>
<td></td>
</tr>
<tr>
<td><strong>Interventions</strong></td>
<td></td>
</tr>
<tr>
<td>Group 1 N= 213</td>
<td></td>
</tr>
<tr>
<td>Placebo - 2 week taper period. All patients received 4 capsules daily.</td>
<td></td>
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<tr>
<td>Group 2 N= 216</td>
<td></td>
</tr>
<tr>
<td>Duloxetine. Mean dose 60-120mg/day - Duloxetine continued at same dose as their open label phase treatment (between 60-120 mg/day). The paper does not report mean dose.</td>
<td></td>
</tr>
<tr>
<td><strong>Notes</strong></td>
<td></td>
</tr>
<tr>
<td>FUNDED BY ELI LILLY: Trial report collected (R7108). Quality assessed: +.</td>
<td></td>
</tr>
</tbody>
</table>
## Characteristics of Excluded Studies

### References of Included Studies

**ALLGULANDER2006** *(Published Data Only)*


**DAVIDSON2008** *(Published Data Only)*

References of Excluded Studies

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### Characteristics Table for The Clinical Question: In the treatment of GAD, what are the risks and benefits associated with different complementary therapies?

#### Comparisons Included in this Clinical Question

<table>
<thead>
<tr>
<th>Acupuncture and Chinese medication vs doxepin</th>
<th>Acupuncture vs behavioural desensitisation + acupuncture</th>
<th>Acupuncture vs behavioural desensitization</th>
<th>Acupuncture vs Doxepin Doxepin</th>
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</thead>
<tbody>
<tr>
<td>Acupuncture vs fluoxetine/Paroxetine</td>
<td>Acupuncture vs flupentixol vs combined</td>
<td>Acupuncture vs lorazepam &amp; plant extract propranolol</td>
<td>Acupuncture vs medication + acupuncture</td>
</tr>
<tr>
<td>Chamomile vs placebo</td>
<td>Chinese Taoist psychotherapy vs benzodiazepine</td>
<td>Galphimia glauca vs lorazepam</td>
<td>Ginkgo biloba vs placebo</td>
</tr>
<tr>
<td>Hypnotherapy vs alprazolam</td>
<td>Passionflower vs oxazepam</td>
<td>Silexan vs lorazepam</td>
<td>Study drug vs placebo</td>
</tr>
<tr>
<td>ZHAO 2005</td>
<td>AKHONDZADEH 2001A</td>
<td>WOELK 2010</td>
<td>HANUS 2004</td>
</tr>
<tr>
<td>Valerian extract vs diazepam</td>
<td>Valerian extract vs placebo</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ANDREATINI 2002</td>
<td>ANDREATINI 2002</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### Characteristics of Included Studies

<table>
<thead>
<tr>
<th>Study Description: 4 week double-blind study comparing passion flower extract and oxazepam.</th>
<th>Type of Analysis: Completers</th>
<th>Duration (days): Mean 28</th>
<th>Setting: Outpatients: Iran.</th>
<th>Notes: RANDOMISATION: no details provided. Info on Screening Process: No details provided.</th>
</tr>
</thead>
</table>

| AMSTERDAM 2009 | Study Type: RCT | Study Description: Efficacy and tolerability trial of chamomile extract therapy in patients with GAD. | Type of Analysis: ITT (LOCF) | Notes: Funding: no details provided. Quality assessed: - . To date, the only published clinical trial looking at effects of passionflower on treatment of anxiety. |

