D.3 Injectable local anaesthetics

Overview of the PICO structure

Definition of the intervention	
Injectable local anaesthetics include the subcutaneous, myofascial or intramuscular delivery of anaesthetic agents (lidocaine, articaine, bupivacaine, chloroprocaine, mepivacaine, procaine, ropivacaine and tetracaine) into local soft and/or connective tissues in the region of the lower back, between the 12th rib and gluteal fold. The injectate is delivered only to the extraspinal soft tissue and not delivered to intra-spinous structures, as is the case with intradiscal, epidural, intrathecal, facet joint and nerve root injections.	
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

Web Annex D.D3: ETD summary for WHO Guideline on non-surgical management of chronic primary low back pain in adults

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

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	**# Review findings GRADE-CERQual Assessment of confidence** 6 Many participants experienced that medication was often the only thing that made a difference to the severity of their pain. However, they were apprehensive of, or dissatisfied with, medication for a number of reasons, often viewing it as a quick fix, temporary relief or that it just masked the pain. Many participants were apprehensive of taking too many medications, the side effects, addiction or did not like how the medications made them feel. Some avoided taking medication all together, did not fill their prescriptions or adjusted medication themselves because of this. MODERATE

Summary of *resource considerations*	
All adults	**Older people**
No evidence synthesis commissioned for all adults. Judgements made based on experience of GDG members	**# Review findings GRADE-CERQual Assessment of confidence** 8 In rural Nigeria, participants considered medicines as a legitimate form of treatment (cultural norm that disease was treated and 'cured' with medication) and depended on them to be able to perform daily tasks. Other treatments were looked down on or stigmatized, such as exercise. Some participants took medication only to comply with this cultural norm. However, there was a constant struggle to be able to afford the drugs on which they depended to function normally. LOW

Web Annex D.D3: ETD summary for WHO Guideline on non-surgical management of chronic primary low back pain in adults

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	**# Review findings GRADE-CERQual Assessment of confidence** 9 Many participants expressed fear of addiction to medication, especially to opioids. This led them to not fill prescriptions, to adjust the dosage or stop taking the medication often without consulting their health care provider. MODERATE 10 Some participants in rural Nigeria stated that when the locally produced drugs did not work (they felt that they were substandard or counterfeit), they believed they were fake or substandard. These participants believed that foreign imported drugs were stronger and could lead to a cure. LOW

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

Web Annex D.D3: ETD summary for WHO Guideline on non-surgical management of chronic primary low back pain in adults

Summary of judgements

Domain	All adults	Older people
Benefits	Trivial; uncertain	Trivial; uncertain
Harms	Trivial; uncertain	Trivial; uncertain
Balance benefits to harms	Probably does not favour local anaesthetic injections; uncertain	Probably does not favour local anaesthetic injections; uncertain
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	Large costs; moderate costs; varies	Large costs; moderate costs; varies
Equity and human rights	Probably reduced; reduced; no impact; uncertain; varies	Probably reduced; reduced; no impact; uncertain; varies
Acceptability	Probably yes; probably no; uncertain; varies	Probably yes; probably no; uncertain; varies
Feasibility	Yes; probably yes	Yes; probably yes

GRADE Table 1. ***What are the benefits and harms of local anaesthetic injections 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/sham injections?***

Certainty assessment							№ of patients		Effect		Certainty	Comments
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Local anaesthetic	Placebo/sham	Relative (95% CI)	Absolute (95% CI)		
Pain - short term (assessed with: VAS; Scale from: 0 to 100)[a]												
2[b,c]	randomized trials	serious[d]	serious[e]	not serious	serious[f]	none	138	137	-	MD **10 lower** (25.44 lower to 5.43 higher)	⨁◯◯◯ Very low	Analysis 1.1
Population subgroups 1, 2 and 3 - not reported (no subgroup analysis was performed)												
Population subgroup 4: regional economic development												
High income 1[g]	randomized trials	serious[h]	not serious[i]	serious[j]	very serious[k]	none	12	12	-	MD **22.4 lower** (45.51 lower to 0.71 higher)	⨁◯◯◯ Very low	
Low/middle income 1[l]	randomized trials	serious[m]	not serious[i]	serious[n]	serious[o]	none	126	125	-	MD **5 lower** (11.32 lower to 1.32 higher)	⨁◯◯◯ Very low	
Pain - short term (assessed with: decrease of at least 30% in VAS score)												
1	randomized trials	serious[m]	not serious[i]	not serious	Very serious[k]	none	71/126	62/125	RR 1.14 (0.90 to 1.44)	69 more per 1000 (50 fewer to 218 more)	⨁◯◯◯ Very low	

