B.3 Spinal manipulative therapy (SMT)

Overview of the PICO structure

Definition of the intervention	
Spinal manipulative therapy (SMT) is considered to be any "hands-on" treatment that involves movement of the spinal joints, including both high-velocity, low-amplitude manipulation and low-velocity, low-amplitude mobilization. Mobilization uses low-grade velocity (relative to manipulation) and small- or large-amplitude passive movement techniques within the person's spinal joint range of motion and control, while manipulation uses a high-velocity impulse or thrust applied to a synovial joint over a short amplitude at, or close to, the end of the passive or physiological range of motion, which is often accompanied by an audible "crack".	
PICO question	
Population and subgroups	Community-dwelling adults (aged 20 years and over) experiencing chronic primary low back pain, with or without leg pain, including older people (aged 60 years and older). Subgroups: • Age (all adults and those aged 60 years and over) • Gender and/or sex • Presence of leg pain (radicular, non-radicular, mixed) • Race/ethnicity - studies of populations who were historically marginalized compared with studies of those who were not • Regional economic development - studies carried out in high-income countries compared with studies in low- to middle-income countries
Comparators	a) Placebo/sham b) No or minimal intervention, or where the effect of the intervention can be isolated c) Usual care (described as usual care in the trial) d) Adjuvant therapy, i.e. where the additional effect of the intervention could be isolated

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Outcomes	Critical outcomes constructs (all adults) Critical outcomes constructs (older adults, aged ≥ 60 years) • Pain • Back-specific function/disability • General function/disability • Health-related quality of life • Psychosocial function • Social participation • Adverse events (as reported in trials) Pain • Back-specific function/disability • General function/disability • Health-related quality of life • Psychosocial function • Adverse events (as reported in trials) • Change in the use of medications • Falls

Other Evidence-to-Decision (EtD) considerations

Summary of *values and preferences*	
All adults	**Older people**
No evidence synthesis commissioned for all adults. Judgements made based on experience of GDG members	No evidence identified

Summary of *resource considerations*	
All adults	**Older people**

No evidence synthesis commissioned for all adults. Judgements made based on experience of GDG members	No evidence identified

Summary of *equity and human rights considerations*	
All adults	**Older people**
No evidence synthesis commissioned for all adults. Judgements made based on experience of GDG members	No evidence identified

Summary of *acceptability considerations*	
All adults	**Older people**
No evidence synthesis commissioned for all adults. Judgements made based on experience of GDG members	No evidence identified.

Summary of *feasibility considerations*	
All adults	**Older people**
No evidence synthesis commissioned for all adults. Judgements made based on experience of GDG members	No evidence identified

Summary of judgements

Domain	**All adults**	**Older people**
Benefits	Moderate; small; trivial; uncertain; varies	Moderate; small; trivial; uncertain
Harms	Small; trivial; uncertain	Small; trivial; uncertain

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Balance benefits to harms	Probably favours SMT; probably does not favour SMT; uncertain	Probably favours SMT; probably does not favour SMT; uncertain
Overall certainty	Very low; low	Very low
Values and preferences	Probably important uncertainty or variability; possibly important uncertainty or variability	Probably important uncertainty or variability; possibly important uncertainty or variability
Resource considerations	Moderate costs; varies	Moderate costs; varies
Equity and human rights	No impact; probably reduced (traction especially); uncertain; varies	No impact; probably reduced (traction especially); uncertain; varies
Acceptability	Yes; probably yes; probably no; uncertain; varies	Yes; probably yes; probably no; uncertain; varies
Feasibility	Yes; probably yes; varies	Yes; probably yes; varies

GRADE Table 1. ***What are the benefits and harms of SMT in the management of community-dwelling adults (including older adults aged 60 years and over) with chronic primary low back pain (with or without leg pain) compared with sham SMT/placebo treatment?***

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of trials	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	WHO SMT	sham/placebo SMT	Relative (95% CI)	Absolute (95% CI)		
Pain intensity (higher scores mean more pain)												
Pain - Pain at 1 month												
15	randomized trials	serious[a]	serious[b]	not serious[c]	serious[d]	none	719	683	-	MD **6.07 lower** (13.09 lower to 0.95 higher)	⨁◯◯◯ Very low	
Population subgroups 1, 2 and 3 - not reported (no subgroup analysis performed)												
Population subgroup 4: regional economic development - high-income countries												
11	randomized trials	serious[a]	serious[b]	serious[c]	serious[d]	none	670	614	-	MD **4.9 lower** (14.57 lower to 4.77 higher)	⨁◯◯◯ Very low	
Population subgroup 4: regional economic development – low- or lower middle-income countries												
4	randomized trials	serious[e]	not serious[f]	serious[g]	very serious[h]	none	88	122	-	MD **8.25 lower** (14.62 lower to 1.88 lower)	⨁◯◯◯ Very low	
Population subgroup 5: participants over 60 years of age												

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Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of trials	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	WHO SMT	sham/placebo SMT	Relative (95% CI)	Absolute (95% CI)		
1	randomized trials	serious[a]	serious[r]	serious[i]	very serious[h]	none	69	67	-	MD **2.48 lower** (9.87 lower to 4.91 higher)	⨁◯◯◯ Very low	
Pain - Pain at 3 months												
8	randomized trials	serious[a]	serious[j]	not serious[c]	serious[m]	none	514	449	-	MD **0.9 lower** (4.68 lower to 2.87 higher)	⨁◯◯◯ Very low	
Population subgroups 1, 2 and 3 - not reported (no subgroup analysis performed)												
Population subgroup 4: regional economic development - high-income countries												
6	randomized trials	serious[a]	serious[j]	not serious[c]	serious[s]	none	494	412	-	MD **0.78 lower** (6.00 lower to 4.43 higher)	⨁◯◯◯ Very low	
Population subgroup 4: regional economic development - low- or lower middle-income income countries												
2	randomized trials	serious[e]	not serious[f]	serious[g]	very serious[h]	none	58	69	-	MD 0.**49 lower** (3.83 lower to 2.84 higher)	⨁◯◯◯ Very low	
Population subgroup 5: participants over 60 years of age												