<table>
<thead>
<tr>
<th>Methods</th>
<th>Participants</th>
<th>Outcomes</th>
<th>Interventions</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>AKHONDZADEH 2001A</td>
<td>n= 36</td>
<td>Data Used</td>
<td>Interventions</td>
<td></td>
</tr>
<tr>
<td>Study Type: RCT</td>
<td>Age: Range 19-47</td>
<td>Group 1 N= 18</td>
<td>Oxazepam. Mean dose 30mg/day - 30mg/day plus placebo drops.</td>
<td></td>
</tr>
<tr>
<td>Study Description: 4 week double-blind study comparing passion flower extract and oxazepam.</td>
<td>Sex: 16 males 20 females</td>
<td>Group 2 N= 18</td>
<td>Other active treatments. Mean dose 45 drops/day - Passionflower 'passiflora' extract. 45 drops per day plus placebo tablet.</td>
<td></td>
</tr>
<tr>
<td>Type of Analysis: Completers</td>
<td>Diagnosis: 100% GAD by DSM-IV</td>
<td>Notes: Assesssed by a psychiatrist at baseline and 4, 7, 14, 21 and 28 days after the medication started.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blindness: Double blind</td>
<td>Exclusions: History of serious suicide attempt or current acute suicidal ideation, an unexpected recent panic attack or full DSM-IV panic disorder within the previous 6 months, a life-time diagnosis of DSM-IV mania, psychosis, paranoia or dementia, concurrent or recent diagnosis of substance misuse, drug psychosis, OCD, hypomania, or major depression. Pregnant and lactating women.</td>
<td>Notes: Participants had a HAM-A score &gt;=14. Participants were free from all psychotopic medication for a minimum of 7 days before starting study. Baseline: No data provided.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| AMSTERDAM 2009 | n= 57 | Data Used | Interventions | Notes: Quality assessment Funded by the National Institutes of Health/National Center for Complementary and Alternative Medicine grant |
| Study Type: RCT | Age: Mean 46 | Group 1 N= 28 | Chamomile extract therapy. Mean dose 220mg - Capsules containing pharmaceutical grade German chamomile extract standardised to a content of 1.2% apigenin. 1-5 capsules |
| Study Description: Efficacy and tolerability trial of chamomile extract therapy in patients with GAD. | Sex: no information | Beck Anxiety Inventory | Cromwell's 2007-2011. 100% GAD by DSM-IV | Psychological General Well Being Index |
| Type of Analysis: ITT (LOCF) | Diagnosis: 100% GAD by DSM-IV | Response (50% reduction in HAM-A score) | Notes: | |
### ANDREATINI2002

**Study Type:** RCT

**Study Description:** ITT using LOCF included all those who completed at least 1 week of treatment

**Type of Analysis:** ITT

**Blindness:** Double blind

**Duration (days):** Mean 28

**Setting:** Sao Paulo, BRAZIL

**Notes:** RANDOMISATION: used a computer programme

**Info on Screening Process:** 132 people were screened. 4 failed (1 for non compliance and 3 for no consent) 57 randomised.

**Diagnosis:** N= 12

**Notes:** RANDOMISATION: Unclear

**Setting:** Department of Family Medicine and Community Health outpatient clinic.

**Notes:** Blocked randomisation with varying block sizes.

**Exclusions:**
- patients under treatment with benzodiazepines were excluded if anxiety was secondary to these disorders
- Patients under treatment with benzodiazepines were excluded if:
  1) they had a clinical response or no evidence of side effects to the current drug
  2) they did not undergo a gradual reduction of medication followed by a 2-week wash-out period
- Social phobia or simple phobia excluded if anxiety was secondary to these disorders
- females not using a medically accepted form of birth control

**Sex:** 109 males  131 females

**Age:** Range 16-73

**N:** 240

**Data Used**

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>Drug</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>12</td>
<td>Diazepam</td>
<td>Mean dose 6.5mg/day</td>
</tr>
<tr>
<td>2</td>
<td>12</td>
<td>Placebo</td>
<td>58.9 (14.1)</td>
</tr>
<tr>
<td>3</td>
<td>12</td>
<td>Valepotriates</td>
<td>2/12 (16.6%), Placebo 2/12 (16.6%)</td>
</tr>
</tbody>
</table>

**Baseline**

- HAM-A: Chamomile 15.4 (4.2) Placebo 14.3 (2.8)
- STAI-trait: Baseline: 58.9 (14.1)

**Notes:**
- Capsules made identical in appearance and aroma.
- Outcome measures obtained at baseline, 2,4,6,8 weeks of treatment. 8 dropouts: 2 had adverse events, 3 withdrew consent, 2 lost to follow up and 1 non compliance.

