Supplementary Online Content

Supplemental file 1. Deviations from protocol

Supplemental file 2. Search strategy Ovid MEDLINE

Supplemental file 3. Search strategies for trial registries

Supplemental file 4. Interventions of interest

Supplemental file 5. GRADE framework

Supplemental file 6. Calculation of effect sizes for pain intensity

Supplemental file 7. Calculation of effect sizes for disability

Supplemental file 8. Characteristics of included studies

Supplemental file 9. Risk of bias assessments

Supplemental file 10. Narrative description of trials not included in meta-analysis for pain intensity (≤ 2 weeks)

Supplemental file 11. Forest plot pain intensity 3-13 weeks

Supplemental file 12. Forest plot disability ≤ 2 weeks

Supplemental file 13. Forest plot disability 3-13 weeks

Supplemental file 14. Forest plot acceptability

Supplemental file 15. Forest plot adverse events

Supplemental file 16. Forest plot serious adverse events

Supplemental file 17. Forest plot tolerability

Supplemental file 18. Forest plot dose subgroup analysis

Supplemental file 19. Funnel plots for all meta-analyses with ≥2 trials

Supplemental file 20. Sensitivity analyses for non-benzodiazepine antispasmodic medicines in acute LBP

Supplemental file 1. Deviations from protocol

We deviated from our pre-registered protocol (accessed from https://osf.io/mu2f5/) to improve both the clinical interpretability and comparability of the review findings.

The deviations are as follows:

- We redefined the follow-up timepoints in relation to 'post-randomisation' as opposed to 'post-treatment' to ensure comparable follow-up between trials. The follow-up timepoints are now immediate (≤ 2 weeks) and short-term (3-13 weeks).
- We redefined how the muscle relaxant medicines were grouped to better reflect clinical utility from (antispasmodic or antispastic) to (non-benzodiazepine antispasmodic, antispastic, benzodiazepine and miscellaneous).
- We conducted additional *ad hoc* sensitivity analyses investigating the effect of removing trials at high risk of bias, trials primarily reported as trial registry records, trials without a placebo comparison, and trials investigating the muscle relaxant medicine carisoprodol.
- We did not report the extended funnel plot following reviewer recommendations.

Supplemental file 2. Search strategy Ovid MEDLINE

Search Strategy for Ovid MEDLINE:

Part A: Generic search for randomized controlled trials
1. randomized controlled trial.pt.
2. controlled clinical trial.pt.
3. comparative study.pt.
4. clinical trial.pt.
5. random*.ab,ti.
6. placebo.ab,ti.
7. drug therapy.fs.
8. trial.ab,ti.
9. groups.ab,ti.
10. or/1-9
11. (animals not (humans and animals)).sh.
12. (adolescent* or teen* or youth? or puberty or childhood or children* or p?ediatri* or preschool or pre-school or nursery or kindergarten or infant? or newborn? or neonat* or prematurity or fetal or foetal).mp.
13. 11 or 12
14. 10 not 13

Part B: Specific search for low back, sacrum and coccyx problems
15. dorsalgia.ti,ab.
16. exp Back Pain/
17. backache.ti,ab.
18. (lumbar adj pain).ti,ab.
19. coccydynia.ti,ab.
20. sciatica.ti,ab.
21. spondylosis.ti,ab.
22. lumbago.ti,ab.
23. back disorder$.ti,ab
24. or/15-23

Part C: Specific search for other spinal disorders
25. Coccyx.sh
26. Lumbar Vertebrae.sh
27. Intervertebral disc.sh
28. Sacrum.sh
29. Intervertebral disc degeneration.sh
30. (disc adj degeneration).ti,ab.
31. (disc adj prolapse).ti,ab.
32. (disc adj herniation).ti,ab.
33. spinal fusion.sh.
34. (facet adj joints).ti,ab.
35. Intervertebral Disc Displacement.sh.
36. or/25-35

Part D: Specific search for interventions of interest
37. suxamethonium.mp. or Succinylcholine/
38. exp Botulinum Toxins/
39. pancuronium/
40. Vecuronium Bromide/

41. Atracurium/
42. Rocuronium/
43. mivacurium bromide.mp.
44. cisatracurium.mp.
45. Carisoprodol/
46. Methocarbamol/
47. Chlorzoxazone/
48. Orphenadrine/
49. Baclofen/
50. tizanidine.mp.
51. Tolperisone/
52. thiocolchicoside.mp.
53. cyclobenzaprine.mp.
54. Dantrolene/
55. Clonazepam/
56. exp Diazepam/
57. Chlordiazepoxide/
58. Oxazepam/
59. Lorazepam/
60. Bromazepam/
61. Clobazam/
62. Alprazolam/
63. clotiazepam.mp.
64. Flurazepam/
65. Nitrazepam/
66. Flunitrazepam/
67. Estazolam/
68. Triazolam/
69. lormetazepam.mp.
70. Temazepam/
71. Midazolam/
72. quazepam.mp.
73. Zolpidem/
74. zaleplon.mp.
75. Eszopiclone/
76. metaxalone.mp.
77. or/37-76 (all interventions of interest)

Results

78. 24 or 36 (all back pain)
79. 77 and 78 (all back pain and all interventions of interest)
80. 14 and 79 (all RCTs of interventions of interest in back pain)

Supplemental file 3. Search strategies for trial registries

	Muscle Relaxant Medicines
WHO ICTRP: Advanced search	
Title:	–
Condition:	'back pain'
Intervention:	*1-40*
Recruitment status:	ALL
Phases are:	ALL
ClinicalTrials.gov: Advanced search	
Study Type:	Interventional Studies
Study Results:	All studies
Recruitment:	All studies
Age:	Adult and Senior
Gender:	All studies
Conditions:	'back pain'
Interventions:	*1-40*
Titles:	–
Outcome Measures:	–
Sponsor/Collaborators:	–
Sponsor (Lead):	–
Study IDs:	–
Locations:	–
Phase:	–
Funder Type:	–
First Received:	–
Last Updated:	–

EU ClinicalTrials Register: Advanced search	**Muscle Relaxant Medicines**
Search Term:	back pain AND ‘intervention’ (1-40)
Country:	–
Age Range:	Adult and Elderly
Trial Status:	–
Trial Phase:	–
Gender:	Both
Date Range:	–
Results Status:	–

Supplemental file 4. Interventions of interest

	Drug name	ATC code	Licenses		
Number			**ARTG**	**FDA**	**EMA**
1	suxamethonium	M03AB01	yes	-	yes
2	botulinum toxin	M03AX01	yes	yes	yes
3	pancuronium	M03AC01	yes	yes	-
4	vecuronium	M03AC03	yes	yes	yes
5	atracurium	M03AC04	-	yes	-
6	rocuronium bromide	M03AC09	-	-	yes
7	mivacurium bromide	M03AC10	yes	-	yes
8	cisatracurium	M03AC11	yes	yes	yes
9	carisoprodol	M03BA02	-	yes	yes
10	methocarbamol	M03BA03	-	yes	-
11	chlorzoxazone	M03BB03	-	yes	-
12	orphenadrine citrate	M03BC01	yes	yes	-
13	baclofen	M03BX01	yes	yes	yes
14	tizanidine	M03BX02	-	yes	yes
15	tolperisone	M03BX04	-	-	yes
16	thiocolchicoside	M03BX05	-	-	yes
17	cyclobenzaprine	M03BX08	-	yes	-
18	dantrolene	M03CA01	yes	yes	yes
19	clonazepam	N03AE01	yes	yes	yes
20	diazepam	N05BA01	yes	yes	-
21	chlordiazepoxide	N05BA02	-	yes	-
22	oxazepam	N05BA04	yes	yes	-
23	lorazepam	N05BA06	yes	yes	yes
24	bromazepam	N05BA08	yes	-	yes
25	clobazam	N05BA09	yes	yes	-
26	alprazolam	N05BA12	yes	yes	yes
27	clotiazepam	N05BA21	-	-	yes
28	flurazepam	N05CD01	-	yes	-
29	nitrazepam	N05CD02	yes	-	yes
30	flunitrazepam	N05CD03	yes	-	yes
31	estazolam	N05CD04	-	yes	-
32	triazolam	N05CD05	yes	yes	yes
33	lormetazepam	N05CD06	-	-	yes
34	temazepam	N05CD07	yes	yes	-
35	midazolam	N05CD08	yes	yes	yes
36	quazepam	N05CD10	-	yes	-
37	zolpidem	N05CF02	yes	yes	-
38	zaleplon	N05CF03	yes	yes	-

	Drug name	ATC code	Licenses		
Number			**ARTG**	**FDA**	**EMA**
39	eszopiclone	N05CF04	yes	yes	-
40	metaxalone	-	-	yes	-

Supplemental file 5. GRADE framework

Certainty in the evidence was assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) working group methodology.[1] The certainty of evidence was initially classified as 'high' (very certain that the true effect lies close to that of the estimate of the effect) and possibly downgraded to 'moderate' (moderately certain in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different), 'low' (certainty in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect), or 'very low' (very little certainty in the effect estimate: The true effect is likely to be substantially different from the estimate of effect).

We graded the evidence in the following recommended domains in the following manner:

- Risk of bias: we downgraded by one level if > 25% but < 50% of the participants in our analysis came from trials assessed as 'high' risk of bias, and we downgraded by two levels if > 50% of the patients came from trials assessed as 'high' risk of bias.[2]
- Inconsistency: we downgraded by one level if we identified important heterogeneity. We assessed heterogeneity using the between-study variance parameter (τ^2) and the proportion of study variance not due to sampling error (I^2).[3]
- Indirectness: we did not consider this domain because the eligibility criteria ensures patients, interventions, and comparators were similar across studies.[4]
- Imprecision: we downgraded by one level if the width of the confidence intervals (for continuous variables as pain intensity and disability) by crossing either the null or the threshold for a clinically meaningful effect (10 points on a 0 to 100 scale) and two levels if the interval spanned both. For dichotomous variables (like harms) we downgraded by one level if the interval spanned the null.[5]
- Publication bias: we downgraded by only one level if we strongly detected publication bias. We assessed publication bias by visually assessing funnel plot and sensitivity analysis.[6]

References

1. Balshem H, Helfand M, Schunemann HJ, et al. GRADE guidelines: 3. Rating the quality of evidence. *J Clin Epidemiol*. 2011;64(4):401-406
2. Guyatt GH, Oxman AD, Vist G, et al. GRADE guidelines: 4. Rating the quality of evidence - study 3limitations (risk of bias). *J Clin Epidemiol.* 2011;64(4):407-415.
3. Guyatt GH, Oxman AD, Kunz R, et al. GRADE guidelines: 7. Rating the quality of evidence - inconsistency. *J Clin Epidemiol.* 2011;64(12):1294-1302.
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5. Guyatt GH, Oxman AD, Kunz R, et al. GRADE guidelines 6. Rating the quality of evidence - imprecision. *J Clin Epidemiol.* 2011;64(12):1283-1293.
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Supplementary file 6. Calculation of effect sizes for pain intensity

Author, year	Muscle relaxant medicine	Outcome scale	Type of data extracted	Type of measure	Point estimate (variability) extracted			Mean (SD), converted[a]			Number of participants	
					Muscle Relaxant	Comparator		Muscle Relaxant	Comparator		Muscle Relaxant	Comparator
Immediate term (≤ 2 weeks)												
Acute LBP												
Aparna 2016	Thiocolchicoside	0-10 VAS	Mean	FV	0.7	1.15		6.7 (30)[b]	11.5 (30)[b]		79	74
Baratta 1982	Cyclobenzaprine	0-10 VAS	Mean (p-value)	CS	-5.5	-5		-55 (48.9)[c]	-40 (48.9)[c]		58	59
Friedman 2015	Cyclobenzaprine	0-10 VAS	Mean (95% CI)	FV	3.6	3.9		36 (35.8)[e]	39 (30.9)[e]		103	104
Friedman 2017	Diazepam	VRS-4	Mean (SD)	FV	1 (1)	0.9 (1)		31.7 (31.7)	29.7 (32)		57	55
Friedman 2018	Orphenadrine	VRS-4	Mean (SD)	FV	1.1 (1)	1.2(1)		38 (33)	39 (32)		78	38[f]
Friedman 2018	Methocarbamol	VRS-4	Mean (SD)	FV	1.3 (1)	1.2(1)		43 (32.7)	39 (32)		80	38[f]
Friedman 2019	Baclofen	VRS-4	Mean (SD)	FV	1.1 (1)	1.2 (0.9)		37.7 (32)	38.3 (29.3)		79	24[f]
Friedman 2019	Metaxalone	VRS-4	Mean (SD)	FV	1.3 (1)	1.2 (0.9)		42 (33)	38.3 (29.3)		76	24[f]
Friedman 2019	Tizanidine	VRS-4	Mean (SD)	FV	1.2 (1)	1.2 (0.9)		38.7 (31.7)	38.3 (29.3)		76	25[f]
Hindle 1972	Carisoprodol	0-100 VAS	Mean	FV	15.5	64		15.5 (30)[b]	64 (30)[b]		14	14
Lepisto 1979	Tizanidine	VRS-4	Mean	CS	-1.5	-1.6		-51 (30)[b]	-52.7 (30)[b]		15	15
Pareek 2009	Tizanidine	0-10 VAS	Mean (SD)	CS	-5.9 (2.1)	-4.4 (2.1)		-58.8 (21.4)	-43.5 (20.6)		94	91
Ralplh 2008	Carisoprodol	VRS-4	Mean (SE)	CS	-1.9 (0.2)	-1.2 (0.2)		-47 (19.5)[d]	-30 (66.7)[d]		269	278
Serfer 2010	Carisoprodol A	VRS-5	Mean (SE)	CS	-1.8 (0.1)	-1.4 (0.1)		-44.5 (48.4)[d]	-34.3 (44)[d]		260	128[f]
Serfer 2010	Carisoprodol B	VRS-5	Mean (SE)	CS	-1.8 (0.1)	-1.4 (0.1)		-44.5 (47.5)[d]	-34.3 (44)[d]		251	128[f]
NCT00671879	Carisoprodol A	0-100 VAS	Mean (SE)	CS	-15.5 (1.3)	-15.2 (1.3)		-15.5 (22.1)[d]	-15.2 (21.4)[d]		271	132[f]
NCT00671879	Carisoprodol B	0-100 VAS	Mean (SE)	CS	-16.4 (1.3)	-15.2 (1.3)		-16.4 (21.4)[d]	-15.2 (21.4)[d]		270	132[f]
NCT00671502	Carisoprodol A	0-100 VAS	Mean	CS	-27.5	-28.6		-27.5 (30)[b]	-28.6 (30)[b]		280	140[f]
NCT00671502	Carisoprodol B	0-100 VAS	Mean	CS	-28	-28.6		-28 (30)[b]	-28.6 (30)[b]		281	139[f]
Mixed LBP												
Akhter 2017	Thiocolchicoside	0-10 VAS	Mean (SE)	FV	0.94 (0.1)	1.35 (0.1)		9.4 (11.5)[d]	13.5 (11.5)[d]		144	144

