NKR 58 Angst voksne PICO 4 Benzodiazepiner

Review information

Authors

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Characteristics of studies

Characteristics of included studies

Pollack 2014

Methods	**Study design:** Randomized controlled trial **Study grouping:** Parallel group
Participants	**Baseline Characteristics** Intervention ● *Age, y. (mean SD)*: 34.8 (12.3) ● *Female, %*: 40 Control ● *Age, y. (mean SD)*: 35.3 (14.3) ● *Female, %*: 34 Overall ● F*emale, %*: 37 **Included criteria:** Inclusion criteria were1) outpatients who were at least 18 years old with a currentprincipal diagnosis of generalized social anxiety disorder byDSM-IV criteria (including designation by the patient as the mostimportant source of distress or impairment), 2) a total score onthe Liebowitz Social Anxiety Scale (LSAS) (10) of 60 or greater,and 3) no clinically significant medical abnormalities based onphysical and laboratory examination. **Excluded criteria:** Exclusion criteria were 1) a history of more than two unsuccessful adequate pharmacological treatment trials, operationalizedas lack of response to at least 10 weeks of any of the following: SSRIs at adequate dosage (e.g., paroxetine, 40 mg/day or its equivalent); benzodiazepines (e.g., clonazepam,. 2.5 mg/day) plus an antidepressant (at adequate dosages as above); MAOIs (e.g., phenelzine, 60 mg/day or its equivalent); or a single failed trial of at least 10 weeks of venlafaxine ($ 150 mg/day); 2) pregnant women, lactating women, and women of childbearing potential not using medically accepted forms of contraception; 3) psychotic disorders, mental retardation, organic medical disorders, bipolar disorder, obsessive-compulsive disorder (OCD) with a Yale-Brown Obsessive Compulsive Scale (YBOCS) score $ 25, or a recent history of eating disorders or alcohol or substance abuse or dependence; 4) concurrent use of other psychotropic medications with discontinuation of regular benzodiazepine or antidepressant therapy at least 2 weeks before the baseline evaluation (5 weeks for fluoxetine); patients with comorbid adult attention deficit hyperactivity disorder (ADHD) could remain on stimulant medication if the dosage had been stable for at least 1 month; 5) current or recent significant

	suicidality; and 6) any concurrent psychotherapy initiated within 3 months or ongoing psychotherapy of any duration directed specifically toward the treatment of the generalized social anxiety disorder (e.g., CBT). Inclusion of patients with major depression, panic disorder, generalized anxiety disorder, adult ADHD, or posttraumatic stress disorder (PTSD) was permitted if the generalized social anxiety disorder wasjudged to be the predominant disorder.
Interventions	**Intervention Characteristics** Intervention ● *Description*: Eligible participants were enrolled into the two-phase pro-tocol. Phase 1 comprised 10 weeks of open prospective treatmentwith sertraline initiated at 25 mg/day, with all symptomaticpatients titrated up to their maximally tolerated dosage (#200mg/day) by week 8. Participants who were unable to reach atleast 50 mg/day by the end of phase 1 were discontinued fromthe study and referred for clinical treatment. Participants wereseen weekly for thefirst 2 weeks of phase 1 and then biweeklythereafter. In addition, phase 1 participants were randomly assignedto receive either brief exposure instructions or no specificinstruc-tions regarding activity. Responders to open treatment (phase 1) atweek 10 were continued on the same dosage of sertraline and seenat week 14 and week 22 for efficacy and safety assessments.In phase 2, participants who remained symptomatic at the endof phase 1 (operationalized as an LSAS score.50 to identifyindividuals with at least a moderate level of severity and forwhom additional intervention was warranted) were randomlyassigned to one of three treatment groups: sertraline plusplacebo; sertraline plus clonazepam, up to 3.0 mg/day; orswitch to venlafaxine withflexible titration up to 225 mg/day.Randomization was stratified by site (Massachusetts GeneralHospital, University of California at San Diego, and McMasterUniversity) and by LSAS severity at week 10 (LSAS total score#70compared with.70). The sertraline dosage in the sertraline plusplacebo and sertraline plus clonazepam arms was held at thesame level as at entry into phase 2. ● *Dose*: Sertraline 25 mg/d + Clonazepam 3 mg/d ● *Duration*: 12 weeks Control ● *Description*: ● *Dose*: Sertraline 25 mg/d + placebo ● *Duration*: 12 weeks
Outcomes	*Grad af angst, HAM-A, mean SD* ● **Outcome type**: ContinuousOutcome ● **Scale**: HAM-A, mean SD ● **Direction**: Lower is better ● **Data value**: Endpoint *Funktionsniveau, Sheean Disability Scale, self report, mean, SD* ● **Outcome type**: ContinuousOutcome ● **Reporting**: Fully reported ● **Scale**: Sheean Disability Scale, self report, mean, SD ● **Direction**: Lower is better ● **Data value**: Endpoint *Livskvalitet, The Quality of Life Enjoyment and Satisfaction Questionnaire, mean SD* ● **Outcome type**: ContinuousOutcome ● **Reporting**: Fully reported ● **Scale**: Q-LES Q, total

