NKR 16 Smerte PICO 12 SNRI

Review information

Authors

Sundhedsstyrelsen¹

¹[Empty affiliation]

Citation example: S. NKR 16 Smerte PICO 12 SNRI. Cochrane Database of Systematic Reviews [Year], Issue [Issue].

Contact person

[Empty name]

Characteristics of studies

Characteristics of included studies

Arnold 2004

Methods	
Participants	
Interventions	
Outcomes	
Notes	See Lunn et al "Duloxetine for treating painful neuropathy, chronic pain and fibromyalgia". Cochrane Library 2014

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	See Lunn et al "Duloxetine for treating painful neuropathy, chronic pain and fibromyalgia". Cochrane Library 2014
Allocation concealment (selection bias)	Low risk	See Lunn et al "Duloxetine for treating painful neuropathy, chronic pain and fibromyalgia". Cochrane Library 2014
Blinding of participants and personnel (performance bias)	Low risk	See Lunn et al "Duloxetine for treating painful neuropathy, chronic pain and fibromyalgia". Cochrane Library 2014
Incomplete outcome data (attrition bias)	High risk	See Lunn et al "Duloxetine for treating painful neuropathy, chronic pain and fibromyalgia". Cochrane Library 2014
Selective reporting (reporting bias)	Unclear risk	See Lunn et al "Duloxetine for treating painful neuropathy, chronic pain and fibromyalgia". Cochrane Library 2014
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Arnold 2005

Methods	
Participants	
Interventions	
Outcomes	
Notes	See Lunn et al "Duloxetine for treating painful neuropathy, chronic pain and fibromyalgia". Cochrane Library 2014

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Arnold 2010

Methods	
Participants	
Interventions	
Outcomes	
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Arnold 2012

Methods	
Participants	
Interventions	
Outcomes	
Notes	See Lunn et al "Duloxetine for treating painful neuropathy, chronic pain and fibromyalgia". Cochrane Library 2014

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Other bias	Low risk	See Lunn et al "Duloxetine for treating painful neuropathy, chronic pain and fibromyalgia". Cochrane Library 2014

Chappell 2008

Methods	
Participants	
Interventions	
Outcomes	
Notes	See Lunn et al "Duloxetine for treating painful neuropathy, chronic pain and fibromyalgia". Cochrane Library 2014

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Selective reporting (reporting bias)	Low risk	See Lunn et al "Duloxetine for treating painful neuropathy, chronic pain and fibromyalgia". Cochrane Library 2014
Other bias	Unclear risk	See Lunn et al "Duloxetine for treating painful neuropathy, chronic pain and fibromyalgia". Cochrane Library 2014

Murakami 2015

Methods	Study design: Randomized controlled trial Study grouping: Parallel group
Participants	Baseline Characteristics Duloxetine • Age, median (range): 47.8 (12.0) mean, SD • No. of females (n): 157 • BPI, average score mean (SD): 6.05 (1.29) Control • Age, median (range): 49.5 (11.7) mean, SD • No. of females (n): 164 • BPI, average score mean (SD): 6.13 (1.35) Overall • Age, median (range): • No. of females (n):

	BPI, average score mean (SD):
	Included criteria: The criteria used in a previous study of duloxetine [25]were adopted. Briefly, male and female outpatients agedbetween 20 and 75 years who met the ACR 1990 criteria for fibromyalgia [2] and had a Brief Pain Inventory (BPI)average pain score≥ 4 [26, 27] at visits 1 and 2 were included. Excluded criteria: Exclusion criteria were as follows: past duloxe-tine treatment; serious or medically unstable disease, clinically significant abnormal laboratory values, or ab-normal electrocardiogram (ECG) findings; pain causedby non-fibromyalgia diseases; poorly controlled thyroid dysfunction; rheumatoid, inflammatory, or infectiousarthritis; autoimmune disorders other than thyroid dys-function; psychiatric disorders other than major de-pressive disorder within the past year; and suicidal tendencies as assessed using the Columbia-SuicideSeverity Rating Scale (C-SSRS). Pretreatment: Both groups were balanced in terms of baseline demographic characteristics
Interventions	Intervention Characteristics Duloxetine • Dosage: In theduloxetine group, patients received 20 mg for 1 week followed by 40 mg for 1 week and then 60 mg for 12 weeks during the treatment phase. • Longest follow-up after end of treatment: • Length of treatment: 14 weeks Control
	 Dosage: In the placebo group, subjects received placebo for 14 weeks through-out the treatment phase. Longest follow-up after end of treatment: Length of treatment: 14 weeks
Outcomes	Functioning. SF-36 (physical functioning), SEM. final Outcome type: ContinuousOutcome Quality of life SF-36 (total score) final. SEM Outcome type: ContinuousOutcome Functioning SF-36 (physical functioning) change. SE Outcome type: ContinuousOutcome Proporting: Fully reported Proporting: Fully reported
	 Data value: Change from baseline Pain. BPI (BOCF) Change, SE Outcome type: ContinuousOutcome Reporting: Fully reported Data value: Change from baseline Pain BPI (pain on average). Final, SEM
	 Outcome type: ContinuousOutcome Drowsiness, % Outcome type: DichotomousOutcome Data value: Endpoint
	Nausea, % ● Outcome type: DichotomousOutcome
	Dry mouth, %
	Constipation, % ■ Outcome type: DichotomousOutcome ■ Reporting: Fully reported

