



Local Infiltration Analgesia versus Interscalene Nerve Block for Pain Control After Shoulder Arthroplasty: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

Journal:	<i>Science Progress</i>
Manuscript ID	SCI-25-1566
Manuscript Type:	Meta-analysis
Date Submitted by the Author:	09-Jul-2025
Complete List of Authors:	Chaouch, Mohamed Ali; Université de Monastir Frederic, Salmeron; Perpignan Hospital Centre Jacem, Saadana; Université de Monastir Fethi, Jebali; Université de Monastir Adriano Carneiro, Da Costa; Federal University of Pernambuco Abdallah Amine, Lahdhiri; Hospital Centre Gonesse Daghmouri, Mohamed Aziz; Habib Thameur Hospital
Keywords:	surgery, arthroscopy, infiltration, Analgesia, block
Abstract:	<p>Background: Shoulder arthroplasty procedures are increasing, requiring effective pain management strategies. Interscalene nerve block (ISB) is widely used but carries potential complications. Local infiltration analgesia (LIA) presents a simpler alternative, but its efficacy compared to ISB remains uncertain. We aimed to compare the effectiveness and safety of local infiltration analgesia versus interscalene nerve block to treat postoperative pain after shoulder arthroplasty.</p> <p>Methods: A systematic review and meta-analysis of randomized controlled trials (RCT) was conducted according to PRISMA and Cochrane guidelines. The databases searched included PubMed, Embase, Cochrane, Scopus, and others. The primary outcome was postoperative opioid consumption (converted to morphine equivalents) within 24 hours. Secondary outcomes included pain scores (VAS) at different time points, chronic pain at two weeks, duration of hospital stay, and complication rates.</p> <p>Results: Twelve RCTs met the inclusion criteria with data from 855 patients. ISB was associated with significantly lower opioid use in 24 hours (mean difference: 7.68 mg of equivalent morphine, 95% CI: 0.96–14.40). Pain scores at 4 and 8 hours favored ISB (mean differences: 1.96 and 1.33, respectively), while no significant differences were observed at 12 and 24 hours or 2 weeks post-op. No differences were found in hospital stay or complications. The certainty of the evidence ranged from high (opioid consumption) to low (hospital stay).</p> <p>Conclusions: ISB provides superior early postoperative analgesia and reduces opioid consumption. However, LIA demonstrates comparable results beyond the immediate postoperative period and may be preferred in resource-limited settings due to lower cost and fewer complications.</p>

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60



1 Local Infiltration Analgesia versus Interscalene Nerve Block for Pain Control After
2 Shoulder Arthroplasty: A Systematic Review and Meta-Analysis of Randomized
3 Controlled Trials

4 Mohamed Ali Chaouch¹, Frederic Salmeron², Jacem Saadana³, Fethi Jebali⁴, Adriano
5 Carneiro da Costa⁵, Abdallah Amine Lahdhiri⁶, Mohamed Aziz Daghmouri⁷

6 1. Department of Visceral and Digestive Surgery, Monastir University Hospital,
7 Tunisia

8 2. Department of orthopedic, Perpignan Hospital, Perpignan, France

9 3. Department of Orthopedic, Monastir University Hospital, Tunisia

10 4. Department of Critical Care Medicine and Anesthesiology B, Monastir
11 University Hospital, Monastir, Tunisia

12 5. Department of Surgery, Federal University of Pernambuco, Recife,
13 Pernambuco, Brazil

14 6. Department of Critical Care Medicine and Anesthesiology, Gonesse Hospital,
15 Gonesse, France

16 7. Department of Anesthesia, Montreuil Intercommunal Hospital Center, France

17 Corresponding author:

18 Mohamed Ali Chaouch, MD

19 Department of Visceral and Digestive Surgery, Fattouma Bourguiba Hospital,
20 University of Monastir, Tunisia

21 Email: docmedalichaouch@gmail.com

22

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

ABSTRACT:

Background: Shoulder arthroplasty procedures are increasing, requiring effective pain management strategies. Interscalene nerve block (ISB) is widely used but carries potential complications. Local infiltration analgesia (LIA) presents a simpler alternative, but its efficacy compared to ISB remains uncertain. We aimed to compare the effectiveness and safety of local infiltration analgesia versus interscalene nerve block to treat postoperative pain after shoulder arthroplasty.

