Appendix A

Total titles: 12091, after deduplication 7803.

Embase.com (n = 6863, after deduplication n = 6738)

('backache'/exp OR 'spinal pain'/de OR (backache OR ((back OR lowback OR spinal OR discogenic* OR lumb*) NEAR/6 (ache OR pain OR syndrome*)) OR backpain OR lumbalgia OR lumbago OR lumbodynia OR dorsalgia):ab,ti,kw) AND ('placebo'/exp OR 'placebo effect'/exp OR 'sham procedure'/exp OR (placebo* OR mock* OR sham OR fake* OR vehicle* OR dumm* OR (pseudo* NEAR/3 treat*) OR (minimal* NEAR/3 acupunture*)):ab,ti,kw) AND ('Controlled clinical trial'/exp OR 'Crossover procedure'/de OR 'Double-blind procedure'/de OR 'Single-blind procedure'/de OR (random* OR factorial* OR crossover* OR (cross NEXT/1 over*) OR ((doubl* OR singl*) NEXT/1 blind*) OR assign* OR allocat* OR volunteer* OR trial OR groups):ab,ti,kw) NOT ([animals]/lim NOT [humans]/lim)

Medline ovid (n = 2126, after deduplication n = 217)

(exp Back Pain/ OR (backache OR ((back OR lowback OR spinal OR discogenic* OR lumb*) ADJ6 (ache OR pain OR syndrome*)) OR backpain OR lumbalgia OR lumbago OR lumbodynia OR dorsalgia).ab,ti,kf.) AND (Placebos/ OR Placebo Effect/ OR (placebo* OR mock* OR sham OR fake* OR vehicle* OR dumm* OR (pseudo* ADJ3 treat*) OR (minimal* ADJ3 acupunture*)).ab,ti,kf.) AND (Exp Controlled clinical trial/ OR "Double-Blind Method"/ OR "Single-Blind Method"/ OR "Random Allocation"/ OR (random* OR factorial* OR crossover* OR cross over* OR ((doubl* OR singl*) ADJ blind*) OR assign* OR allocat* OR volunteer* OR trial OR groups).ab,ti,kf.) NOT (Animals/ NOT Humans/)

Cochrane CENTRAL (n = 3102, after deduplication n = 848)

((backache OR ((back OR lowback OR spinal OR discogenic* OR lumb*) NEAR/6 (ache OR pain OR syndrome*)) OR backpain OR lumbalgia OR lumbago OR lumbodynia OR dorsalgia):ab,ti) AND ((placebo* OR mock* OR sham OR fake* OR vehicle* OR dumm* OR (pseudo* NEAR/3 treat*) OR (minimal* NEAR/3 acupunture*)):ab,ti)

Appendix B

Name, year of publication	
Study design	
Aim of the study	
Patient population	
Baseline Comparability of Groups	Yes/No
Interventions	
Follow-up time	
Primary outcome	
Results for main outcome Mean Standard deviation Sample size 	
Secondary outcomes	
Results for secondary outcomes Mean Standard deviation Sample size Funding source	