	Data value: Endpoint
	Weight gain, % ● Outcome type: DichotomousOutcome
	Fatigue/somnolence, % Outcome type: DichotomousOutcome Reporting: Fully reported Data value: Endpoint
	Dizziness, % ■ Outcome type: DichotomousOutcome ■ Reporting: Fully reported ■ Data value: Endpoint
	Dropout pga bivirkninger ● Outcome type: DichotomousOutcome
	Severe adverse events, n ● Outcome type: DichotomousOutcome
Notes	

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)		Quote: "After the screening phase, patients were assigned randomly to receive duloxetine or placebo in a 1:1 ratio, using a web-based patient regis- tration system (ACRONET Corp., Tokyo, Japan) with a stochastic minimization procedure. The following alloca- tion factors were used: (1) BPI average pain score at visit 2 (<6 vs. ≥ 6) and (2) presence or absence of concomitant major depressive disorder diagnosed on the basis of the M.I.N.I. International Neuropsychiatric Interview–Japanese version 5.0.0 [29]. It was ensured that the maxi- mum between-group difference in the number of subjects in each medical institution did not exceed two."
Allocation concealment (selection bias)		Quote: "The drug allocation con- troller confirmed the study drugs were undiscernible in terms of appearance, packaging, and labeling, and mock titration of placebo pills was also performed to maintain blinding. Only the drug allocation controller was aware of the type of drugs being dispensed."
Blinding of participants and personnel (performance bias)		Quote: "two. Blinding was maintained until the end of the study by the person responsible for the study drug assignment." Quote: "The drug allocation con- troller confirmed the study drugs were undiscernible in terms of appearance, packaging, and labeling, and mock titration of placebo pills was also performed to maintain blinding. Only the drug allocation controller was aware of the type of drugs being dispensed."
Incomplete outcome data (attrition bias)	High risk	Judgement Comment: 76% of the patients in the placebo completed and 85% in the duloxetine group completed.
Selective reporting (reporting bias)	High risk	Judgement Comment: Not all the primary oputcome mentioned in the protocol are reproted.
Other bias	Low risk	Judgement Comment: No other apparent sources of bias

Russell 2008

Methods	
Participants	
Interventions	
Outcomes	
Notes	See Lunn et al "Duloxetine for treating painful neuropathy, chronic pain and fibromyalgia". Cochrane Library 2014

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	See Lunn et al "Duloxetine for treating painful neuropathy, chronic pain and fibromyalgia". Cochrane Library 2014
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Other bias	Low risk	See Lunn et al "Duloxetine for treating painful neuropathy, chronic pain and fibromyalgia". Cochrane Library 2014

Footnotes

Characteristics of excluded studies

Footnotes

Characteristics of studies awaiting classification

Footnotes

Characteristics of ongoing studies

Footnotes

References to studies

Included studies

Arnold 2004

[Empty]

Arnold 2005

[Empty]

Arnold 2010

[Empty]

Arnold 2012

[Empty]

Chappell 2008

[Empty]

Murakami 2015

Murakami, Masato; Osada, Kenichi; Mizuno, Hiromichi; Ochiai, Toshimitsu; Alev, Levent; Nishioka, Kusuki. A randomized, double-blind, placebo-controlled phase III trial of duloxetine in Japanese fibromyalgia patients.. Arthritis Research & Therapy 2015;17(Journal Article):224. [DOI: https://dx.doi.org/10.1186/s13075-015-0718-y]

