

## NKR 58 Angst hos voksne, PICO 6 pregabalin eller antidepressiva ved generaliseret angst

### Review information

#### Authors

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### Characteristics of studies

#### Characteristics of included studies

##### Cvetkovic Bosnjak 2015

<b>Methods</b>	<p><b>Study design:</b> Randomized controlled trial</p> <p><b>Study grouping:</b> Parallel group</p>
<b>Participants</b>	<p><b>Baseline Characteristics</b></p> <p>Intervention 1</p> <ul style="list-style-type: none"> <li>● <i>Mean age, years (SD):</i> 37.8 (2.2)</li> <li>● <i>No of female, %:</i> 67 (31)</li> <li>● <i>HAM-A total score, mean (SD):</i> 23.80 (5.8)</li> </ul> <p>Kontrol</p> <ul style="list-style-type: none"> <li>● <i>Mean age, years (SD):</i> 37.4 (5.2)</li> <li>● <i>No of female, %:</i> 41 (19)</li> <li>● <i>HAM-A total score, mean (SD):</i> 23.50 (3.4)</li> </ul> <p><b>Included criteria:</b> All patients had a diagnosis of GAD (according to ICD-X, and DSM-IV) Inclusion criteria: at the beginning of the investigation, all observed patients had a HAM-A total score &gt; 20.</p> <p><b>Excluded criteria:</b> Patients with comorbid mental disorders (depression, alcoholism, personal disorders, psychotic disorders), or somatic dysfunction (diabetes mellitus, hypertension, cardiomyopathy, thyroiddysfunktion) were not included in the study.</p>
<b>Interventions</b>	<p><b>Intervention Characteristics</b></p> <p>Intervention 1</p> <ul style="list-style-type: none"> <li>● <i>Description:</i> Pregabalin</li> <li>● <i>Dose:</i> Mean daily dosis of 225 mg/day. Doses of psychoactive drugs were titrated during the first week</li> <li>● <i>Duration:</i> 4 weeks</li> </ul> <p>Kontrol</p> <ul style="list-style-type: none"> <li>● <i>Description:</i> Sertraline</li> <li>● <i>Dose:</i> Mean daily dosis of 150 mg/day. Doses of psychoactive drugs were titrated during the first week</li> </ul>

	<p>● <b>Duration:</b> 4 weeks</p> <p><i>Grad of angstsymptomer</i></p> <ul style="list-style-type: none"> <li>● <b>Outcome type:</b> Continuous Outcome</li> <li>● <b>Reporting:</b> Fully reported</li> <li>● <b>Scale:</b> HAM-A, total score</li> <li>● <b>Range:</b> 0-56</li> <li>● <b>Direction:</b> Lower is better</li> </ul> <p><i>Bedring (respons), CGI-I, %</i></p> <ul style="list-style-type: none"> <li>● <b>Outcome type:</b> Dichotomous Outcome</li> <li>● <b>Reporting:</b> Fully reported</li> <li>● <b>Scale:</b> CGI-I</li> <li>● <b>Direction:</b> Higher is better</li> </ul> <p><i>Adverse events (AE), Antal personer</i></p> <ul style="list-style-type: none"> <li>● <b>Outcome type:</b> Dichotomous Outcome</li> <li>● <b>Reporting:</b> Fully reported</li> <li>● <b>Direction:</b> Lower is better</li> <li>● <b>Data value:</b> Endpoint</li> </ul>
<p><b>Identification</b></p>	<p><b>Sponsorship source:</b> No information</p> <p><b>Country:</b> Serbia</p> <p><b>Setting:</b> Outward patients at a Psychiatric Clinic</p> <p><b>Comments:</b></p> <p><b>Authors name:</b> M.CVJETKOVIC-BOSNJAK</p> <p><b>Institution:</b> PsychiatricClinic,ClinicalCenterofVojvodina,Serbia,MedicalFacultyofNoviSad,Serbia</p> <p><b>Email:</b> minacvjet@gmail.com</p> <p><b>Address:</b></p>
<p><b>Notes</b></p>	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement Comment: No information of how the allocation sequence was generated
Allocation concealment (selection bias)	Unclear risk	Judgement Comment: No information of allocation concealment
Blinding of participants and personnel (performance bias)	High risk	Judgement Comment: Insufficient information on blinding

Blinding of outcome assessment (detection bias)	High risk	Judgement Comment: Insufficient information on blinding
Incomplete outcome data (attrition bias)	Unclear risk	Judgement Comment: 107 were randomized, no information of attrition, no diagram of patient flow
Selective reporting (reporting bias)	Unclear risk	Judgement Comment: No information of a protocol, no protocol at Clinicaltrials.gov Only Severe of symptoms, responses and adverse events are reported. No reporting of withdrawal, quality of life, disability or serious adverse events
Other bias	Low risk	Quote: Conflict of Interest: The Authors declare that there are no conflicts of interest. Judgement Comment: The study appears to be free from other sources of bias