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Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of trials	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	WHO SMT	sham/placebo SMT	Relative (95% CI)	Absolute (95% CI)		
1	randomized trials	serious[a]	serious[r]	serious[i]	very serious[h]	none	69	66	-	MD **2.22 lower** (9.96 lower to 5.52 higher)	⨁◯◯◯ Very low	
Pain - Pain at 6 months												
2	randomized trials	serious[k]	serious[l]	serious[g]	very serious[h]	none	58	56	-	MD **0.96 higher** (6.34 lower to 8.26 higher)	⨁◯◯◯ Very low	
Population subgroup 4: regional economic development - high-income countries												
1	randomized trials	very serious[e]	serious[r]	serious[g]	very serious[h]	none	32	19	-	MD **7.1 higher** (5.16 lower to 19.36 higher)	⨁◯◯◯ Very low	
Population subgroup 4: regional economic development - low- or lower middle-income income countries												
1	randomized trials	serious[m]	serious[r]	serious[g]	very serious[h]	none	26	37	-	MD **1.3 lower** (6.31 lower to 3.71 higher)	⨁◯◯◯ Very low	
Population subgroup 5: participants over 60 years of age - not reported (no subgroup analysis performed; no trial reporting outcomes at this follow-up **Pain - Pain at 12 months**												

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Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of trials	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	WHO SMT	sham/placebo SMT	Relative (95% CI)	Absolute (95% CI)		
1	randomized trials	serious[m]	Serious[r]	serious[g]	very serious[h]	none	26	37	-	MD **0.2 higher** (5.33 lower to 5.73 higher)	⨁◯◯◯ Very low	
Population subgroups 1, 2 and 3 - not reported (no subgroup analysis performed)												
Population subgroup 4: regional economic development - high-income countries - not reported (no subgroup analysis performed; no trial reporting outcomes at this follow-up)												
Population subgroup 4: regional economic development - low- or lower middle-income income countries												
1	randomized trials	serious[m]	Serious[r]	serious[g]	very serious[h]	none	26	37	-	MD **0.2 higher** (5.33 lower to 5.73 higher)	⨁◯◯◯ Very low	
Population subgroup 5: participants over 60 years of age - not reported												
Back-specific functional status (higher scores mean more disability)												
Back-specific functional status - back-specific functional status at 1 month												
12	randomized trials	serious[n]	serious[b]	not serious[c]	serious[o]	none	678	642	-	SMD **0.43 lower** (0.74 lower to 0.12 lower)	⨁◯◯◯ Very low	
Population subgroups 1, 2 and 3 - not reported (no subgroup analysis performed)												
Population subgroup 4: regional economic development - high-income countries												

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Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of trials	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	WHO SMT	sham/placebo SMT	Relative (95% CI)	Absolute (95% CI)		
9	randomized trials	serious[n]	serious[b]	not serious[c]	serious[o]	none	622	572	-	SMD **0.34 SD lower** (0.68 lower to 0)	⨁◯◯◯ Very low	
Population subgroup 4: regional economic development - low- or lower middle-income income countries												
3	randomized trials	serious[e]	serious[p]	serious[g]	very serious[h]	none	56	70	-	SMD **0.79 SD lower** (1.36 lower to 0.21 lower)	⨁◯◯◯ Very low	
Population subgroup 5: participants over 60 years of age												
1	randomized trials	serious[a]	Serious[r]	serious[i]	very serious[h]	none	69	67	-	SMD **0.07 SD lower** (0.4 lower to 0.27 higher)	⨁◯◯◯ Very low	
Population subgroup 6: ODI												
8	randomized trials	serious[n]	serious[b]	serious[c]	very serious[h]	none	214	250	-	SMD **0.65 SD lower** (1.2 lower to 0.11 lower)	⨁◯◯◯ Very low	
Population subgroup 6: RMDQ												
4	randomized trials	serious[a]	serious[b]	not serious[c]	very serious[h]	none	398	325	-	SMD **0.71 SD lower** (1.48 lower to 0.06 higher)	⨁◯◯◯ Very low	
Back-specific functional status - back-specific functional status at 3 months												

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Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of trials	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	WHO SMT	sham/placebo SMT	Relative (95% CI)	Absolute (95% CI)		
7	randomized trials	serious[n]	not serious[f]	not serious[c]	serious[s]	none	512	449	-	SMD **0.14 SD lower** (0.27 lower to 0.01 lower)	⨁⨁◯◯ Low	
Population subgroups 1, 2 and 3 - not reported (no subgroup analysis performed)												
Population subgroup 4: regional economic development - high-income countries												
5	randomized trials	serious[n]	not serious[f]	not serious[c]	very serious[d]	none	454	380	-	SMD **0.14 SD lower** (0.28 lower to 0)	⨁◯◯◯ Very low	
Population subgroup 4: regional economic development - low- or lower middle-income income countries												
2	randomized trials	serious[e]	not serious[f]	serious[g]	very serious[h]	none	58	69	-	SMD **0.13 SD lower** (0.18 lower to 0.22 higher)	⨁◯◯◯ Very low	
Population subgroup 5: participants over 60 years of age												
1	randomized trials	serious[a]	serious[i]	serious[i]	very serious[h]	none	67	67	-	SMD **0.29 SD lower** (0.63 lower to 0.05 higher)	⨁◯◯◯ Very low	
Population subgroup 6: ODI												

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Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of trials	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	WHO SMT	sham/placebo SMT	Relative (95% CI)	Absolute (95% CI)		
3	randomized trials	serious[n]	not serious[f]	serious[g]	very serious[h]	none	125	136	-	SMD 0.**26 SD lower** (0.48 lower to 0.03 lower)	⨁◯◯◯ Very low	
Population subgroup 6: RMDQ												
3	randomized trials	serious[a]	not serious[f]	not serious[c]	very serious[h]	none	367	295	-	SMD **0.09 SD lower** (0.24 lower to 0.07 higher)	⨁◯◯◯ Very low	
Back-specific functional status - back-specific functional status at 6 months												
2	randomized trials	serious[m]	not serious	serious[g]	very serious[h]	none	58	56	-	SMD **0.12 lower** (0.5 lower to 0.25 higher)	⨁◯◯◯ Very low	
Population subgroups 1, 2 and 3 - not reported (no subgroup analysis performed)												
Population subgroup 4: regional economic development - high-income countries												
1	randomized trials	very serious[e]	serious[i]	serious[i]	very serious[h]	none	32	19	-	SMD **0.04 SD higher** (0.52 lower to 0.61 higher)	⨁◯◯◯ Very low	
Population subgroup 4: regional economic development - low- or lower middle-income income countries												