Russell 2008

[Empty]

Excluded studies

Data and analyses

3 Duloxetine versus placebo in the treatment of fibromyalgia

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
3.1 Functionality (SF-36, physical functioning) Change	6	2238	Mean Difference (IV, Random, 95% CI)	2.13 [0.46, 3.79]
3.2 Pain (BPI, average pain+BOCF) Change	7	2474	Std. Mean Difference (IV, Random, 95% CI)	-0.28 [-0.38, -0.17]
3.3 Quality of life (BPI, enjoyment of life, QoL in depressionsn scale) Change	2	513	Std. Mean Difference (IV, Random, 95% CI)	-0.40 [-0.58, -0.22]
3.6 Serious adverse event	6	2356	Risk Ratio (M-H, Random, 95% CI)	0.66 [0.28, 1.55]
3.6.6 End of treatment	6	2356	Risk Ratio (M-H, Random, 95% CI)	0.66 [0.28, 1.55]
3.7 Droput due to adverse events	7	2639	Risk Ratio (M-H, Random, 95% CI)	1.61 [1.29, 2.01]
3.7.6 End of treatment	7	2639	Risk Ratio (M-H, Random, 95% CI)	1.61 [1.29, 2.01]
3.8 Tired/Somnolence	4	1548	Risk Ratio (M-H, Random, 95% CI)	2.76 [1.89, 4.02]
3.8.2 End of treatment	4	1548	Risk Ratio (M-H, Random, 95% CI)	2.76 [1.89, 4.02]
3.9 Dizziness	3		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
3.9.3 End of treatment	3	1440	Risk Ratio (M-H, Random, 95% CI)	2.16 [1.16, 4.00]
3.10 Nausea	5	2078	Risk Ratio (M-H, Random, 95% CI)	3.12 [2.28, 4.27]
3.10.2 End of treatment	5	2078	Risk Ratio (M-H, Random, 95% CI)	3.12 [2.28, 4.27]
3.11 Constipation	4	1770	Risk Ratio (M-H, Random, 95% CI)	3.36 [2.32, 4.87]
3.12 Weigt gain	1	520	Risk Ratio (M-H, Fixed, 95% CI)	6.51 [0.87, 48.48]
3.13 Dry mouth	4	1770	Risk Ratio (M-H, Random, 95% CI)	2.89 [2.00, 4.17]
3.15 EKG differences	0		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
3.16 Confusion	0		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
3.17 Hypotension	0		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
3.18 Agitation	0		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only

Figures

Figure 1 (Analysis 3.1)

	SNRI							Mean Difference	Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	ABCDEF
Arnold 2004	8.44	16.114	92	3.82	16.2099	92	10.0%	4.62 [-0.05, 9.29]	-	
Arnold 2010	13.5	21.0825	263	8.1	21.2422	267	14.7%	5.40 [1.80, 9.00]		$lackbox{0} lackbox{0} lac$
Arnold 2012	4.75	9	155	3.91	9.03	153	27.9%	0.84 [-1.17, 2.85]	+	$lackbox{\bullet} ? lackbox{\bullet} lackbox{\bullet} lackbox{\bullet}$
Chappell 2008	4.66	18.2483	148	3.52	17.9464	162	12.5%	1.14 [-2.89, 5.17]		• • ? • • ?
Murakami 2015	7.4	29.43718567	191	3.04	30.02311609	195	6.8%	4.36 [-1.57, 10.29]	+-	$\bullet \bullet \bullet \bullet \bullet \bullet$
Russell 2008	4.7154	10.1298	376	4.01	10.44	144	28.2%	0.71 [-1.28, 2.69]	<u>†</u>	● ? ● ● ? ●
Total (95% CI)			1225			1013	100.0%	2.13 [0.46, 3.79]	*	
Heterogeneity: Tau² = Test for overall effect:			(P = 0.1	15); I²=	38%				-20 -10 0 10 20 Favours control Favours SNRI	-

Risk of bias legend

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

Forest plot of comparison: 3 Duloxetine versus placebo in the treatment of fibromyalgia, outcome: 3.1 Functionality (SF-36, physical functioning) Change.