### GUIZHEN1998

**Study Type:** RCT

**Study Description:** Comparative study on acupuncture combined with behavioural desensitisation for treatment of anxiety neurosis on 240 patients

**Type of Analysis:** ITT

**Blindness:** No mention

**Duration (days):**

**Setting:** China

**Notes:** RANDOMISATION: Unclear

**Info on Screening Process:** Unclear

**Diagnosis:** N= 12

**Notes:** Diagnosis tool unclear. Chung self assessment scores (SAS) were greater than 50 (i.e moderate to severe anxiety)

**Sex:** 17 males  19 females

**Age:** Range 16-73

**N:** 1240

**Data Used**

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>Drug</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>80</td>
<td>Acupuncture</td>
<td>Mean dose 10-30 sessions</td>
</tr>
</tbody>
</table>
| 2     | 29 | Placebo | Capsule containing lactose monohydrate National Formulary. 1 per day one week. 2 per day in second week. 1-5 capsules per day depending on tolerability.

**Baseline**

- Baseline: Duration of disease: Acupuncture = 1 month to 16 years, Behavioural desensitisation = 6 months to 12 years, Combined = 2 weeks to 16 years
<table>
<thead>
<tr>
<th>Study</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>N= 80</strong></td>
<td>Behavioural desensitisation. Mean dose 10 sessions (twice per week for 30 minutes) - Treatment consisted of self-relaxation techniques, psychotherapy, &amp; a program of behavioural desensitisation. Received instruction in muscle relaxation techniques to be practiced daily. Psychotherapy incorporated desensitisation techniques.</td>
<td><strong>N= 80</strong></td>
<td>Behavioural desensitisation + acupuncture. Mean dose 10-40 sessions - Underwent the above programme of behavioural desensitisation followed by acupuncture treatments on the same day, as described for the acupuncture group. Received 1-4 courses of treatment with an interval of 3-7 days between courses.</td>
</tr>
</tbody>
</table>

**HANUS2004**

**Study Type:** RCT  
**Study Description:** Clinical efficacy of fixed quantities of two plant extracts and magnesium vs placebo in anxiety disorders with functional disturbances.  
**Type of Analysis:** ITT (LOCF)  
**Blindness:** Double blind  
**Duration (days):** Mean 90  
**Setting:** Multi outpatient centers in Paris.  
**Notes:** Randomised box design used for randomisation.  
**Info on Screening Process:** Not mentioned

<table>
<thead>
<tr>
<th>n= 264</th>
<th>Data Used</th>
<th>Data Not Used</th>
</tr>
</thead>
</table>
| **Age:** Mean 45  
**Sex:** 50 males, 214 females | HAM-A  
**Visual Analog Scale (VAS)**  
Response (50% reduction in HAM-A score) | **CGI - no data**  
**Notes:** Efficacy assessment before at baseline and 7, 14, 30, 60 and 90 days after treatment. 31 drop outs due to inefficacy. |
| **Diagnosis:**  
100% GAD by DSM-III-R  
**Exclusions:** <18 years. No consent. No GAD according to DSM-III-R criteria. Patients with suicide risk. Use of psychotropic drugs or drugs with psychotropic properties or magnesium salts within 1 month.  
**Notes:** Total HAM-A score between 16 and 28  
**Baseline:** HAM-A: Study group 22.7 Placebo 22.4 |

**HERRERA-ARELLANO2007**

**Study Type:** RCT  
**Study Description:** 4-week double-blind study of galphimia glauca vs. placebo in outpatients with GAD  
**Type of Analysis:** Unclear  
**Blindness:** Double blind  
**Duration (days):** Mean 28  
**Setting:** Outpatients: Mexico  
**Notes:** RANDOMISATION: no details provided  
**Info on Screening Process:** No details provided

