

# Needle in the Haystack: Finding Morphine's Sweet Spot: a meta-analysis

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## Literature review:

### Morphine:

Morphine is a powerful opioid painkiller derived from the opium poppy. It works by binding to specific receptors in the brain and spinal cord, blocking pain signals and reducing the perception of pain. Morphine is widely used to manage severe pain, but its use is carefully monitored due to its addictive potential and serious side effects, such as respiratory depression.

### Neuropathic pain:

Neuropathic pain is a chronic nerve pain affecting about 10% of adults over 30. Caused by nerve damage, it leads to burning or shooting pain. While opioids like morphine can reduce pain intensity by up to 30%, they're not a cure and have side effects. Other treatments like surgery and physical therapy are often combined.

### Cancer pain:

Cancer pain is often caused by tumors pressing on organs or by cancer treatments. Morphine is considered a gold standard treatment for moderate to severe cancer pain. While effective, it can cause side effects like constipation, drowsiness, nausea, and vomiting.

### Musculoskeletal pain:

Musculoskeletal pain is a common issue affecting bones, muscles, and joints, causing significant discomfort and reduced quality of life. Morphine has been widely used to treat severe cases, but its use has increased dramatically in recent years. While it can provide pain relief, it also carries risks like sleepiness and respiratory problems.

### Post operative pain:

Postoperative pain is a common, often intense discomfort experienced after surgery. Morphine is a frequently used opioid for managing this pain due to its rapid action. While effective, it can cause serious side effects including difficulty breathing, nausea, and vomiting.

## Aim and Objective:

**Aim:** How does morphine compare with comparative placebo drugs with the management of different types of pain (neuropathic, cancer, post operative and musculoskeletal pain.) and which type of pain is morphine able to manage more efficiently?