Short term (3-13 weeks)												
Acute LBP												
Friedman 2015	Cyclobenzaprine	0-10 VAS	Mean (95% CI)	FV	0.6 (1)	0.7 (1.1)		19.3 (31.7)	24.3 (35.3)		108	107
Friedman 2017	Diazepam	VRS-4	Mean (SD)	FV	0.3 (0.7)	0.4 (0.8)		11.3 (23)	12.3 (25.7)		50	53
Friedman 2018	Orphenadrine	VRS-4	Mean (SD)	FV	0.6 (0.9)	0.7 (1)		21.3 (29)	22.7 (34.7)		70	34[f]
Friedman 2018	Methocarbamol	VRS-4	Mean (SD)	FV	0.7 (1)	0.7 (1)		24.7 (32)	22.7 (34.7)		70	34[f]
Friedman 2019	Baclofen	VRS-4	Mean (SD)	FV	0.6 (0.9)	0.4 (0.7)		18.3 (31)	14.3 (23)		76	23[f]
Friedman 2019	Metaxalone	VRS-4	Mean (SD)	FV	0.6 (0.9)	0.4 (0.7)		20 (31)	14.3 (23)		72	23[f]
Friedman 2019	Tizanidine	VRS-4	Mean (SD)	FV	0.6 (0.9)	0.4 (0.7)		19.7 (29.3)	14.3 (23)		70	24[f]
Sub-acute LBP												
Herskowitz 2004	Botulinum toxin A	0-10 VAS	Mean (p-value)	CS	-2.2	-0.3		-22 (29.8)[c]	-3 (32.1)[c]		13	15

SD, standard deviation; MD, mean difference; 95% CI, 95% confidence interval; FV, Final Value; CS, Change Score; VAS, Visual Analogue Scale; VRS-4, Verbal Rating Scale 4 levels; VRS-5, Verbal Rating Scale 5 levels

[a] Mean and variability measures divided by the top number of scale and multiplied by 100, e.g. 0-10 VAS score divided by 10 and multiplied by 100.

[b] SD imputed as variability measures not available

[c] SD estimated from p-value

[d] SD estimated from standard error

[e] SD estimated from 95% Confidence Interval

[f] Sample size in the placebo group was divided by the number of groups to avoid double-counting

Supplementary file 7. Calculation of effect sizes for disability

Author, year	Muscle relaxant medicine	Outcome scale (range)	Type of data extracted	Type of measure	Point estimate (variability) extracted		Mean (SD), converted[a]		Number of participants	
					Muscle Relaxant	Comparator	Muscle Relaxant	Comparator	Muscle Relaxant	Comparator
Immediate term (≤ 2 weeks)										
Acute LBP										
Friedman 2015	Cyclobenzaprine	0-24 RMDQ	Mean (95% CI)	FV	8.2	8.9	34.2 (35)[b]	37.1 (34.8)[b]	108	107
Friedman 2017	Diazepam	0-24 RMDQ	Mean (95% CI)	CS	-11	-11	-45.8 (31.4)[b]	-45.8 (39.3)[b]	57	55
Friedman 2018	Orphenadrine	0-24 RMDQ	Mean (95% CI)	CS	-9.4	-10.9	-39.2 (37.)9[b]	-45.4 (36.5)[b]	78	38[g]
Friedman 2018	Methocarbamol	0-24 RMDQ	Mean (95% CI)	CS	-8.1	-10.9	-33.8 (37.4)[b]	-45.4 (36.5)[b]	80	38[g]
Friedman 2019	Baclofen	0-24 RMDQ	Mean (95% CI)	CS	-10.6	-11.1	-44.2 (38.1)[b]	-46.3 (38.7)[b]	79	24[g]
Friedman 2019	Metaxalone	0-24 RMDQ	Mean (95% CI)	CS	-10.1	-11.1	-42.1 (39.2)[b]	-46.3 (38.7)[b]	76	25[g]
Friedman 2019	Tizanidine	0-24 RMDQ	Mean (95% CI)	CS	-11.2	-11.1	-46.7 (36.5)[b]	-46.3 (38.7)[b]	76	26[g]
Hindle 1972	Carisoprodol	VRS-4	Mean	FV	1.8	3.4	45 (30)[c]	85 (30)[c]	14	14
NCT00671879 2012	Carisoprodol A	0-24 RMDQ	Mean (SE)	CS	-5 (0.6)	-4.3 (0.7)	-20.8 (31.7)[d]	-17.9 (32.3)[d]	141	71[g]
NCT00671879 2012	Carisoprodol B	0-24 RMDQ	Mean (SE)	CS	-4.2 (0.6)	-4.3 (0.7)	-17.5 (31)[d]	-17.9 (32.3)[d]	135	71[g]
Ralph 2008	Carisoprodol	0-24 RMDQ	Mean (p-value)	FV	4.1	6.2	17.1 (36.6)[e]	25.8 (37.2)[e]	269	278
Serfer 2010	Carisoprodol A	0-24 RMDQ	Mean (SE)	CS	-5.7 (0.3)	-4.4 (0.3)	-23.8 (21.2)[d]	-18.3 (21.7)[d]	269	133[g]
Serfer 2010	Carisoprodol B	0-24 RMDQ	Mean (SE)	CS	-5.4 (0.3)	-4.4 (0.3)	-22.5 (21.5)[d]	-18.3 (21.7)[d]	259	132[g]
Mixed LBP										
Aksoy 2002	Thiocolchicoside	0-24 RMDQ	Mean (SD)	FV	7.2 (8.8)	11.8 (10)	30 (36.7)	49.2 (41.7)	174	155
Short term (3-13 weeks)										
Acute LBP										
Friedman 2015	Cyclobenzaprine	0-24 RMDQ	Mean (95% CI)	FV	4.5	3.8	18.8 (31.7)[b]	15.8 (27.2)[b]	108	107

Friedman 2017	Diazepam	0-24 RMDQ	Median (IQR)	FV	0 (0-1)	0 (0-6)		1.4 (3.2)[f]	8.3 (19.1)[f]		50	53
Friedman 2018	Orphenadrine	0-24 RMDQ	Mean (SD)	FV	5.6 (8)	3.8 (6.7)		23.3 (33.4)	16 (27.7)		69	34[g]
Friedman 2018	Methocarbamol	0-24 RMDQ	Mean (SD)	FV	4.9 (7.6)	3.8 (6.7)		20.6 (31.5)	16 (27.7)		70	34[g]
Chronic LBP												
Goforth 2015	Eszoplicone	0-24 RMDQ	Mean (SD)	FV	6.6 (5.5)	7.9 (7)		27.5 (22.9)	33.1 (29.1)		32	20
Zaringhalam 2010	Baclofen A	0-24 RMDQ	Mean (SD)	FV	8.8 (3.8)	9.8 (3.9)		36.7 (15.8)	40.8 (16.3)		20	20
Zaringhalam 2010	Baclofen B	0-24 RMDQ	Mean (SD)	FV	5.7 (1.4)	6.4 (2.9)		23.8 (5.8)	26.7 (12.1)		20	20

SD, standard deviation; MD, mean difference; 95% CI, 95% confidence interval; FV, Final Value; CS, Change Score; RMDQ, Roland Morris Disability Questionnaire; VRS-4, Verbal Rating Scale 4 levels

[a] Mean and variability measures divided by the top number of scale and multiplied by 100, e.g. 0-24 RMDQ score divided by 24 and multiplied by 100.

[b] SD estimated from 95% Confidence Interval

[c] SD imputed as variability measures not available

[d] SD estimated from standard error

[e] SD estimated from p-value

[f] SD estimated from median and IQR

[g] Sample size in the placebo group was divided by the number of groups to avoid double-counting

Supplemental file 8. Characteristics of included studies

Study, Year (Reference)	Study sample Mean age (SD) and percentage female (%)	Setting	Number of relevant trial arms	Test intervention, *n*	Comparison intervention, *n*	Duration of treatment	Outcome measure (Pain, Disability)	Overall risk of Bias	Source of data
Akhter 2017[1]	288 participants with mixed acute and subacute LBP Age and sex not reported	India	2	Oral thiocolchicoside 150mg/day + diclofenac sodium, 144	Oral diclofenac sodium, 144	7 days	10cm VAS, NA	High	Published
Aksoy 2002[2]	329 participants with mixed acute and subacute LBP thiocolchicoside group 39.7 (11) yrs, 67% female; standard treatment group 40.2 (11.3) yrs, 61% female	Turkey	2	Oral thiocolchicoside 16mg/day + standard treatment (NSAID or an analgesic), 174	Standard treatment (oral NSAID or another analgesic), 155	5-7 days	100mm VAS, RMDQ	High	Published
Aparna 2016[3]	200 participants with acute LBP Age and sex not reported	India	2	Oral thiocolchicoside 8mg/day + aceclofenac, 100	Oral aceclofenac, 100	7 days	10cm VAS, NA	High	Published
Baratta 1982[4]	120 participants with acute LBP cyclobenzaprine group 35 yrs [a], 41% female; placebo group 38 yrs [a], 41% female	USA	2	Oral cyclobenzaprine 30mg/day, 60	Oral placebo, 60	10 days	10cm VAS, NA	High	Published
Berry (a) 1988[5]	105 participants with acute LBP tizanidine group 43 (12.4) yrs, 47% female; placebo group 42 (12.4) years, 43% female	UK	2	Oral tizanidine 12mg/day + ibuprofen, 51	Oral placebo + ibuprofen, 54	7 days	100mm VAS, NA	High	Published
Berry (b) 1988[6]	112 participants with acute LBP tizanidine group 44 (13) yrs, 49% female; placebo group 38 (13) yrs, 49% female	UK	2	Oral tizanidine 12mg/day, 59	Oral placebo, 53	7 days	100mm VAS, NA	High	Published
Borenstein 1990[7]	40 participants with acute LBP	USA	2	Oral cyclobenzaprine 30mg/day + naproxen, 20	Oral naproxen, 20	14 days	NR, VRS-4 [b]	High	Published

	cyclobenzaprine group 37 yrs [a], 35% female; comparator group 37 yrs [a], 25% female								
Casale 1988[8]	20 participants with acute LBP dantrolene group 46.7 yrs [a], 30% female; placebo group 47.1 yrs [a], 20% female	Italy	2	Oral dantrolene 25mg/day, 10	Oral placebo, 10	4 days	NR, NR	Moderate	Published
Cogné 2017[9] (crossover)	19 participants with chronic LBP botulinum toxin A group 38.1 (5.94) yrs, 67% female; placebo group 38.2 (10.27) yrs, 100% female	France	2	IM botulinum toxin A 200 units, 9	IM placebo, 10	Single dose	100mm VAS[b], QBPDS[b]	High	Published
Dapas 1985[10]	200 participants with acute LBP baclofen group 42.7 yrs [a], 48% female; placebo group 41.8 yrs [a], 56% female	USA	2	Oral baclofen range 30-80mg/day, 100	Oral placebo, 100	14 days	VRS-5[b], NA	High	Published
Emrich 2015[11]	202 participants with acute LBP methocarbamol group 45.3 (11) yrs, 63% female; placebo group 43.8 (11.6) yrs, 71% female	Germany	2	Oral methocarbamol 4500mg/day, 98	Oral placebo, 104	8 days	100mm VAS, NR	High	Published
Fathie 1964[12]	200 participants with acute LBP Age and sex not reported	USA	2	Oral metaxalone 3200mg/day, 101	Oral placebo, 99	7 days	VRS-4[b], NA	High	Published
Foster 2001[13]	31 participants with chronic LBP botulinum toxin A group 46.4 yrs [a], 53% female; placebo group 47 yrs [a], 50% female	USA	2	IM botulinum toxin A 200 units	IM placebo	Single dose	10cm VAS[b], ODI [b]	Low	Published
Friedman 2015[14]	323 participants with acute LBP cyclobenzaprine group 38 (11) yrs, 42% female; oxycodone group 39 (11) yrs, 56% female [not synthesized]; placebo 39 (11) yrs, 50% female	USA	2	Oral cyclobenzaprine range 5-30mg/day + naproxen, 108	Oral placebo +naproxen, 107	10 days	10cm VAS, RMDQ	Low	Published

Friedman 2017[15]	114 participants with acute LBP diazepam group 34 (12) yrs, 47% female; placebo group 38 (12) yrs, 42% female	USA	2	Oral diazepam range 5-20mg/day + naproxen, 57	Oral placebo + naproxen	7 days	VRS-4, RMDQ	Low	Published
Friedman 2018[16]	240 participants with acute LBP orphenadrine group 40 (12) yrs, 43% female; methocarbamol group 38 (12) yrs, 51% female; placebo group 39 (12) yrs, 43% female	USA	3	Oral orphenadrine 200mg/day + naproxen, 80 Oral methocarbamol range 2250-4500mg/day + naproxen, 81	Oral placebo + naproxen, 79	7 days	VRS-4, RMDQ	Low	Published
Friedman 2019[17]	320 participants with acute LBP tizanidine group 40 (11) yrs, 48% female; metaxalone group 37 (10) yrs, 45% female; baclofen group 39 (12) yrs, 29% female; placebo group 39 (11) yrs, 45% female	USA	4	Oral tizanidine range 2-16mg/day + ibuprofen, 80 Oral metaxalone range 400-3200mg/day+ ibuprofen, 80 Oral baclofen range 10-80mg/day + ibuprofen, 80	Oral placebo + ibuprofen, 80	7 days	VRS-4, RMDQ	Low	Published
Goforth 2014[18]	58 participants with chronic LBP eszopiclone group 45.7 (11) yrs, 61% female; placebo group 40.1 (12.8) yrs, 72% female	USA	2	Oral eszopiclone 3mg/day + naproxen, 33	Oral placebo + naproxen, 25	28 days	100mm VAS, RMDQ	Low	Published
Gold 1978[19]	60 participants with acute LBP Age and sex not reported	USA	2	Oral orphenadrine 200mg/day, 20	Oral placebo, 20	7 days	NR, NA	High	Published
Herskowitz 2004[20]	28 participants with subacute LBP Age and sex not reported	USA	2	IM botulinum toxin A 400 units, 13	IM placebo, 15	Single dose	10cm VAS, NA	High	Published (conference abstract)
Hindle 1972[21]	48 participants with acute LBP	USA	2	Oral carisoprodol 1400mg/day, 16	Oral placebo, 16	4 days	100mm VAS, VRS-4	High	Published