Figure 2 (Analysis 3.2)

		SNRI			Control			Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	ABCDEF
Arnold 2004	-1.83	2.4	100	-0.94	2.3229	102	10.2%	-0.38 [-0.65, -0.10]		
Arnold 2005	-2.395	2.345	230	-1.16	2.2812	118	13.6%	-0.53 [-0.76, -0.30]		? ? \varTheta \varTheta ? 🖜
Arnold 2010	-2.6	2.7423	188	-1.7	2.8071	197	15.7%	-0.32 [-0.52, -0.12]		lacksquare
Arnold 2012	-2.04	2.4	155	-1.7	2.32	153	13.8%	-0.14 [-0.37, 0.08]	 	lacksquare
Chappell 2008	-1.62	2.514	158	-1.13	2.4553	167	14.2%	-0.20 [-0.41, 0.02]	 	• • ? • • ?
Murakami 2015	-1.38	3.45506874	191	-0.92	3.49106001	195	15.9%	-0.13 [-0.33, 0.07]	-• 	$\bullet \bullet \bullet \bullet \bullet \bullet$
Russell 2008	-2.1399	2.5363	376	-1.43	2.52	144	16.5%	-0.28 [-0.47, -0.09]	-	● ? ● ● ? ●
Total (95% CI)			1398			1076	100.0%	-0.28 [-0.38, -0.17]	•	
Heterogeneity: Tau² = Test for overall effect:			(P = 0.	15); I²=	36%				-2 -1 0 1 2 Favours SNRI Favours Control	

Risk of bias legend

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

Forest plot of comparison: 3 Duloxetine versus placebo in the treatment of fibromyalgia, outcome: 3.2 Pain (BPI, average pain+BOCF) Change.

Figure 3 (Analysis 3.3)

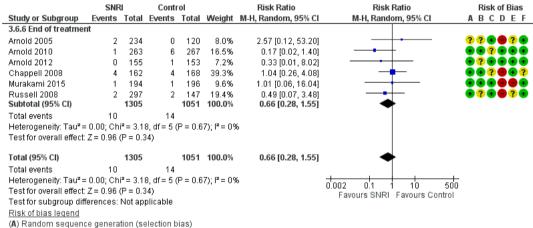
	SNRI Control							Std. Mean Difference	Std. Mean Difference	Risk of Bias
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	ABCDEF
Arnold 2004	-1.52	4.8575	84	0.11	4.86	81	34.8%	-0.33 [-0.64, -0.03]	-	
Arnold 2005	-2.895	2.7791	230	-1.68	2.7157	118	65.2%	-0.44 [-0.66, -0.22]	-	? ? 🗨 🖨 ? 🖜
Total (95% CI)			314			199	100.0%	-0.40 [-0.58, -0.22]	•	
Heterogeneity: Tau 2 = 0.00; Chi 2 = 0.30, df = 1 (P = 0.59); $ ^2$ = 0% Test for overall effect: Z = 4.36 (P < 0.0001)									-2 -1 0 1 2 Favours SNRI Favours Control	_

Risk of bias legend

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

Forest plot of comparison: 3 Duloxetine versus placebo in the treatment of fibromyalgia, outcome: 3.3 Quality of life (BPI, enjoyment of life, QoL in depressionsn scale) Change.

Figure 5 (Analysis 3.6)



- (B) Allocation concealment (selection bias)
- (C) Blinding of participants and personnel (performance bias)
- (D) Incomplete outcome data (attrition bias)
- (E) Selective reporting (reporting bias)
- (F) Other bias

Forest plot of comparison: 3 Duloxetine versus placebo in the treatment of fibromyalgia, outcome: 3.6 Serious adverse event.