**Kasper 2009**

<b>Methods</b>	<p><b>Study design:</b> Randomized controlled trial <b>Study grouping:</b> Parallel group</p>
<b>Participants</b>	<p><b>Baseline Characteristics</b></p> <p>Intervention 1</p> <ul style="list-style-type: none"> <li>● Mean age, years (SD): 39.5 (11.9)</li> <li>● No of female, %: 64%</li> <li>● HAM-A total score, mean (SE): 27.6 (0.4)</li> </ul> <p>Kontrol</p> <ul style="list-style-type: none"> <li>● Mean age, years (SD): 42.6 (11.8)</li> <li>● No of female, %: 58%</li> <li>● HAM-A total score, mean (SE): 27.4 (0.4)</li> </ul> <p><b>Included criteria:</b> Male and female outpatients aged 18-65 years were eligible for study entry if they met DSM-IV-Text Revision criteria for a primary diagnosis of GAD based on a structured Mini International Neuropsychiatric Interview (M.I.N.I. Plus; version 5.0.0; Sheehan et al., 1997), and if their HAM-A total score was <math>\geq 20</math> at both the screening and baseline visits. The HAM-A psychic and somatic anxiety factors also were required to be <math>\geq 10</math> at both the screening and baseline visits. Women of childbearing potential were required to have a negative serum human chorionic gonadotropin pregnancy test and be practicing a medically accepted form of birth control.</p> <p><b>Excluded criteria:</b> Patients were excluded if they presented with any of the following: (i) a current or past DSM-IV diagnosis of bipolar disorder, schizophrenia, or any other psychotic disorder; (ii) a DSM-IV diagnosis in the past 6 months of MDD, dysthymic disorder, obsessive-compulsive disorder, post-traumatic stress disorder, an eating disorder, or alcohol or substance dependence and/or abuse; (iii) a 17-item Hamilton Depression Rating scale (HAM-D) total score <math>\geq 15</math>; (iv) a history of seizure disorder (except febrile seizures in childhood); (v) any clinically significant acute or unstable medical condition; (vi) a positive urine drug screen (for benzodiazepines, ethanol, amphetamines, barbiturates, cocaine, opiates, cannabinoids, phen-cyclidine); (vii) creatinine clearance rates <math>\leq 60</math> ml/min; (viii) concurrent psychotherapy for GAD (psychotherapy not targeting GAD symptoms was permitted if initiated &gt; 3 months before study enrollment); (ix) use of concomitant psychotropic medications within 2 weeks of the baseline visit (5 weeks for fluoxetine; except, zopiclone or zolpidem were permitted on two nights, as needed, during the 1-week washout period); (x) current suicide risk based on the clinical judgment of the investigator; (xi) previous treatment with either PGB or VXR; and (xii) lactating women.</p> <p><b>Pretreatment:</b> No significant baseline differences.</p>

<p><b>Interventions</b></p>	<p><b>Intervention Characteristics</b></p> <p>Intervention 1</p> <ul style="list-style-type: none"> <li>● <i>Description:</i> Pregabalin (PGB) 150-600 mg/day.</li> <li>● <i>Dose:</i> PGB treatment was started at a dose of 150 mg twice daily for the first week; thereafter, PGB dosing was flexible, based on clinical response and tolerability, in the range of 300-600 mg/day.</li> <li>● <i>Duration:</i> 8 weeks.</li> </ul> <p>Kontrol</p> <ul style="list-style-type: none"> <li>● <i>Description:</i> Venlafaxine (VXR) 75-225 mg/day</li> <li>● <i>Dose:</i> VXR treatment was started at a dose of 75 mg/day (administered in the morning, with matching placebo in the evening) for the first week. Thereafter, VXR dosing was flexible in the range of 75-225 mg/day.</li> <li>● <i>Duration:</i> 8 weeks</li> </ul>
<p><b>Outcomes</b></p>	<p><i>Grad af angstsymptomer</i></p> <ul style="list-style-type: none"> <li>● <b>Outcome type:</b> Continuous Outcome</li> <li>● <b>Reporting:</b> Fully reported</li> <li>● <b>Scale:</b> HAM-A, total score</li> <li>● <b>Range:</b> 0-56</li> <li>● <b>Direction:</b> Lower is better</li> </ul> <p><i>Funktionsniveau</i></p> <ul style="list-style-type: none"> <li>● <b>Outcome type:</b> Continuous Outcome</li> <li>● <b>Reporting:</b> Fully reported</li> <li>● <b>Scale:</b> Sheehan Disability Scale</li> <li>● <b>Range:</b> 0-30</li> <li>● <b>Direction:</b> Lower is better</li> </ul> <p><i>Livskvalitet, EQ5D</i></p> <ul style="list-style-type: none"> <li>● <b>Outcome type:</b> Continuous Outcome</li> <li>● <b>Reporting:</b> Fully reported</li> <li>● <b>Scale:</b> EuroQol EQ5D</li> <li>● <b>Range:</b></li> <li>● <b>Direction:</b> Higher is better</li> </ul> <p><i>Bedring (respons), CGI-I, mean change, SE</i></p> <ul style="list-style-type: none"> <li>● <b>Outcome type:</b> Continuous Outcome</li> <li>● <b>Reporting:</b> Fully reported</li> <li>● <b>Scale:</b> CGI-I</li> <li>● <b>Range:</b> 1-7</li> <li>● <b>Direction:</b> Lower is better</li> </ul> <p><i>Fratakt, alle årsager</i></p> <ul style="list-style-type: none"> <li>● <b>Outcome type:</b> Dichotomous Outcome</li> <li>● <b>Reporting:</b> Fully reported</li> </ul>

