C.2 Respondent therapy

Overview of the PICO structure

Definition of the intervention	
Respondent therapy aims to modify the physiological response system to pain through the reduction of muscular tension through biofeedback, progressive relaxation and applied relaxation. This type of therapy is aligned with relaxation therapy.	
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)

Web Annex D.C2: ETD summary for WHO Guideline on non-surgical management of chronic primary low back pain in adults

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 • Self-efficacy • 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)

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	Small; trivial; uncertain	Uncertain
Harms	Trivial; uncertain	Uncertain
Balance benefits to harms	Uncertain	Uncertain

Web Annex D.C2: ETD summary for WHO Guideline on non-surgical management of chronic primary low back pain in adults

Overall certainty	Very low	Very low
Values and preferences	Important uncertainty or variability; possibly important uncertainty or variability	Important uncertainty or variability; possibly important uncertainty or variability
Resource considerations	Moderate; large; varies	Moderate; large; varies
Equity and human rights	Possibly reduced; no impact; uncertain; varies	Possibly reduced; no impact; uncertain; varies
Acceptability	Probably yes; probably no; varies	Probably yes; probably no; varies
Feasibility	Varies	Varies

Web Annex D.C2: ETD summary for WHO Guideline on non-surgical management of chronic primary low back pain in adults

GRADE Table 1. ***What are the benefits and harms of respondent 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) compared with placebo?***

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Respondent therapy	Placebo	Relative (95% CI)	Absolute (95% CI)		
Pain - short term												
2	randomized trials	serious[a]	not serious	not serious	serious[b]	none	29	29	-	MD **6.21 lower** (14.94 lower to 2.52 higher)	⨁⨁◯◯ Low	
Population subgroups 1, 2, 3 and 4 - not reported (no subgroup analysis was performed)												
Pain - intermediate term or long term – no studies identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	
Back-specific functional status – short term												
2	randomized trials	serious[a]	not serious	not serious	serious[b]	none	29	29	-	SMD **0.07 higher** (0.45 lower to 0.58 higher)	⨁⨁◯◯ Low	
Population subgroups 1, 2, 3 and 4 - not reported (no subgroup analysis was performed)												
Back-specific functional status - intermediate term or long term: no studies identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	
General functional status - short term, intermediate term or long term: no studies identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	
Health-related quality of life - short term, intermediate term or long term: no studies identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	

Web Annex D.C2: 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 studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Respondent therapy	Placebo	Relative (95% CI)	Absolute (95% CI)		
Adverse events or serious adverse events: no studies identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	
Psychological functioning - short term, intermediate term or long term: no studies identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	
Social participation - short term, intermediate term or long term: no studies identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	
Self-efficacy - short term, intermediate term or long term: no studies identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	

CI: confidence interval; MD: mean difference; SMD: standardized mean difference

Explanations

[a]Risk of bias downgraded by 1 level: due to unclear or high risk of bias in one study regarding random sequence generation, allocation concealment, blinding of care providers, blinding of outcome assessment, incomplete outcome data, selective reporting, similarity of groups at baseline, co-interventions, and compliance with the intervention.

[b]Imprecision downgraded by 1 level: low number of participants

GRADE Table 2.1. ***What are the benefits and harms of respondent therapy (biofeedback) 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 studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Respondent therapy	No intervention	Relative (95% CI)	Absolute (95% CI)		
Pain - short term												
3	randomized trials	very serious[a]	not serious	not serious	serious[b]	none	53	47	-	SMD **0.66 lower** (1.1 lower to 0.22 lower)	⨁◯◯◯ Very low	
Population subgroups 1, 2 and 3 - not reported (no subgroup analysis was performed)												
Population subgroup 4: regional economic development												
Low/middle income 1	randomized trials	very serious[a]	not serious	not serious	serious[b]	None	27	25	-	SMD **0.53 lower** (1.08 lower to 0.03 higher)	⨁◯◯◯ Very low	
High income 2	randomized trials	very serious[a]	not serious	not serious	serious[b]	None	26	22	-	SMD **0.79 lower** (1.6 lower to 0.01 higher)	⨁◯◯◯ Very low	
Pain - intermediate term or long term: no studies identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	
Back-specific functional status – short term												
2	randomized trials	very serious[a]	not serious	not serious	serious[b]	none	43	37	-	SMD **0.62 lower** (1.07 lower to 0.17 lower)	⨁◯◯◯ Very low	

Web Annex D.C2: 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 studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Respondent therapy	No intervention	Relative (95% CI)	Absolute (95% CI)		
Population subgroups 1, 2 and 3 - not reported (no subgroup analysis was performed)												
Population subgroup 4: regional economic development												
Low/middle income 1	randomized trials	very serious[a]	not serious	not serious	serious[b]	None	27	25	-	SMD **0.51 lower** (1.06 lower to 0.04 higher)	⨁◯◯◯ Very low	
High income 1	randomized trials	very serious[a]	not serious	not serious	serious[b]	None	16	12	-	SMD **0.85 lower** (1.64 lower to 0.06 lower)	⨁◯◯◯ Very low	
Back-specific functional status - intermediate term or long term: no studies identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	
General functional status - short term, intermediate term or long term: no studies identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	
Health-related quality of life - short term, intermediate term or long term: no studies identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	
Adverse events or serious adverse events: no studies identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	
Psychological functioning (anxiety) - short term												
2	randomized trials	very serious[a]	not serious	not serious	serious[b]	none	43	37	-	MD **5.15 lower** (8.74 lower to 1.57 lower)	⨁◯◯◯ Very low	
Population subgroups 1, 2 and 3 - not reported (no subgroup analysis was performed)												