	carisoprodol group 37 yrs [a]; butabarbital group 34.6 yrs [a]; placebo group 43.5 yrs [a] Entire sample 44% female								
Hingorani 1966[22]	50 participants with acute LBP Age not reported Entire sample 20% female	UK	2	IM diazepam 40mg + oral diazepam 8mg/day, 25	IM placebo + oral placebo, 25	6 days	NR, NA	High	Published
Jazayeri 2011[23]	50 participants with chronic LBP botulinum toxin A group 41.7 yrs [a], 52% female; placebo group 42.3 yrs [a], 56% female	Iran	2	IM botulinum toxin A 200 units, 25	IM placebo 25	Single dose	10cm VAS[b], ODI [b]	High	Published
Ketenci 2005[24]	97 participants with acute LBP thiocolchicoside group 37 yrs [a], 42% female; tizanidine group 37 yrs [a], 63% female; placebo group 40 yrs [a], 52% female	Turkey	3	Oral thiocolchicoside 16mg/day, 38 Oral tizanidine 6mg/day, 32	Oral placebo, 27	7 days	10cm VAS, NA	High	Published
Klinger 1988[25]	80 participants with acute LBP orphenadrine group 35.7 (12.4) yrs, 1% female; placebo group 31.9 (11.7) yrs, 30% female	USA	2	IV orphenadrine 60mg, 40	IV placebo, 40	Single dose	VRS-4[b], NA	Low	Published
Lepisto 1979[26]	30 participants with acute LBP tizanidine group 42.5 yrs [a], 47% female; placebo group 40.8 yrs [a], 53% female	Finland	2	Oral tizanidine 6mg/day, 15	Oral placebo, 15	7 days	VRS-4, NA	Moderate	Published
Machado 2016[27]	43 participants with chronic LBP botulinum toxin A group 51.3 yrs [a], 67% female; placebo group 48.6 yrs [a], 45% female	USA	2	IM botulinum toxin A range 500-1000 units, 21	IM placebo, 22	Single injection	10cm VAS[b], ODI [b]	Moderate	Published
Moll 1973[28]	68 participants with acute LBP	Germany	2	IM diazepam 4ml + oral diazepam 40-60mg/day, 33	IM placebo + oral placebo, 35	5-10 days	NR, NA	High	Published

	Diazepam group 45.8 (13.9) yrs, 39% female; placebo group 45.4 (13.3) yrs, 49% female								
Pareek 2009[29]	197 participants with acute LBP tizanidine group 43.3 (12.7) yrs, 39% female; comparator group 43.5 (10.9) yrs, 40% female	India	2	Oral tizanidine 4mg/day + aceclofenac, 101	Oral aceclofenac, 96	7 days	10cm VAS, NA	High	Published
Ralph 2008[30]	562 participants with acute LBP carisoprodol group 39.3 (11.8) yrs, 47% female; comparator group 41.5 (11.7) yrs, 54% female	USA	2	Oral carisoprodol 1000mg/day, 277	Oral placebo, 285	7 days	VRS-5, RMDQ	High	Published
Salvini 1986[31]	30 participants with LBP Age and sex not reported	Italy	2	Oral dantrolene 1200mg/day + ibuprofen, 15	Oral ibuprofen, 15	8 days	VRS-4[b], NA	High	Published
Schliessbach 2017[32] (crossover)	98 participants with chronic LBP Age and sex not reported	Switzerland	2	Oral clobazam 20mg, 49	Oral placebo, 49	2 hours	11pt NRS, NA	Low	Published
Serfer 2010[33]	828 participants with acute LBP carisoprodol (350mg) group 40.5 (12.4) yrs, 54% female; carisoprodol (250mg) group 40.9 (11.7) yrs, 51% female; placebo group 40.7 (13.1) yrs, 59% female	USA	3	Oral carisoprodol (350mg) 1400mg/day, 281 Oral carisoprodol (250mg) 1000mg/day, 271	Oral placebo, 276	7 days	VRS-5, RMDQ	High	Published
Tervo 1976[34]	50 participants with acute LBP Age not reported Entire sample 66% female	Finland	2	IM orphenadrine 60mg + oral orphenadrine 210mg/day & paracetamol, 25	IM placebo + oral paracetamol, 25	7-10 days	NR, NR	High	Published
Thompson 1983[35]	76 participants with acute LBP Age and sex not reported	UK	2	Oral tizanidine 6mg/day	Oral placebo	10 days	100mm VAS[b], NA	High	Published (conference abstract)
Tüzün 2003[36]	149 participants with acute LBP	Turkey	2	IM thiocolchicoside 8mg/day, 77	IM placebo, 72	5 days	100mm VAS, NA	High	Published

	thiocolchicoside group 40.7 (10.3) yrs, 48% female; placebo group 41 (11) yrs, 56% female								
Zaringhalam 2010[37]	84 participants with chronic LBP baclofen group 55.1 (3.3) yrs; no treatment group 54.3 (4.2) yrs; acupuncture group 54.2 (5.4) yrs; baclofen + acupuncture group 54.2 (5.6) yrs Entire sample 0% female	Iran	4	Oral baclofen 30mg/day, 21 Oral baclofen 30mg/day + acupuncture, 21	No treatment, 21 Acupuncture, 21	35 days	100mm VAS, RMDQ	High	Published
ACTRN12616000017426[38] (status: terminated)	Participants with acute LBP	Australia	2	Oral zoplicone 7.5mg/day	Oral placebo	14 days	NA	NA	Clinical trial registry
EUCTR2017-004530-29[39]	134 participants with acute LBP Age and sex not reported	Greece	2	IM thiocolchicoside 4mg + diclofenac	IM diclofenac	Single injection	NA	NA	Clinical trial registry
EUCTR2019-001885-14[40] (status: ongoing)	Participants with acute LBP and/or sciatica	Hungry	2	Oral tolperisone	Oral placebo	14 days	NA	NA	Clinical trial registry
IRCT20111109008035N4[41]	46 participants with LBP Age and sex not reported	Iran	2	Oral zolpidem 5mg/day	Oral placebo	28 days	NA	NA	Clinical trial registry
NCT00671879[42]	840 participants with acute LBP carisoprodol (500mg) group 41.6 (11.8) yrs, 52% female; carisoprodol (700mg) group 41.5 (12.4) yrs, 53% female; placebo group 41.4 (11.9) yrs, 51% female	USA	3	Oral carisoprodol (500mg) 1000mg/day, 279 Oral carisoprodol (700mg) 1400mg/day, 281	Oral placebo, 280	14 days	100mm VAS, RMDQ	High	Clinical trial registry
NCT00671502[43]	840 participants with acute LBP carisoprodol (500mg) group 41.4 (12.6) yrs, 51% female; carisoprodol (700mg) group 40.3 (13.1) yrs, 47%	USA	3	Oral carisoprodol (500mg) 1000mg/day, 280	Oral placebo, 279	14 days	100mm VAS, RMDQ [b]	High	Clinical trial registry

	female; placebo group 40.9 (12.7) yrs, 49% female			Oral carisoprodol (700mg) 1400mg/day, 281					
NCT00817986[44]	161 participants with acute LBP Age and sex not reported	USA	4	Oral arbaclofen placarbil (20mg) 40mg/day Oral arbaclofen placarbil (30mg) 60mg/day Oral arbaclofen placarbil (40mg) 80mg/day	Oral placebo	14 days	NA	NA	Clinical trial registry
NCT00404417[45] (crossover, status: active not recruiting)	Participants with chronic LBP	USA	4	IM botulinum toxin A	IM placebo	Single dose	NA	NA	Clinical trial registry
NCT00384579[46] (status: terminated)	Participants with acute LBP	USA	2	IM botulinum toxin B	IM placebo	Single dose	NA	NA	Clinical trial registry
NCT00384371[47] (status: terminated)	Participants with subacute LBP	USA	2	IM botulinum toxin A	IM placebo	Single dose	NA	NA	Clinical trial registry
NCT02887534[48] (status: withdrawn)	Participants with acute LBP	Not reported	5	Oral tizanidine Oral SPARC1401-low dose Oral SPARC1401-mid dose Oral SPARC1401-high dose	Oral placebo	Not reported	NA	NA	Clinical trial registry
NCT01587508[49]	Participants with acute LBP	Brazil	3	Oral cyclobenzaprine 20mg/day	Oral meloxicam & cyclobenzaprine	7 days	NA	NA	Clinical trial registry

(status: withdrawn)				Oral meloxicam					

[a] Standard deviation not reported. [b] Data not available. Abbreviations: LBP, Low Back Pain; SD, Standard Deviation; IM, Intramuscular; IV, Intravenous; NA, Not Applicable; NR Not Reported; NRS, Numerical Rating Scale; VAS, Visual Rating Scale; VRS-4, Verbal Rating Scale 4 levels; VRS-5, Verbal Rating Scale 5 levels; RMDQ, Roland Morris Disability Questionnaire; QBPDS, Quebec Back Pain Disability Scale

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Supplemental file 9. Risk of bias assessments

Study	Year	Random sequence generation	Allocation concealment	Blinding (Patients)	Blinding (Care-providers)	Blinding (Outcome assessors)	Drop Outs	Intention-to-treat analysis?	Selective outcome reporting	Similarity at baseline	Co-interventions	Compliance	Timing of assessment	Other bias	Overall Risk of Bias
Fathie	**1964**	Low risk	Unclear	Low risk	Low risk	Low risk	Low risk	High risk	Low risk	Unclear	Unclear	Unclear	Low risk	Unclear	**High**
Hingorani	**1966**	Unclear	Unclear	Low risk	Low risk	Low risk	Low risk	Low risk	Unclear	Unclear	High risk	Unclear	Low risk	Unclear	**High**
Hindle	**1972**	Low risk	Unclear	Low risk	Low risk	Low risk	Low risk	High risk	Low risk	Low risk	Unclear	Unclear	Low risk	Unclear	**High**
Moll	**1973**	Unclear	Unclear	Low risk	Low risk	Low risk	Low risk	Unclear	Low risk	High risk	High risk	High risk	Low risk	Unclear	**High**
Tervo	**1976**	Unclear	Low risk	Low risk	Low risk	Low risk	Unclear	High risk	Unclear	Low risk	Unclear	Unclear	Low risk	Unclear	**High**
Gold	**1978**	Unclear	Unclear	Low risk	Low risk	Low risk	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Low risk	Unclear	**High**
Lepisto	**1979**	Unclear	Unclear	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Unclear	Low risk	Unclear	**Moderate**
Baratta	**1982**	Low risk	Unclear	Low risk	Low risk	Low risk	Low risk	High risk	Low risk	Low risk	Unclear	Unclear	Low risk	Low risk	**High**
Thompson	**1983**	Unclear	Unclear	Low risk	Low risk	Low risk	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Low risk	Unclear	**High**
Dapas	**1985**	Unclear	Unclear	Low risk	Low risk	Low risk	High risk	High risk	High risk	Low risk	Unclear	Unclear	Low risk	Unclear	**High**
Salvini	**1986**	Unclear	Unclear	High risk	High risk	High risk	Low risk	Unclear	Unclear	Unclear	Unclear	Unclear	Low risk	Unclear	**High**
Berry (a)	**1988**	Unclear	Unclear	Low risk	Low risk	Low risk	Low risk	Unclear	High risk	Low risk	Low risk	Unclear	Low risk	Unclear	**High**
Berry (b)	**1988**	Unclear	Unclear	Low risk	Low risk	Low risk	Low risk	Unclear	Low risk	Low risk	Low risk	Unclear	Low risk	Unclear	**High**

Casale	**1988**	Unclear	Unclear	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Unclear	Low risk	Unclear	**Moderate**
Klinger	**1988**	Unclear	Unclear	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Unclear	**Low**
Borenstein	**1990**	Unclear	Unclear	High risk	High risk	High risk	Low risk	Low risk	Low risk	Low risk	Low risk	Unclear	Low risk	Unclear	**High**
Foster	**2001**	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Unclear	**Low**
Aksoy	**2002**	Low risk	Unclear	High risk	High risk	High risk	Unclear	Unclear	Low risk	Low risk	Low risk	Unclear	Low risk	Low risk	**High**
Tuzun	**2003**	Unclear	Unclear	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Unclear	Unclear	Low risk	Unclear	**High**
Herskowitz	**2004**	Unclear	Unclear	Low risk	Low risk	Low risk	Low risk	Unclear	Unclear	Unclear	Unclear	Low risk	Low risk	Unclear	**High**
Ketenci	**2005**	Unclear	Unclear	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	High risk	Unclear	Low risk	Unclear	**High**
Ralph	**2008**	Unclear	Unclear	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	High risk	**High**
Pareek	**2009**	Unclear	Unclear	Unclear	Unclear	Unclear	Low risk	High risk	Low risk	Low risk	Unclear	Unclear	Low risk	High risk	**High**
Serfer	**2010**	Low risk	Unclear	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	High risk	Low risk	High risk	**High**
Zaringhalam	**2010**	Low risk	High risk	High risk	High risk	High risk	Low risk	High risk	Low risk	Low risk	Low risk	Unclear	Low risk	Low risk	**High**
Jazayeri	**2011**	Unclear	Unclear	Low risk	High risk	Low risk	Low risk	Low risk	Low risk	Low risk	Unclear	Low risk	Low risk	Low risk	**High**
NCT00671502	**2011**	Unclear	Unclear	Low risk	Low risk	Low risk	Low risk	Unclear	High risk	Unclear	Unclear	Unclear	Low risk	Unclear	**High**
NCT00671879	**2012**	Unclear	Unclear	Low risk	Low risk	Low risk	Low risk	Unclear	Low risk	Unclear	Unclear	Unclear	Low risk	Unclear	**High**
Goforth	**2014**	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Unclear	Unclear	Low risk	Unclear	**Low**
Emrich	**2015**	Unclear	Unclear	Low risk	Low risk	Low risk	High risk	Low risk	Unclear	Low risk	Low risk	Low risk	Low risk	Unclear	**High**
Friedman	**2015**	Low risk	Unclear	Low risk	Low risk	Low risk	Unclear	Low risk	Low risk	Low risk	Unclear	Low risk	Low risk	Low risk	**Low**
Aparna	**2016**	Unclear	Unclear	High risk	High risk	High risk	High risk	Unclear	Unclear	Unclear	Unclear	Unclear	Low risk	Low risk	**High**