	<ul style="list-style-type: none"> <li>● <b>Direction:</b> Lower is better</li> <li>● <b>Data value:</b> Endpoint</li> </ul> <p><i>Frafaid grundet bivirkninger</i></p> <ul style="list-style-type: none"> <li>● <b>Outcome type:</b> Dichotomous Outcome</li> <li>● <b>Reporting:</b> Fully reported</li> <li>● <b>Direction:</b> Lower is better</li> <li>● <b>Data value:</b> Endpoint</li> </ul> <p><i>Alvorlige bivirkninger (SAE), antal personer</i></p> <ul style="list-style-type: none"> <li>● <b>Outcome type:</b> Dichotomous Outcome</li> <li>● <b>Reporting:</b> Fully reported</li> <li>● <b>Direction:</b> Lower is better</li> <li>● <b>Data value:</b> Endpoint</li> </ul> <p><i>Adverse events (AE), Antal personer</i></p> <ul style="list-style-type: none"> <li>● <b>Outcome type:</b> Dichotomous Outcome</li> <li>● <b>Reporting:</b> Fully reported</li> <li>● <b>Direction:</b> Lower is better</li> <li>● <b>Data value:</b> Endpoint</li> </ul>
<b>Identification</b>	<p><b>Sponsorship source:</b> The study was funded by Pfizer  <b>Country:</b> 47 international sites in Belgium, Canada, France, Ireland, Italy, The Netherlands, Spain and Sweden.  <b>Setting:</b> Outpatient  <b>Comments:</b>  <b>Authors name:</b> Siegfried Kasper  <b>Institution:</b> Department of General Psychiatry and Psychotherapy, Medical University of Vienna, Vienna, Austria  <b>Email:</b> e-mail: Sekretariat.Bandelow@med.uni-goettingen.de  <b>Address:</b> Correspondence to Professor Borwin Bandelow, Department of Psychiatry and Psychotherapy, University of Gottingen, von-Siebold-Str 5, D-37085 Gottingen, Germany</p>
<b>Notes</b>	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Patients were randomized to one of the three treatment groups based on a computer-generated randomization list."
Allocation concealment (selection bias)	Unclear risk	Judgement Comment: No information allocation concealment

Blinding of participants and personnel (performance bias)	Low risk	Quote: "double-blind, placebo-controlled" Quote: "This was an 8-week, double-blind, placebo-controlled study of PGB and VXR for the treatment of GAD patients who met Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV) criteria." Judgement Comment: Double-blinded and placebo controlled
Blinding of outcome assessment (detection bias)	Low risk	Quote: "This was an 8-week, double-blind, placebo-controlled study of PGB and VXR for the treatment of GAD patients who met Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV) criteria. After" Judgement Comment: Self reported, patients were blinded
Incomplete outcome data (attrition bias)	Low risk	Quote: "All statistical analyses were performed using SAS statistical package (version 8) (SAS Institute, Cary, North Carolina, USA, 2000) on the intention-to-treat population consisting of all randomized patients who received at least one dose of study medication."
Selective reporting (reporting bias)	Low risk	Quote: "ClinicalTrials.gov Identifier: NCT00151450. Funded" Judgement Comment: Protocol at clinicaltrials.gov, but outcome measures are not stated in the protocol at clinicaltrials. All expected outcomes are reported
Other bias	Low risk	Quote: "Acknowledgements. The study was funded by Pfizer Inc. Paid editorial support was provided by Edward Schweizer, MD, and funded by Pfizer Inc. The authors acknowledge the contribution of the many individual investigators for their participation in this trial. Dr Kasper has received grants/research support, consulting fees, and honoraria within the last 3 years from AstraZeneca, Bristol-Myers Squibb, CSC, Eli Lilly, GlaxoSmithKline, Janssen Pharmaceutical, Lundbeck, MSD, Novartis, Organon, Pierre Fabre, Pfizer, Schwabe, Sepracor, Servier, Wyeth. Dr Herman is a full-time employee of Pfizer Inc. Dr Nivoil has no disclosures to declare. Dr Van Ameringen has received grant/research support from AstraZeneca, Cephalon, GlaxoSmithKline, Janssen-Ortho Inc., National Institute of Health, Novartis, Pfizer, and Wyeth-Ayerst; has served as a consultant for Biovail, Cephalon, GlaxoSmithKline, Janssen-Ortho Inc., Novartis, Pfizer, and Wyeth-Ayerst. Dr Petralia has no disclosures to declare Dr Mandel is a full-time employee of Pfizer Inc. Dr Balinetti was a full-time employee of Pfizer Inc. at the time this study was conducted, and at the time the initial draft manuscript was prepared. She currently is affiliated with IRCCS S. Lucia Foundation-Neurology Department, University of Rome, Rome, Italy. Dr Bandelow has received consulting fees and honoraria within the last 3 years from AstraZeneca, Bristol-Myers-Squibb, Cephalon, Dainippon-Sumitomo, Glaxo, Janssen, Jazz, Lilly, Lundbeck, Pfizer, Roche, Servier, Solvay, and Wyeth. ClinicalTrials.gov Identifier: NCT00151450. Funded by Pfizer Inc.</b> References Algulander C, Hackett D," Judgement Comment: Appears to be free from other sources of bias