	● **Direction**: Higher is better ● **Data value**: Endpoint *Bedring respons, Liebowitz Social Anciety Scale (LSAS) (LSAS≤ 50), nN* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Scale**: Liebowitz Social Anciety Scale (LSAS) (LSAS≤ 50) ● **Data value**: Endpoint *Frafald, alle årsager* ● **Outcome type**: DichotomousOutcome ● **Reporting**: Fully reported ● **Direction**: Lower is better ● **Data value**: Endpoint *SAE* ● **Outcome type**: DichotomousOutcome ● **Direction**: Lower is better ● **Data value**: Endpoint
Identification	**Sponsorship source:** Supported by NIMH (grant 1R01MH070919). Support for study drug and packaging received from Pfizer and Wyeth Pharmaceuticals. **Country:** USA **Authors name:** Mark H. Pollack, M.D. **Institution:** Rush University Medical Center, Chicago; McMaster University, Hamilton, Ontario; Massachusetts General Hospital, Boston; and the University of California, San Diego **Email:** mark_pollack@rush.edu
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Randomization was stratified by site (Massachusetts General Hospital, University of California at San Diego, and McMaster University) and by LSAS severity at week 10 (LSAS total score #70 compared with .70)." Judgement Comment: Insufficient information on sequence generation
Allocation concealment (selection bias)	Unclear risk	Judgement Comment: Insufficient information on allocation concealment
Blinding of participants and personnel (performance bias)	Unclear risk	Quote: "A double-dummy design was employed in which patients received an identical number of study capsules at each visit (a mixture of study medication and placebo depending on treatment assignment and dose) to enable maintenance of the double blind for all three treatment arms." Judgement Comment: Likely participants were blinded. No information about blinding of personnel.