Methods: A systematic review and meta-analysis of randomized controlled trials (RCT) was conducted according to PRISMA and Cochrane guidelines. The databases searched included PubMed, Embase, Cochrane, Scopus, and others. The primary outcome was postoperative opioid consumption (converted to morphine equivalents) within 24 hours. Secondary outcomes included pain scores (VAS) at different time points, chronic pain at two weeks, duration of hospital stay, and complication rates.

Results: Twelve RCTs met the inclusion criteria with data from 855 patients. ISB was associated with significantly lower opioid use in 24 hours (mean difference: 7.68 mg of equivalent morphine, 95% CI: 0.96–14.40). Pain scores at 4 and 8 hours favored ISB (mean differences: 1.96 and 1.33, respectively), while no significant differences were observed at 12 and 24 hours or 2 weeks post-op. No differences were found in hospital stay or complications. The certainty of the evidence ranged from high (opioid consumption) to low (hospital stay).

III

Conclusions: ISB provides superior early postoperative analgesia and reduces opioid consumption. However, LIA demonstrates comparable results beyond the immediate postoperative period and may be preferred in resource-limited settings due to lower cost and fewer complications.

Keywords: Shoulder arthroplasty; interscalene nerve block; local infiltration analgesia; postoperative pain management; opioid consumption; visual analog scale

INTRODUCTION

The annual incidence of total shoulder arthroplasty has seen a significant increase, showing a growth rate that exceeds that of total hip or knee arthroplasty (1). This escalation is primarily attributed to the aging population and the introduction of new surgical techniques (2). Considering this trend, establishing effective postoperative pain management protocols has become crucial. Traditional methods, predominantly based on opioids, are associated with several side effects, including respiratory depression, somnolence, and drug dependence (3). Ineffective postoperative pain can lead to reduced patient satisfaction, delayed mobilization, increased healthcare costs, and extended hospital stays (4). Consequently, interscalene nerve block (ISB) has been recognized as a highly effective pain management technique after shoulder arthroplasty, in correlation with shorter hospital stays and reduced opioid consumption (5). However, ISB also carries potential risks of neurological or respiratory complications, such as hemi-diaphragmatic paresis and a nerve blockade failure rate between 10% and 20% (6). Recently, local infiltration at the surgical site has gained

IV

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

popularity, but the efficacy and limitations of this technique need to be fully elucidated (7). Various meta-analyses have been published that compare local infiltration with liposomal bupivacaine and ISB (8), but these often include retrospective trials and focus solely on liposomal bupivacaine. Therefore, our meta-analysis of randomized controlled trials (RCTs) assessed the efficiency and safety of regional infiltration analgesia compared to interscalene nerve block in managing pain after shoulder arthroplasty.

METHODS

This systematic review and meta-analysis was structured according to the PRISMA 2020 guidelines (Preferred Reporting Items for Systematic Review and was Meta-analysis) (9) and checked according to the AMSTAR 2 guidelines (evaluating the methodological quality of systematic reviews) (10). The protocol of this study is registered in PROSPERO under the number CRD420251022581.

Electronics searches: An extensive electronic search of the relevant literature, with no language restrictions, was performed in March 2025, using the following databases: "Cochrane Library's Controlled Trials Registry and Database of Systematic Review", "United States National Library of Medicine", "National Institutes of Health PubMed/MEDLINE", "Excerpt Medica Database", "Embase", "Scopus", and "Google Scholar". Keywords used for the final search in all databases were "interscalene nerve block", "local infiltration", "total shoulder arthroplasty", "total shoulder replacement", "pain control", "pain management", and "analgesia". The Boolean operators "OR" and

"AND" were used to combine literature searches. We manually checked the reference list of trials included to identify additional studies. Studies including a patient population of less than 10 patients, case reports, and editorials were not considered.

Included studies: All randomized controlled trials (RCTs) reporting a comparison between interscalene nerve plane block and local infiltration analgesia with respect to postoperative analgesia in total shoulder arthroplasty, published in a peer-reviewed journal, were considered for analysis. Data from nonrandomized trials, non-comparative studies, editorials, letters to editors, review articles, and case series were excluded from the analysis. RCTs comparing ISB and local infiltration in another type of shoulder surgery were also excluded. The study was excluded if a direct comparison of ISB and local infiltration could not be determined.