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Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of trials	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	WHO SMT	sham/placebo SMT	Relative (95% CI)	Absolute (95% CI)		
1	randomized trials	serious[m]	serious[i]	serious[i]	very serious[h]	none	26	37	-	SMD **0.25 SD lower** (0.76 lower to 0.25 higher)	⨁◯◯◯ Very low	
Population subgroup 5: participants over 60 years of age - not reported												
Population subgroup 6: ODI												
1	randomized trials	serious[m]	serious[i]	serious[i]	very serious[h]	none	26	27	-	SMD **0.25 SD lower** (0.76 lower to 0.25 higher)	⨁◯◯◯ Very low	
Population subgroup 6: RMDQ												
1	randomized trials	very serious[e]	serious[i]	serious[i]	very serious[h]	none	32	19	-	SMD **0.04 SD higher** (0.52 lower to 0.61 higher)	⨁◯◯◯ Very low	
Back-specific functional status - back-specific functional status 12 months												
1	randomized trials	serious[m]	serious[i]	serious[i]	very serious[h]	none	26	37	-	SMD **0.19 lower** (0.69 lower to 0.31 higher)	⨁◯◯◯ Very low	
Population subgroups 1, 2 and 3 - not reported (no subgroup analysis performed)												
Population subgroup 4: regional economic development - high-income countries - not reported (no subgroup analysis performed; one trial performed in high-income countries)												

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Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of trials	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	WHO SMT	sham/placebo SMT	Relative (95% CI)	Absolute (95% CI)		
Population subgroup 4: regional economic development - low- or lower middle-income income countries												
1	randomized trials	serious[m]	serious[i]	serious[i]	very serious[h]	none	26	37	-	SMD **0.19 SD lower** (0.69 lower to 0.31 higher)	⨁◯◯◯ Very low	
Population subgroup 5: participants over 60 years of age - not reported												
Population subgroup 6: ODI												
1	randomized trials	serious[m]	serious[i]	serious[i]	very serious[h]	none	26	37	-	SMD **0.19 SD lower** (0.69 lower to 0.31 higher)	⨁◯◯◯ Very low	
Population subgroup 6: RMDQ - not reported												
Health-related quality of life (higher scores mean better health)												
Health-related quality of life – Health-related quality of life at 1 month												
1	randomized trials	very serious[e]	serious[r]	serious[i]	very serious[h]	none	26	37	-	MD **4.5 SD higher** (0.46 higher to 8.54 higher)	⨁◯◯◯ Very low	
Health-related quality of life – Health-related quality of life at 3 months												

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Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of trials	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	WHO SMT	sham/placebo SMT	Relative (95% CI)	Absolute (95% CI)		
1	randomized trials	very serious[e]	serious[ir]	serious[i]	very serious[h]	none	26	37	-	MD **2.8 SD higher** (1.24 lower to 6.84 higher)	⨁◯◯◯ Very low	
Health-related quality of life – Health-related quality of life at 6 months												
1	randomized trials	very serious[e]	serious[r]	serious[i]	very serious[h]	none	26	37	-	MD **1.7 SD higher** (2.34 lower to 5.74 higher)	⨁◯◯◯ Very low	
Health-related quality of life – Health-related quality of life at 12 months												
1	randomized trials	very serious[e]	serious[r]	serious[i]	very serious[h]	none	26	37	-	MD **1.7 SD higher** (2.34 lower to 5.74 higher)	⨁◯◯◯ Very low	
Return to work - Return to work at 1 month												
1	randomized trials	very serious[e]	serious[ir]	serious[i]	very serious[h]	none	1/2 (50.0%)	7/17 (41.2%)	**RR 1.21** (0.27 to 5.43)	**86 more per 1.000** (from 301 fewer to 1.000 more)	⨁◯◯◯ Very low	
Return to work - Return to work at 3 months												

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Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of trials	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	WHO SMT	sham/placebo SMT	Relative (95% CI)	Absolute (95% CI)		
1	randomized trials	very serious[e]	serious[ir]	serious[i]	very serious[h]	none	2/3 (66.7%)	11/17 (64.7%)	**RR 1.03** (0.43 to 2.47)	**19 more per 1.000** (from 369 fewer to 951 more)	⨁◯◯◯ Very low	
General functional status (higher scores mean less disability)												
General functional status - General functional status at 1 month												
2	randomized trials	serious[m]	serious[b]	not serious[c]	very serious[h]	none	111	90	-	SMD 0.**57 higher** (0.55 lower to 1.69 higher)	⨁◯◯◯ Very low	
Population subgroups 1, 2, 3 and 4 - not reported (no subgroup analysis performed)												
Population subgroup 5: participants over 60 years of age												
1	randomized trials	serious[a]	serious[r]	serious[i]	very serious[h]	none	69	67	-	SMD **0.02 SD higher** (0.32 lower to 0.36 higher)	⨁◯◯◯ Very low	
General functional status - General functional status at 3 months												
2	randomized trials	serious[m]	not serious[f]	not serious[c]	very serious[h]	none	103	85	-	SMD **0.07 lower** (0.36 lower to 0.22 higher)	⨁◯◯◯ Very low	
Population subgroups 1, 2, 3 and 4 - not reported (no subgroup analysis performed)												
Population subgroup 5: participants over 60 years of age												

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Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of trials	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	WHO SMT	sham/placebo SMT	Relative (95% CI)	Absolute (95% CI)		
1	randomized trials	serious[a]	serious[r]	serious[i]	very serious[h]	none	67	67	-	SMD **0.02 SD lower** (0.36 lower to 0.32 higher)	⨁◯◯◯ Very low	
General functional status - General functional status at 6 months												
1	randomized trials	very serious[q]	serious[ir]	serious[i]	very serious[h]	none	32	19	-	SMD **0** (0.57 lower to 0.57 higher)	⨁◯◯◯ Very low	
Population subgroups 1, 2, 3, 4 and 5 - not reported (no subgroup analysis performed)												
General functional status - Functional status at 12 months - not reported												
Psychological functioning - at 1 month												
2	randomized trials	very serious[t]	Serious[j]	Serious[g]	very serious[h]	none			-	Data was not pooled, because they used different measurements	⨁◯◯◯ Very low	
Psychological functioning - at 3 months												
1	randomized trials	very serious[t]	Serious[j]	Serious[i]	very serious[h]	none			-	Data was not pooled, because they used different measurements	⨁◯◯◯ Very low	
Psychological functioning - at 6 months												