Appendix C

Forest plots of subgroup analysis

1: intervention studies vs open label placebo studies pain short term follow-up

	Placeb	oInterven	tion	Nol	nterventio	n	S	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	ABCDE
1.6.1 intervention trials										
Bialosky 2014	29.13	22.28	54	25.75	26.21	28	5.8%	0.14 [-0.32, 0.60]	_ 	$\mathbf{+}\mathbf{+}\mathbf{+}\mathbf{-}\mathbf{+}$
Borges 2014	4.7	0.66	15	5.9	0.66	14	3.0%	-1.77 [-2.64, -0.89]		$\mathbf{+}\mathbf{+}\mathbf{+}\mathbf{-}\mathbf{+}$
Brinkhaus 2006	43.7	29.8	70	58.6	25.1	74	6.9%	-0.54 [-0.87, -0.21]		$\mathbf{+}\mathbf{+}\mathbf{+}\mathbf{-}\mathbf{+}$
Celenay 2019	1.56	1.84	21	4.5	2.88	21	4.2%	-1.19 [-1.86, -0.53]		$\mathbf{+}\mathbf{+}\mathbf{+}\mathbf{-}\mathbf{+}$
Eardley 2013	36	19.8	20	57.7	19.2	17	4.0%	-1.09 [-1.78, -0.39]		
arasyn 2006	59	21	20	52	21	20	4.5%	0.33 [-0.30, 0.95]	-+	+++=?
mamura 2016	4.9	2.4	125	4.9	2.7	127	7.6%	0.00 [-0.25, 0.25]	-+-	$\bullet \bullet \bullet \bullet \bullet \bullet \bullet$
(oroglu 2017	4.8	3.4	20	5.5	2.9	20	4.5%	-0.22 [-0.84, 0.40]		++++
eichtfried 2014	3.5	2.31	36	4.5	2.17	33	5.6%	-0.44 [-0.92, 0.04]		• ? • • ?
_ewis 2010	1.5	1.9	8	2.3	1.1	5	2.1%	-0.45 [-1.59, 0.69]		?? 🕂 🛑 ?
icciardone 2003	3.07	2.25	23	4.64	2.14	16	4.2%	-0.70 [-1.36, -0.04]		••••
uz 2015	6.3	2	20	5.5	1.9	20	4.4%	0.40 [-0.22, 1.03]	+	$\mathbf{+}\mathbf{+}\mathbf{+}\mathbf{-}\mathbf{+}$
larchand 1993	25.51	25.15	12	28.6	29.6	16	3.7%	-0.11 [-0.86, 0.64]		++?+?
/lolsberger 2002	43	23	61	52	19	60	6.6%	-0.42 [-0.78, -0.06]		++++
Noura 2019	3.61	3.49	36	3.73	2.86	37	5.7%	-0.04 [-0.50, 0.42]	-+-	+++
Pach 2011	41.8	34.2561	43	53	35.3553	50	6.2%	-0.32 [-0.73, 0.09]	+	
Schmitz 2019	2.95	2.36	38	5.36	1.98	14	4.3%	-1.05 [-1.69, -0.40]		+ - ? - ?
Nepner 2008	47.5	31	18	52.4	27.2	18	4.3%	-0.16 [-0.82, 0.49]		••••
Subtotal (95% CI)			640			590	87.4%	-0.37 [-0.59, -0.16]	\bullet	
leterogeneity: Tau ² = 0.1	3; Chi ² =	51.68, df =	17 (P <	0.0001)	; l ² = 67%					
est for overall effect: Z =	3.40 (P =	= 0.0007)		,						
I.6.2 placebo trials										
Carvalho 2016	3.52	1.7	41	4.36	1.8	42	5.9%	-0.48 [-0.91, -0.04]		••••
Kleine-Borgmann 2019	4.64	2.04	63	5.1	1.86	59	6.6%	-0.23 [-0.59, 0.12]	+	
Subtotal (95% CI)			104			101	12.6%	-0.33 [-0.61, -0.05]	\bullet	
eterogeneity: Tau ² = 0.0	0; Chi ² = (0.70, df = 1	I (P = 0.4	40); l ² =	0%					
Fest for overall effect: Z =	2.35 (P =	= 0.02)								
Total (95% CI)			744			691	100.0%	-0.37 [-0.55, -0.18]	•	
Heterogeneity: Tau ² = 0.1	1: Chi ² =	52.43. df =	19 (P <	0.0001	: ² = 64%					
Fest for overall effect: Z =				0.0001					-2 -1 0 1 2	
Test for subgroup differen			- 1 (P -	0.81) 8	2 - 0%				Favours Placebo Int. Favours No Intervention	

2: forest plot placebo acupuncture vs no treatment on pain short term follow-up

	Placebo	Interven	tion	NoInt	ervent	ion	9	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	ABCDE
Brinkhaus 2006	43.7	29.8	70	58.6	25.1	74	39.0%	-0.54 [-0.87, -0.21]		
Molsberger 2002	43	23	61	52	19	60	35.4%	-0.42 [-0.78, -0.06]	_	••••
Moura 2019	3.61	3.49	36	3.73	2.86	37	25.5%	-0.04 [-0.50, 0.42]		••••
Total (95% CI)			167			171	100.0%	-0.37 [-0.64, -0.10]	-	
	terogeneity: Tau ² = 0.02; Chi ² = 3.07, df = 2 (P = 0.21); st for overall effect: Z = 2.68 (P = 0.007)				² = 35%	b			-1 -0.5 0 0.5 1 Favours Placebo Int. Favours No Interve	ntion