Machado	**2016**	Unclear	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Unclear	Low risk	Unclear	Unclear	Low risk	Low risk	**Moderate**
Akhter	**2017**	Unclear	Unclear	High risk	High risk	High risk	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Low risk	Low risk	**High**
Cogne	**2017**	Low risk	Unclear	Low risk	Low risk	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	**High**
Friedman	**2017**	Low risk	Unclear	Low risk	Low risk	Low risk	Unclear	Low risk	Low risk	Low risk	Unclear	Low risk	Low risk	Low risk	**Low**
Schliessbach	**2017**	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Unclear	Low risk	Unclear	Low risk	Low risk	Low risk	Low risk	**Low**
Friedman	**2018**	Low risk	Unclear	Low risk	Low risk	Low risk	Unclear	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	**Low**
Friedman	**2019**	Low risk	Unclear	Low risk	Low risk	Low risk	Unclear	Low risk	Low risk	Low risk	Unclear	Low risk	Low risk	Low risk	**Low**

Supplemental file 10. Narrative description of trials not included in meta-analysis for pain intensity (≤ 2 weeks)

Study, Year (Reference)	Outcome (Pain intensity)
Borenstein 1990[1]	"The total pain scores, as determined by the patients daily and physicians during scheduled visits, were not significantly different."
Casale 1988[2]	"VAS [visual analogue scale] pain measurements during the maximal voluntary movements showed a decrease in pain rating clearly in favor of dantrolene, with a percentage variation of 50% for the drug and 8.6% for placebo. Statistical comparison between the two treatments showed dantrolene to have a higher effectiveness ($p<0.001$)."
Cogné 2017[3] (crossover)	First phase crossover data was not available. The study found "no significant difference between the groups' [botulinum toxin A vs placebo] average LBP [low back pain] during the last 8 days at Day 30 ($p = 0.97$)".
Dapas 1985[4]	Patients were categorised into subgroups based on low back symptom severity, moderate initial pain and sever or extremely severe initial pain. "When the severity of symptoms at visits 2 and 3 [day 4 and 10] was compared with baseline values at visit 1 [day 1] within the placebo and the baclofen treatment groups, all efficacy variables [including local pain in lumbar area] showed a statistically significant ($P<0.05$) improvement for the severe- and moderate-pain groups."
Emrich 2015[5]	"The proportion of patients treated with methocarbamol who achieved a pain-free state rose more rapidly to over 80% and accordingly the proportion of patients who were not yet pain-free after 8 days is below 20% - in contrast to ~ 60% in the placebo group"
Fathie 1964[6]	"A medically significant response was observed in 69.6% of the 46 metaxalone-treated patients who complete the course of therapy and returned for re-examination". Compared to "17.4% of the placebo-treatment patients who completed the course of therapy [and] showed a medically significant improvement".
Foster 2001[7]	"At 3 weeks, 11 of 15 patients who received botulinum toxin (73.3%) had >50% pain relief vs four of 16 (25%) in the saline group ($p < 0.012$). At 8 weeks, nine of 15 (60%) in the botulinum toxin group and two of 16 (12.5%) in the saline group had relief ($p < 0.009$)."
Gold 1978[8]	At the 48-hour evaluation, 7/20 patients treated with orphenadrine improved compared to 0/20 in the placebo group.

Hingorani 1966[9]	"Of the 25 patients in the placebo group, 18 showed improvement, 5 showed no change, and 2 were worse. Of the 25 patients in the diazepam group, 19 showed improvement, 5 showed no change, and 1 was worse. The difference would therefore seem to be marginal, patients in the treated group having almost no better results than those in the placebo group."
Jazayeri 2011[10]	"After 4 weeks, 76% of patients in the BoNT-A [botulinum toxin A] group reported pain relief compared to 20% in the saline group ($P < 0.005$). Additionally, greater pain relief was experienced by patients in the BoNT-A group at 8 weeks (64% vs. 12%; $P < 0.001$)."
Klinger 1988[11]	"Based on both the physicians' evaluations of signs and symptoms and the patients' assessments of pain, intravenous orphenadrine was highly effective compared with placebo in reducing these patients' lumbar paravertebral muscle pain and spasm."
Machado 2016[12]	"The primary outcome of this study was the proportion of responders with a visual analogue scale (VAS) of <4 at 6 weeks. At 6 weeks, 5 subjects in the [abobotulinum toxin A] toxin group and 3 subjects in the placebo group (28% and 16%) met this criterion ($p = 0.4470$)."
Moll 1973[13]	There was a larger overall therapeutic effect of diazepam vs placebo. Therapeutic effect was determined based on the patient's subjective rating of improvement in pain intensity, and alterations in clinical status as determined by the examiner.
Salvini 1986[14]	There was no significant difference between the groups dantrolene and ibuprofen vs ibuprofen for pain on movement and pain at rest at 4 and 8 days of treatment.
Schliessbach 2017[15] (crossover)	First phase crossover data was not available. The study found "pain intensity in the supine position was significantly reduced by clobazam compared to active placebo (60 min: 2.9 vs. 3.5, p = 0.008; 90 min: 2.7 vs. 3.3, p = 0.024; 120 min: 2.4 vs. 3.1, p = 0.005). Pain intensity in the sitting position was not significantly different between groups."
Tervo 1976[16]	No statistically significant difference was observed for symptom relief from low back for orphenadrine vs saline immediately after the injection or at 7-10 days follow-up.
Thompson 1983[17]	Tizanidine was "generally better than placebo and significantly so in respect of VAS [visual analogue scale pain intensity]".
ACTRN12616000017426[18]	Trial terminated

EUCTR2017-004530-29[19]	No data available
EUCTR2019-001885-14[20]	Trial ongoing
NCT00817986[21]	No data available
NCT00404417[22]	Trial active but not recruiting
NCT00384579[23]	Trial terminated
NCT02887534[24]	Trial withdrawn
NCT01587508[25]	Trial withdrawn

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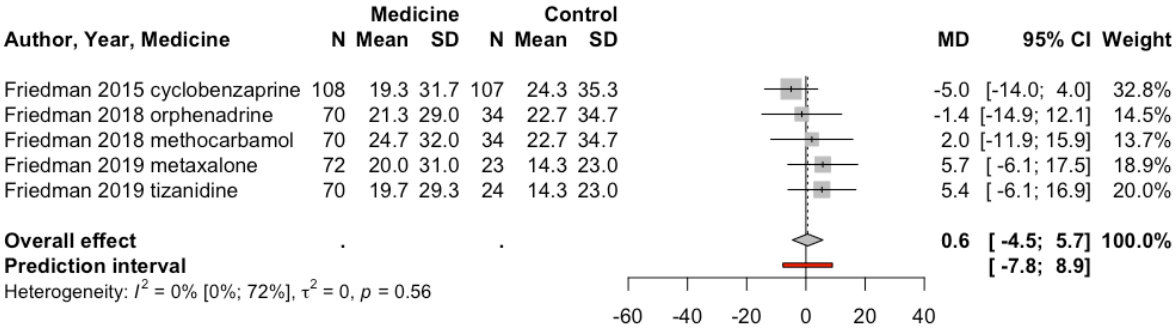
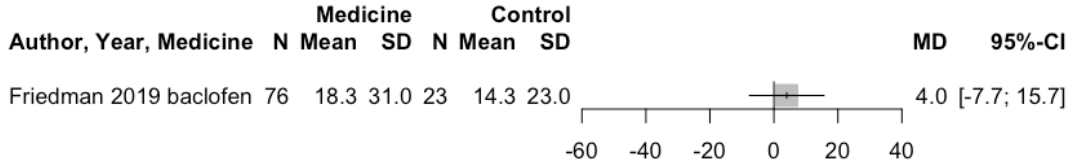
Supplemental file 11. Forest plot pain intensity 3-13 weeks

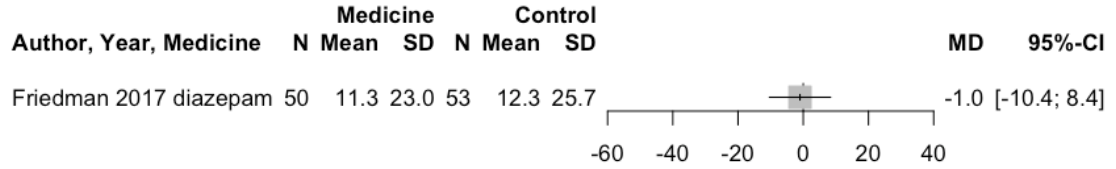
Acute LBP – Non-benzodiazepine antispasmodic



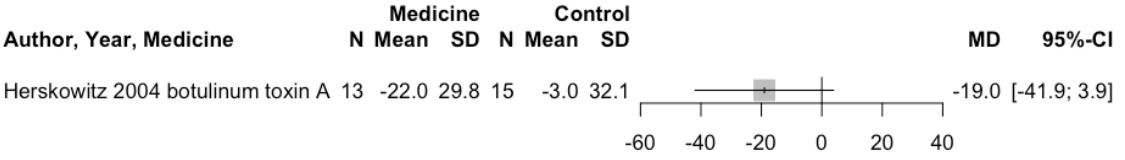
Acute LBP – Antispastic



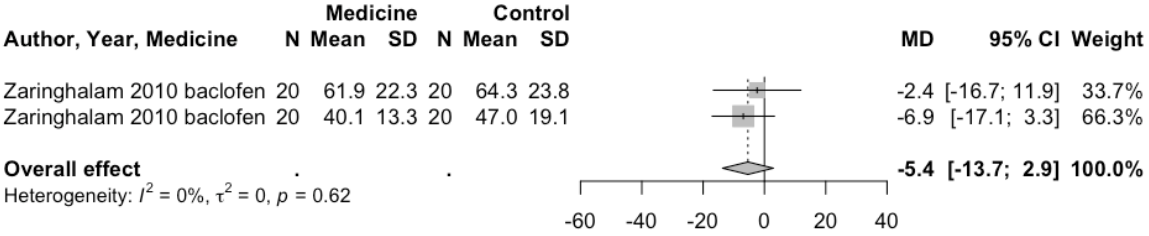
Acute LBP – Benzodiazepine



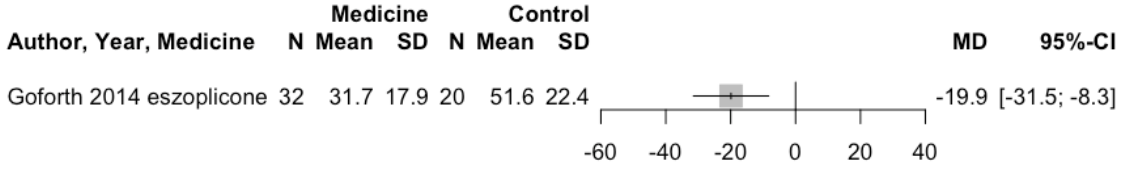
Subacute LBP – Miscellaneous



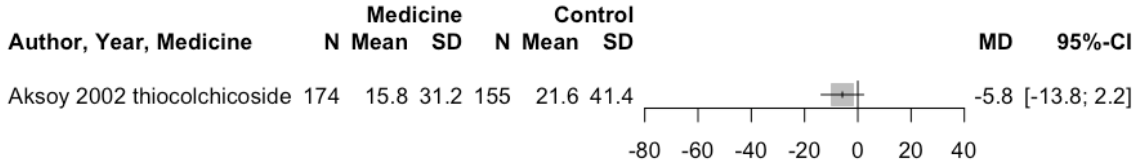
Chronic LBP – Antispastic



Chronic LBP – Miscellaneous

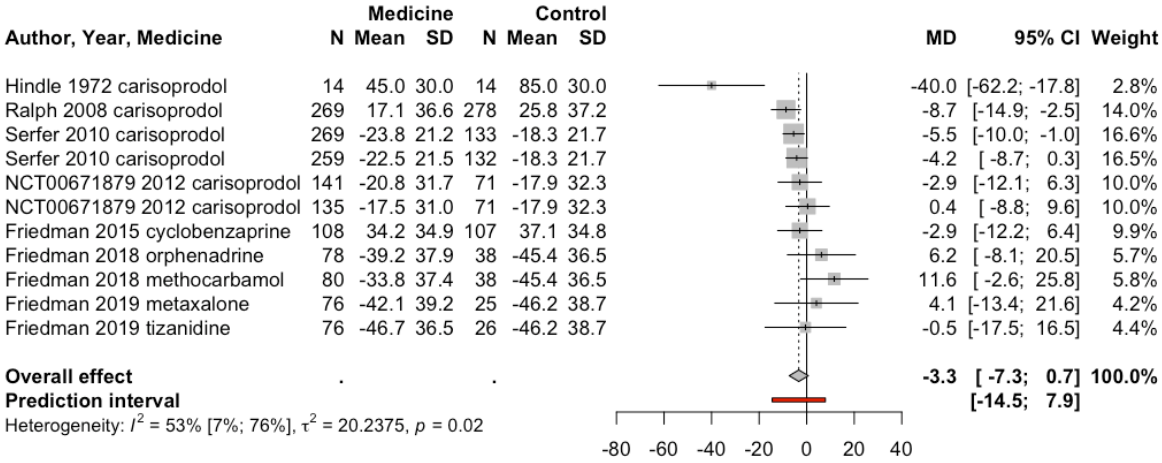


Mixed LBP – Non-benzodiazepine antispasmodic

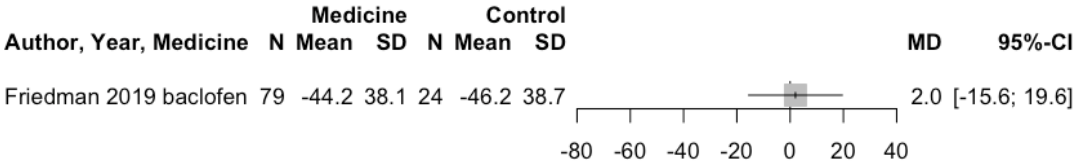


Supplemental file 12. Forest plot disability ≤ 2 weeks

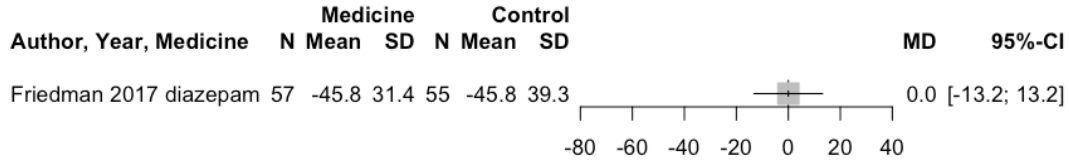
Acute LBP – Non-benzodiazepine antispasmodic