<table>
<thead>
<tr>
<th>n= 152</th>
<th>Data Used</th>
<th>Data Not Used</th>
</tr>
</thead>
</table>
| **Age:** Mean 38  
**Sex:** 35 males, 117 females | CG-H  
HAM-A  
**Leaving the study due to adverse events**  
**Leaving the study early for any reason** | **Notes:** Funding: unknown. Quality assessed: -. |
| **Diagnosis:**  
100% GAD by DSM-IV  
**Exclusions:** No pharmacological intervention for GAD within past 4 weeks, no drug or alcohol misuse for at least 6 months prior to study initiation, no suicidal behaviour or psychiatric comorbidity of higher clinical importance than GAD.  
**Notes:** Participants scored >=19 on HAM-A. 7% of participants had had a drug/alcohol addiction. Baseline: None provided. |

**RUAN2003**

**Study Type:** RCT  
**Study Description:** compare efficacy of combined treatment (acupuncture and Chinese medicine) versus doxepin for treatment of anxiety neurosis  
**Type of Analysis:** unknown

<table>
<thead>
<tr>
<th>n= 169</th>
<th>Data Used</th>
<th>Data Not Used</th>
</tr>
</thead>
</table>
| **Age:** Range 14-62  
**Sex:** 63 males, 106 females | SAS-CR  
**Notes:** Quality assessed: all selection, performance, attrition, detection bias are unclear |
| **Diagnosis:** Anxiety neurosis by CCMD-2-R | **Group 1 N= 80**  
**Study drug. Mean dose 375mg - 2 plant extracts (Crataegus oxyacantha and eschscholzia californica) and magnesium. Drug name: Sympathyl. Tablet form.  
75mg Crataegus oxyacantha, 20mg Eschscholzia californica, 75mg elemental magnesium. 2 tablets per day for 3 months.** | **Group 1 N= 134**  
**Lorazepam. Mean dose 2mg/day - 1mg twice daily.**  
**Group 2 N= 72**  
**Other active treatments. Mean dose 620mg/day - Galphimia glauca. Contained 310mg of dried aqueous G.G. extract twice a day.**  
**Group 2 N= 130**  
**Study drug. Mean dose 375mg - 2 plant extracts (Crataegus oxyacantha and eschscholzia californica) and magnesium. Drug name: Sympathyl. Tablet form.  
75mg Crataegus oxyacantha, 20mg Eschscholzia californica, 75mg elemental magnesium. 2 tablets per day for 3 months.** |

**Quality assessment:** low risk of bias. Funded by Laboratoires Innothera, France
Blindness: No mention
Duration (days): Mean 30
Setting: unknown. Probably inpatients

Information on Screening Process: not reported

Exclusions: Excluded those who scored below 50 on CCMD-2 and SAS-CR

Baseline: Did not report if both groups are comparable at baseline. Baseline score (SAS-CR) for acupuncture group is 78.56 (17.64) and Doxepin group is 77.68 (18.23).

Duration of diagnosis ranges from 1 month to 8 years.

Data Used
HAM-A
Notes: Assessment took place at baseline and on days 4, 8, 15, and 29.

Data Not Used
Group 2 N = 86
Acupuncture. Mean dose 30 days - Acupuncture combined with Chinese medicine. Participants took the Chinese medicine twice a day for 30 days. They also receive acupuncture once per day for 30-60 min each session.

Group 1 N = 37
Ginkgo biloba. Mean dose n/a - Patients took 2 film-coated tablets t.i.d (no active drug). Active drug and placebo were of same appearance.

Group 2 N = 36
Ginkgo biloba. Mean dose 240 mg - Patients took 2 film-coated tablets t.i.d (40 mg). Active drug and placebo were of same appearance.

Group 3 N = 34
Ginkgo biloba. Mean dose 480 mg - Patients took 2 film-coated tablets t.i.d (80 mg). Active drug and placebo were of same appearance.

Quality assessment: Attrition bias: Unclear

Group 1 N = 37
Lorazepam. Mean dose 0.5 mg - Patients received 1 capsule lorazepam and 1 capsule silexan placebo.

Group 2 N = 40
Silexan. Mean dose 80 mg - Patients received one capsule of silexan and 1 capsule lorazepam placebo. Silexan is an oil produced from lavender.