Blinding of outcome assessment (detection bias)	Unclear risk	Judgement Comment: Likely the participants were blinded - relevant for the PRO (SDS and QLES). No information about blinding of the trained study clinicians asessing remission criteria (LSAS) and HAM-A.
Incomplete outcome data (attrition bias)	Low risk	Quote: "Early discontinuation rates were highest among patients randomly assigned to venlafaxine (20%), followed by patients assigned to sertraline plus placebo (15%) and sertraline plus clonazepam (10%), al- though the differences were not significant."
Selective reporting (reporting bias)	High risk	Quote: "Clinicaltrials.gov identifier NCT00282828." Judgement Comment: Protocol available however, no secondary outcome measures reported in the article where pre-specified in the protocol registered.
Other bias	Low risk	Quote: "Pollack (mark_pollack@rush.edu). Clinicaltrials.gov identifier NCT00282828. Supported by NIMH (grant 1R01MH070919). Support for study drug and packaging received from Pfizer and Wyeth Pharmaceuticals. Dr. Pollack has received advisory board or consulting fees from Brain Cells, Concept Pharma, Corcept, Edgemont, Eli Lilly, Ironwood Pharma- ceuticals, Johnson and Johnson, Labopharm, Medavante, Merck, Mindsite, Otsuka, Pfizer, Sepracor, Targia, and Transcept; grant support from Bristol-Myers Squibb, Eli Lilly, Euthymics, Forest Laboratories, GlaxoSmithKline, the National Center for Complementary and Alterna- tive Medicine, National Institute on Drug Abuse, NIMH, and Sepracor; CME activity support from AstraZeneca, Pfizer, and Sepracor; royalty or patent funds from the Structured Interview Guide for the Hamilton Anxiety Scale, SAFER interviews; and equity from Doyen Medical, Medavante, Mensante Corporation, Mindsite, and Targia. Dr. Van Ameringen has received grant or research support from the Canadian Foundation for Innovation, Forest Laboratories, Janssen-Ortho, NIH, Pfizer, Servier, and Wyeth-Ayerst and has received speakers bureau, consultant, or advisory board fees from AstraZeneca, Biovail, Eli Lilly, Forest Laboratories, GlaxoSmithKline, Janssen-Ortho, Labo Pharm, Lundbeck, Pfizer, Shire, and Valiant. Dr. Simon has received grant support or consulting fees from the American Cancer Society, American Foundation for Suicide Prevention, Department of Defense, Eli Lilly, Forest Research, GlaxoSmithKline, Highland Street Founda- tion, Massachusetts General Hospital Psychiatry Academy, NARSAD, NIH, NIMH, Pfizer, and Sepracor and her spouse has equity in Elan, Dandreon, G Zero, and Gatekeeper. Dr. Worthington has received grant or research support from Eli Lilly, Forest Pharmaceuticals, Pfizer, and Sepracor. Dr. Stein has a patent on the use of genetic testing to predict treatment outcomes in social anxiety disorder and receives payment for his work as Co-Editor-in-Chief of UpToDate in Psychiatry and as Deputy Editor of Depression and Anxiety and Biological Psy- chiatry. Dr. Hoge and Ms. Keshaviah report no financial relationships with commercial interests. The authors thank Laura Fischer," Judgement Comment: No other sources of bias are suspected.

Footnotes

Characteristics of excluded studies

Footnotes

Characteristics of studies awaiting classification

Footnotes

Characteristics of ongoing studies

Footnotes

References to studies

Included studies

Pollack 2014

Pollack, M. H.; Van Ameringen, M.; Simon, N. M.; Worthington, J. W.; Hoge, E. A.; Keshaviah, A.; Stein, M. B.. A double-blind randomized controlled trial of augmentation and switch strategies for refractory social anxiety disorder. The American Journal of Psychiatry 2014;171(1):44-53. [DOI: 10.1176/appi.ajp.2013.12101353 [doi]]