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Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of trials	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	WHO SMT	sham/placebo SMT	Relative (95% CI)	Absolute (95% CI)		
1	randomized trials	very serious[t]	serious[i]	serious[i]	very serious[h]	none			-	Data was not pooled, because they used different measurements	⨁◯◯◯ Very low	

Psychological functioning - at **12 months - not reported** (subgroup analysis of psychological functioning not conducted as data could not be pooled)

CI: confidence interval; **MD:** mean difference; **RR:** risk ratio; **SMD:** standardised mean difference

Explanations

a. Downgrade due to the presence of performance bias (lack of patient blinding) in all trials. We did not downgrade for the other risk of bias domains because most of the weight (>50%) comes from trials with a low risk of bias.
b. Downgrade because $I^2 > 75\%$, and treatment effects were in different directions, and were not able to be explained. Poor overlap of 95% CIs
c. We did not downgrade because trials were included from different countries, from different settings and populations.
d. Downgraded for the following: 1) sample <2000 participants; anTd 2) the lower 95% CI crosses the barrier of a potentially clinically-relevant threshold and the upper border is in favour of the control group.
e. Downgraded due to selection bias (unclear treatment allocation), performance bias (unclear risk due to co-interventions and compliance), and high risk of attrition bias.
f. Not downgraded due to treatment effect are similar, $I^2<50\%$ and CIs overlap
g. Downgraded because all trials that provided data were small for this outcome; single-center trials and not from different settings or countries .
h. Downgraded because <2,000 participants were included.
i. Downgraded because just one (small) trial provided data for this outcome; single-center trial and therefore not from different settings or countries.
j. Downgrade because treatment effects were in different directions. Poor overlap of 95% CIs. $I^2 > 50\%$
k. Downgrade due to attrition bias.
l. Downgraded although the $I^2 < 50\%$, the treatment effects were in different directions.
m. Downgraded due to selection bias (unclear treatment allocation), and high risk of attrition bias.
n. Downgraded because of a high risk of performance bias (patients and clinicians were not blinded in a majority of the trials) and unclear risk of selection bias (e.g. treatment allocation).
o. Downgraded one level because there were <2,000 participants but more than 1000 and the 95% CI was relatively broad (including a strong, clinically-relevant effect and no effect).
p. Not downgraded due to treatment effect are similar, $I^2<75\%$ and CIs overlap
q. Downgraded due to selection bias (unclear treatment allocation), performance bias (unclear risk of blinding patients and clinicians), and high risk of attrition bias and selective outcome reporting bias.
r. Downgraded because data comes one trial, small in size.
s. Downgraded one level as almost 1000 participants were included
t. Downgraded due to presence of performance bias and high risk of attrition bias.

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GRADE Table 2. ***What are the benefits and harms of SMT in the management of community-dwelling adults (including older adults aged 60 years and over) with chronic primary low back pain (with or without leg pain) compared with no intervention?***

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of trials	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	SMT	no intervention	Relative (95% CI)	Absolute (95% CI)		
Pain intensity (higher scores mean more pain)												
Pain - Pain at 1 month												
4	randomized trials	serious[a]	serious[b]	serious[c]	very serious[e]	none	218	107	-	MD **14 lower** (27.35 lower to 0.64 lower)	⨁◯◯◯ Very low	
Population subgroups 1, 2 and 3 - not reported (no subgroup analysis performed)												
Population subgroup 4: regional economic development - High-income countries												
3	randomized trials	serious[a]	serious[b]	serious[c]	very serious[e]	none	198	87	-	MD **8.8 lower** (18.17 lower to 0.57 higher)	⨁◯◯◯ Very low	
Population subgroup 4: regional economic development - Low- or lower middle-income Income countries												
1	randomized trials	serious[a]	serious[i]	serious[c]	very serious[e]	none	20	20	-	MD **36 lower** (43.9 lower to 28.1 higher)	⨁◯◯◯ Very low	
Pain - Pain at 3 months												
1	randomized trials	very serious[f]	serious[i]	serious[c]	very serious[e]	none	36	16	-	MD **14.2 lower** (26.89 lower to 1.51 lower)	⨁◯◯◯ Very low	
Population subgroups 1, 2 and 3 - not reported (no subgroup analysis performed) **Population subgroup 4: regional economic development - High-income countries**												
1	randomized trials	serious[f]	serious[i]	serious[c]	very serious[e]	none	36	16	-	MD **14.2 lower** (26.89 lower to 1.51 lower)	⨁◯◯◯ Very low	

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Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of trials	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	SMT	no intervention	Relative (95% CI)	Absolute (95% CI)		
Population subgroup 4: regional economic development - Low- or lower middle-income Income countries - not reported												
Pain - Pain at 6 months												
1	randomized trials	very serious[f]	serious[i]	serious[c]	very serious[e]	none	32	15	-	MD **4.9 lower** (18.68 lower to 8.88 higher)	⨁◯◯◯ Very low	
Population subgroups 1, 2 and 3 - not reported (no subgroup analysis performed)												
Population subgroup 4: regional economic development - High-income countries												
1	randomized trials	very serious[f]	serious[i]	serious[c]	very serious[e]	none	32	15	-	MD **4.9 higher** (18.68 higher to 8.88 higher)	⨁◯◯◯ Very low	
Population subgroup 4: regional economic development - Low- or lower middle-income Income countries - not reported												
Pain - Pain at 12 months - not reported												
Back-specific functional status (higher scores mean more disability)												
Back-specific functional status - back-specific functional status at 1 month –												
4	randomized trials	serious[a]	not serious[g]	serious[c]	very serious[e]	none	205	107	-	SMD **0.57 lower** (0.82 lower to 0.32 lower)	⨁◯◯◯ Very low	
Population subgroups 1, 2, and 3 - not reported **Population subgroup 4: regional economic development - High-income countries**												
3	randomized trials	serious[a]	not serious[g]	serious[c]	very serious[e]	none	185	87	-	SMD **0.6 SD lower** (0.89 lower to 0.31 lower)	⨁◯◯◯ Very low	
Population subgroup 4: regional economic development - Low- or lower middle-income countries												