3: forest plot placebo taping vs no treatment on pain short term follow-up

	Placebo	Interven	tion	NoInte	ervent	ion	5	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	ABCDE	
Koroglu 2017	4.8	3.4	20	5.5	2.9	20	50.2%	-0.22 [-0.84, 0.40]		+++?	
Luz 2015	6.3	2	20	5.5	1.9	20	49.8%	0.40 [-0.22, 1.03]	+ - -		
Total (95% CI)			40			40	100.0%	0.09 [-0.52, 0.70]	-		
• •	erogeneity: Tau² = 0.09; Chi² = 1.89, df = 1 (P = 0.17); l² = t for overall effect: Z = 0.29 (P = 0.77)				= 47%	6			-2 -1 0 1 2 Favours Placebo Int. Favours No Interventio	n	

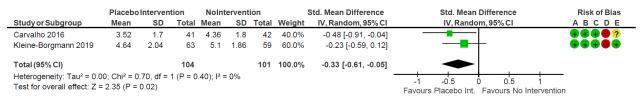
4: forest plot placebo injection vs no treatment on pain short term follow-up

	Placebo	Placebo Intervention NoInterven					5	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	ABCDE		
Imamura 2016	4.9	2.4	125	4.9	2.7	127	73.2%	0.00 [-0.25, 0.25]	-#-			
Pach 2011	41.8	39.16	43	37	42.23	50	26.8%	0.12 [-0.29, 0.52]		$\bullet \bullet \bullet \bullet \bullet$		
Total (95% CI)			168			177	100.0%	0.03 [-0.18, 0.24]	•			
Heterogeneity: Tau ² = 0.00; Chi ² = 0.23, df = 1 (P = 0.63); l ² = 0% Test for overall effect: Z = 0.29 (P = 0.77)									-1 -0.5 0 0.5 1 Favours Placebo Int. Favours No Interve	ntion		

5: forest plot placebo spinal manipulation vs no treatment on pain short term follow-up

	Placebo	Interven	tion	Noln	tervent	ion	:	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	ABCDE		
Bialosky 2014	29.13	22.28	27	25.75	26.21	27	53.2%	0.14 [-0.40, 0.67]				
Licciardone 2003	2.87	2.14	19	4.51	2.12	16	46.8%	-0.75 [-1.44, -0.06]		••••?		
Total (95% CI)			46			43	100.0%	-0.28 [-1.15, 0.59]				
leterogeneity: Tau² = 0.30; Chi² = 3.98, df = 1 (P = 0.05); l² = 75%				6				<u> </u>				
Test for overall effect:	st for overall effect: Z = 0.63 (P = 0.53)						Favours Placebo Int. Favours No Interve	- ention				

6: forest plot open label placebo pills vs no treatment on pain short term follow-up



Risk of bias legend

(A) Allocation concealment (selection bias)

 $({\bf B})$ Blinding of participants and personnel (performance bias)

(C) Incomplete outcome data (attrition bias)(D) Blinding of outcome assessment (detection bias)

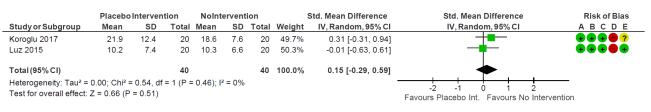
(E) Selective reporting (reporting bias)

Subgroup analysis physical functioning short term follow-up

1: forest plot open label placebo pills vs no treatment on physical functioning short term follow-up

Carvalho 2016 7.04 5.2 41 8.48 4.6 42 40.7% -0.29 [-0.72, 0.14] Image: Carvalho 2019 Kleine-Borgmann 2019 25.96 11.98 63 30.79 13.37 59 59.3% -0.38 [-0.74, -0.02] Image: Carvalho 2019 Image: Carvalho 2019 <td< th=""><th></th><th colspan="5">PlaceboIntervention NoIntervention</th><th>ion</th><th>:</th><th>Std. Mean Difference</th><th>Std. Mean Difference</th><th colspan="3">Risk of Bias</th></td<>		PlaceboIntervention NoIntervention					ion	:	Std. Mean Difference	Std. Mean Difference	Risk of Bias		
Kleine-Borgmann 2019 25.96 11.98 63 30.79 13.37 59 59.3% -0.38 [-0.74, -0.02]	Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI	ABCDE		
	Carvalho 2016	7.04	5.2	41	8.48	4.6	42	40.7%	-0.29 [-0.72, 0.14]		••••		
Total (95% CI) 104 101 100.0% -0.34 F-0.62 -0.071	Kleine-Borgmann 2019	25.96	11.98	63	30.79	13.37	59	59.3%	-0.38 [-0.74, -0.02]		••••		
	Total (95% CI)			104			101	100.0%	-0.34 [-0.62, -0.07]				