Montgomery 2006

Methods	Study design: Randomized controlled trial Study grouping: Parallel group
Participants	<p><b>Baseline Characteristics</b></p> <p>Intervention 1</p> <ul style="list-style-type: none"> <li>● Mean age, years (SD): 45 (12)</li> <li>● No of female, %: 59</li> <li>● HAM-A total score, mean (SD): 26.3(4.4)</li> </ul> <p>Intervention 2</p> <ul style="list-style-type: none"> <li>● Mean age, years (SD): 42(12)</li> <li>● No of female, %: 65</li> </ul>

	<p>● <i>HAM-A total score, mean (SD):</i> 26.5 (4.6)</p> <p>Kontrol</p> <ul style="list-style-type: none"> <li>● <i>Mean age, years (SD):</i> 46(12)</li> <li>● <i>No of female, %:</i> 65</li> <li>● <i>HAM-A total score, mean (SD):</i> 26.0 (4.6)</li> </ul> <p><b>Included criteria:</b> Adult male or female outpatients who were at least 18 years of age and who met DSM-IV diagnostic criteria for primary GAD using the Mini-International Neuropsychiatric Interview (MINI) were eligible for inclusion. At baseline assessment and prior to randomization, patients were re-quired to have a total score <math>\geq 20</math> on the Hamilton Rating Scale for Anxiety (HAM-A). To ensure that current symptoms of anxiety rather than those of depression predominated, a <math>\geq 9</math> on the Covi Anxiety Scale and a score <math>\leq 7</math> on the Raskin Depression Scale were also required.</p> <p><b>Excluded criteria:</b> Patients were excluded from the study if they were diagnosed with any other current Axis I disorders except depression not otherwise specified, dysthymia, simple phobia, or somatization disorder. Additional exclusion criteria included clinically relevant hematologic, autoimmune, endocrine, cardiovascular, renal, hepatic, gastrointestinal, or neurologic disorders; a history of seizure disorder; borderline, avoidant, or antisocial personality disorder; alcohol or substance use disorder within the past 6 months; and patients considered at risk of suicide. Women who were pregnant or lactating were not eligible for the study; also ineligible were women of childbearing potential who were not using a reliable method of contraception. Other reasons for exclusion were the use of gabapentin or a benzodiazepine within 1 week of the first baseline visit, the use of other psychotropic medications within 2 weeks prior to study entry, or ongoing psychodynamic or cognitive-behavioral psychotherapy for GAD. Use of corticosteroids (except topical or inhaled corticosteroids <math>&lt; 100 \mu\text{g/day}</math>), antihypertensive agents, captopril, betablockers, and psychotropic medication was not permitted during the study. Patients were allowed to take zolpidem for insomnia, but not for more than 2 nights per week or the night before clinic visits.</p>
<p><b>Interventions</b></p>	<p><b>Intervention Characteristics</b></p> <p>Intervention 1</p> <ul style="list-style-type: none"> <li>● <i>Description:</i> Pregabalin 400 mg/day.</li> <li>● <i>Dose:</i> Patients assigned to pregabalin 400 mg/day received 100 mg/day for 2 days, then 200 mg/day for 2 days, before receiving the full dosage of 400 mg/day on day 5.</li> <li>● <i>Duration:</i> Six weeks.</li> </ul> <p>Intervention 2</p> <ul style="list-style-type: none"> <li>● <i>Description:</i> Pregabalin 600 mg/day.</li> <li>● <i>Dose:</i> Patients assigned to pregabalin 600 mg/day received 150 mg/day for 2 days, 300 mg/day for 2 days, and 450 mg/day for 2 days, before receiving the full dosage of 600 mg/day after their day 7 visit.</li> <li>● <i>Duration:</i> Six weeks.</li> </ul> <p>Kontrol</p> <ul style="list-style-type: none"> <li>● <i>Description:</i> Venlafaxine 75 mg/day.</li> <li>● <i>Dose:</i> Patients assigned to venlafaxine began treatment at the full 37.5 mg b.i.d. dosage.</li> <li>● <i>Duration:</i> Six weeks.</li> </ul>
<p><b>Outcomes</b></p>	<p><i>Grad of angstsymptomer</i></p> <ul style="list-style-type: none"> <li>● <b>Outcome type:</b> Continuous Outcome</li> <li>● <b>Reporting:</b> Fully reported</li> <li>● <b>Scale:</b> HAM-A, total score</li> </ul>