Figure 6 (Analysis 3.7)

	SNR	i i	Contr	ol		Risk Ratio	Risk Ratio	Risk of Bias	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI	ABCDEF	
3.7.6 End of treatmen	rt								
Arnold 2004	18	104	11	103	10.1%	1.62 [0.81, 3.26]	+	• • • • ? •	
Arnold 2005	52	234	14	120	16.5%	1.90 [1.10, 3.29]		? ? 🗨 🖨 ? 🖜	
Arnold 2010	41	263	24	267	22.0%	1.73 [1.08, 2.79]		$lackbox{0} lackbox{0} lackbox{0} lackbox{0} lackbox{0} lackbox{0} lackbox{0} lackbox{0} lackbox{0} lackbox{0}$	
Arnold 2012	14	155	9	153	7.6%	1.54 [0.69, 3.44]	+-	$lackbox{0.5}{\bullet}$	
Chappell 2008	30	162	19	168	17.4%	1.64 [0.96, 2.79]		• ? • ?	
Murakami 2015	14	194	15	196	10.0%	0.94 [0.47, 1.90]			
Russell 2008	62	376	14	144	16.5%	1.70 [0.98, 2.93]	-	????	
Subtotal (95% CI)		1488		1151	100.0%	1.61 [1.29, 2.01]	•		
Total events	231		106						
Heterogeneity: Tau² =	0.00; Chi	$i^2 = 2.7$	5, df = 6 (P = 0.8	4); $I^2 = 09$	6			
Test for overall effect:	Z = 4.19 ((P < 0.0	1001)						
Total (95% CI)		1488		1151	100.0%	1.61 [1.29, 2.01]	•		
Total events	231		106						
Heterogeneity: Tau ² =	0.00; Chi	$i^2 = 2.7$	5, df = 6 (P = 0.8	4); $I^2 = 0.9$	6		-	
Test for overall effect:	Z = 4.19 ((P < 0.0)	1001)				0.2 0.5 1 2 5 Favours SNRI Favours Control		
Test for subgroup differences: Not applicable									
Risk of bias legend									

(A) Random sequence generation (selection bias)

(B) Allocation concealment (selection bias)

(C) Blinding of participants and personnel (performance bias)

(C) Blinding of participants and personnel (performance bias)

(D) Incomplete outcome data (attrition bias) (E) Selective reporting (reporting bias)

(F) Other bias

(D) Incomplete outcome data (attrition bias)

(E) Selective reporting (reporting bias)

(F) Other bias

Forest plot of comparison: 3 Duloxetine versus placebo in the treatment of fibromyalgia, outcome: 3.7 Droput due to adverse events.

Figure 7 (Analysis 3.8)

	SNR	1	Contr	ol		Risk Ratio	Risk Ratio	Risk of Bias				
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI	ABCDEF				
3.8.2 End of treatmer	nt											
Arnold 2012	9	155	4	153	10.6%	2.22 [0.70, 7.06]	+-	lacksquare				
Chappell 2008	12	162	2	168	6.5%	6.22 [1.41, 27.37]						
Murakami 2015	51	194	20	196	62.3%	2.58 [1.60, 4.15]	-					
Russell 2008 Subtotal (95% CI)	46	376 887	6	144 661	20.7% 100.0 %	2.94 [1.28, 6.73] 2.76 [1.89, 4.02]	<u>→</u>	•?••?•				
Total events	118		32									
Heterogeneity: Tau ² =	Heterogeneity: Tau² = 0.00; Chi² = 1.41, df = 3 (P = 0.70); I² = 0%											
Test for overall effect:	Z=5.28 ((P < 0.0	10001)									
Total (95% CI)		887		661	100.0%	2.76 [1.89, 4.02]	•					
Total events	118		32									
Heterogeneity: Tau² =	0.00; Chi	$i^2 = 1.4^\circ$	1, df = 3 (P = 0.7	$0); I^2 = 09$	6	0.01 0.1 1 10 100	•				
Test for overall effect:	Z = 5.28 (P < 0.0	10001)				Favours SNRI Favours Control					
Test for subgroup diff	erences:	Tavours Oraci Tavours Control										
Risk of bias legend												
(A) Random sequenc	(A) Random sequence generation (selection bias)											
(B) Allocation conceal	ment (se	lection	bias)									

Forest plot of comparison: 3 Duloxetine versus placebo in the treatment of fibromyalgia, outcome: 3.8 Tired/Somnolence.

