Cochrane Clinical Answers

Question:

How does oxycodone compare with placebo in adults with neuropathic pain?

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Answer

Adults with neuropathic pain (associated with post-herpetic neuralgia or diabetic neuropathy) might experience moderate pain relief with modified-release oxycodone (on average, 514 vs 309 per 1000 people), along with an increased risk of adverse events (on average, 131 vs 55 per 1000 people), compared with people given placebo. However, as only very low-quality evidence is available, results are uncertain.

Of note, quality of life and long-term effects of oxycodone were not assessed, although these are of great importance given that oxycodone can have detrimental psychological and physiological impact, including dependency. Physicians prescribing oxycodone should be aware of possible interactions with neuroleptics, tricyclic antidepressants, and selective serotonin reuptake inhibitors (SSRIs).

Comparisons

1. Oxycodone modified-release (MR) versus placebo

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› **OUTCOME 1.1 At least moderate pain relief (≥ 30% reduction in pain or Patient Global Impression of Change (PGIC) much or very much improved**

Narrative result

Three RCTs with 587 participants found that more people had at least moderate pain relief with modified-release oxycodone than with placebo.

Subgroup analyses assessing whether results differed if people were given oxycodone as monotherapy or as add-on therapy (with gabapentin) found similar results to the main analysis.[1]

Quality of the evidence

The reviewers performed a GRADE assessment of the quality of evidence for this outcome at this time point and stated that the evidence was very low quality. See Summary of findings from Cochrane review

Relative effect or mean difference

There was a statistically significant difference between groups, in favor of oxycodone (RR 1.66, 95% CI 1.32 to 2.09).

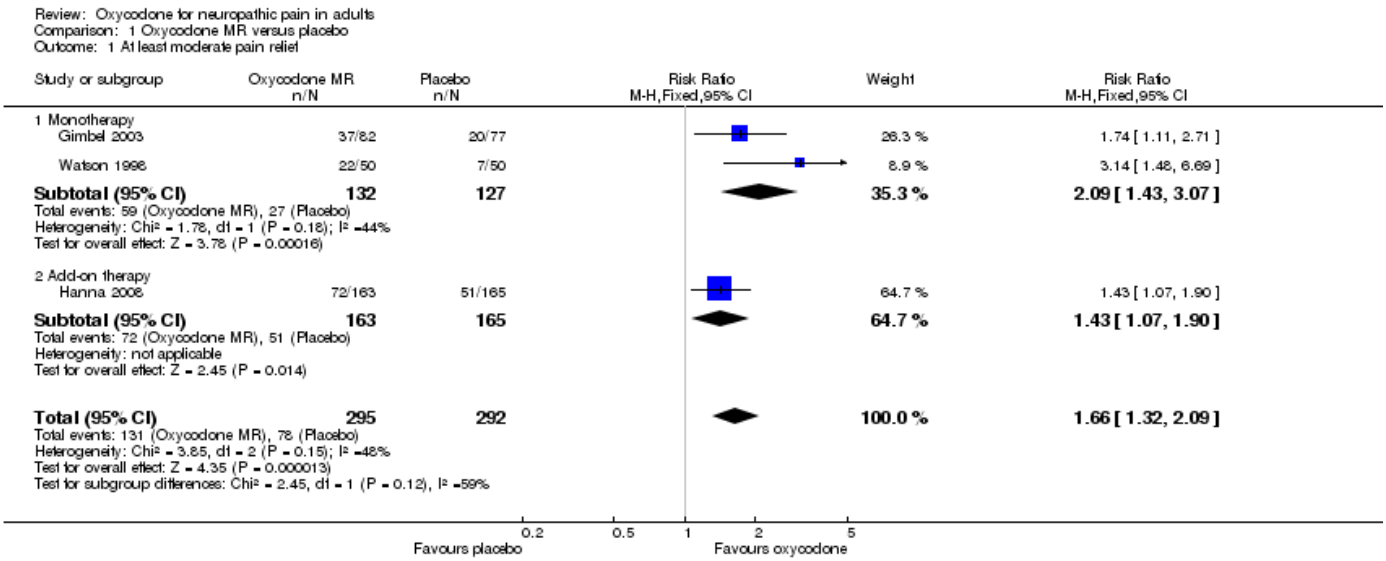

Figure 1

Open in figure viewer

Forest plot from Cochrane Review

Absolute effect

514 per 1000 people (95% CI 409 to 647) with modified-release oxycodone compared with 309 per 1000 people with placebo. The number needed to treat (NNT) for one additional person to achieve at least moderate pain relief was 5.7 (95% CI 4.0 to 9.9).