	<ul style="list-style-type: none"> <li>● <b>Range:</b> 0-56</li> <li>● <b>Direction:</b> Lower is better</li> </ul> <p><i>Bedring (respons), CGI-I, %</i></p> <ul style="list-style-type: none"> <li>● <b>Outcome type:</b> Continuous Outcome</li> <li>● <b>Reporting:</b> Fully reported</li> <li>● <b>Scale:</b> CGI-I</li> <li>● <b>Range:</b> 1-7</li> <li>● <b>Direction:</b> Lower is better</li> </ul> <p><i>Frafaid, alle årsager</i></p> <ul style="list-style-type: none"> <li>● <b>Outcome type:</b> Dichotomous Outcome</li> <li>● <b>Reporting:</b> Fully reported</li> <li>● <b>Direction:</b> Lower is better</li> <li>● <b>Data value:</b> Endpoint</li> </ul> <p><i>Frafaid grundet bivirkninger</i></p> <ul style="list-style-type: none"> <li>● <b>Outcome type:</b> Dichotomous Outcome</li> <li>● <b>Reporting:</b> Fully reported</li> <li>● <b>Direction:</b> Lower is better</li> <li>● <b>Data value:</b> Endpoint</li> </ul> <p><i>Alvorlige bivirkninger (SAE), antal personer</i></p> <ul style="list-style-type: none"> <li>● <b>Outcome type:</b> Dichotomous Outcome</li> <li>● <b>Reporting:</b> Fully reported</li> <li>● <b>Direction:</b> Lower is better</li> <li>● <b>Data value:</b> Endpoint</li> </ul> <p><i>Adverse events (AE), Antal personer</i></p> <ul style="list-style-type: none"> <li>● <b>Outcome type:</b> Dichotomous Outcome</li> <li>● <b>Reporting:</b> Fully reported</li> <li>● <b>Direction:</b> Lower is better</li> <li>● <b>Data value:</b> Endpoint</li> </ul>
	<p><b>Sponsorship source:</b> This study was funded by Pfizer Inc, New York, N.Y</p> <p><b>Country:</b> 76 centers in 5 European countries (Austria, Belgium, Germany, the Netherlands, and the United Kingdom).</p> <p><b>Setting:</b> 52 of 76 centers were primary care centers (the remainder were psychiatric centers).</p> <p><b>Comments:</b></p> <p><b>Authors name:</b> Montgomery</p> <p><b>Institution:</b> Imperial College School of Medicine, London, U.K. (Dr. Montgomery)</p> <p><b>Email:</b> e-mail: Stuart@samontgomery.co.uk</p> <p><b>Address:</b> Stuart A. Montgomery, M.D.,Ph.D., P.O. Box 8751, London W13 8WH, UK</p>
	<p><b>Notes</b></p>



Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Judgement Comment: No information of how the allocation sequence was generated
Allocation concealment (selection bias)	Unclear risk	Judgement Comment: No information allocation concealment
Blinding of participants and personnel (performance bias)	Low risk	Quote: "randomized, double-blind, 4-arm, parallel- group, fixed-dose comparison study of 2 dosages of pregabalin, placebo, and venlafaxine in patients diagnosed with GAD." Judgement Comment: Double-blinded treatment, matched placebo.
Blinding of outcome assessment (detection bias)	Low risk	Judgement Comment: double-blinded.
Incomplete outcome data (attrition bias)	Low risk	Quote: "Primary efficacy and safety analyses were performed on the intention-to-treat (ITT) population, which consisted of all randomized patients who received at least 1 dose of study drug." Judgement Comment: Unequal attrition in the groups, more participants discontinued in the Venlafaxine group due to adverse events
Selective reporting (reporting bias)	Low risk	Judgement Comment: The study protocol is not available, but the study appears to report on all outcomes of interest.
Other bias	Low risk	Judgement Comment: Appears to be free from other sources of bias

Footnotes

Characteristics of excluded studies

Footnotes

Characteristics of studies awaiting classification

Footnotes

Characteristics of ongoing studies

Footnotes

## References to studies

### Included studies

#### **Cvijetkovic-Bosnjak 2015**

Cvijetkovic-Bosnjak, M.; Soldatovic-Stajic, B.; Babovic, S. S.; Boskovic, K.; Jovicevic, M.. Pregabalin versus sertraline in generalized anxiety disorder. An open label study. European review for medical and pharmacological sciences 2015;19(11):2120-2124. [DOI: 9052 [pii]]

#### **Kasper 2009**

Kasper, S.; Herman, B.; Nivoli, G.; Van Ameringen, M.; Petralia, A.; Mandel, F. S.; Baldinetti, F.; Bandelow, B.. Efficacy of pregabalin and venlafaxine-XR in generalized anxiety disorder: results of a double-blind, placebo-controlled 8-week trial. International clinical psychopharmacology 2009;24(2):87-96. [DOI: ]