Quality assessment: Attrition bias: Unclear

Group 1 N = 29
Jin-3-Needling therapy - Needles inserted from four sites to produce a tightening or heavy sensation on the patient's scalp. Needles retained for 45 minutes and run every 15 minutes, once everyday, 6 times per week for 6 weeks.


**WOELK2007**

Study Type: RCT

Study Description: Anxiolytic-effects of ginkgo biloba in patients with GAD and adjustment disorder. Dosage EGB 761: 480mg, 240mg.

Type of Analysis: ITT with LOCF

Blindness: Double blind

Duration (days): Mean 28 Range 18-70

Setting: Private practices of specialists in neurology/ psychiatry, internal medicine, GPs and outpatient clinic of a psychiatric university hospital

Notes: Validated computer program randomly assigned numbers to 3 treatment groups. Randomisation code sealed and stored safely.

Info on Screening Process: 109 screened. 2 excluded. 1 responded to placebo treatment and 1 withdrew consent.

Data Used
HAM-A
Notes: Assessment at baseline, 1, 2, 4, 6 and 8 weeks. 11 drop outs/incomplete assessment.

Data Not Used

Quality assessment: Detection bias: Low risk of bias.

Group 1 N = 37
Ginkgo biloba. Mean dose 240 mg - Patients took 2 film-coated tablets t.i.d (40 mg). Active drug and placebo were of same appearance.

Group 2 N = 36
Ginkgo biloba. Mean dose 240 mg - Patients took 2 film-coated tablets t.i.d (40 mg). Active drug and placebo were of same appearance.

Group 3 N = 34
Ginkgo biloba. Mean dose 480 mg - Patients took 2 film-coated tablets t.i.d (80 mg). Active drug and placebo were of same appearance.

Quality assessment: Attrition bias: Unclear

Group 1 N = 37
Lorazepam. Mean dose 0.5mg - Patients received 1 capsule lorazepam and 1 capsule silexan placebo.

Group 2 N = 40
Silexan. Mean dose 80 mg - Patients received one capsule of silexan and 1 capsule lorazepam placebo. Silexan is an oil produced from lavender.

Quality assessment: Attrition bias: Unclear

Group 1 N = 29
Jin-3-Needling therapy - Needles inserted from four sites to produce a tightening or heavy sensation on the patient's scalp. Needles retained for 45 minutes and run every 15 minutes, once everyday, 6 times per week for 6 weeks.


**WOELK2010**

Study Type: RCT

Study Description: To investigate the therapeutic efficacy and tolerability of silexan compared to lorazepam in the treatment of GAD.

Type of Analysis: ITT

Blindness: Double blind

Duration (days): Mean 42

Followup: 2-week discontinuation phase

Setting: Multi outpatient centers in Germany.

Notes: Randomisation by validated computer program

Info on Screening Process: 1-week screening. Patients received placebo. Patients with decrease of 25% or more of HAM-A during this phase were excluded.

Data Used
HAM-A
Notes: Assessment took place at baseline and on days 4, 8, 15, and 29.

Data Not Used

Quality assessment: Detection bias: Low risk of bias.

Group 1 N = 37
Ginkgo biloba. Mean dose n/a - Patients took 2 film-coated tablets t.i.d (no active drug). Active drug and placebo were of same appearance.

Group 2 N = 36
Ginkgo biloba. Mean dose 240 mg - Patients took 2 film-coated tablets t.i.d (40 mg). Active drug and placebo were of same appearance.

Group 3 N = 34
Ginkgo biloba. Mean dose 480 mg - Patients took 2 film-coated tablets t.i.d (80 mg). Active drug and placebo were of same appearance.

Quality assessment: Attrition bias: Unclear

Group 1 N = 37
Lorazepam. Mean dose 0.5 mg - Patients received 1 capsule lorazepam and 1 capsule silexan placebo.

Group 2 N = 40
Silexan. Mean dose 80 mg - Patients received one capsule of silexan and 1 capsule lorazepam placebo. Silexan is an oil produced from lavender.