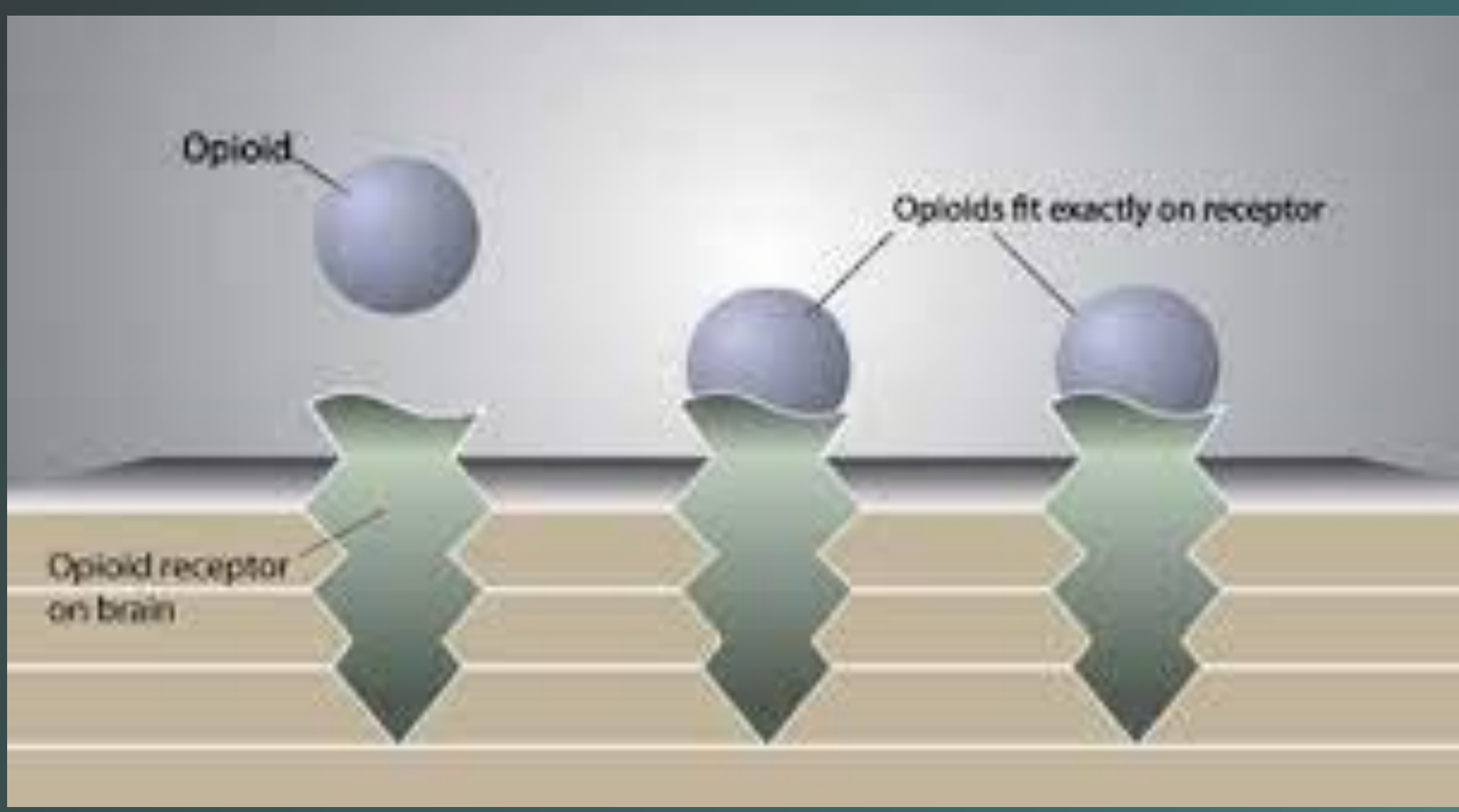
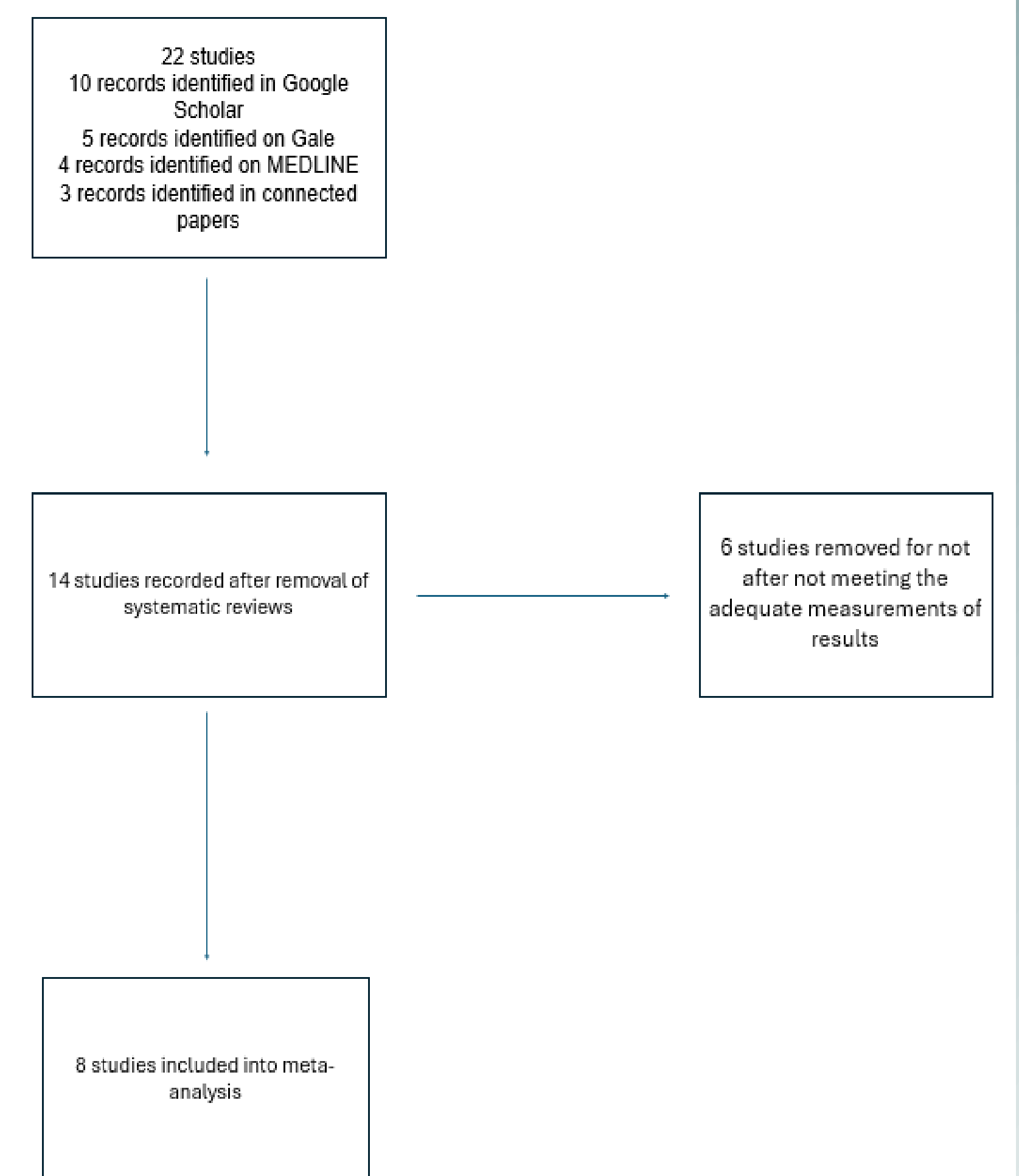
**Hypothesis:** Due to morphine's nerve-blocking effects there will be a correlation between morphine and the treatment of each pain type. The data collected will indicate that morphine will be able to treat neuropathic pain most effectively due to the origin of neuropathic pain.