Reference

Gaskell H, Derry S, Stannard C, Moore RA. Oxycodone for neuropathic pain in adults. *Cochrane Database of Systematic Reviews* 2016, Issue 7. Art. No.: CD010692. DOI: 10.1002/14651858.CD010692.pub3. Search date December 2015

OUTCOME 1.2 Withdrawals due to lack of efficacy

Narrative result

Five RCTs with 775 participants found that fewer people withdrew due to lack of efficacy with modified-release oxycodone (plus naloxone) compared with placebo/benztropine.

Subgroup analyses assessing whether results differed if people were given oxycodone as monotherapy or as add-on therapy (with gabapentin or naloxone) found similar results to the main analysis.[2]

Quality of the evidence

The reviewers performed a GRADE assessment of the quality of evidence for this outcome at this time point and stated that the evidence was very low quality. See Summary of findings from Cochrane review

Relative effect or mean difference

There was a statistically significant difference between groups, in favor of oxycodone (RR 0.21, 95% CI 0.10 to 0.44).

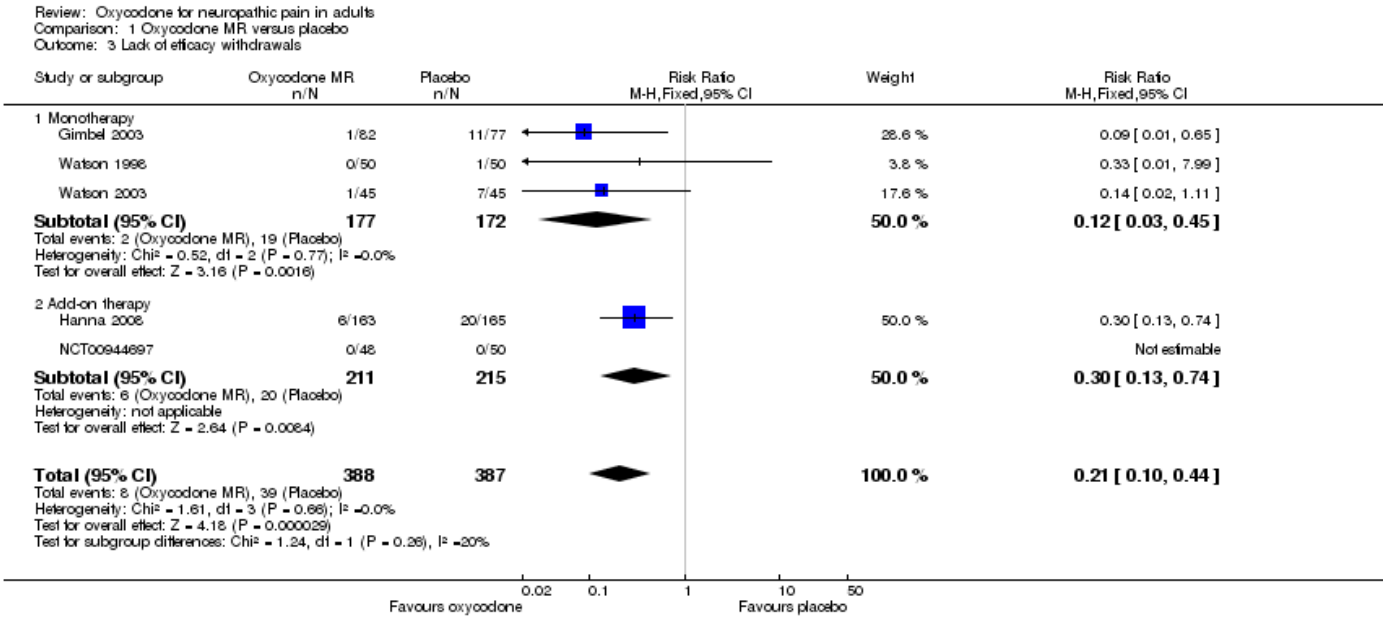

Figure 2 Open in figure viewer

Forest plot from Cochrane Review

Absolute effect

26 per 1000 people (95% CI 13 to 53) with modified-release oxycodone (plus naloxone) compared with 121 per 1000 people with placebo/benztropine. The number needed to treat (NNT) for one additional person to withdraw was 12 (95% CI 8.8 to 21).

Reference

Gaskell H, Derry S, Stannard C, Moore RA. Oxycodone for neuropathic pain in adults. *Cochrane Database of Systematic Reviews* 2016, Issue 7. Art. No.: CD010692. DOI: 10.1002/14651858.CD010692.pub3. Search date December 2015

OUTCOME 1.3 Withdrawals due to adverse events

Narrative result

Five RCTs with 775 participants found that more people withdrew because of adverse events with modified-release oxycodone (plus naloxone) than with placebo/benztropine.