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Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of trials	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	SMT	no intervention	Relative (95% CI)	Absolute (95% CI)		
1	randomized trials	serious[a]	serious[i]	serious[c]	very serious[e]	none	20	20	-	SMD **0.38 SD lower** (1.01 lower to 0.24 higher)	⨁◯◯◯ Very low	
Population subgroup 5: ODI												
2	randomized trials	serious[a]	not serious[g]	serious[c]	very serious[e]	none	34	48	-	SMD **0.36 SD lower** (0.81 lower to 0.09 higher)	⨁◯◯◯ Very low	
Population subgroup 5: RMDQ												
2	randomized trials	serious[a]	not serious[g]	serious[c]	very serious[e]	none	171	59	-	SMD **0.66 SD lower** (1 lower to 0.33 lower)	⨁◯◯◯ Very low	
Back-specific functional status - back-specific functional status at 3 months												
1	randomized trials	very serious[f]	serious[i]	serious[c]	very serious[e]	none	36	17	-	SMD **0.03 higher** (0.54 lower to 0.61 higher)	⨁◯◯◯ Very low	
Population subgroups 1, 2 and 3 - not reported (no subgroup analysis performed) **Population subgroup 4: regional economic development - High-income countries**												
1	randomized trials	very serious[f]	serious[e]	serious[e]	very serious[e]	none	36	17	-	SMD **0.03 higher** (0.54 lower to 0.61 higher)	⨁◯◯◯ Very low	
Back-specific functional status - back-specific functional status at 6 months												
1	randomized trials	very serious[f]	serious[e]	serious[e]	very serious[e]	none	32	15	-	SMD **0.18 lower** (0.8 lower to 0.43 higher)	⨁◯◯◯ Very low	

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Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of trials	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	SMT	no intervention	Relative (95% CI)	Absolute (95% CI)		
Population subgroups 1, 2 and 3 - not reported (no subgroup analysis performed) **Population subgroup 4: regional economic development - High-income countries**												
1	randomized trials	serious[f]	serious[e]	serious[e]	very serious[e]	none	32	15	-	SMD **0.18 lower** (0.8 lower to 0.43 higher)	⨁◯◯◯ Very low	
Back-specific functional status - back-specific functional status at 12 months - not reported												
Health-related quality of life (higher scores mean better health) **Health-related quality of life - Health-related quality of life at 1 month**												
1	randomized trials	serious[i]	serious[e]	serious[e]	very serious[e]	none	129	42	-	MD **4.95 higher** (3.2 higher to 6.71 higher)	⨁◯◯◯ Very low	
Health-related quality of life - Health-related quality of life at 3 months, 6 months or 12 months - not reported												
General functional status (higher scores mean less disability) **General functional status - functional status at 1 month**												
1	randomized trials	very serious[f]	serious[i]	serious[c]	very serious[e]	none	42	17	-	MD **5.5 higher** (1.99 lower to 12.99 higher)	⨁◯◯◯ Very low	
General functional status - functional status at 3 months												
1	randomized trials	very serious[f]	serious[e]	serious[e]	very serious[e]	none	36	17	-	MD **10.4 higher** (2.79 higher to 18.01 higher)	⨁◯◯◯ Very low	
General functional status - functional status at 6 months												

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Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of trials	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	SMT	no intervention	Relative (95% CI)	Absolute (95% CI)		
1	randomized trials	very serious[f]	serious[e]	serious[e]	very serious[e]	none	32	15	-	MD **8.5 higher** (0.12 higher to 16.88 higher)	⨁◯◯◯ Very low	
General functional status - Functional status at 12 months - not reported												
Psychological functioning - at 1 month												
2	randomized trials	very serious[f]	Serious[i]	Serious[c]	very serious[e]	none			-	Data was not pooled, because they used different measurements	⨁◯◯◯ Very low	
Psychological functioning - at 3 months												
1	randomized trials	very serious[f]	Serious[i]	Serious[c]	very serious[e]	none			-	Data was not pooled, because they used different measurements	⨁◯◯◯ Very low	
Psychological functioning - at 6 months												
1	randomized trials	very serious[f]	serious[i]	serious[c]	very serious[e]	none			-	Data was not pooled, because they used different measurements	⨁◯◯◯ Very low	
Psychological functioning - at **12 months - not reported**												
Subgroups for psychological functioning were not conducted as data could not be pooled												

CI: confidence interval; **MD:** mean difference; **SMD:** standardised mean difference

Explanations

a. Downgraded due to the presence of performance bias (lack of patient blinding) in all trials. We did not downgrade for the other risk of bias domains because most of the weight (>50%) comes from trials with a low risk of bias.

b. Downgraded due to the presence of statistical heterogeneity (I2 = 68%) which could not be explained by subgroup analysis. In addition, the treatment effects and corresponding 95% CI varied in direction.
c. Downgraded because data comes from only single-centre trials and data does not come from different settings or countries.
d. Downgraded because the upper 95% CI crosses the barrier of a potentially clinically-relevant threshold and the lower border is close to no effect.
e. Downgraded because less than 2000 participants provided data for this outcome.
f. Downgraded due to the presence of high risk of performance bias (lack of patient blinding), attrition bias and selective reporting.
g. Not downgraded because the $I^2 < 50\%$, and there was sufficient overlap of the 95% CI's.
h. Downgraded because relatively few participants were recruited.
i. Downgraded due to the presence of performance bias (lack of patient blinding).
j. Downgraded because data comes from one trial small in size.

GRADE Table 3. ***What are the benefits and harms of SMT in the management of community-dwelling adults (including older adults aged 60 years and over) with chronic primary low back pain (with or without leg pain) compared with usual care?***

One trial: data could not be extracted for GRADE assessment.