Excluded studies

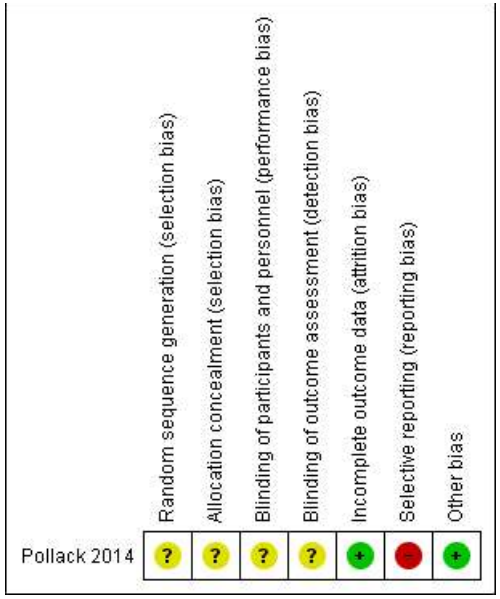
Data and analyses

1 Benzodiazepin+SSRI vs SSRI+placebo

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
1.1 Grad af angst (severity of anxiety)	1	122	Mean Difference (IV, Fixed, 95% CI)	-1.10 [-3.28, 1.08]
1.2 Funktionsniveau (disability)	1	122	Mean Difference (IV, Fixed, 95% CI)	-0.10 [-2.40, 2.20]
1.3 Livskvalitet (quality of life)	1	122	Mean Difference (IV, Fixed, 95% CI)	0.20 [-2.84, 3.24]
1.4 Bedring respons (response LSAS <= 50))	1	122	Risk Ratio (IV, Fixed, 95% CI)	1.56 [1.04, 2.35]
1.5 Frafald, alle årsager (dropout all cause)	1	122	Risk Ratio (IV, Fixed, 95% CI)	0.70 [0.26, 1.90]
1.6 Alvorlige bivirkninger (SAE)	1	122	Risk Difference (IV, Fixed, 95% CI)	0.05 [-0.01, 0.11]
1.7 Alvorlige bivirkninger (SAE)	1	122	Risk Ratio (M-H, Fixed, 95% CI)	6.56 [0.35, 124.41]