Web Annex D.C2: 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 studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Respondent therapy	No intervention	Relative (95% CI)	Absolute (95% CI)		
Population subgroup 4: regional economic development												
Low/middle income 1	randomized trials	very serious[a]	not serious	not serious	serious[b]	None	27	25	-	MD **5.3 lower** (9.32 lower to 1.28 lower)	⨁◯◯◯ Very low	
High income 1	randomized trials	very serious[a]	not serious	not serious	serious[b]	None	16	12	-	MD **4.58 lower** (12.46 lower to 3.3 higher)	⨁◯◯◯ Very low	
Psychological functioning (depression) - short term												
2	randomized trials	very serious[a]	not serious	not serious	serious[b]	none	43	37	-	MD **3.78 lower** (8.06 lower to 0.5 higher)	⨁◯◯◯ Very low	
Population subgroups 1, 2 and 3 - not reported (no subgroup analysis was performed)												
Population subgroup 4: regional economic development												
Low/middle income 1	randomized trials	very serious[a]	not serious	not serious	serious[b]	None	27	25	-	MD **0.52 lower** (7.37 lower to 6.33 higher)	⨁◯◯◯ Very low	
High income 1	randomized trials	very serious[a]	not serious	not serious	serious[b]	None	16	12	-	MD **5.24 lower** (9.03 lower to 1.45 lower)	⨁◯◯◯ Very low	
Psychological functioning (coping) - short term												

Web Annex D.C2: 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 studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Respondent therapy	No intervention	Relative (95% CI)	Absolute (95% CI)		
1	randomized trials	very serious[a]	not serious[c]	not serious	serious[b]	none	16	12	-	MD **6.92 higher** (10.83 lower to 24.67 higher)	⨁◯◯◯ Very low	
Population subgroups 1, 2, 3 and 4 - not reported (no subgroup analysis was performed; only one included study on this outcome)												
Psychological functioning - intermediate term or long term: no studies identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	
Social participation - short term, intermediate term or long term: no studies identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	
Self-efficacy - short term, intermediate term or long term: no studies identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	

CI: confidence interval; MD: mean difference; SMD: standardized mean difference

Explanations

[a]Risk of bias downgraded by 2 levels: due to unclear or high risk of bias across all studies regarding random sequence generation, allocation concealment, blinding of participants, blinding of care providers, blinding of outcome assessment, incomplete outcome data, selective reporting, similarity of groups at baseline, co-interventions, and compliance with the intervention.

[b]Imprecision downgraded by 1 level: low number of participants.

[c]Inconsistency not assessed because only one study included in this analysis.

GRADE Table 2.2. ***What are the benefits and harms of respondent therapy (relaxation) 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 studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Respondent therapy	No intervention	Relative (95% CI)	Absolute (95% CI)		
Pain - short term												
2	randomized trials	very serious[a]	serious[b]	not serious	very serious[c]	none	31	27	-	MD **21.8 lower** (45.78 lower to 2.17 higher)	⨁◯◯◯ Very low	
Population subgroups 1, 2, 3 and 4 - not reported (no subgroup analysis was performed)												
Pain - intermediate term or long term – no studies identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	
Back-specific functional status – short term												
2	randomized trials	very serious[a]	not serious	not serious	serious[d]	none	31	27	-	SMD **0.97 lower** (1.52 lower to 0.41 lower)	⨁◯◯◯ Very low	
Population subgroups 1, 2, 3 and 4 - not reported (no subgroup analysis was performed)												
Back-specific functional status - intermediate term or long term: no studies identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	
General functional status - short term, intermediate term or long term: no studies identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	
Health-related quality of life - short term, intermediate term or long term: no studies identified that reported on this outcome												

Web Annex D.C2: 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 studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Respondent therapy	No intervention	Relative (95% CI)	Absolute (95% CI)		
-	-	-	-	-	-	-	-	-	-	-	-	
Adverse events or serious adverse events: no studies identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	
Psychological functioning (depression) - short term												
2	randomized trials	very serious[a]	serious[e]	not serious	very serious[c]	none	31	27	-	MD **6.8 lower** (19.73 lower to 6.12 higher)	⨁◯◯◯ Very low	
Population subgroups 1, 2, 3 and 4 - not reported (no subgroup analysis was performed)												
Psychological functioning - intermediate term or long term: no studies identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	
Social participation - short term, intermediate term or long term: no studies identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	
Self-efficacy - short term, intermediate term or long term: no studies identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	

CI: confidence interval; MD: mean difference; SMD: standardized mean difference

Explanations

[a]Risk of bias downgraded by 2 levels: due to unclear or high risk of bias across all studies regarding random sequence generation, allocation concealment, blinding of participants, blinding of care providers, blinding of outcome assessment, incomplete outcome data, selective reporting, similarity of groups at baseline, co-interventions, and compliance with the intervention.