#### **Montgomery 2006**

Montgomery, S. A.; Tobias, K.; Zomberg, G. L.; Kasper, S.; Pande, A. C.. Efficacy and safety of pregabalin in the treatment of generalized anxiety disorder: a 6-week, multicenter, randomized, double-blind, placebo-controlled comparison of pregabalin and venlafaxine. The Journal of clinical psychiatry 2006;67(5):771-782. [DOI: ]

### Excluded studies

## Data and analyses

### 1 Pregabalin vs Antidepressiva

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
1.1 Grad af angstsymptomer (anxiety severity)	3	661	Mean Difference (IV, Random, 95% CI)	-0.58 [-2.18, 1.03]
1.2 Funktionsniveau	1	246	Mean Difference (IV, Fixed, 95% CI)	-2.00 [-4.22, 0.22]
1.3 Livskvalitet (quality of life), EQ5D	1	246	Mean Difference (IV, Fixed, 95% CI)	0.01 [-0.07, 0.09]
1.4 Bedring (response), CGI-I	2	415	Risk Ratio (IV, Random, 95% CI)	1.00 [0.93, 1.08]
1.5 Frafald, alle årsager (Dropouts, all causes)	3	673	Risk Ratio (IV, Random, 95% CI)	0.77 [0.59, 1.02]
1.6 Frafald grundet bivirkninger (Dropouts due to adverse events)	3	673	Risk Ratio (IV, Random, 95% CI)	0.58 [0.39, 0.87]
1.7 Alvorlige bivirkninger (Serious adverse events), antal personer	2	566	Risk Ratio (IV, Random, 95% CI)	0.51 [0.32, 0.83]
1.8 Bivirkninger (Adverse events), antal personer	1	107	Risk Ratio (IV, Random, 95% CI)	1.04 [0.56, 1.94]
1.9 Grad af undgåelse (avoidance)	0	0	Mean Difference (IV, Fixed, 95% CI)	Not estimable

1.10 Afhængighed (dependence)	0	0	Odds Ratio (M-H, Fixed, 95% CI)	Not estimable
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**Figures**

**Figure 1**

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Cvijetkovic Bosnjak 2015	?	?	+	+	?	?	+
Kasper 2009	+	?	+	+	+	+	+
Montgomery 2006	?	?	+	+	+	+	+

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

**Figure 2 (Analysis 1.1)**

Study or Subgroup	Pregabalin		Antidepressiva		Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI	Risk of Bias
	Mean	SD	Mean	SD			
Cvijetkovic Bosnjak 2015	14.2	5.8	4.7	13.7	3	0.50 [-1.32, 2.32]	A ? ? ? ? ? ? ? ?
Kasper 2009	-14.5	9.9	121	-12	125	-2.50 [-4.99, -0.01]	B ? ? ? ? ? ? ? ?
Montgomery 2006	-14.3848	7.9558	198	-14.1	8.3905	-0.28 [-2.20, 1.64]	C ? ? ? ? ? ? ? ?
<b>Total (95% CI)</b>			<b>366</b>		<b>295</b>	<b>-0.58 [-2.18, 1.03]</b>	

Heterogeneity: Tau<sup>2</sup> = 0.92; Chi<sup>2</sup> = 3.67, df = 2 (P = 0.16); I<sup>2</sup> = 45%  
 Test for overall effect: Z = 0.70 (P = 0.48)

Risk of bias legend

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

Forest plot of comparison: 1 Pregabalin vs Antidepressiva, outcome: 1.1 Grad af angstsymptomer (anxiety severity).

**Figure 3 (Analysis 1.2)**

Study or Subgroup	Pregabalin		Antidepressiva		Mean Difference IV, Fixed, 95% CI	Mean Difference IV, Fixed, 95% CI	Risk of Bias
	Mean	SD	Mean	SD			
Kasper 2009	-6.7	8.8	121	-4.7	8.94427191	-2.00 [-4.22, 0.22]	A ? ? ? ? ? ? ? ?
<b>Total (95% CI)</b>			<b>121</b>		<b>125</b>	<b>-2.00 [-4.22, 0.22]</b>	