Quality assessment: Attrition bias: Unclear

Group 1 N = 29
Jin-3-Needling therapy - Needles inserted from four sites to produce a tightening or heavy sensation on the patient's scalp. Needles retained for 45 minutes and run every 15 minutes, once everyday, 6 times per week for 6 weeks.


**YUAN2007**

Study Type: Quasi-randomised

Study Description: To observe the therapeutic efficacy of Jin-3-needling (NL) therapy on GAD through Clinical Global Impression scale (CGI).

Type of Analysis: Completer

Blindness: No mention

Duration (days): Mean 36

Setting: The first affiliated hospital of Guangzhou Traditional Chinese Medical

Notes: Randomisation by validated computer program

Data Used
HAM-A
Notes: Assessment took place at baseline and on days 4, 8, 15, and 29.

Data Not Used

Quality assessment: Detection bias: Low risk of bias.
University, Guangzhou Municipal Hospital of the Brain.

Notes: Assigned to treatment groups according to the sequence of their visiting between Oct 2004 - Dec 2005.

Info on Screening Process: 86 enrolled upon meeting the inclusion criteria.

In pregnancy or lactation period were excluded.

Notes: Diagnostic standard for GAD in the Chinese classification scheme and diagnostic standard for psychiatric diseases (CCMD-3-R)

Baseline: HAM-A: WM 26.74 (3.51) NL 27.65 (2.86) CT 27.33 (3.71). Severity Index: WM 5.12 (1.04) NL 5.36 (0.93) CT 5.71 (1.35). No significant difference.

Notes: Clinical Global Impression (CGI) scale scored before and after 6-week treatment with 3 scales. SI, GI and EI. 7 dropouts. 3 worsening condition 2 intolerability to side-effects 1 'economic uptightness' 1-emigration.

**Group 2 N= 29**

Western medicine - 1. Fluoxetine or paroxetine (20mg) 2. Alprazolam (0.4-1.6mg) per day. One or two of the above drugs were chosen with the former as the dominant drug and alprazolam was used in addition according to the patient's condition. 6-week course.

**Group 3 N= 28**

Western medicine + Jin-3-Needling therapy - Combination of method for western medicine and J3N therapy. Dosage and manipulation as used in other 2 groups were applied simultaneously to these patients.

## ZHANG2002

**Study Type:** RCT

**Study Description:** Combines elements of cognitive therapy and Taoist philosophy. Looks at efficacy of CTCP, BDZ and combined treatment in people with GAD.

**Type of Analysis:** ITT (no mention of drop out analysis)

**Blindness:** No mention

**Duration (days):** Mean 168

**Setting:** 4 mental health centres in China

Notes: Patients were randomly assigned to treatment groups. Procedure not mentioned.

Info on Screening Process: 143 patients with GAD included. Exclusions not mentioned. Study lasted 6 months with two phases. One month of weekly sessions and 5 months of twice monthly sessions.

**n= 143**

Age: Mean 35

Sex: 80 males 53 females

Diagnosis:

100% GAD by CCMD-2-R

Exclusions: Patients in psychiatric treatment prior to study. No consent given.

Notes: CCMD-2-R criteria for GAD is the same as ICD-10 and DSM-IV except that condition has duration of 3 rather than 6 months.

Baseline: SCL-90: CTCP 90.7, Drug 113.8 Combined 107.0  No significant difference in baseline characteristics

**Data Used**

EPQ

SCL-90 Chinese version

Coping Style Questionnaire

Type A Personality Scale

Notes: Phase 1-1 month weekly sessions. Phase II-5 months of twice monthly sessions. 13 drop outs. Reason not mentioned.

**Group 1 N= 48**

BDZ - Each session lasted 10 minutes. Drug dosage unaltered after phase I. Variable doses of oral BDZ (diazepam or alprazolam) administered according to patient condition. 10-20mg diazepam equivalent.

**Group 2 N= 46**

Chinese Taoist Cognitive Psychotherapy - Each session lasted 1 hour. Carried out by first author and experienced psychiatrists trained for method.