Web Annex D.D3: ETD summary for WHO Guideline on non-surgical management of chronic primary low back pain in adults

Certainty assessment							№ of patients		Effect		Certainty	Comments
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Local anaesthetic	Placebo/sham	Relative (95% CI)	Absolute (95% CI)		
Population subgroups 1, 2, 3 and 4 - not reported (no subgroup analysis was performed; only one study reported on this outcome)												
Pain - short term (assessed with: "feeling improved" pain severity compared with baseline)												
1	randomized trials	serious[h]	not serious[i]	not serious	very serious[k]	none	7/12	1/12	RR 7.00 (1.01 to 48.53)	500 more per 1000 (1 more to 1000 more)	⨁◯◯◯ Very low	
Population subgroups 1, 2, 3 and 4 - not reported (no subgroup analysis was performed; only one study reported on this outcome)												
Pain - intermediate or long term: no studies were identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	
Back-specific functional status – short term, intermediate term or long term: no studies were identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	
General functional status – short term, intermediate term or long term: no studies were identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	
Health related quality of life – short term, intermediate term or long term: no studies were identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	
Adverse events assessed: any unfavourable symptom, regardless of its relationship to treatment, during the treatment period												
1[l]	randomized trials	serious[m]	not serious[i]	not serious	very serious[p]	none	7/126 (5.6%)	2/125 (1.6%)	**RR 3.47** (0.74 to 16.39)	**40 more per 1,000** (from 4 fewer to 246 more)	⨁◯◯◯ Very low	Analysis 1.4
Population subgroups 1, 2, 3 and 4 - not reported (no subgroup analysis was performed)												
Serious adverse events												

Web Annex D.D3: ETD summary for WHO Guideline on non-surgical management of chronic primary low back pain in adults

Certainty assessment							№ of patients		Effect		Certainty	Comments
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Local anaesthetic	Placebo/sham	Relative (95% CI)	Absolute (95% CI)		
1[g]	randomized trials	serious[h]	not serious[i]	not serious	very serious[q]	none	0/12 (0.0%)	0/12 (0.0%)	not estimable		⨁◯◯◯	Analysis 1.5
Population subgroups 1, 2, 3 and 4 - not reported (no subgroup analysis was performed; only one study reported on this outcome)												
Psychological functioning (depression) – short term, intermediate term or long term: no studies were identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	
Social participation – short term, intermediate term or long term: no studies were identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	