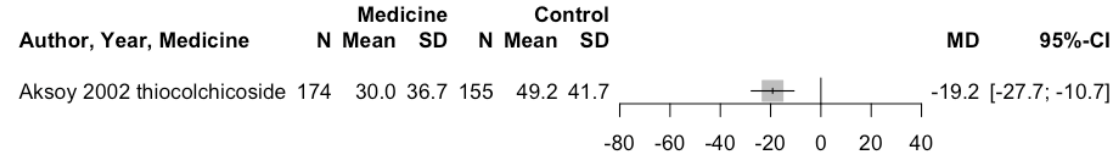
Acute LBP – Antispastic



Acute LBP – Benzodiazepine

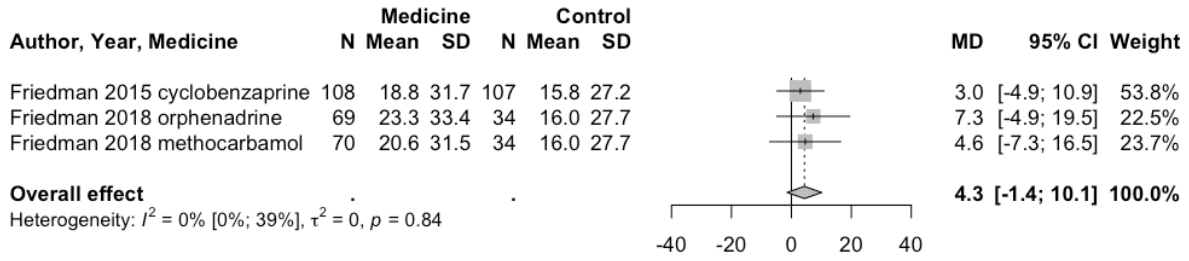


Mixed LBP – Non-benzodiazepine antispasmodic

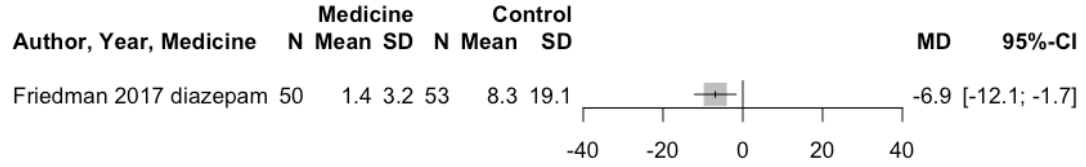


Supplemental file 13. Forest plot disability 3-13 weeks

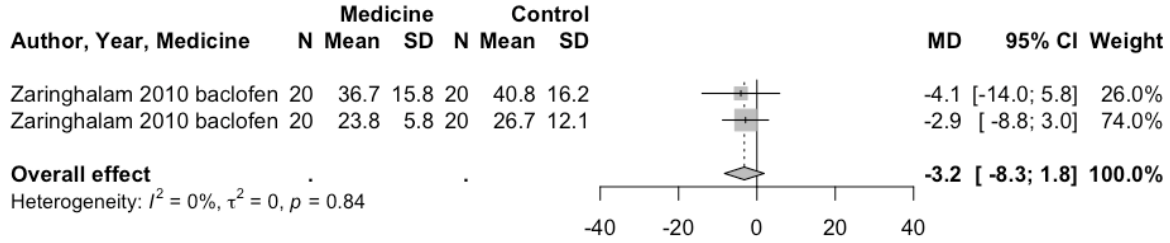
Acute LBP – Non-benzodiazepine antispasmodic



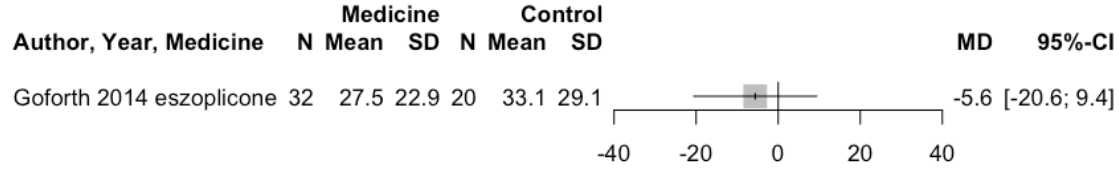
Acute LBP – Benzodiazepine



Chronic LBP – Antispastic

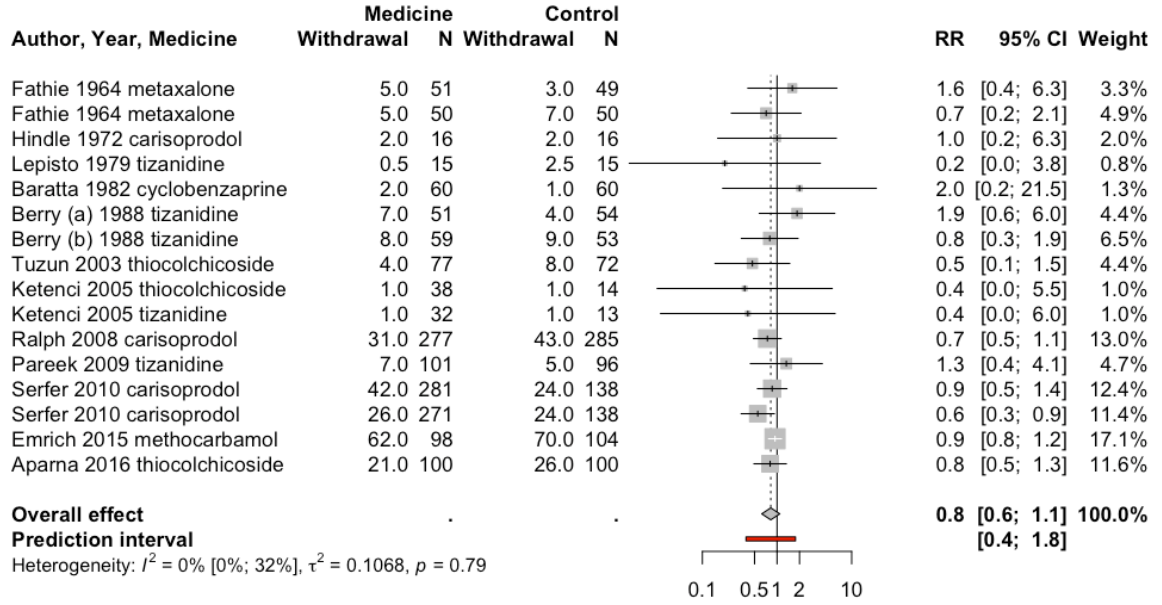


Chronic LBP – Miscellaneous

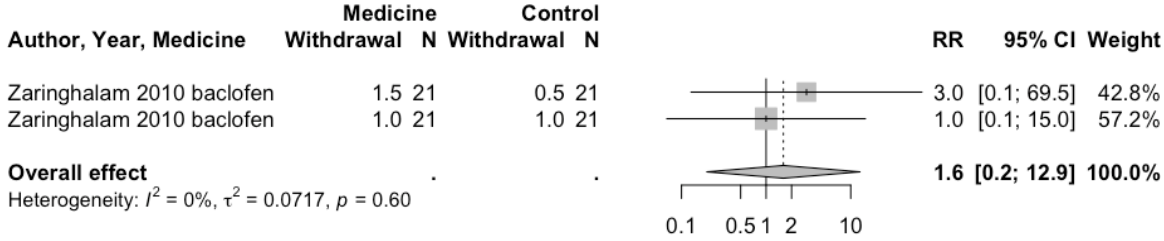


Supplemental file 14. Forest plot acceptability

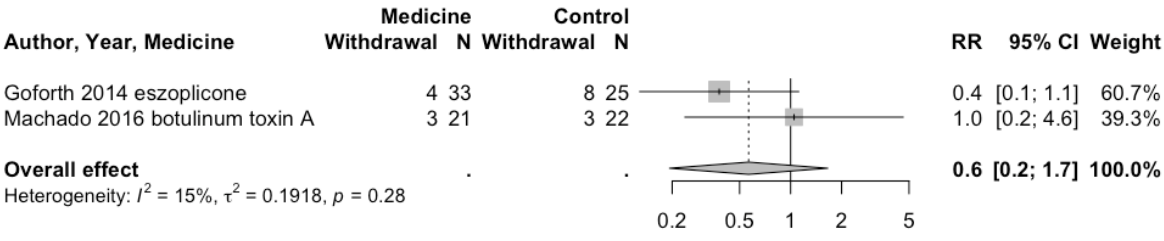
Acute LBP – Non-benzodiazepine antispasmodic



Chronic LBP – Antispastic

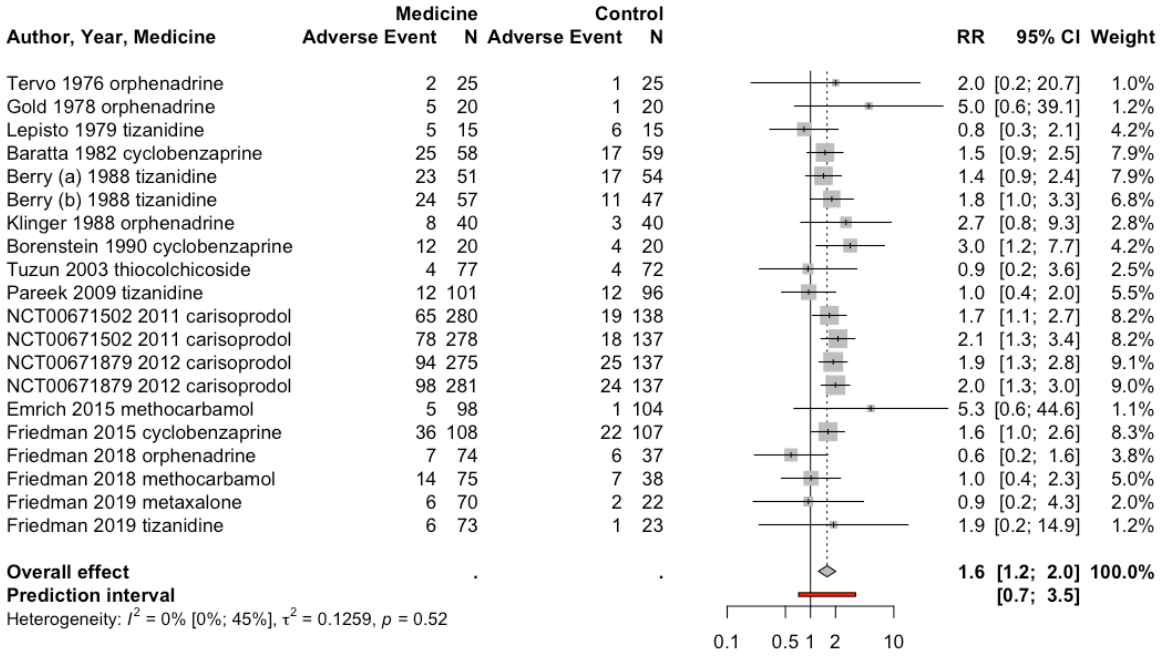


Chronic LBP – Miscellaneous

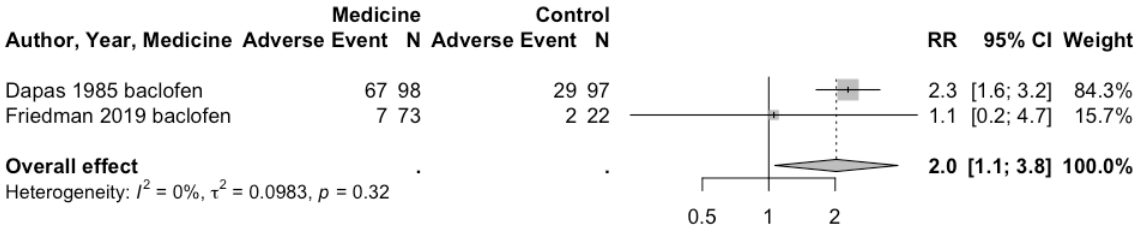


Supplemental file 15. Forest plot adverse events

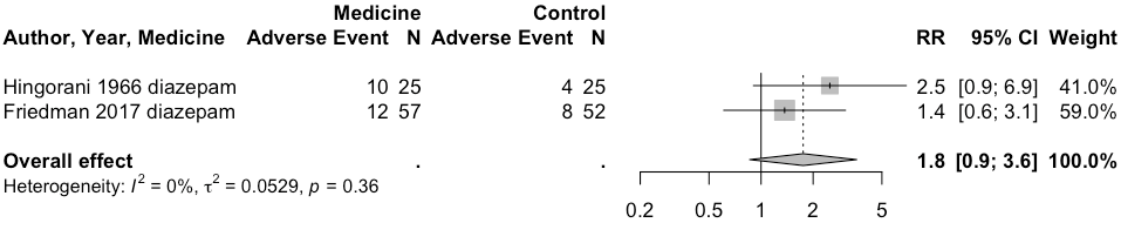
Acute LBP – Non-benzodiazepine antispasmodic



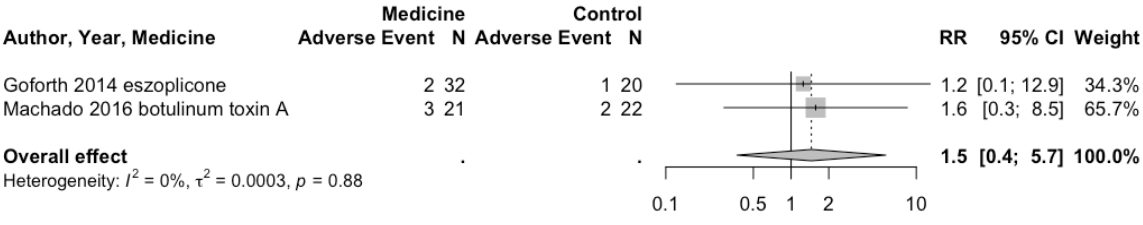
Acute LBP – Antispastic



Acute LBP – Benzodiazepine

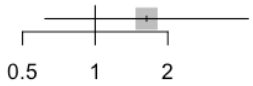


Chronic LBP – Miscellaneous



Mixed LBP – Non-benzodiazepine antispasmodic

Author, Year, Medicine	Medicine Adverse Event	Medicine N	Control Adverse Event	Control N	RR	95%-CI
Aksoy 2002 thiocolchicoside	11	174	6	155	1.6	[0.6; 4.3]