The subgroup analysis of oxycodone as add-on therapy (with gabapentin or naloxone) found similar results to the main analysis. The analysis assessing oxycodone as monotherapy found no statistically significant difference between groups.[3]

Quality of the evidence

The reviewers performed a GRADE assessment of the quality of evidence for this outcome at this time point and stated that the evidence was very low quality. See Summary of findings from Cochrane review

Relative effect or mean difference

There was a statistically significant difference between groups, in favor of placebo (RR 2.41, 95% CI 1.47 to 3.94).

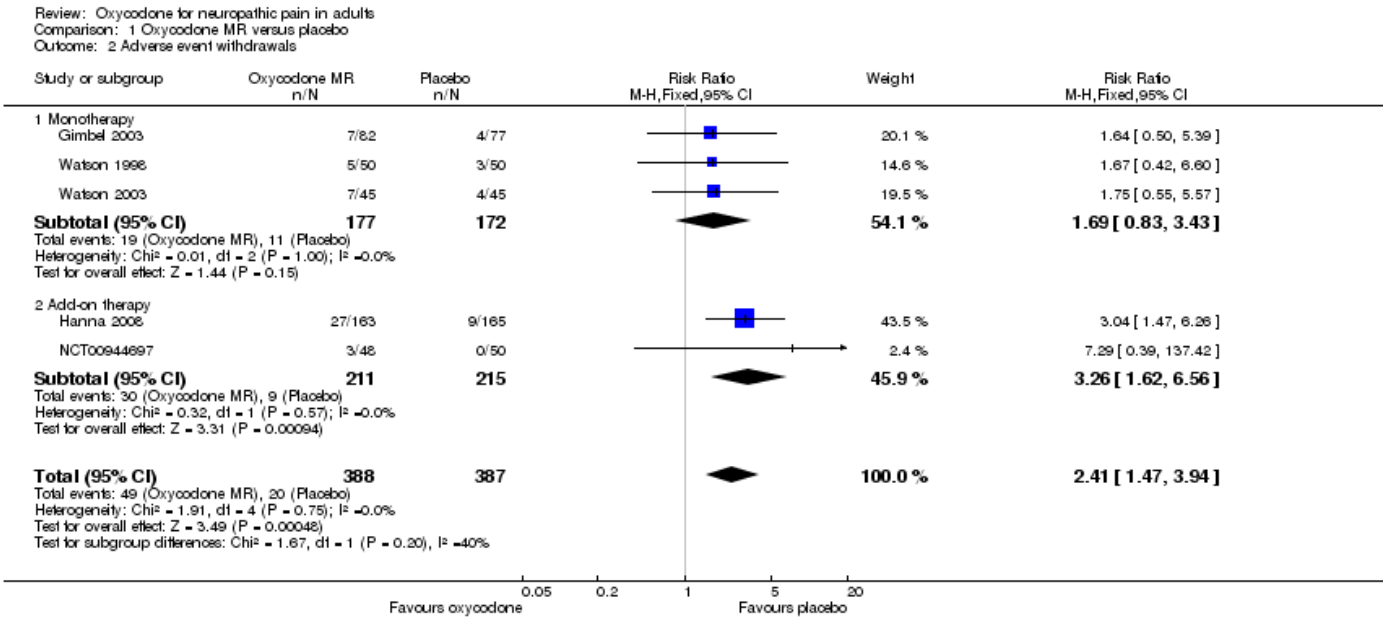

Figure 3 Open in figure viewer

Forest plot from Cochrane Review

Absolute effect

131 per 1000 people (95% CI 80 to 215) with modified-release oxycodone (plus naloxone) compared with 55 per 1000 people with placebo/benztropine.

Reference

Gaskell H, Derry S, Stannard C, Moore RA. Oxycodone for neuropathic pain in adults. *Cochrane Database of Systematic Reviews* 2016, Issue 7. Art. No.: CD010692. DOI: 10.1002/14651858.CD010692.pub3. Search date December 2015

OUTCOME 1.4 Any adverse event

Narrative result

Five RCTs with 782 participants found that more people had any adverse event with modified-release oxycodone (plus naloxone) than with placebo/benztropine. Adverse events included constipation, dizziness, nausea and somnolence.

Subgroup analyses assessing whether results differed if people were given oxycodone as monotherapy or as add-on therapy (with gabapentin or naloxone) found similar results to the main analysis.[4]

Risk of bias of studies

The reviewers performed a GRADE assessment of the quality of evidence for this outcome at this time point and stated that the evidence was very low quality. Reported in the main text of the Cochrane review

Relative effect or mean difference

There was a statistically significant difference between groups, in favor of placebo (RR 1.34, 95% CI 1.24 to 1.46).