2: forest plot placebo taping vs no treatment on physical functioning short term follow-up



Risk of bias legend

(A) Allocation concealment (selection bias)

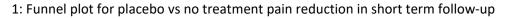
 $({\bf B})$ Blinding of participants and personnel (performance bias)

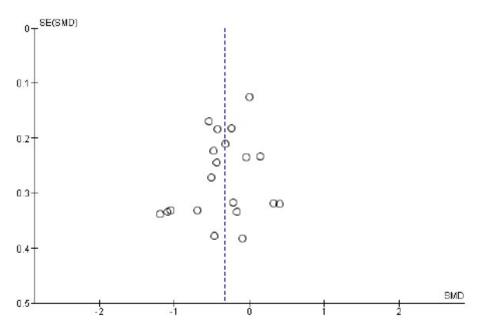
(C) Incomplete outcome data (attrition bias)

(D) Blinding of outcome assessment (detection bias)

(E) Selective reporting (reporting bias)

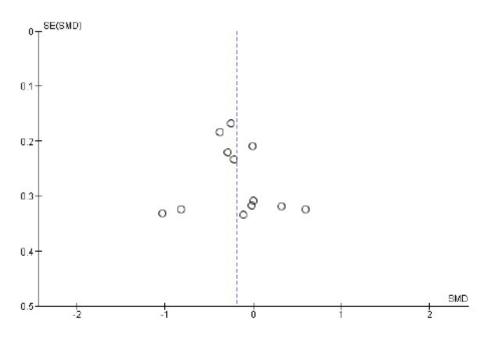
Appendix D: Funnel plots.





Funnel plot of comparison: 1 placebo vs. control intervention, outcome: 1.1 Pain intensity, short term follow-up.

2: funnel plot for placebo vs no treatment physical functioning in short term follow-up



Funnel plot of comparison: 1 placebo vs. control intervention, outcome: 1.3 Physical Functioning, short term follow-up.

Appendix E:

Grade approach for the primary outcomes

Placebo treatment compared to no treatment control for non specific lower back pain Bibliography:

		Certair	nty asse		Summary of findings						
Posticio						0	_	event (%)	Relat	abso	pated plute ects
Particip ants (studie s) Follow up	Ris k of bia s	Inconsis tency	Indirect ness	Imprec ision	Public ation bias	Overa II certai nty of evide nce	With no treat ment contr ol	With place bo treat ment	ive effec t (95 % CI)	Risk with no treat ment contr ol	Risk differ ence with place bo treat ment

Pain intensity (follow up: range 1 days to 3 months; assessed with: visual analog scale ; Scale from: 0 to 100)

1443 (19 RCTs)	not seri ous a	serious ^b	not serious	not serious	none	⊕⊕⊕ ○ MODE RATE	698	745	_	-	SMD 0.37 SD lower (0.55 lower to 0.18 lower)
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Physical functioning (follow up: range 1 days to 3 months; assessed with: Oswestry disability index; Scale from: 0 to 100)

Pain intensity (follow up: range 3 months to 6 months; assessed with: visual analog scale; Scale from: 0 to 100)

Placebo treatment compared to no treatment control for non specific lower back pain

Bibliography:

		Certair	nty asse	ssment			S	umma	ry of t	finding	S
154 (3 RCTs)	not seri ous a	not serious	not serious	serious ^c	none	⊕⊕⊕ ○ MODE RATE	80	74	_	-	SMD 0.26 lower (0.58 lower to 0.06 higher)

ST SF-36 PCS (follow up: range 1 days to 3 months; assessed with: Short-Form 36 physical component summary score; Scale from: 0 to 100)

267 (3 RCTs)	not seri ous ª	not serious	not serious	not serious	none	⊕⊕⊕ ⊕ HIGH	139	128	-	The mean ST SF- 36 PCS was 0	MD 2.55 lower (4.63 lower to 0.47 lower)	
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ST SF-36 MCS (follow up: range 1 days to 3 months; assessed with: Sort-Form 36 mental component summary score; Scale from: 0 to 100)

CI: Confidence interval; SMD: Standardised mean difference; MD: Mean difference

Explanations

a. High risk of bias in measurement of the outcome

- b. I² is between 40 and 75%
- c. The sample size for the specific outcome is less than 100.