GRADE Table 4. ***What are the benefits and harms of SMT as an adjuvant therapy in the management of community-dwelling adults (including older adults aged 60 years and over) with chronic primary low back pain (with or without leg pain)*?**

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Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of trials	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	SMT with an intervention	Same intervention alone	Relative (95% CI)	Absolute (95% CI)		
Pain intensity (higher scores mean more pain)												
Pain - Pain at 1 month												
10	randomized trials	serious[a]	serious[b]	not serious[c]	not serious[d]	none	650	864	-	MD **5.16 lower** (9.32 lower to 1 lower)	⨁⨁◯◯ Low	
Population subgroups 1, 2 and 3 - not reported (no subgroup analysis performed)												
Population subgroup 4: regional economic development - high-income countries												
6	randomized trials	serious[a]	serious[b]	not serious[c]	not serious[d]	none	479	691	-	MD **3.13 lower** (7.73 higher to 1.48 higher)	⨁⨁◯◯ Low	
Population subgroup 4: regional economic development low- or lower middle-income income countries												
4	randomized trials	serious[a]	not serious[e]	serious[f]	very serious[g]	none	171	173	-	MD **9.05 lower** (14.71 lower to 3.39 lower)	⨁◯◯◯ Very low	
Population subgroup 5: participants over 60 years of age												
1	randomized trials	serious[a]	serious[n]	serious[h]	very serious[g]	none	87	79	-	MD **2.9 lower** (8.85 lower to 3.05 higher)	⨁◯◯◯ Very low	
Pain - Pain at 3 months												

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Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of trials	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	SMT with an intervention	Same intervention alone	Relative (95% CI)	Absolute (95% CI)		
5	randomized trials	serious[a]	not serious[e]	not serious[c]	not serious[d]	none	739	658	-	MD **4.34 lower** (8.83 lower to 0.15 higher)	⨁⨁⨁◯ Moderate	
Population subgroups 1 and 2 - not reported (no subgroup analysis performed)												
Population subgroup 3: presence of radicular pain												
1	randomized trials	serious[a]	Serious[n]	serious[h]	very serious[g]	none	96	96	-	MD **9 lower** (24.42 lower to 6.42 higher)	⨁◯◯◯ Very low	
Population subgroup 4: regional economic development - high-income countries												
4	randomized trials	serious[a]	not serious[e]	not serious[c]	not serious[d]	none	722	640	-	MD **6.4 lower** (9.053 lower to 3.76 higher)	⨁⨁⨁◯ Moderate	
Population subgroup 4: regional economic development - low- or lower middle-income income countries												
1	randomized trials	serious[a]	serious[i]	serious[f]	very serious[g]	none	171	173	-	MD **1.20 lower** (1.32 lower to 3.72 higher)	⨁◯◯◯ Very low	
Population subgroup 5: participants 60 years and older												

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Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of trials	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	SMT with an intervention	Same intervention alone	Relative (95% CI)	Absolute (95% CI)		
1	randomized trials	serious[a]	serious[n]	serious[h]	very serious[g]	none	80	76	-	MD **7.9 lower** (13.89 lower to 1.91 lower)	⨁◯◯◯ Very low	
Pain - Pain at 6 months												
3	randomized trials	serious[a]	serious[b]	not serious[c]	very serious[i]	none	206	204	-	MD **4.22 lower** (15.12 lower to 6.67 higher)	⨁◯◯◯ Very low	
Population subgroups 1, 2 and 3 - not reported (no subgroup analysis performed)												
Population subgroup 4: regional economic development - high-income countries												
1	randomized trials	serious[a]	serious[n]	serious[h]	very serious[g]	none	79	77	-	MD **1.2 higher** (4.82 lower to 7.22 higher)	⨁◯◯◯ Very low	
Population subgroup 4: regional economic development - low- or lower middle-income income countries												
2	randomized trials	serious[a]	serious[l]	serious[f]	very serious[g]	none	127	127	-	MD **10.8 lower** (13.2 lower to 8.4 lower)	⨁◯◯◯ Very low	
Population subgroup 5: participants 60 years and older												

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Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of trials	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	SMT with an intervention	Same intervention alone	Relative (95% CI)	Absolute (95% CI)		
1	randomized trials	serious[a]	serious[n]	serious[f]	very serious[g]	none	79	77	-	MD **1.2 higher** (4.82 lower to 7.22 higher)	⨁◯◯◯ Very low	
Pain - Pain at 12 months												
5	randomized trials	serious[a]	not serious [e]	not serious[c]	not serious[d]	none	823	745	-	MD **3.92 higher** (8.53 lower to 0.69 higher)	⨁⨁⨁◯ Moderate	
Population subgroups 1 and 2 - not reported (no subgroup analysis performed)												
Population subgroup 3: presence of radicular pain												
1	randomized trials	serious[a]	Serious[n]	serious[h]	very serious[g]	none	96	96	-	MD **4 lower** (21.45 lower to 13.45 higher)	⨁◯◯◯ Very low	
Population subgroup 4: regional economic development - high-income countries												
4	randomized trials	serious[a]	not serious[k]	not serious[c]	not serious[d]	none	713	635	-	MD **2.42 lower** (5.19 lower to 0.35 higher)	⨁⨁⨁◯ Moderate	
Population subgroup 4: regional economic development - low- or lower middle-income income countries												

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Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of trials	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	SMT with an intervention	Same intervention alone	Relative (95% CI)	Absolute (95% CI)		
1	randomized trials	serious[a]	serious[b]	serious[h]	very serious[g]	none	110	110	-	MD **10.4 lower** (13.01 lower to 7.79 lower)	⨁◯◯◯ Very low	
Population subgroup 5: participants 60 years and older												
1	randomized trials	serious[a]	Serious[n]	serious[h]	very serious[g]	none	80	76	-	MD **1.30 lower** (4.69 lower to 7.29 higher)	⨁◯◯◯ Very low	
Back-specific functional status - back-specific functional status at 1 month (higher score mean more disability)												
7	randomized trials	serious[a]	serious[b]	not serious[c]	serious[i]	none	573	792	-	SMD **0.38 lower** (0.73 lower to 0.04 lower)	⨁◯◯◯ Very low	
Population subgroups 1, 2 and 3 - not reported (no subgroup analysis performed)												
Population subgroup 4: regional economic development - high-income countries												
5	randomized trials	serious[a]	serious[b]	not serious[c]	serious[i]	none	446	663	-	SMD **0.14 SD lower** (0.36 lower to 0.09 higher)	⨁◯◯◯ Very low	
Population subgroup 4: regional economic development - low- or lower middle-income income countries												