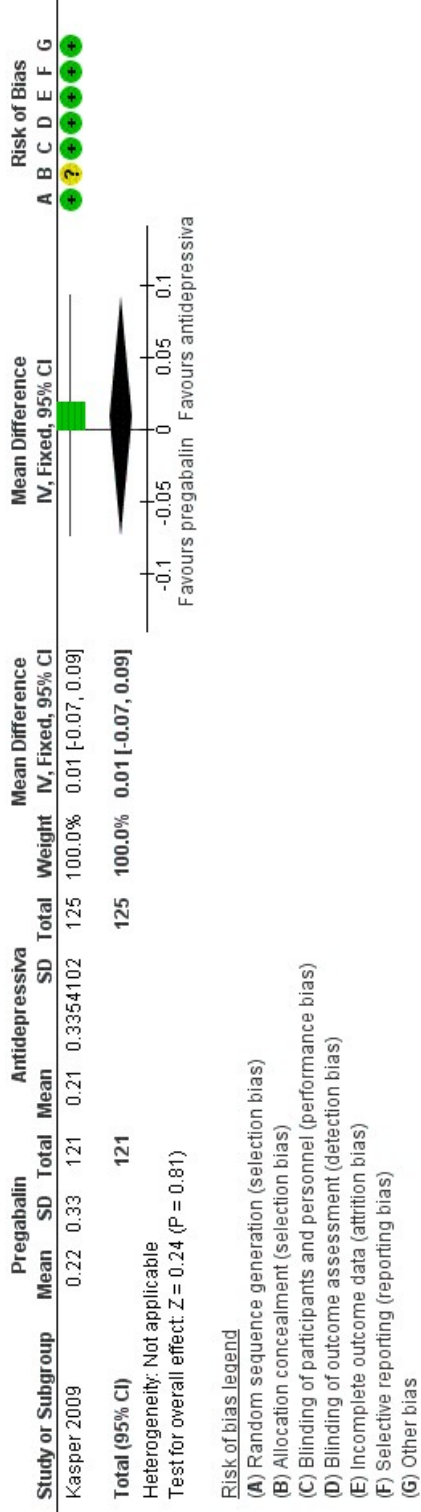
Heterogeneity: Not applicable  
 Test for overall effect: Z = 1.77 (P = 0.08)

Risk of bias legend

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

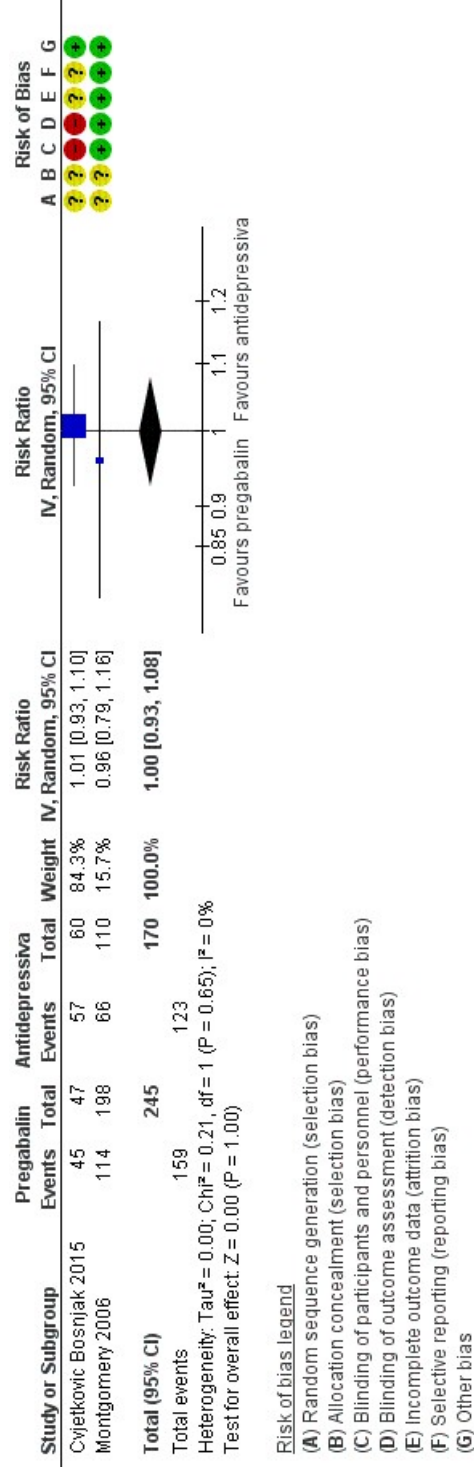
Forest plot of comparison: 1 Pregabalin vs Antidepressiva, outcome: 1.2 Funktionsniveau.

Figure 4 (Analysis 1.3)



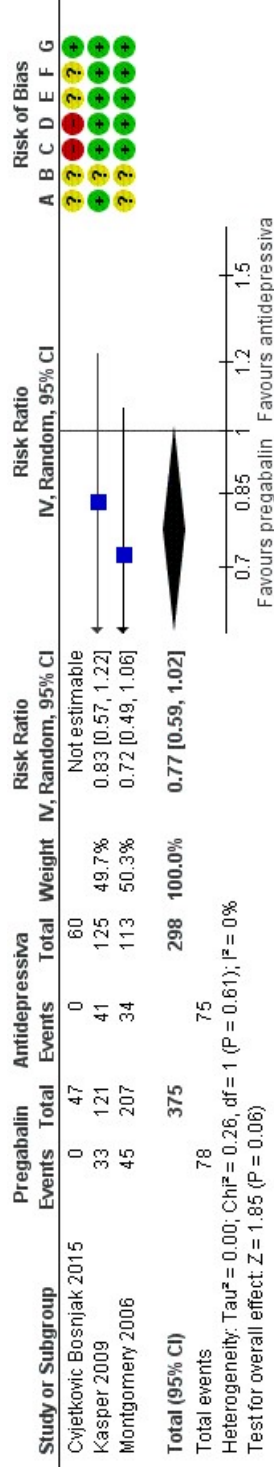
Forest plot of comparison: 1 Pregabalin vs Antidepressiva, outcome: 1.3 Livskvalitet (quality of life), EQ5D.