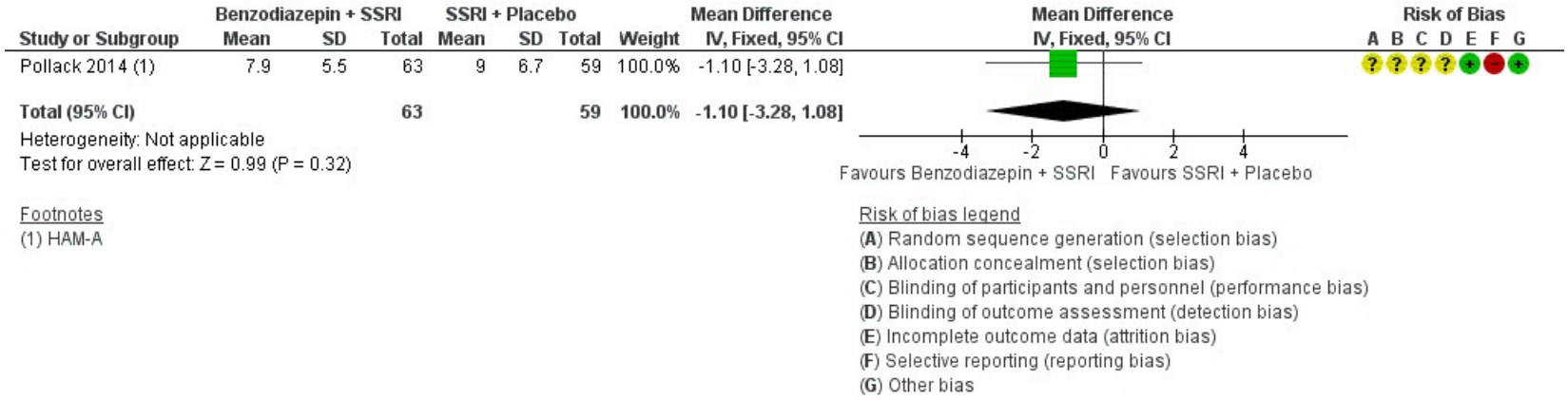
Figures

Figure 1



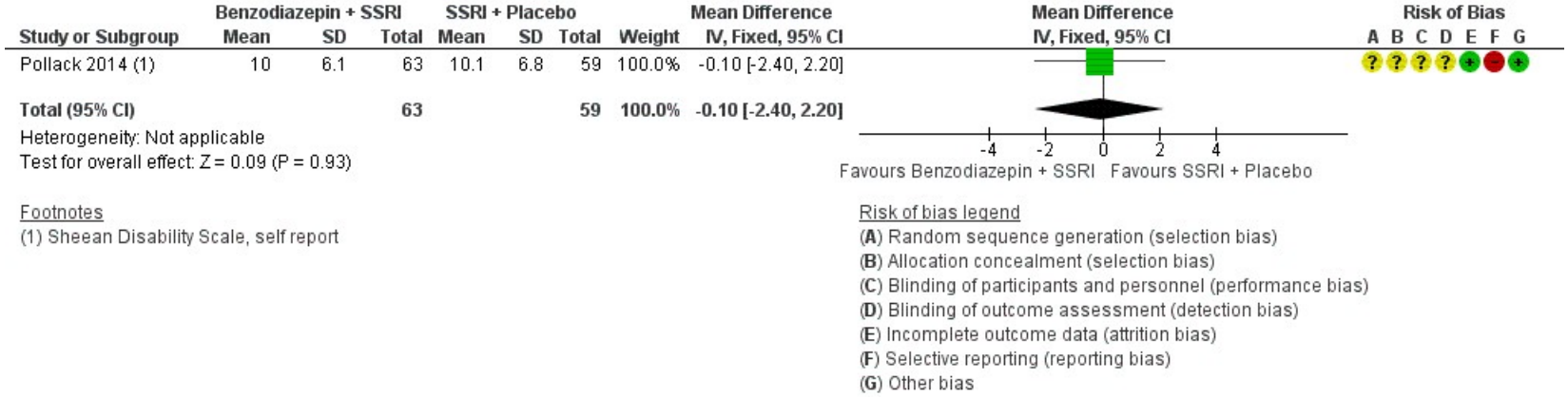
Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

Figure 2 (Analysis 1.1)



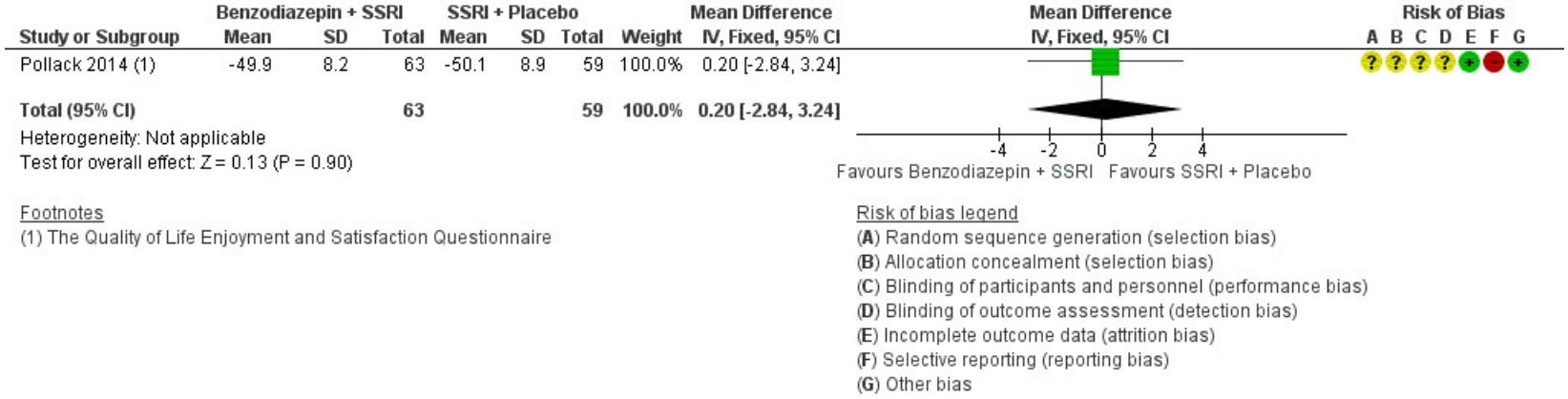
Forest plot of comparison: 1 Benzodiazepin+SSRI vs SSRI+placebo, outcome: 1.1 Grad af angst (severity of anxiety).