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Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of trials	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	SMT with an intervention	Same intervention alone	Relative (95% CI)	Absolute (95% CI)		
2	randomized trials	serious[a]	serious[k]	serious[f]	very serious[g]	none	127	129	-	SMD **1.05 SD lower** (1.39 lower to 0.71 lower)	⨁◯◯◯ Very low	
Population subgroup 5: participants 60 years and older												
1	randomized trials	serious[a]	serious[n]	serious[h]	very serious[g]	none	81	79	-	SMD **0.08 SD higher** (0.23 lower to 0.39 higher)	⨁◯◯◯ Very low	
Population subgroup 6: ODI												
3	randomized trials	serious[a]	serious[b]	serious[f]	very serious[g]	none	75	80	-	SMD **0.73 SD lower** (1.48 lower to 0.02 higher)	⨁◯◯◯ Very low	
Population subgroup 6: RMDQ												
6	randomized trials	serious[a]	serious[b]	not serious[c]	serious[i]	none	523	742	-	SMD **0.4 SD lower** (0.8 lower to 0.01 lower)	⨁◯◯◯ Very low	
Back-specific functional status - back-specific functional status at 3 months												
5	randomized trials	serious[a]	not serious[k]	not serious[c]	serious[i]	none	763	696	-	SMD **0.13 lower** (0.29 lower to 0.03 higher)	⨁⨁◯◯ Low	
Population subgroups 1 and 2 - not reported (no subgroup analysis performed)												

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Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of trials	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	SMT with an intervention	Same intervention alone	Relative (95% CI)	Absolute (95% CI)		
Population subgroup 3: presence of radicular pain												
1	randomized trials	serious[a]	serious[h]	serious[h]	very serious[g]	none	96	96	-	SMD **0.19 SD lower** (0.47 lower to 0.1 higher)	⨁◯◯◯ Very low	
Population subgroup 4: regional economic development - high-income countries												
4	randomized trials	serious[a]	not serious[e]	not serious[c]	serious[i]	none	746	687	-	SMD **0.14 SD lower** (0.31 lower to 0.03 higher)	⨁⨁◯◯ Low	
Population subgroup 4: regional economic development - low- or lower middle-income income countries												
1	randomized trials	serious[a]	Serious[n]	serious[f]	very serious[g]	none	17	18	-	SMD **0.11 SD higher** (0.55 lower to 0.77 higher)	⨁◯◯◯ Very low	
Population subgroup 5: participants 60 years and older												
1	randomized trials	serious[a]	Serious[n]	serious[h]	very serious[g]	none	80	76	-	SMD **0.01 SD lower** (0.32 lower to 0.31 higher)	⨁◯◯◯ Very low	
Population subgroup 6: RMDQ												
5	randomized trials	serious[a]	serious[k]	not serious[c]	serious[i]	none	763	696	-	SMD **0.13 SD lower** (0.29 lower to 0.03 higher)	⨁◯◯◯ Very low	

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Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of trials	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	SMT with an intervention	Same intervention alone	Relative (95% CI)	Absolute (95% CI)		
Back-specific functional status (higher scores mean more disability)												
Back-specific functional status - back-specific functional status at 6 months												
3	randomized trials	serious[a]	serious[b]	not serious[c]	very serious[i]	none	206	204	-	SMD **0.4 lower** (0.91 lower to 0.11 higher)	⨁◯◯◯ Very low	
Population subgroups 1, 2 and 3 - not reported (no subgroup analysis performed)												
Population subgroup 4: regional economic development - high-income countries												
1	randomized trials	serious[a]	Serious[n]	serious[h]	very serious[g]	none	79	77	-	SMD **0.28 SD lower** (0.6 lower to 0.04 higher)	⨁◯◯◯ Very low	
Population subgroup 4: regional economic development - low- or lower middle-income income countries												
2	randomized trials	serious[a]	serious[b]	serious[f]	very serious[g]	none	127	127	-	SMD **0.43 SD lower** (1.34 lower to 0.49 higher)	⨁◯◯◯ Very low	
Population subgroup 5: participants 60 years and older												
1	randomized trials	serious[a]	Serious[n]	serious[h]	very serious[g]	none	79	77	-	SMD **0.28 SD lower** (0.6 lower to 0.04 lower)	⨁◯◯◯ Very low	
Population subgroup 6: ODI												

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Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of trials	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	SMT with an intervention	Same intervention alone	Relative (95% CI)	Absolute (95% CI)		
1	randomized trials	serious[a]	Serious[n]	serious[h]	very serious[g]	none	17	17	-	SMD **0.05 SD higher** (0.62 lower to 0.73 higher)	⨁◯◯◯ Very low	
Population subgroup 6: RMDQ												
3	randomized trials	serious[a]	serious[b]	not serious[c]	very serious[g]	none	206	204	-	SMD **0.4 SD lower** (0.91 lower to 0.11 higher)	⨁◯◯◯ Very low	
Back-specific functional status - back-specific functional status at 12 months												
4	randomized trials	serious[a]	not serious[e]	not serious[c]	serious[i]	none	816	746	-	SMD **0.23 lower** (0.43 lower to 0.03 lower)	⨁⨁◯◯ Low	
Population subgroups 1 and 2 - not reported (no subgroup analysis performed)												
Population subgroup 3: presence of radicular pain												
1	randomized trials	serious[a]	Serious[n]	serious[f]	very serious[g]	none	96	96	-	SMD **0.1 SD lower** (0.38 lower to 0.19 higher)	⨁◯◯◯ Very low	
Population subgroup 4: regional economic development - high-income countries												
3	randomized trials	serious[a]	not serious[k]	not serious[c]	serious[i]	none	706	636	-	SMD **0.16 SD lower** (0.27 lower to 0.05 lower)	⨁⨁◯◯ Low	

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Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of trials	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	SMT with an intervention	Same intervention alone	Relative (95% CI)	Absolute (95% CI)		
Population subgroup 4: regional economic development - low- or lower middle-income income countries												
1	randomized trials	serious[a]	Serious[n]	serious[h]	very serious[g]	none	110	110	-	SMD **0.67 SD lower** (0.94 lower to 0.4 lower)	⨁◯◯◯ Very low	
Population subgroup 5: participants 60 years and older												
1	randomized trials	serious[a]	Serious[n]	serious[h]	very serious[g]	none	80	76	-	SMD **0.08 SD higher** (0.23 lower to 0.4 higher)	⨁◯◯◯ Very low	
Population subgroup 6: RMDQ												
4	randomized trials	serious[a]	serious[b]	not serious[c]	serious[i]	none	816	746	-	SMD **0.23 SD lower** (0.43 lower to 0.03 lower)	⨁◯◯◯ Very low	
Health-related quality of life - Health-related quality of life at 1 month (higher scores mean better health)												
1	randomized trials	serious[a]	Serious[n]	serious[h]	very serious[h]	none	81	79	-	MD **0.6 SD higher** (1.25 lower to 2.45 higher)	⨁◯◯◯ Very low	
Population subgroups 1, 2 and 3 - not reported (no subgroup analysis performed)												
Population subgroup 4: regional economic development - not reported (No subgroup analysis performed; only one trial)												
Population subgroup 5: participants 60 years and older												