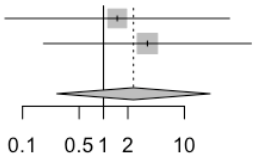


Supplemental file 16. Forest plot serious adverse events

Acute LBP – Non-benzodiazepine antispasmodic

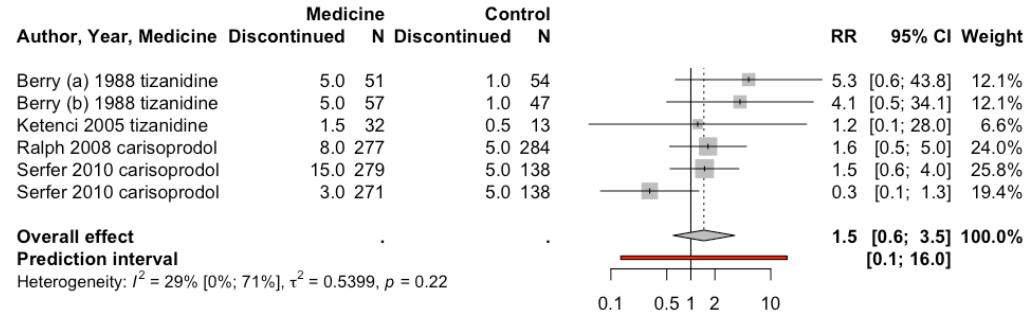
Author, Year, Medicine	Medicine Serious AE	Medicine N	Control Serious AE	Control N	RR	95% CI	Weight
NCT00671502 2011 carisoprodol	1.5	280	0.5	138	1.5	[0.1; 36.1]	46.2%
NCT00671879 2012 carisoprodol	3.5	275	0.5	137	3.5	[0.2; 67.0]	53.8%
Overall effect	.		.		**2.3**	**[0.3; 20.8]**	**100.0%**

Heterogeneity: I^2 = 0%, τ^2 = 0.0256, p = 0.70

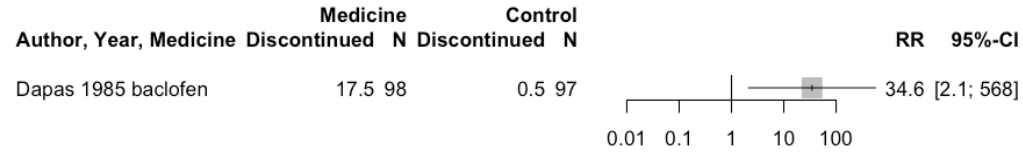


Supplemental file 17. Forest plot tolerability

Acute LBP – Non-benzodiazepine antispasmodic



Acute LBP – Antispastic



Supplemental file 18. Forest plot dose subgroup analysis

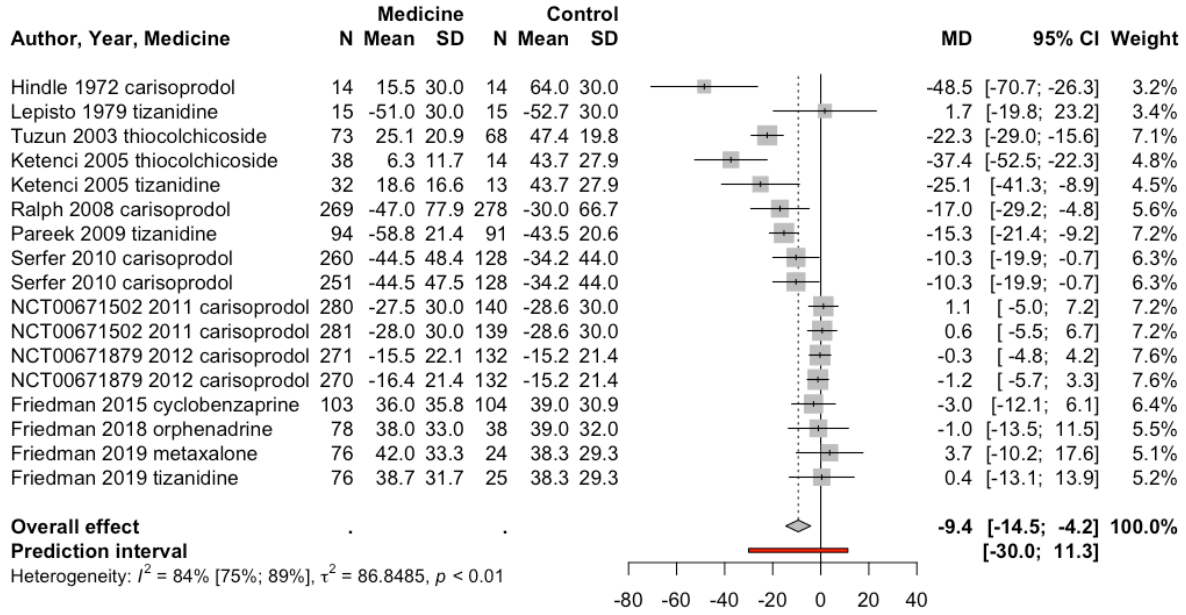
Population: Acute low back pain

Medicine: Non-benzodiazepine antispasmodic

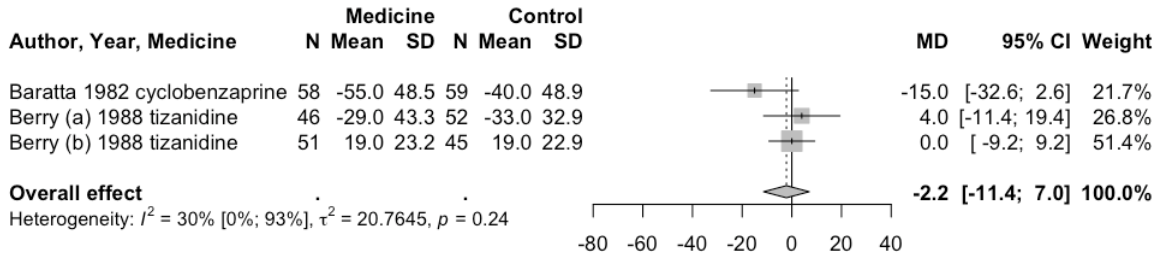
Outcome: Pain intensity

Follow-up: Immediate (≤ 2 weeks)

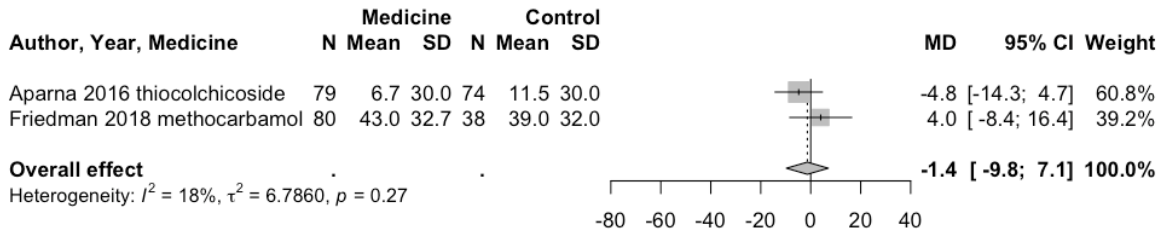
Standard dose



Above dose



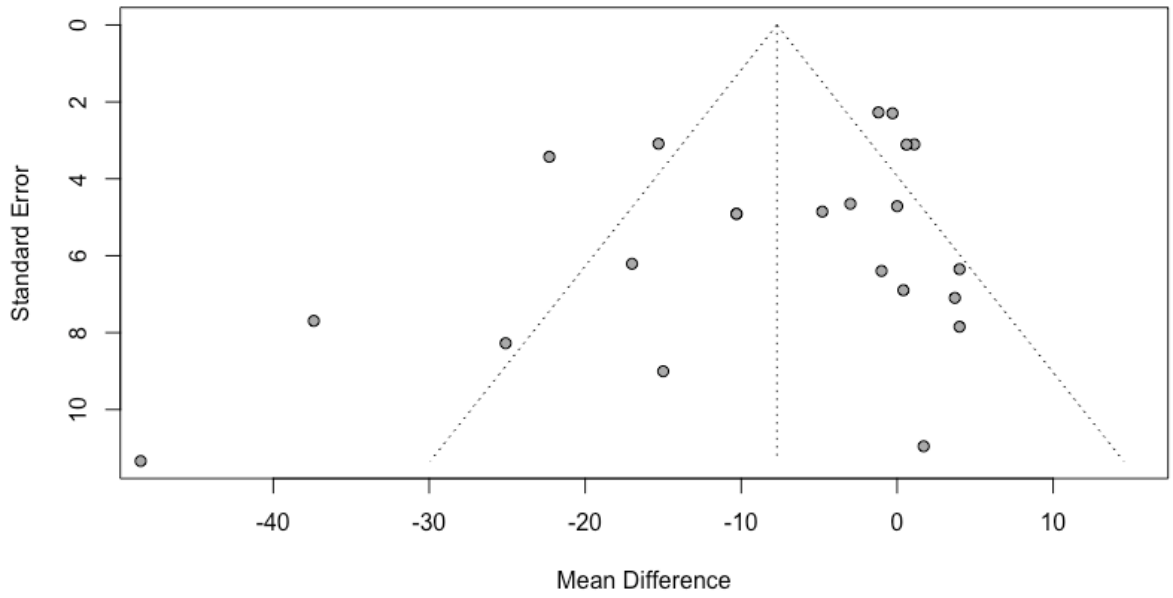
Below dose



Supplemental file 19. Funnel plots for all meta-analyses with ≥2 trials

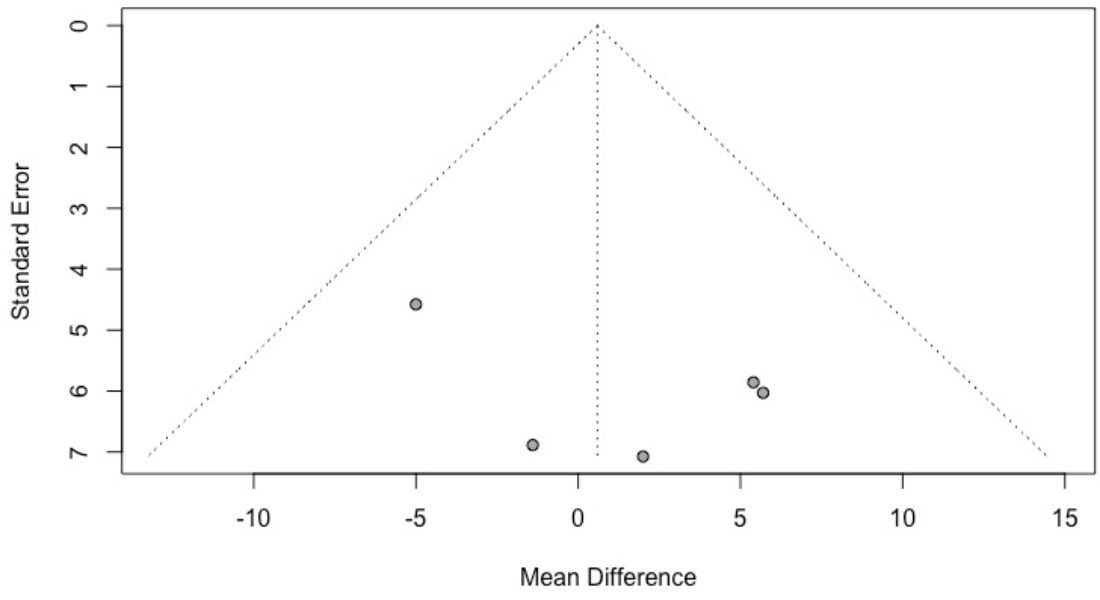
Results for Egger's regression test for funnel plot asymmetry are reported alongside funnel plots which included comparisons with 10 or more trials.[1]

Acute LBP Non-benzodiazepine antispasmodics, Pain intensity ≤2 weeks

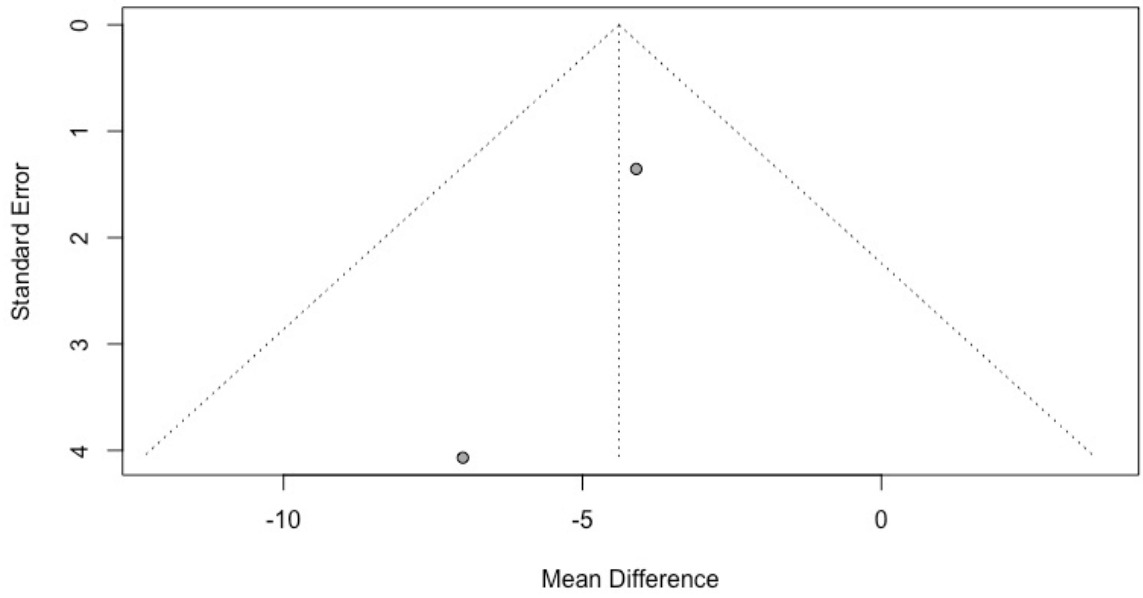


	Intercept	Confidence Interval	t-value	p-value
Egger's test	-1.6	-3.7 to 0.4	-1.5	0.1

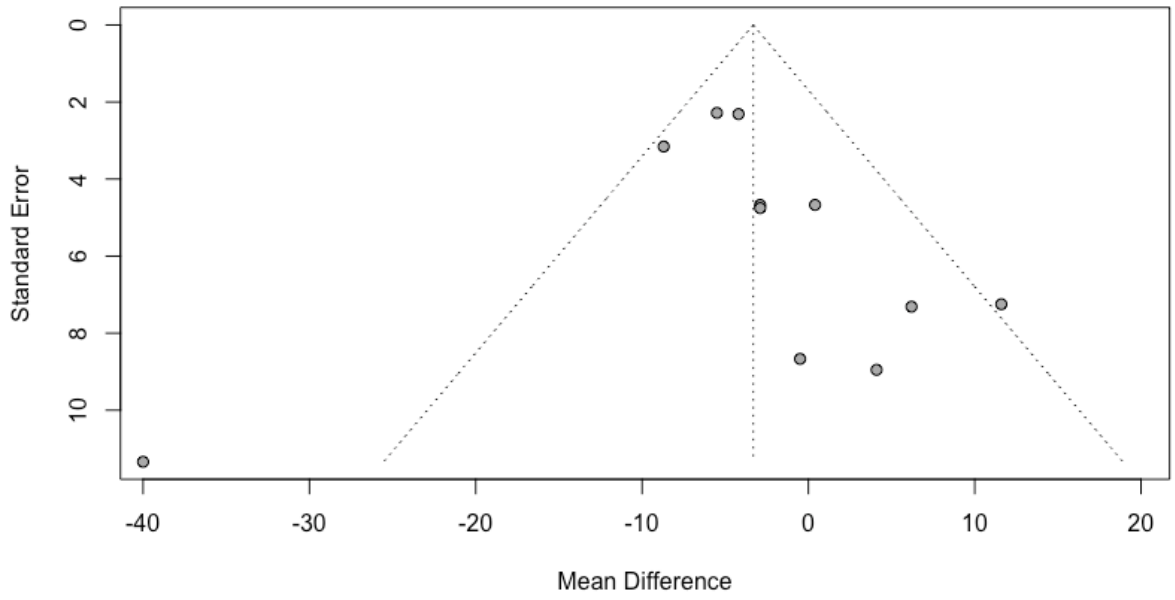
Acute LBP Non-benzodiazepine antispasmodics, Pain intensity 3-13 weeks