Figure 8 (Analysis 3.9)

	SNRI		Control		Risk Ratio		Risk Ratio	Risk of Bias
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI	ABCDEF
3.9.3 End of treatment	nt							
Arnold 2010	26	263	14	267	49.9%	1.89 [1.01, 3.53]	-	
Murakami 2015	11	194	1	196	8.4%	11.11 [1.45, 85.25]		— •••••
Russell 2008 Subtotal (95% CI)	38	376 833	8	144 607	41.7% 100.0 %	1.82 [0.87, 3.80] 2.16 [1.16, 4.00]	•	● ? ● ? ●
Total events	75		23					
Heterogeneity: Tau ² =	0.10; Ch	$i^2 = 2.9$	2, df = 2 (P = 0.2	3); $I^2 = 31$	1%		
Test for overall effect:	Z = 2.44	(P = 0.0)	01)					
							0.01 0.1 1 10	100
							Favours SNRI Favours Con	trol

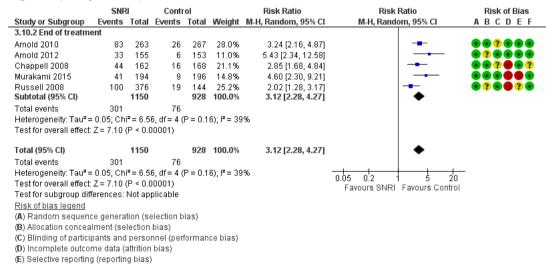
Risk of bias legend

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

(F) Other bias

Forest plot of comparison: 3 Duloxetine versus placebo in the treatment of fibromyalgia, outcome: 3.9 Dizziness.

Figure 9 (Analysis 3.10)



Forest plot of comparison: 3 Duloxetine versus placebo in the treatment of fibromyalgia, outcome: 3.10 Nausea.

Figure 10 (Analysis 3.11)

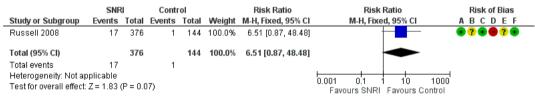
	SNR	IRI Control				Risk Ratio	Risk Ratio	Risk of Bias
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI	ABCDEF
Arnold 2010	34	263	10	267	29.5%	3.45 [1.74, 6.84]	-	$lackbox{0}$
Chappell 2008	26	162	9	168	26.1%	3.00 [1.45, 6.20]		3 (1)3 (2)4 (2)5 (2)6 (2)7 (2)7 (2)8 (2)9 (2)
Murakami 2015	28	194	8	196	23.9%	3.54 [1.65, 7.56]	 -	$\bullet \bullet \bullet \bullet \bullet \bullet$
Russell 2008	55	376	6	144	20.5%	3.51 [1.55, 7.97]		● ? ● ● ? ●
Total (95% CI)		995		775	100.0%	3.36 [2.32, 4.87]	•	
Total events	143		33					
Heterogeneity: Tau ² =	0.00; Ch	$i^2 = 0.13$	3, df = 3 (P = 0.9	$9); I^2 = 09$	6	0.005 0.1 1 10 2	1 -
Test for overall effect:	Z= 6.39	(P < 0.0	00001)				Favours SNRI Favours Conti	

Risk of bias legend

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

Forest plot of comparison: 3 Duloxetine versus placebo in the treatment of fibromyalgia, outcome: 3.11 Constipation.

Figure 11 (Analysis 3.12)



Risk of bias legend

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

Forest plot of comparison: 3 Duloxetine versus placebo in the treatment of fibromyalgia, outcome: 3.12 Weigt gain.

Figure 12 (Analysis 3.13)

	SNRI		Control		Risk Ratio		Risk Ratio		Risk of Bias
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Rando	m, 95% CI	ABCDEF
Arnold 2010	31	263	12	267	32.6%	2.62 [1.38, 4.99]		-	$lackbox{0}$
Chappell 2008	32	162	9	168	27.0%	3.69 [1.82, 7.48]		-	• • ? • • ?
Murakami 2015	13	194	7	196	16.8%	1.88 [0.77, 4.60]	+	-	$\bullet \bullet \bullet \bullet \bullet \bullet$
Russell 2008	62	376	7	144	23.6%	3.39 [1.59, 7.24]		-	9 ? 9 9 ? 9
Total (95% CI)		995		775	100.0%	2.89 [2.00, 4.17]		•	
Total events	138		35						
Heterogeneity: Tau ² = 0.00; Chi ² = 1.61, df = 3 (P = 0.66); I ² = 0%							0.005 0.1 1	40 200	-
Test for overall effect: $Z = 5.65$ (P < 0.00001)								10 200 Favours Control	

Risk of bias legend

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

Forest plot of comparison: 3 Duloxetine versus placebo in the treatment of fibromyalgia, outcome: 3.13 Dry mouth.