**Group 3 N= 49**

CTCP + BDZ - Same as above

Notes: Assigned to treatment groups according to patient condition. 6-week course.

Exclusions: No diagnosis of GAD, not between age range of 100% Anxiety neurosis by CCMD-2-R

100% GAD by CCMD-2-R

**Group 1 N= 139**

Doxepin. Mean dose 25 mg + - The dose for each session in the first week was 25mg & it could be modified properly based on the therapeutic effects and the adverse effect of the drug.

**Group 2 N= 157**

Acupuncture. Mean dose 30 sessions - The treatment was given once a day, with a 1 day interval every 6 consecutive treatments. Treatment followed four different methods which are described in detail in the paper.

**FUNDING:** no mention,

Quality assessment: low quality

## ZHANG2003

**Study Type:** RCT

**Study Description:** Examined the effectiveness of acupuncture treatment against doxepin in the treatment of anxiety neurosis.

**Type of Analysis:** ITT

**Blindness:** No mention

**Duration (days):** Mean 30

**Setting:** In and outpatients, China

Notes: RANDOMISATION: no mention

Info on Screening Process: No mention

**n= 296**

Age: Range 16-60

Sex: 130 males 166 females

Diagnosis:

100% Anxiety neurosis by CCMD-2-R

Exclusions: Did not achieve a score of greater than 50 on the SAS-CR.

Notes: Duration of illness ranged from 1-month to 6 years

Baseline: no data

**Data Used**

Remission (symptoms disappeared & stable emotions)

Response (symptoms relieved, some fluctuations)

SAS-CR

Notes: No drop outs

**Group 1 N= 139**

Doxepin. Mean dose 25 mg + - The dose for each session in the first week was 25mg & it could be modified properly based on the therapeutic effects and the adverse effect of the drug.

**Group 2 N= 157**

Acupuncture. Mean dose 30 sessions - The treatment was given once a day, with a 1 day interval every 6 consecutive treatments. Treatment followed four different methods which are described in detail in the paper.

**FUNDING:** no mention,

Quality assessment: low quality

## ZHAO2005

**Study Type:** RCT

**Study Description:** compared the clinical efficacy of hypnotherapy and alprazolam in the treatment of GAD.

**Type of Analysis:** Completers (no drop outs)

**Blindness:** No mention

**Duration (days):** Mean 14

**n= 62**

Age: Mean 38 Range 20-45

Sex: 23 males 39 females

Diagnosis:

100% GAD by CCMD-3

Exclusions: No diagnosis of GAD, not between age range of

**Data Used**

HAM-A

Hospital Anxiety and Depression Scale (anxiety)

Body Sensations Questionnaire

Social Adjustment Scale

**Group 1 N= 32**

Hypnotherapy. Mean dose 2 - Use different technique of hypnotherapy (catered to each individual's need) to reduce the patient's anxiety. Each session takes 30-40 minutes

**Quality assessment:** low-high risk of bias
Notes: Assessments (HAM-A and self report SAS) were given to both groups at pre-treatment (2 weeks before treatment) and follow up (4 weeks). Clinical significance is defined as reduction > 50% on HAM-A scale. No drop outs

Group 2 N=30
Alprazolam. Mean dose 2 - visits clinic twice a week, each session takes at least 30 minutes, the GP prescribes 0.8mg dose (taken twice a day).

Notes: RANDOMISATION: according to patient number & date entered into trial.

Setting: Outpatients, China

Notes: In experimental group, the duration of diagnosis ranges from 1-11 years, with an average of 4 (+/-3) years. In control group, duration of diagnosis is 1-10 years, average 4 (+/-2) years.

Baseline: HAM-A (total) 28.8 (3.9)
Psychological anxiety (subscale) 16.6 (2.3)
Sensation (subscale) 12.2 (3.3)
SAS 60.9 (4.9)
There was no statistically significant difference between the 2 groups (chi square= 0.005, P>0.05)

Notes: Remission criteria: disappearance of symptoms with stable emotions.

Data Used
Self-rating Anxiety Scale (SAS)
Remission
Notes: Remission criteria: disappearance of symptoms with stable emotions.