Mixed LBP Non-benzodiazepine antispasmodics, Pain intensity ≤2 weeks

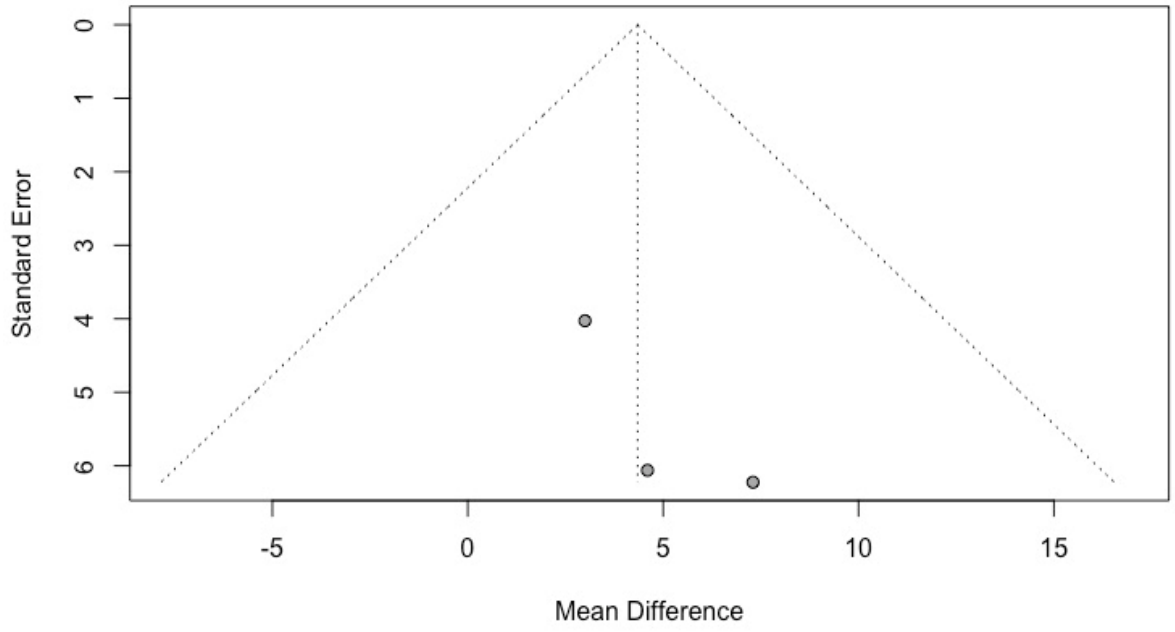


Acute LBP Non-benzodiazepine antispasmodics, Disability ≤2 weeks

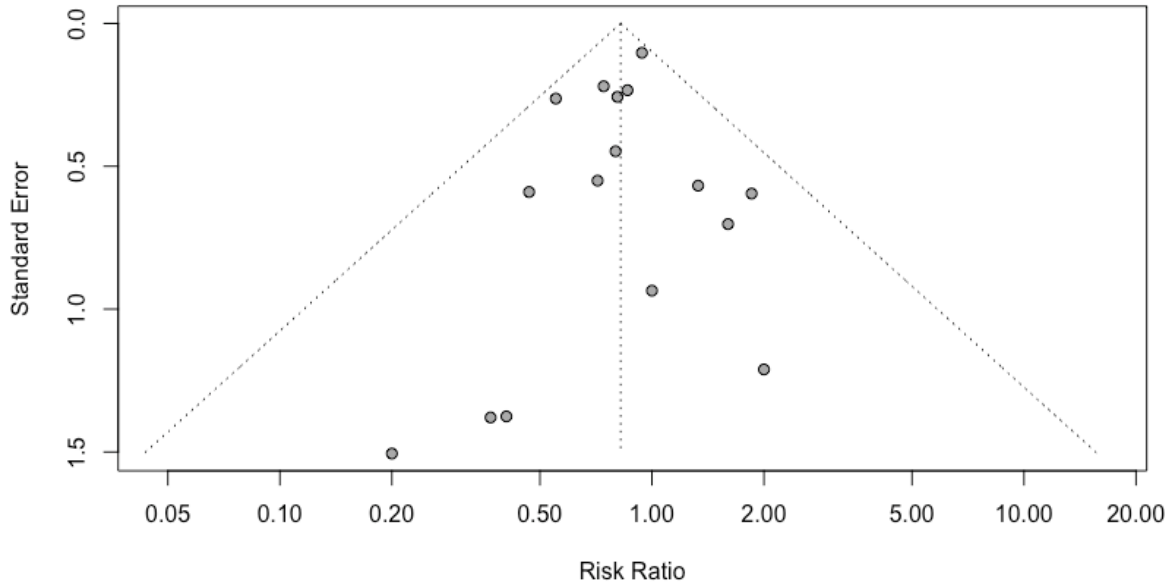


	Intercept	Confidence Interval	t-value	p-value
Egger's test	0.5	-1.3 to 2.4	0.6	0.6

Acute LBP Non-benzodiazepine antispasmodics, Disability 3-13 weeks

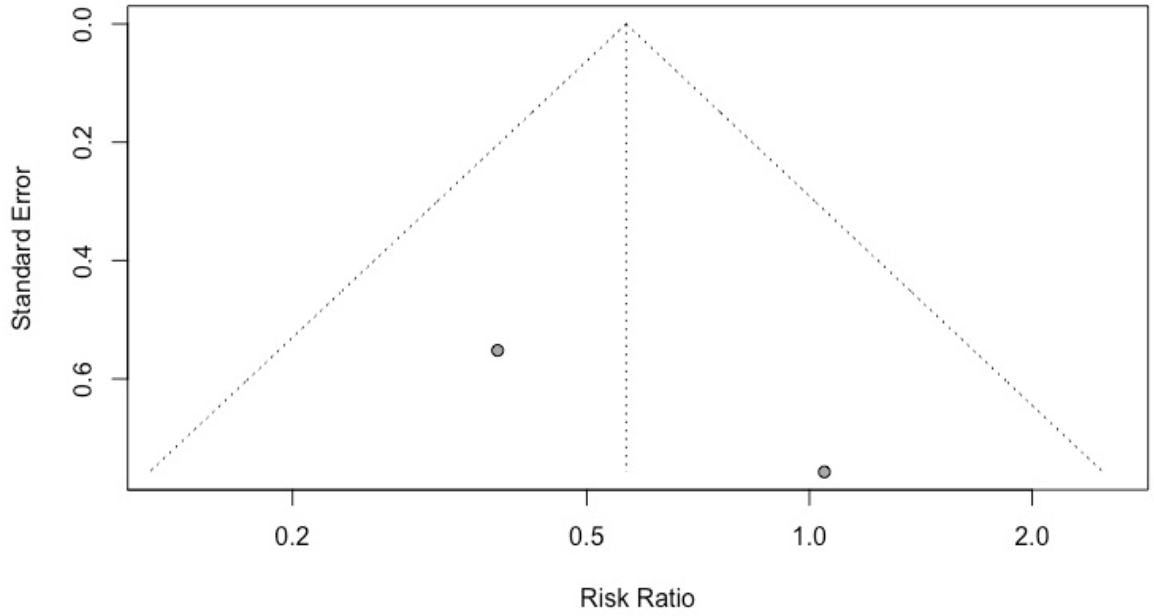


Acute LBP Non-benzodiazepine antispasmodics, Acceptability

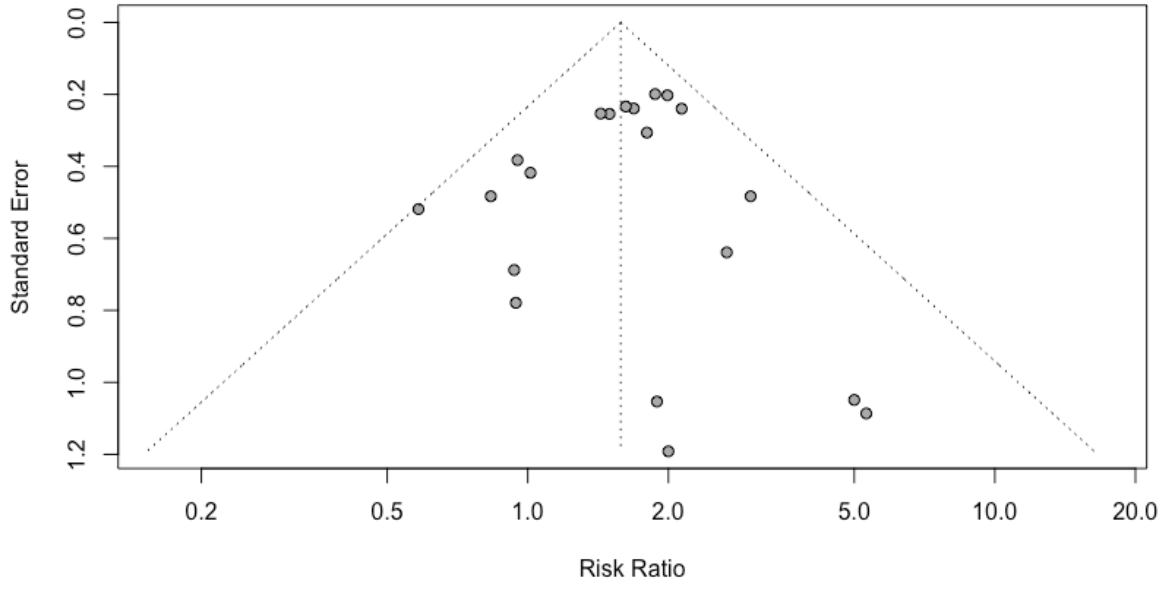


	Intercept	Confidence Interval	t-value	p-value
Egger's test	-0.2	-0.8 to 0.4	-0.6	0.5

Chronic LBP Miscellaneous, Acceptability

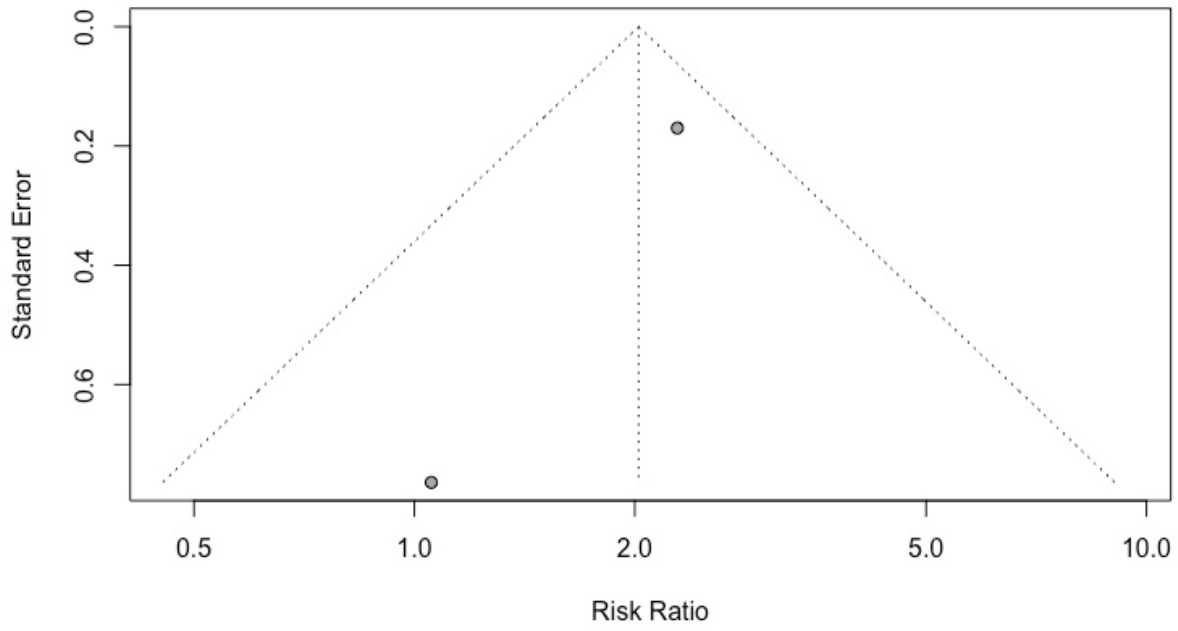


Acute LBP Non-benzodiazepine antispasmodics, Adverse events

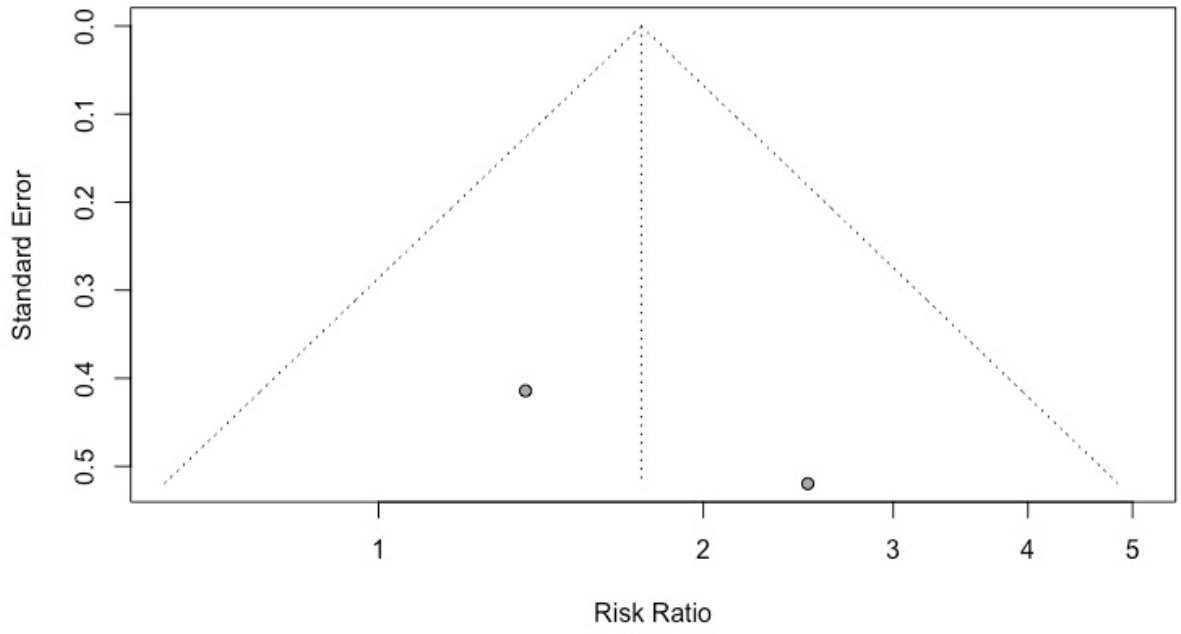


	Intercept	Confidence Interval	t-value	p-value
Egger's test	-0.3	-1.2 to 0.7	-0.6	0.6