Participants: adults (aged over 18 years) of any sex undergoing shoulder arthroplasty and receiving local infiltration analgesia or ISB pain control.

Intervention group: regional infiltration analgesia group (infiltration group).

Control group: interscalene nerve block group (ISB group).

Primary outcome: Postoperative intravenous opioid consumption was reported 24 hours after surgery. It was converted to intravenous milligram equivalents (morEq) (11).

Secondary outcomes:

- Acute postoperative pain score at rest at different periods (4 hours (H4), 8 hours (H8), 12 hours (H12), and 24 hours (H24)) using the visual analog scale (VAS) score (0 = no pain and 10 = extreme pain).

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

- Chronic postoperative pain score (2 weeks postoperative).
- Duration of postoperative hospital stay and complications.

Study selection: Two authors (MAD and MAC) independently reviewed all abstracts. All studies, accompanied by the full text that met the inclusion criteria, were retained. Disagreements were resolved by discussion after consulting a third member of the review team (LR).

Quality assessment of studies and the risk of bias: All studies that met the selection criteria were independently evaluated. The risk of bias of randomized clinical trials was assessed using the RoB2 (risk of bias) assessment containing the 5-domain noted in the Cochrane Handbook (12).

Data extraction: The data extracted from the studies were the author’s name, publication year, age, dosage and type of anesthetic drug, sample size, duration of follow-up, and results. Postoperative pain intensity was measured using a 10-point VAS score (a 100-point VAS was converted to a 10-point VAS). Data in other forms (median, interquartile range, and mean±95% range confidence interval) were converted to mean ± standard deviation by using the Cochrane Handbook guidelines. If the data were not reported numerically, we extracted them from the figures or contacted the corresponding authors for more information.

Each author independently extracted data from each study. Disparities were resolved after discussion with the senior authors (LA).

Heterogeneity assessment: To assess heterogeneity, three strategies were used:

VII

1. The Cochrane Chi² test (Q test), Tau², which is the variance of true effects, and 95% predictive interval (index of dispersion) to estimate the degree of heterogeneity (13). We calculate the predictive interval using a comprehensive meta-analysis prediction interval.

2. Graphical exploration with funnel plots (14).

3. Sensitivity analysis with a subgroup analysis when applicable (15). Subgroup analyzes were carried out, if feasible, to assess potential sources of heterogeneity.

Assessment of evidence: Two authors independently assessed the certainty of the evidence. GRADE guidelines were used to assess the quality of evidence. We considered the limitations of the study constancy of effect, imprecision, indirectness, and publication bias. We assessed the certainty of evidence as high, moderate, low, or very low. We considered the following criteria for upgrading the certainty of evidence, if appropriate: large effect, dose-response gradient, and plausible confounding effect. We use the methods and recommendations described in Sections 8.5 and 8.7, and Chapters 11 and 12 of the Cochrane Handbook for systematic reviews of Interventions. GRADEpro GDT software was used to summarize the findings' tables. We explain the reasons for downgrading or upgrading certain included studies using footnotes with comments.

Evaluation of effect size: We used the RevMan 5.4 statistical package from the Cochrane Collaboration for meta-analysis (16). We selected the mean difference (MD) as an effective measure for continuous data. Odds ratios (OR) with 95% confidence

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

intervals (95% CI) were calculated for dichotomous variables. The random-effects model was used and the significance threshold was fixed at 0.05. When the mean and standard deviation (SD) were not reported, they were estimated from the range (R) and median according to the formula described by Hozo et *al.* (17).

RESULTS

Literature search results: We retrieved eight potentially relevant articles (**Figure 1**). In the initial research, a total of 189 articles were identified from the electronic database. After evaluating the abstracts and titles of these studies, only 12 articles were retained. Five studies were excluded for the following reasons: one study (18) included patients undergoing shoulder arthroscopy surgeries, and four studies were not prospective trials (19–22). **Table 1** summarizes data from 12 clinical studies that compare local infiltration (Group Infiltration) and interscalene block (Group ISB) techniques for postoperative pain management in shoulder surgeries. Studies span from 2015 to 2023 and were carried out primarily in the USA, with additional data from Turkey, Denmark, France and Colombia. The ages ranged from early 50s to the early 70s, with relatively balanced gender distributions. Throughout the studies, various anesthetics were used, commonly liposomal bupivacaine, ropivacaine, and bupivacaine, administered in different volumes and concentrations. The results focused primarily on VAS pain scores and opioid consumption, with follow-up periods ranging from 24 hours to 90 days. The of patients of the group sizes were generally comparable within each study, supporting a balanced analysis of the efficacy between techniques. The risk of bias assessment of these studies is reported in **Table 2**.