### Null Hypothesis:

There is no correlation between morphine's nerve-blocking effects and the treatment of each pain type

## Methodology:

A meta-analysis using the software 'Revman' was conducted to assess the effectiveness of morphine for various pain types. The study included adults with chronic neuropathic, cancer, musculoskeletal or post operative pain who received morphine compared to a placebo or other treatment. Pain relief will be measured using numerical rating scales or similar methods. Data was collected from peer-reviewed randomized controlled trials published within the past 22 years. The primary outcomes was the average pain score after treatment for each study and for each pain type. An ANOVA was conducted to finally compare the correlation between morphine and placebo on pain types as well as the efficacy.



(Figure 1 – morphine binding to opioid receptors (University of Colorado, 2018))

## Results:

There were 22 studies identified, 14 excluded which left 8 that were included in the meta-analysis. All 8 studies were cross-sectional, with a total of 1170 participants. The overall risk of bias was moderate, with selective reporting being the main concern.

### Pain Types:

- Neuropathic pain: Morphine significantly reduced pain compared to placebo.
- Cancer pain: Morphine significantly reduced the same pain compared to placebo.
- Postoperative pain: Morphine significantly reduced the same pain compared to placebo.
- Musculoskeletal pain: No significant difference between morphine and placebo.

### Overall Pain Improvement:

- Neuropathic pain had the lowest average pain score after treatment with morphine.
- Statistical analysis indicated significant differences between pain types but not between morphine and placebo for all pain types combined.

Morphine is effective in reducing pain for neuropathic, cancer, and postoperative pain but shows limited benefit for musculoskeletal pain. Further research is needed to address the identified biases and explore other factors influencing pain management.

## Discussion:

**Main findings:** This study compared morphine to a placebo for treating different types of pain. It was found that while morphine generally reduced pain compared to a placebo, the difference wasn't always significant. Neuropathic pain responded best to morphine treatment, while postoperative pain was the most severe.