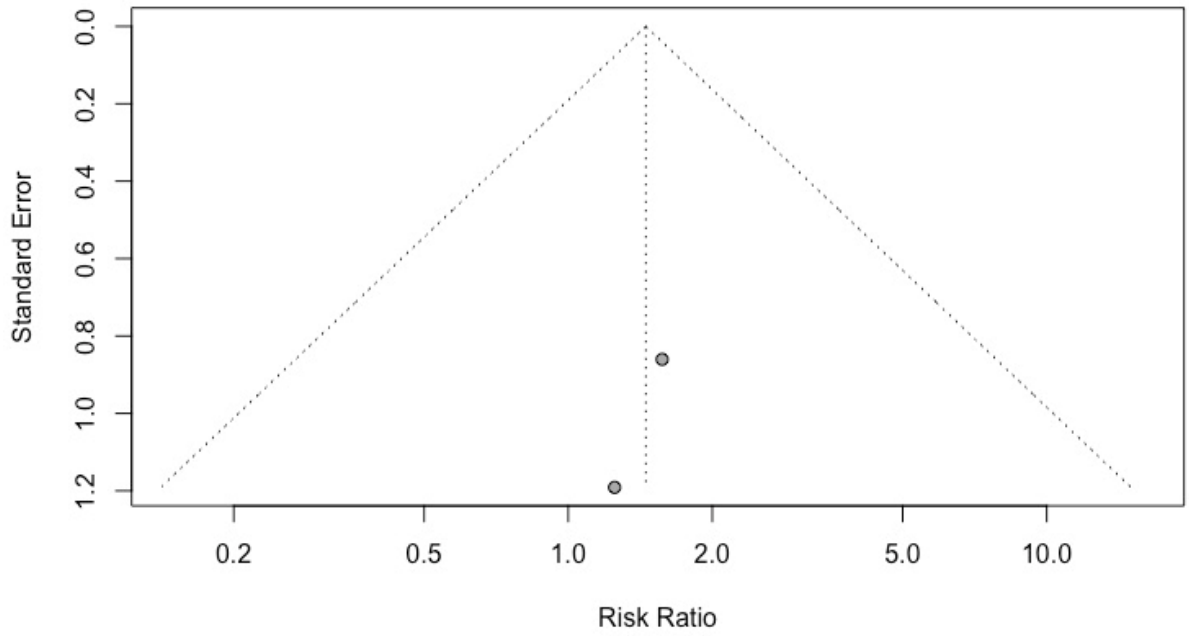
Acute LBP Antispastics, Adverse events



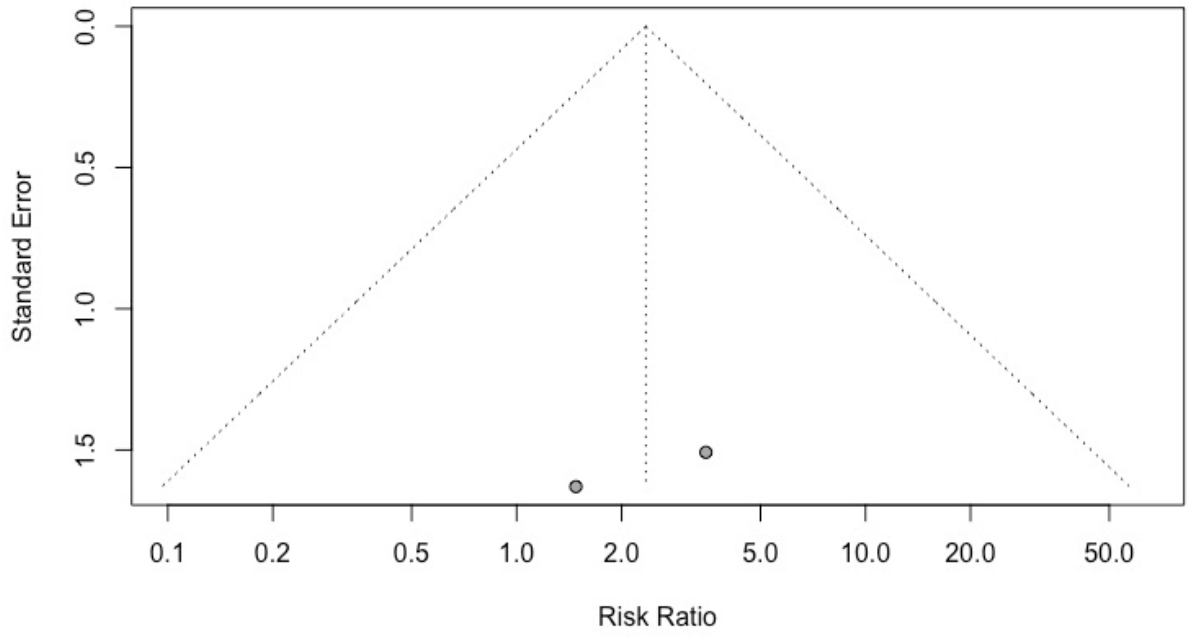
Acute LBP Benzodiazepines, Adverse events



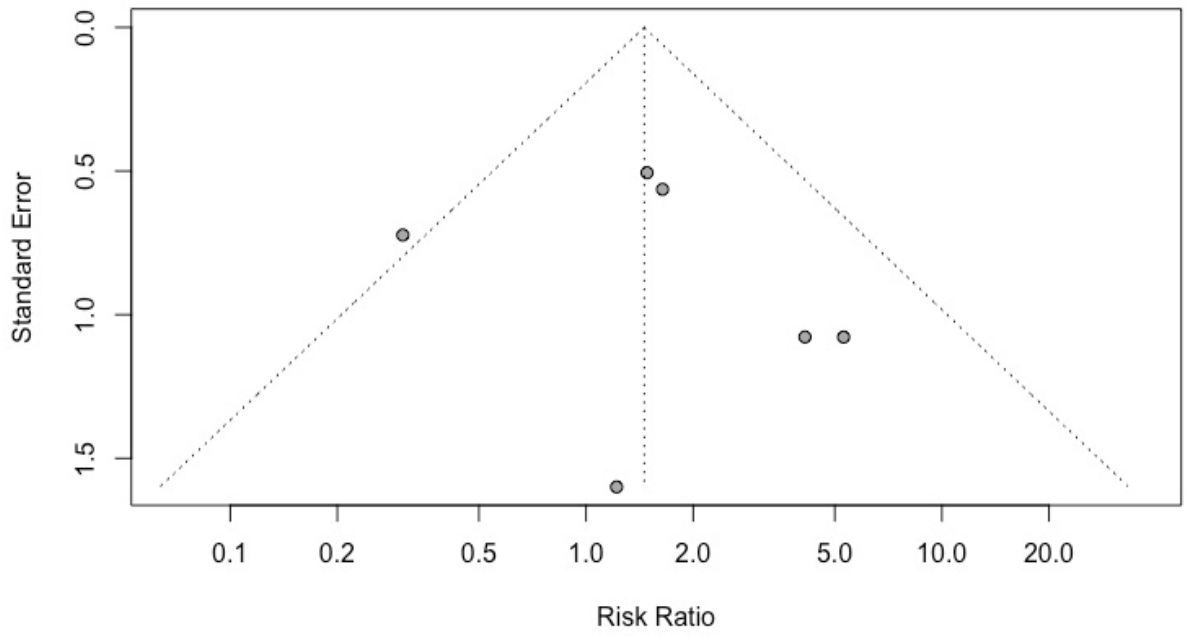
Chronic LBP Miscellaneous, Adverse events



Acute LBP Non-benzodiazepine antispasmodics, Serious adverse events



Acute LBP Non-benzodiazepine antispasmodics, Tolerability



References

1. Sterne JAC, Sutton AJ, Ioannidis JPA, et al. Recommendations for Examining and Interpreting Funnel Plot Asymmetry in Meta-Analyses of Randomised Controlled Trials. *BMJ*. 2011;343. doi:10.1136/bmj.d4002

Supplemental file 20. Sensitivity analyses for non-benzodiazepine antispasmodic medicines in acute LBP

Outcome	Overall	Removed trials with an unclear definition for non-specific LBP	Removed trials measuring pain with a VRS	Removed trials where measures of variance were imputed	Removed trials for carisoprodol	Removed trials for thiocolchicoside	Removed trials at high risk of bias	Removed trials with data from trial registry record	Removed trials without a placebo comparator
	(MD/RR [95% CI]; Tau^2; n]	**(MD/RR [95% CI]; Tau^2; n]**	**(MD/RR [95% CI]; Tau^2; n]**	**(MD/RR [95% CI]; Tau^2; n]**	**(MD/RR [95% CI]; Tau^2; n]**	**(MD/RR [95% CI]; Tau^2; n]**	**(MD/RR [95% CI]; Tau^2; n]**	**(MD/RR [95% CI]; Tau^2; n]**	**(MD/RR [95% CI]; Tau^2; n]**
Pain intensity (≤ 2 weeks)	-7.7 (-12.1 to -3.3), 76.2, n=4546	-8.1 (-12.7 to -3.6), 79.3, n=4450	-9.7 (-15.4 to -3.9), 92.6, n=2767	-8.2 (-13.2 to -3.2), 77.6, n=3495	-8 (-14.3 to -1.7), 103.9, n=1559	-5.3 (-9.2 to -1.4), 43.8, n=4200	0.2 (-4.9 to 5.4), 0, n=672	-10.2 (-15.6 to -4.7), 96.4, n=2901	-11 (-17 to -5.1), 95.9, n=3488
	Change in overall effect size (%) *Change in Tau^2 (%)*	*Increased by -0.4 (5.2%)* *Tau^2 increased by 3.1 (4.1%)*	*Increased by -2 (26%)* *Tau^2 increased by 16.4 (21.8%)*	*Increased by -0.5 (6.5%)* *Tau^2 increased by 1.4 (1.8%)*	*Increased by -0.3 (3.9%)* *Tau^2 increased by 27.2 (36.4%)*	*Reduced by 2.4 (31.2%)* *Tau^2 reduced by 32.4 (42.5%)*	*Reduced by 7.9 (102.6%)* *Tau^2 reduced by 76.2 (100%)*	*Increased by -2.5 (32.5%)* *Tau^2 increased by 20.2 (26.5%)*	*Increased by –3.3 (42.9%)* *Tau^2 increased by 19.7 (25.9%)*
Acceptability	0.8 (0.6 to 1.1), 0.1, n=2834	0.8 (0.6 to 1.1), 0, n=2520	-	-	0.9 (0.6 to 1.3), 0.2, n=1412	0.9 (0.6 to 1.2), 0.1, n=2433	0.2 (0 to 3.8), NA, n=30	-	0.8 (0.6 to 1), 0.1, n=2332
	Change in overall effect size (%) *Change in Tau^2 (%)*	*No change in acceptability* *Tau^2 reduced by 0.1 (100%)*	-	-	*Reduced by 0.1 (12.5%)* *Tau^2 increased by 0.1 (100%)*	*Reduced by 0.1 (12.5%)* *No change in Tau^2*	*Increased by 0.6 (75%)* *NA*	-	*No change in acceptability* *No change in Tau^2*
Disability (≤2 weeks)	-3.3 (-7.3 to 0.7), 20.2, n=2438	-	-	-3.3 (-6.2 to -0.4), 4, n=2410	2.3 (-3.6 to 8.3), 0, n=652	-	2.3 (-3.6 to 8.3), 0, n=652	-3.7 (-8.6 to 1.2), 26.7, n=2020	-5.9 (-10.5 to -1.3), 17.5, n=1786
	Change in overall effect size (%) *Change in Tau^2 (%)*	-	-	*No change in disability* *Tau^2 reduced by 16.2 (80.2%)*	*Reduced by 5.6 (30.3%)* *Tau^2 reduced by 20.2 (100%)*	-	*Reduced by 5.6 (30.3%)* *Tau^2 reduced by 20.2 (100%)*	*Increased by -0.4 (12.1%)* *Tau^2 increased by 6.5 (32.7%)*	*Increased by -2.6 (78.8%)* *Tau^2 reduced by 2.7 (13.4%)*

Adverse events	1.6 (1.2 to 2), 0.1, n=3404	-	-	-	1.4 (1 to 2), 0.2, n=1741	1.6 (1.3 to 2), 0.1, n=3255	1.2 (0.8 to 1.9), 0.1, n=737	1.4 (1 to 2), 0.2, n=1741	1.8 (1.3 to 2.4), 0.1, n=2385
	Change in overall effect size (%) *Change in Tau^2 (%)*	-	-	-	*Reduced by 0.2 (12.5%)* *Tau^2 increased by 0.1 (100%)*	*No change in adverse events* *No change in Tau^2*	*Reduced by 0.4 (25%)* *No change in Tau^2*	*Reduced by 0.2 (12.5%)* *Tau^2 increased by 0.1 (100%)*	*Increased by 0.2 (12.5%)* *No change in Tau^2*
Tolerability	1.5 (0.6 to 3.5), 0.5, n=1641	-	-	-	3.6 (0.9 to 14.7), 0.1, n=254	-	-	-	1.2 (0.5 to 3), 0.4, n=1536
	Change in overall effect size (%) *Change in Tau^2 (%)*	-	-	-	*Increased by 2.1 (140%)* *Tau^2 reduced by 0.4 (80%)*	-	-	-	*Reduced by 0.3 (20%)* *Tau^2 reduced by 0.1 (20%)*

LBP, Low Back Pain; MD, Mean Difference; RR, Risk Ratio; CI, Confidence Interval; VRS, Verbal Rating Scale; NA, Not Applicable