CI: confidence interval; MD: mean difference; RR: risk ratio

Explanations

a. FU time between 2–12 weeks
b. Collee 1991, Imamura 2016
d. Risk of bias downgraded by 1 level due to unclear or high risk of bias regarding random sequence generation, allocation concealment, blinding of participants, blinding of care providers, blinding of outcome assessment, incomplete outcome data, selective reporting, compliance, and other bias.
e. Inconsistency downgraded by 1 level: substantial heterogeneity I^2=51%. Inconsistency is not clearly explained by the subgroup analyses of HIC versus LMIC setting.
f. Imprecision downgraded by 1 level: due to wide confidence interval consistent with the possibility for benefit and the possibility for no effect and low number of participants. This outcome was not downgraded an additional level for imprecision because it was downgraded for inconsistency, which is related to and would have contributed to the severity of the imprecision.
g. Collee 1991
h. Risk of bias downgraded by one level due to unclear or high risk of bias regarding random sequence generation, allocation concealment, incomplete outcome data, selective outcome reporting, compliance, and other bias.
i. Inconsistency not assessed as only one study included in this analysis.
j. Indirectness downgraded by 1 level: only one study included in this subgroup analysis, it is unclear whether it is representative of all high-income country settings.
k. 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.
l. Imamura 2016
m. Risk of bias downgraded by one level due to unclear or high risk of bias regarding blinding of participants, blinding of care providers, blinding of outcome assessment, incomplete outcome data, selective reporting, and compliance.
n. Indirectness downgraded by 1 level: only one study included in this subgroup analysis, it is unclear whether it is representative of all low/middle-income country settings.
o. Imprecision downgraded by 1 level: despite narrow confidence intervals around the effect estimate showing little to no difference, downgraded due to low number of participants.
p. Imprecision downgraded by 2 levels: due to wide confidence interval consistent with the possibility for harm and the possibility for no effect and low number of participants.
q. Imprecision downgraded by 2 levels: no events in either group and a very low number of participants.

GRADE Table 2. ***What are the benefits and harms of local anaesthetic injections 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	Local anaesthetic	no intervention	Relative (95% CI)	Absolute (95% CI)		
Pain - short term (assessed with: VAS; Scale from: 0 to 100)[a]												
1[b,c]	randomized trials	serious[d]	not serious[e]	not serious	very serious[f]	none	126	127	-	MD **5 lower** (11.65 lower to 1.65 higher)	⨁◯◯◯ Very low	Analysis 2.1
Population subgroups 1, 2, 3 and 4 - not reported (no subgroup analysis was performed; only one study reported on this outcome)												
Pain - short term (assessed with: decrease of at least 30% in VAS score)												
1[b]	randomized trials	serious[d]	not serious[e]	not serious	very serious[f]	none	71/126	51/127	RR 1.40 (1.08 to 1.82)	161 more per 1000 (32 more to 329 more)	⨁◯◯◯ Very low	
Pain - intermediate or long term: no studies were identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	
Back-specific functional status – short term, intermediate term or long term: no studies were identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	
General functional status – short term, intermediate term or long term: no studies were identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	
Health related quality of life – short term, intermediate term or long term: no studies were identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	
Adverse events												

Web Annex D.D3: 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	Local anaesthetic	no intervention	Relative (95% CI)	Absolute (95% CI)		
1[b]	randomized trials	serious[d]	not serious[e]	not serious	very serious[g]	none	7/126 (5.6%)	4/127 (3.1%)	**RR 1.76** (0.53 to 5.88)	**24 more per 1,000** (from 15 fewer to 154 more)	⨁◯◯◯ Very low	Analysis 2.3
Population subgroups 1, 2, 3 and 4 - not reported (no subgroup analysis was performed; only one study reported on this outcome)												
Serious adverse events - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	
Psychological functioning (depression) – short term, intermediate term or long term: no studies were identified that reported on this outcome												
-	-	-	-	-	-	-	-	-	-	-	-	
Social participation – short term, intermediate term or long term: no studies were identified that reported on this outcome												
-	-	-	-	-	-	-					-	

CI: confidence interval; MD: mean difference; RR: risk ratio

Explanations

a. FU time 12 weeks
b. Imamura 2016
c. The study measured the outcome on an additional scale as dichotomous outcome as decrease of at least 30% in VAS score compared with baseline at 12 weeks (Analysis 2.2): there were 71/126 events in the intervention group vs 51/127 events in the comparison group (no intervention): RR 1.40 95% CI (1.08 to 1.82)
d. Risk of bias downgraded by one level due to unclear or high risk of bias regarding, blinding of participants, blinding of care providers, blinding of outcome assessment, incomplete outcome data, selective reporting, and compliance.
e. Inconsistency not assessed as only one study included in this analysis.
f. 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.
g. Imprecision downgraded by 2 levels: due to wide confidence interval consistent with the possibility for benefit and the possibility for harm and low number of participants.

GRADE Table 3. ***What are the benefits and harms of local anaesthetic injections 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?***

No trials