Figure 6 (Analysis 1.4)



Forest plot of comparison: 1 Pregabalin vs Antidepressiva, outcome: 1.4 Bedring (response), CGI-I.

Figure 7 (Analysis 1.5)

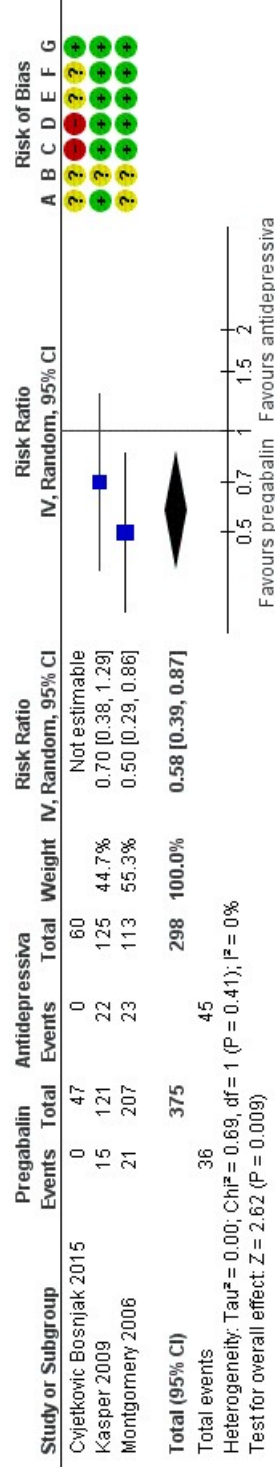


Risk of bias legend

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

Forest plot of comparison: 1 Pregabalin vs Antidepressiva, outcome: 1.5 Frafald, alle årsager (Dropouts, all causes).

Figure 8 (Analysis 1.6)

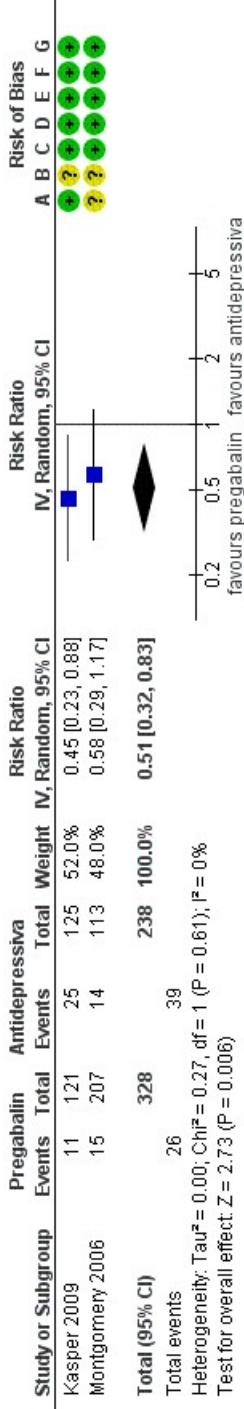


Risk of bias legend

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

Forest plot of comparison: 1 Pregabalin vs Antidepressiva, outcome: 1.6 Frafald grundet bivirkninger (Dropouts due to adverse events).

Figure 9 (Analysis 1.7)

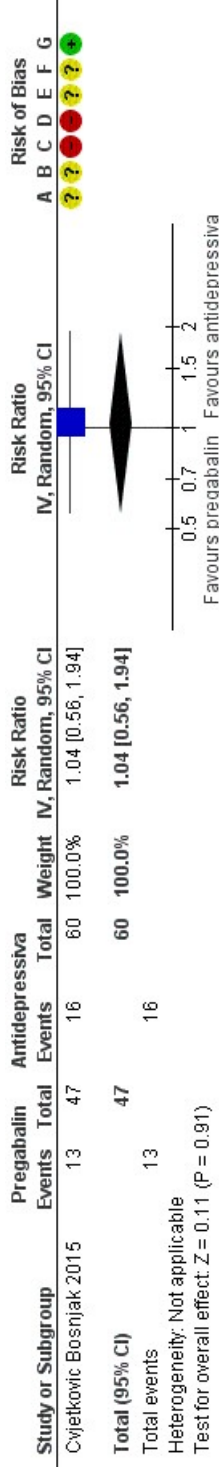


Risk of bias legend

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

Forest plot of comparison: 1 Pregabalin vs Antidepressiva, outcome: 1.7 Alvorlige bivirkninger (Serious adverse events), antal personer.

Figure 10 (Analysis 1.8)



Risk of bias legend

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

Forest plot of comparison: 1 Pregabalin vs Antidepressiva, outcome: 1.8 Bivirkninger (Adverse events), antal personer.