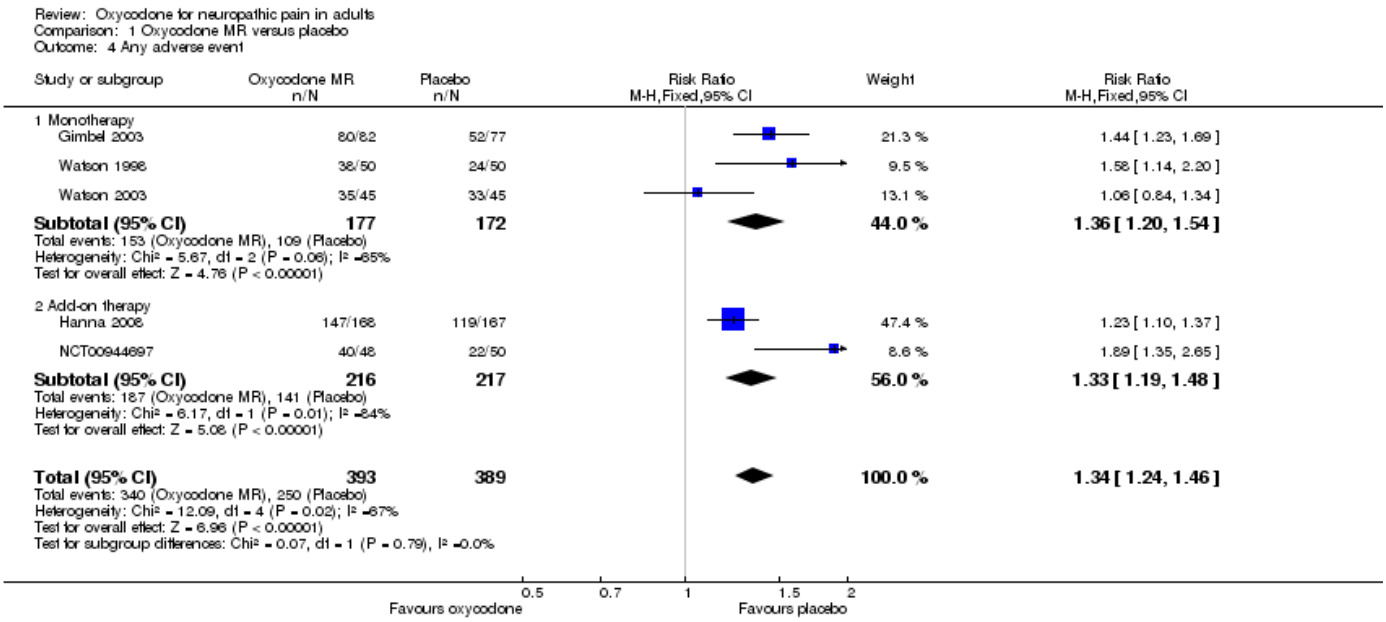

Figure 4 Open in figure viewer

Forest plot from Cochrane Review

Absolute effect

957 per 1000 people (95% CI 881 to 1040) with modified-release oxycodone (plus naloxone) compared with 713 per 1000 people with placebo/benztropine.

Reference

Gaskell H, Derry S, Stannard C, Moore RA. Oxycodone for neuropathic pain in adults. *Cochrane Database of Systematic Reviews* 2016, Issue 7. Art. No.: CD010692. DOI: 10.1002/14651858.CD010692.pub3. Search date December 2015

OUTCOME 1.5 Serious adverse events

Narrative result

Four RCTs with 447 participants found no statistically significant difference between groups, but the confidence intervals could not discard clinically important differences. Serious adverse events typically include any untoward clinical occurrence or effect that at any dose results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in persistent or significant disability or incapacity, is a congenital anomaly or birth defect, is an 'important medical event' that may jeopardize the person, or may require an intervention to prevent one of the above characteristics or consequences.

Subgroup analyses assessing whether results differed if people were given oxycodone as monotherapy or as add-on therapy (with naloxone) were underpowered to draw conclusions due to the low event rates.[5]

Quality of the evidence

The reviewers performed a GRADE assessment of the quality of evidence for this outcome at this time point and stated that the evidence was very low quality. See Summary of findings from Cochrane review

Relative effect or mean difference

There was no statistically significant difference between groups (RR 0.82, 95% CI 0.37 to 1.80).