Figure 3 (Analysis 1.2)



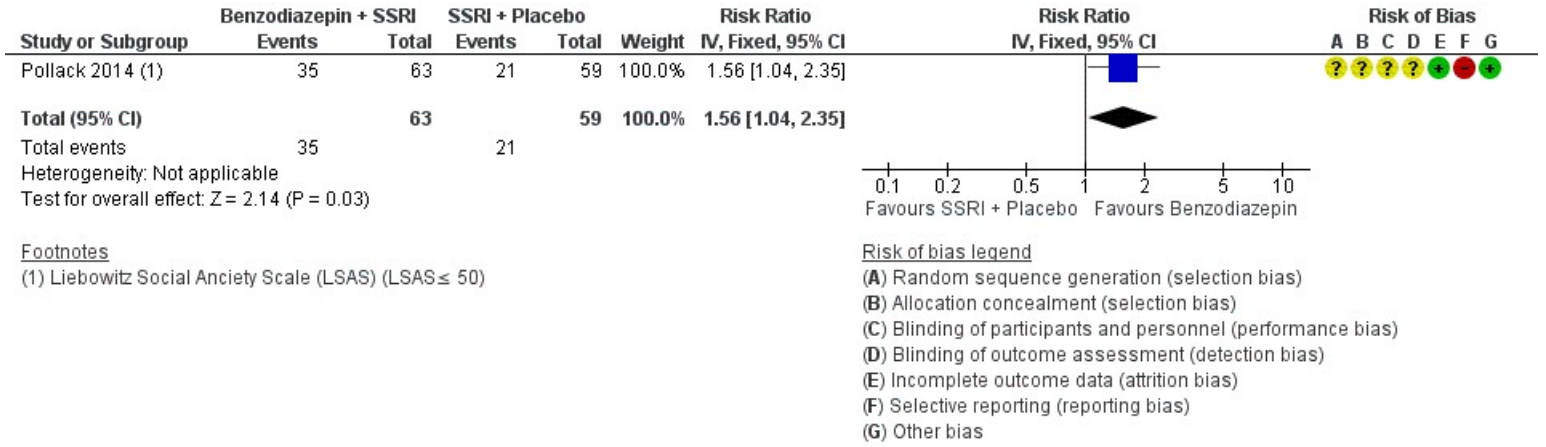
Forest plot of comparison: 1 Benzodiazepin+SSRI vs SSRI+placebo, outcome: 1.2 Funktionsniveau (disability).

Figure 4 (Analysis 1.3)



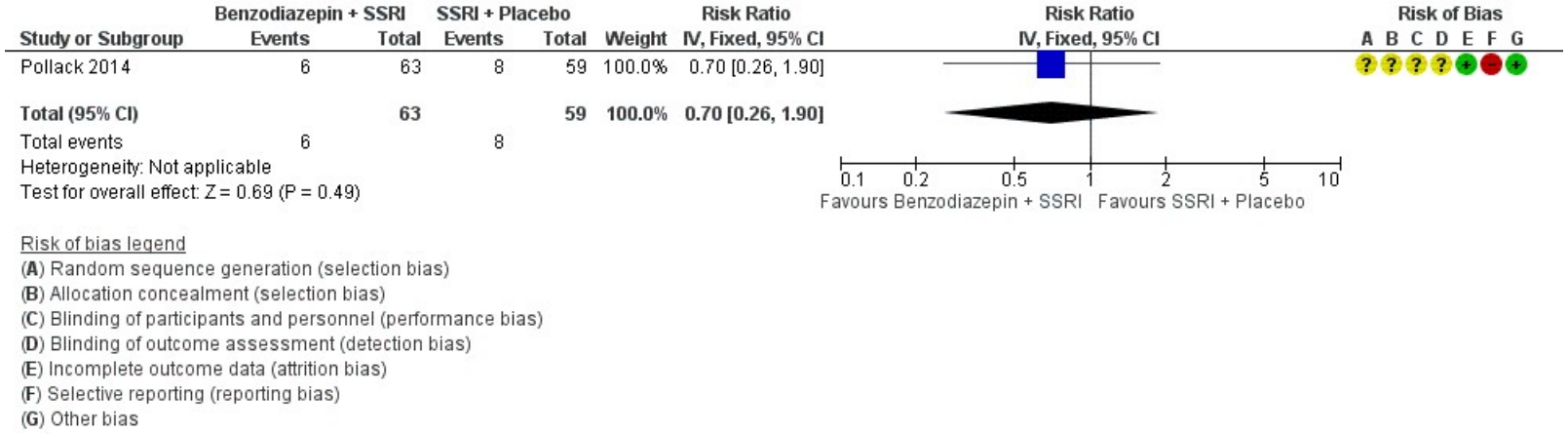
Forest plot of comparison: 1 Benzodiazepin+SSRI vs SSRI+placebo, outcome: 1.3 Livskvalitet (quality of life).