ZHILING2006

Study Type: RCT

Study Description: Treatment of GAD by acupuncture

Type of Analysis: Completers (no dropouts)

Blindness: No mention

Duration (days): Mean 30

Setting: Out and inpatients

Notes: Randomisation method not reported

Info on Screening Process: Not mentioned

Notes: In control group, duration of diagnosis is 1-10 years, average 4 (+/-2) years.

Baseline: HAM-A (total) 28.8 (3.9)
Psychological anxiety (subscale) 16.6 (2.3)
Sensation (subscale) 12.2 (3.3)
SAS 60.9 (4.9)
There was no statistically significant difference between the 2 groups (chi square= 0.005, P>0.05)

Notes: Remission defined as no symptoms, can lead normal daily work task; Response (normal functioning) defined as majority of symptom measures are lowered, can lead normal daily worktask; Response (unstable functioning) as unstable emotions, impaired daily life

Quality assessed: Selection bias-unclear; performance bias-unclear; attrition bias-unclear; detection bias-unclear

Data Not Used
Reliable & clinically significant change
Notes: Remission defined as no symptoms, can lead normal daily work task; Response (normal functioning) defined as majority of symptom measures are lowered, can lead normal daily worktask; Response (unstable functioning) as unstable emotions, impaired daily life

ZHOU2003

Study Type: RCT

Study Description: compare effectiveness of combined treatment of acupuncture with medication versus medication alone for anxiety neurosis

Type of Analysis: unknown

Blindness: No mention

Duration (days): Mean 40

Setting: Unknown. Maybe conducted in The First Hospital of Yuhang District in Zhejiang, China

Info on Screening Process: Did not report

Diagnosis: Anxiety neurosis by CCMD-2-R
Exclusions: Not reported

Notes: SAS score >50

Baseline: Comparable in terms of sex, age and disease course. SAS: Treatment 79.88 (6.32) Control 78.96 (5.98)

Notes: SAS score >50

Quality assessed: Selection bias-unclear; performance bias-unclear; attrition bias-unclear; detection bias-unclear

Data Used
Remission

Data Not Used
Reliable & clinically significant change
Notes: Remission defined as no symptoms, can lead normal daily work task; Response (normal functioning) defined as majority of symptom measures are lowered, can lead normal daily worktask; Response (unstable functioning) as unstable emotions, impaired daily life

Diagnostic anxiety by CCMD-2-R

Exclusions: Not reported

Baseline: No statistical difference between 2 groups on age, gender or chronicity. Patients in treatment group had average 2.5 years of diagnosis. Patients in comparison group average was 2.3 years of diagnosis.

Notes: In control group, duration of diagnosis is 1-10 years, average 4 (+/-2) years.

Baseline: HAM-A (total) 28.8 (3.9)
Psychological anxiety (subscale) 16.6 (2.3)
Sensation (subscale) 12.2 (3.3)
SAS 60.9 (4.9)
There was no statistically significant difference between the 2 groups (chi square= 0.005, P>0.05)

Notes: Remission defined as disappearance of symptoms with stable emotions.

Data Used
Self-rating Anxiety Scale (SAS)
Remission
Notes: Remission criteria: disappearance of symptoms with stable emotions.

References of Included Studies

AKHONDZADEH2001A
References of Excluded Studies

AMSTERDAM2009
(Admin. Data Only)

ANDREATINI2002
(Admin. Data Only)

GUIZHEN1998
(Admin. Data Only)

HANUS2004
(Admin. Data Only)

HERRERA-ARELLANO2007
(Admin. Data Only)

RUAN2003
(Admin. Data Only)

WOELK2007
(Admin. Data Only)

WOELK2010
(Admin. Data Only)

YUAN2007
(Admin. Data Only)

ZHAO2005
(Admin. Data Only)

ZHILING2006
(Admin. Data Only)

ZHUO2003
(Admin. Data Only)

References of Excluded Studies

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(Admin. Data Only)

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Bonne2003a  

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SMITH2007  

WANG2001  

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