172

173 **Primary outcome: Postoperative opioid consumption reported up to 24 hours after**
174 **surgery**

175 Ten studies evaluated opioid consumption postoperatively, comprising 418 patients in
176 the infiltration group and 437 in the ISB group. The infiltration group demonstrated
177 significantly higher opioid use, with a mean difference of 7.68 mg of equivalent
178 morphine (95% CI: 0.96 to 14.40). The heterogeneity was substantial ($\text{Tau}^2 = 93.68$),
179 indicating the variability in effect sizes between studies. Despite this, the consistent
180 direction of effect suggests a clinically significant reduction in opioid use with ISB
181 (Figure 2).

182 **Secondary outcomes:**

183 **Postoperative pain scores at H4, H8, H12 and H24**

184 VAS scores at 4 hours after the operation were analyzed in ten studies with 410
185 patients in the infiltration group and 429 in the ISB group. The pooled mean difference
186 favored ISB, with a statistically significant value of 1.96 (95% CI 1.14 to 2.77). The
187 heterogeneity was little ($\text{Tau}^2 = 1.45$), although the consistent direction of the effect in
188 all studies supports a clear early analgesic advantage for ISB (Figure 3A).

189 Seven studies reported pain outcomes 8 hours following shoulder arthroplasty.

190 According to the studies, 290 patients received infiltration and 298 received ISB. The
191 pooled mean difference was 1.33 points higher in the infiltration group (95% CI: 0.02
192 to 2.64), which favors ISB and suggests a statistically significant reduction in pain at 8

X

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

hours with ISB. However, heterogeneity was very high ($\text{Tau}^2 = 2.89$), indicating substantial variability among the studies (**Figure 3B**).

At 12 hours postoperatively, ten studies contributed data to the analysis, with a total of 314 patients in the infiltration group and 321 in the ISB group. The pooled mean difference was 0.32 (95% CI: -0.82 to 1.47), again indicating that there were no significant differences in pain scores between the two analgesic approaches. Low heterogeneity was present ($\text{Tau}^2 = 2.08$), reflecting the variation in pain outcomes across studies (**Figure 3C**).

Finally, nine studies reported VAS pain scores on the first postoperative day, with 418 patients in the infiltration group and 437 in the ISB group. The pooled mean difference was 0.13 (95% CI: -0.84 to 1.10), which does not show significant differences in pain outcomes between groups at this point. The heterogeneity was low, with $\text{Tau}^2 = 2.17$, reflecting moderate consistency in results across studies (**Figure 3D**).

Postoperative pain score after two weeks

Three studies reported VAS pain scores two weeks postoperatively. The infiltration group included 114 patients, while the ISB group included 115 patients. The mean difference between the groups was 0.60 (95% CI: -0.87 to 2.08), indicating that there were no statistically significant differences. However, heterogeneity was low ($\text{Tau}^2 = 1.55$), suggesting variability among study results and reducing confidence in the pooled estimate. (**Figure 3E**)

Duration of hospital stay

Seven studies examined hospital stay, including 368 patients in the infiltration group and 388 in the ISB group. The pooled mean difference was -0.00 days (95% CI -0.13 to 0.12), indicating no significant differences in the duration of hospitalization between the two analgesic approaches. Heterogeneity was low ($\text{Tau}^2 = 0.01$), suggesting that different hospital discharge practices or patient factors may have influenced results (Figure 4).

Complications

Six studies evaluated postoperative complications, including 377 patients in the infiltration group and 386 in the ISB group. There were 8 reported events in the infiltration group and 16 in the ISB group. The pooled odds ratio was 0.60 (95% CI: 0.25 to 1.42), indicating that there was no statistically significant difference in the risk between the two interventions (Figure 5).