Figure 5 (Analysis 1.4)



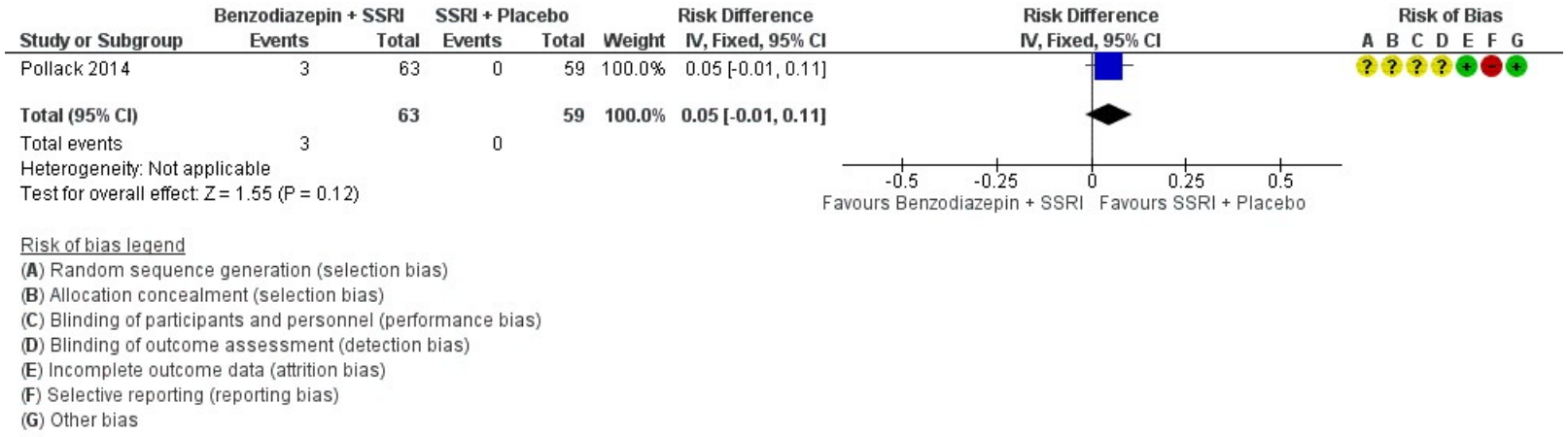
Forest plot of comparison: 1 Benzodiazepin+SSRI vs SSRI+placebo, outcome: 1.4 Bedring respons (response LSAS <= 50)).

Figure 6 (Analysis 1.5)



Forest plot of comparison: 1 Benzodiazepin+SSRI vs SSRI+placebo, outcome: 1.5 Frafald, alle årsager (dropout all cause).

Figure 7 (Analysis 1.6)



Forest plot of comparison: 1 Benzodiazepin+SSRI vs SSRI+placebo, outcome: 1.6 Alvorlige bivirkninger (SAE).