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Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of trials	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	SMT with an intervention	Same intervention alone	Relative (95% CI)	Absolute (95% CI)		
1	randomized trials	serious[a]	serious[n]	serious[h]	very serious[g]	none	81	79	-	MD **0.6 higher** (1.25 lower to 2.45 higher)	⨁◯◯◯ Very low	
Health-related quality of life (higher scores mean better health)												
Health-related quality of life - Health-related quality of life at 3 months												
3	randomized trials	serious[a]	not serious[k]	not serious[c]	very serious[l]	none	435	399	-	MD **1.78 SD higher** (0.19 higher to 3.36 higher)	⨁◯◯◯ Very low	
Population subgroups 1 and 2 - not reported (no subgroup analysis performed)												
Population subgroup 3: presence of radicular pain												
1	randomized trials	serious[a]	serious[n]	serious[h]	very serious[g]	none	96	96	-	MD **3.4 higher** (3.2 lower to 10 higher)	⨁◯◯◯ Very low	
Population subgroup 4: regional economic development - not reported												
Population subgroup 5: participants 60 years and older												
1	randomized trials	serious[a]	serious	serious[h]	very serious[g]	none	80	76	-	MD **0.5 higher** (1.38 lower to 2.38 higher)	⨁◯◯◯ Very low	
Health-related quality of life - Health-related quality of life at 6 months												

Web Annex D.B3: ETD summary for WHO Guideline on non-surgical management of chronic primary low back pain in adults

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of trials	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	SMT with an intervention	Same intervention alone	Relative (95% CI)	Absolute (95% CI)		
1	randomized trials	serious[a]	Serious[n]	serious[h]	very serious[h]	none	79	77	-	SMD **0.3 SD lower** (2.21 lower to 1.61 higher)	⨁◯◯◯ Very low	
Population subgroups 1, 2, 3 and 4 - not reported (no subgroup analysis performed)												
Population subgroup 5: participants 60 years and older												
1	randomized trials	serious[a]	Serious[n]	serious[h]	very serious[g]	none	79	77	-	MD **0.3 lower** (2.21 lower to 1.61 higher)	⨁◯◯◯ Very low	
Health-related quality of life - Health-related quality of life at 12 months												
4	randomized trials	serious[a]	serious[b]	not serious[c]	serious[l]	none	428	393	-	MD **0.31 higher** (2.29 lower to 2.91 higher)	⨁◯◯◯ Very low	
Population subgroups 1 and 2 - not reported (no subgroup analysis performed)												
Population subgroup 3: presence of radicular pain												
1	randomized trials	serious[a]	Seriousn	serious[h]	very serious[g]	none	96	96	-	MD **1.5 higher** (4.96 lower to 7.96 higher)	⨁◯◯◯ Very low	
Population subgroup 4: regional economic development – not reported (No subgroup analysis performed; only one trial)												
Population subgroup 5: participants 60 years and older												

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№ of trials	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	SMT with an intervention	Same intervention alone	Relative (95% CI)	Absolute (95% CI)		
1	randomized trials	serious[a]	Serious	serious[h]	very serious[g]	none	80	76	-	MD **1.5 lower** (3.38 lower to 0.38 higher)	⨁◯◯◯ Very low	
Psychological functioning - Psychological functioning at 1 month												
1	randomized trials	serious[a]	Serious[n]	serious[h]	very serious[g]	none	81	79	-	MD **0.4 SD higher** (1.38 lower to 2.18 higher)	⨁◯◯◯ Very low	
Psychological functioning - Psychological functioning at 3 months												
3	randomized trials	serious[a]	not serious[k]	not serious[c]	very serious[g]	none	435	399	-	MD **1.33 SD higher** (0.91 lower to 3.58 higher)	⨁◯◯◯ Very low	
Psychological functioning - Psychological functioning at 6 months												
1	randomized trials	serious[a]	Serious[n]	serious[h]	very serious[h]	none	79	77	-	MD **1.7 SD higher** (0.18 lower to 3.58 higher)	⨁◯◯◯ Very low	
Psychological functioning - Psychological functioning at 12 months												
3	randomized trials	serious[a]	serious[b]	not serious[c]	very serious[g]	none	428	393	-	MD **0.42 SD higher** (1.42 lower to 2.27 higher)	⨁◯◯◯ Very low	
Subgroup analysis of psychological functioning not conducted.												

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CI: confidence interval; **MD:** mean difference; **SMD:** standardised mean difference

Explanations

a. Downgrade due to the presence of performance bias (lack of patient blinding) in all trials. We did not downgrade for the other risk of bias domains because most of the weight (>50%) comes from trials with a low risk of bias.
b. Downgraded suggesting substantial statistical heterogeneity (I2 >50%). In addition, the treatment effects and corresponding 95% CI varied in direction and could not be explained.
c. We did not downgrade because trials were included from different countries, from different settings and populations.
d. Not downgraded. The 95% CI's are sufficiently narrow and do not across the line of no effect nor the clinically-relevant threshold.
e. Not downgraded because although the I^2 is high, all treatment effects were in the same direction, except one small trial, and there was sufficient overlap of the 95% CI's.
f. Downgraded because only single centered (small) trials and data does not come from different settings or countries.
g. Downgraded because < 2000 participants, very few participants were recruited.
h. Downgraded because just one (small) trial provided data for this outcome, therefore data does not come from different settings or countries..
i. Downgraded for the following: the lower 95% CI crosses the barrier of a potentially clinically-relevant threshold, and the upper border is close to no effect.
j. Downgraded for the following: 1) 410 participants; and 2) the lower 95% CI crosses the barrier of a potentially clinically-relevant threshold and the upper border is in favour of the control group.
k. Not downgraded because the I^2 < 50%, and there was sufficient overlap of the 95% CI's.
l. Downgraded because the upper 95% CI crosses the barrier of a potentially clinically-relevant threshold, and the lower border is close to no effect.
m. Downgraded because data is provided from almost 1000 participants.
n. Downgraded because data comes from one trial, small in size.