[b]Inconsistency downgraded by 1 level: unexplained substantial heterogeneity I^2=57%

[c]Imprecision downgraded by 2 levels: due to wide confidence interval consistent with the possibility for benefit and the possibility for no effect and low number of participants.

[d]Imprecision downgraded by 1 level: low number of participants.

[e]Inconsistency downgraded by 1 level: unexplained considerable heterogeneity I^2=85%

GRADE Table 3. ***What are the benefits and harms of respondent therapy (relaxation) 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?***

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Respondent therapy	Usual care	Relative (95% CI)	Absolute (95% CI)		
Pain - short term												
1	randomized trials	very serious[a]	not serious[b]	not serious	very serious[c]	none	57	43	-	MD **11 lower** (22.22 lower to 0.22 higher)	⨁◯◯◯ Very low	
Population subgroups 1, 2 and 3 - not reported (no subgroup analysis was performed)												
Population subgroup 4: regional economic development (no subgroup analysis was performed; all studies performed in high income settings)												
Pain - intermediate term												
1	randomized trials	very serious[a]	not serious[b]	not serious	serious[d]	none	54	45	-	MD **1.4 lower** (12.65 lower to 9.85 higher)	⨁◯◯◯ Very low	
Population subgroups 1, 2, 3 and 4 - not reported (no subgroup analysis was performed; only one included study on this outcome)												
Pain - long term: no studies identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	
Back-specific functional status - short term												
1	randomized trials	very serious[a]	not serious[b]	not serious	serious[d]	none	57	43	-	MD **3.3 lower** (11.6 lower to 5 higher)	⨁◯◯◯ Very low	
Population subgroups 1, 2, 3 and 4 - not reported (no subgroup analysis was performed; only one included study on this outcome)												

Web Annex D.C2: 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 studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Respondent therapy	Usual care	Relative (95% CI)	Absolute (95% CI)		
Back-specific functional status - intermediate term												
1	randomized trials	very serious[a]	not serious[b]	not serious	serious[d]	none	54	45	-	MD **1.6 lower** (9.22 lower to 6.02 higher)	⨁◯◯◯ Very low	
Population subgroups 1, 2, 3 and 4 - not reported (no subgroup analysis was performed; only one included study on this outcome)												
Back-specific functional status - long term: no studies identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	
General functional status - short term, intermediate term or long term: no studies identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	
Health-related quality of life - short term												
1	randomized trials	very serious[a]	not serious[b]	not serious	serious[d]	none	57	43	-	MD **6.9 higher** (2.51 lower to 16.31 higher)	⨁◯◯◯ Very low	
Population subgroups 1, 2, 3 and 4 - not reported (no subgroup analysis was performed; only one included study on this outcome)												
Health-related quality of life - intermediate term												
1	randomized trials	very serious[a]	not serious[b]	not serious	serious[d]	none	54	45	-	MD **2.6 lower** (11.9 lower to 6.7 higher)	⨁◯◯◯ Very low	
Population subgroups 1, 2, 3 and 4 - not reported (no subgroup analysis was performed; only one included study on this outcome)												
Health-related quality of life - long term: no studies identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	

Web Annex D.C2: 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 studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Respondent therapy	Usual care	Relative (95% CI)	Absolute (95% CI)		
Adverse events or serious adverse events: no studies identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	
Psychological functioning (depression) - short term												
1	randomized trials	very serious[a]	not serious[b]	not serious	serious[d]	none	57	43	-	MD **1.5 lower** (5.87 lower to 2.87 higher)	⨁◯◯◯ Very low	
Psychological functioning (depression) - intermediate term												
1	randomized trials	very serious[a]	not serious[b]	not serious	serious[d]	none	54	45	-	MD **0.2 lower** (4.16 lower to 3.76 higher)	⨁◯◯◯ Very low	
Psychological functioning - long term: no studies identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	
Social participation – short term, intermediate term or long term: no studies identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	
Self-efficacy – short term, intermediate term or long term: no studies identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	

CI: confidence interval; MD: mean difference

Explanations

[a]Risk of bias downgraded by 2 levels: due to unclear or high risk of bias across all studies regarding random sequence generation, allocation concealment, blinding of participants, blinding of care providers, blinding of outcome assessment, incomplete outcome data, selective reporting, similarity of groups at baseline, co-interventions, and compliance with the intervention.

[b]Inconsistency not assessed because only one study included in this analysis.

[c]Imprecision downgraded by 2 levels: due to wide confidence interval consistent with the possibility for benefit and the possibility for no effect and low number of participants.

[d]Imprecision downgraded by 1 level: low number of participants.