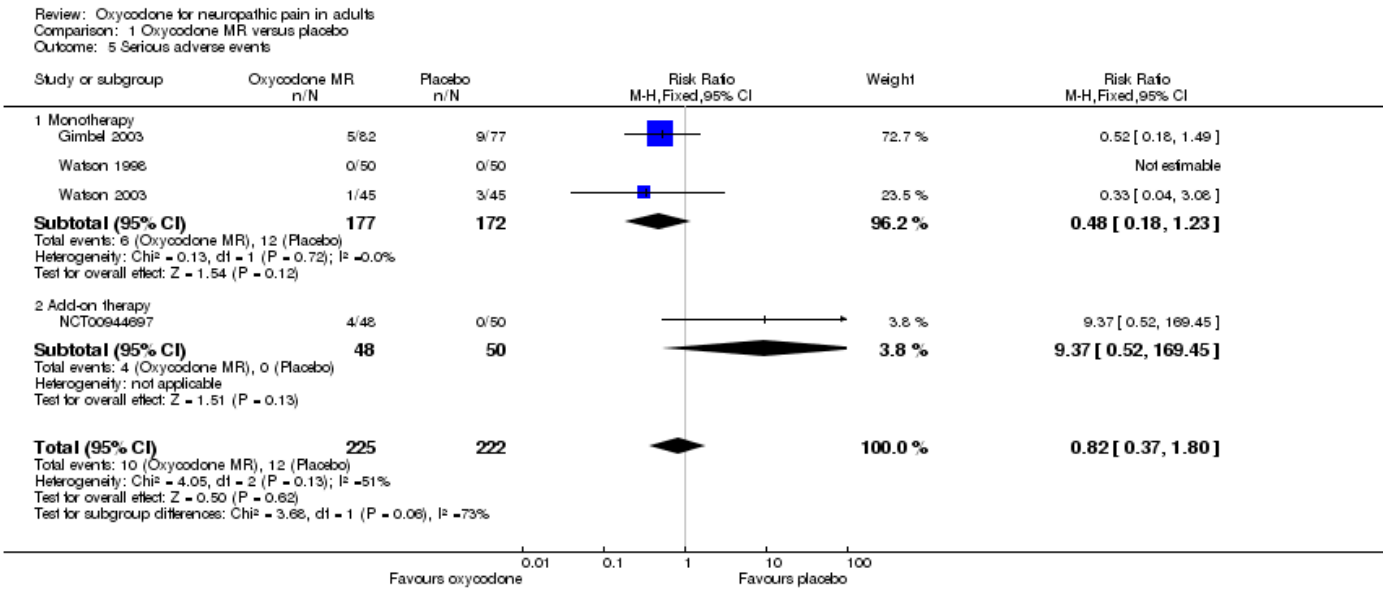

Figure 5 Open in figure viewer

Forest plot from Cochrane Review

Absolute effect

54 per 1000 people (95% CI 25 to 120) with modified-release oxycodone (plus naloxone) compared with 67 per 1000 people with placebo/benztropine.

Reference

Gaskell H, Derry S, Stannard C, Moore RA. Oxycodone for neuropathic pain in adults. *Cochrane Database of Systematic Reviews* 2016, Issue 7. Art. No.: CD010692. DOI: 10.1002/14651858.CD010692.pub3. Search date December 2015

› OUTCOME 1.6 Substantial pain relief (≥ 50% reduction in pain, Patient Global Impression of Change (PGIC) much or very much improved, Quality of life

Narrative result

The reviewers found no RCTs that assessed these outcomes.[6]

Reference

Gaskell H, Derry S, Stannard C, Moore RA. Oxycodone for neuropathic pain in adults. *Cochrane Database of Systematic Reviews* 2016, Issue 7. Art. No.: CD010692. DOI: 10.1002/14651858.CD010692.pub3. Search date December 2015

⌄ Population, Intervention, Comparator

Safety Alerts

Physicians prescribing oxycodone should be aware of possible interactions with neuroleptics, tricyclic antidepressants, and selective serotonin reuptake inhibitors (SSRIs). Click here for details of potential oxycodone interactions.

Population

People (mean age 59-70 years) who had experienced at least moderate neuropathic pain for three months or more, associated with either post herpetic neuralgia (1 trial) or diabetic neuropathy (painful symmetrical distal polyneuropathy) in people with stable diabetes (4 trials). In one trial, all participants were treated with stable doses of gabapentin

Intervention

Oxycodone modified-release (dose reported for three trials, up to 60 to 120 mg/day) (4 trials) or oxycodone plus naloxone (1 trial)

Comparator

Inactive placebo (4 trials) or active placebo (benztropine) (1 trial)

Additional Information

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