### Strengths and Limitations:

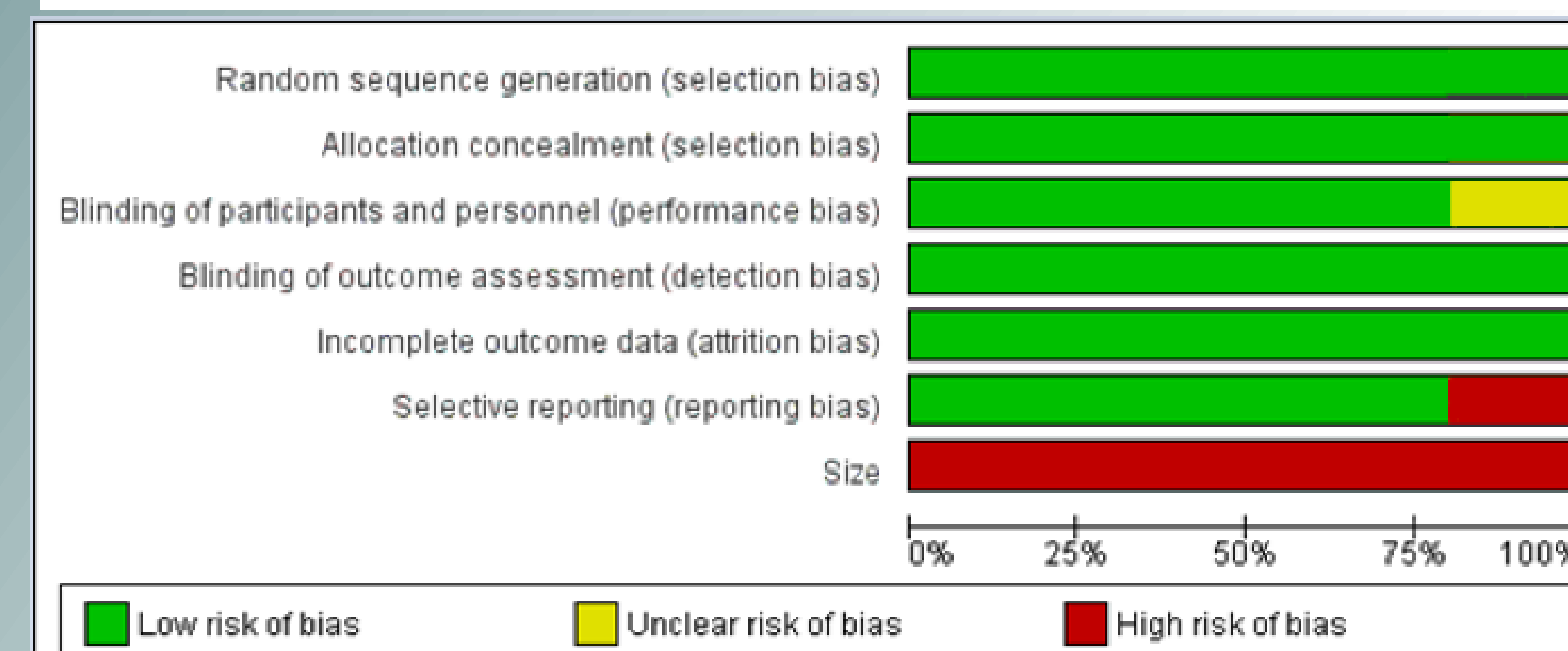
- Limited available studies: There was a shortage of studies for each pain type and those including a comparative drug.
- Difficulty in conducting a meta-analysis: The lack of sufficient data hindered the creation of a robust meta-analysis with reliable risk of bias assessments.
- Unexpected findings: The similarity in pain reduction between morphine and placebo in some cases was unexpected and requires further investigation.
- Data gaps: There was a noticeable lack of studies on severe pain types like postoperative pain, despite its high prevalence.

### Overall Discussion:

The results showed that while morphine was effective for some types of pain, there was no overall difference between morphine and placebo. However, the study did find that morphine worked better for some types of pain than others. This information can be used in future research to identify the best pain treatment for specific conditions. Due to the P value being higher than the alpha value (0.05) ( $P < 0.10548$ .) it is statistically significant that there is no correlation between morphine and the comparative placebo drug. Due to the P value being smaller than the alpha value ( $P > 0.016106$ .) There is a statistically significant difference between the efficacy of morphine on pain types.

Source of Variation	SS	df	MS	F	P-value	F crit
Sample	6.695156	1	6.695156	3.329754	0.10548	5.317655
Columns	38.59682	3	12.86561	6.398551	0.016106	4.066181
Interaction	7.689769	3	2.563256	1.274804	0.346906	4.066181
Within	16.08565	8	2.010706			
Total	69.06739	15				

(Table 1 – ANOVA table of results.)



(Figure 4 – Risk of bias graph for the average of all studies)

## Conclusion:

This meta-analysis investigated the effectiveness of morphine for different types of pain. While morphine generally reduced pain compared to placebo, its impact varied across pain conditions. Neuropathic pain showed the most significant improvement with morphine treatment. However, the study was limited by a small number of included studies. Further research is needed to confirm these findings.