The certainty of evidence of the effect size

Table 3 summarizes the findings comparing local infiltration analgesia with ISB for postoperative pain management in shoulder arthroplasty in several outcomes. ISB demonstrated a clear advantage in early pain control, with significantly lower pain scores at 4 and 8 hours after surgery (moderate certainty evidence) and reduced opioid consumption at 24 hours (high certainty evidence). However, 12 and 24-hour post-op, as well as at 2 weeks, pain scores between groups were similar, with no significant differences observed. Complication rates were slightly lower with infiltration, though the difference was not statistically significant (moderate certainty), and both techniques showed comparable results regarding hospital stay duration (low certainty). In general,

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

236 ISB provides superior immediate analgesia and reduces opioid use, while both
237 methods are equally effective for longer-term pain control and recovery outcomes.

238 **DISCUSSION**

239 To our knowledge, this is the first systematic review and meta-analysis comparing local
240 infiltration analgesia with ISB for pain management after shoulder arthroplasty. ISB
241 was more effective in early postoperative pain relief (at 4 and 8 hours) and significantly
242 reduced opioid use within 24 hours. However, there were no significant differences in
243 pain scores at 12 and 24 hours, duration of hospital stay, or complication rates.
244 Although ISB offers better immediate analgesia, LIA is simpler and safer, making it a
245 suitable alternative, especially in resource-limited settings.

246 Opioids are frequently used as an adjunct therapy for postoperative pain after shoulder
247 arthroplasty. However, their side effects, including nausea, vomiting, respiratory
248 depression, and drug dependence, can impede functional recovery and diminish
249 patient satisfaction (23). Thus, total opioid consumption after surgery is a key indicator
250 of analgesic efficacy. A study by Weller et al. (20) involving 214 arthroplasties reported
251 that average oral morphine equivalent consumption at 24 hours was significantly
252 higher with local infiltration of liposomal bupivacaine compared to the ISB group. Our
253 meta-analysis confirms this difference in total opioid consumption between the two
254 groups up to 24 hours. Beyond opioid consumption, postoperative pain scores were
255 also a critical outcome in our meta-analysis to evaluate the efficacy of analgesics. The
256 aggregated results revealed higher VAS scores at H4 and H8 in the local infiltration
257 group, which then aligned with the ISB group H12 and H24. This initial discrepancy

XIII

could be explained by the type of local anesthetic used: liposomal bupivacaine in four included RCTs and ropivacaine in others. Liposomal bupivacaine, designed for prolonged release for 72 hours, could account for the higher early postoperative pain scores due to delayed bupivacaine release from lipid stores (24,25). However, the meta-analyses by Liu et al. (26) and Kuang et al. (27) advised against recommending liposomal bupivacaine as a long-acting analgesic in local infiltration, citing no significant differences in postoperative pain scores compared to traditional local anesthetics.

The length of hospital stay did not differ significantly between the two groups, a finding consistent with previous meta-analyses (7,8). Yet, Weller et al. (20) noted that the cost of local infiltration mixtures averaged \$289.04 per case, significantly less than \$1559.42 for interscalene catheters, inclusive of equipment and anesthesia fees. This cost-effectiveness of local infiltration is also observed in studies of total joint arthroplasty of the lower extremities (28), which positions it as a more economically viable alternative to ISB for pain management after shoulder arthroplasty. Furthermore, the rates of complication, a vital factor in the evaluation of analgesic techniques, were found to be lower in the local infiltration group compared to ISB. However, due to the limited data available, only a general analysis of various complications was feasible. In particular, ISB is associated with a high incidence of hemi-diaphragmatic paresis (29).

Our systematic review and meta-analysis suggest that both local infiltration and interscalene nerve block are effective and safe for postoperative pain management

XIV

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

after shoulder arthroplasty. However, considering the higher incidence of hemidiaphragmatic paresis after ISB and the associated medical expenses, local infiltration appears more suitable, particularly for patients with limited financial resources.

This study has several limitations. First, although 12 RCTs were initially considered, only eight studies with a combined total of 855 patients (418 in the local infiltration group and 437 in the interscalene block group) were included in the primary outcome analysis, which can limit the robustness of the findings and the ability to assess publication bias. Second, there was significant heterogeneity in some outcomes, likely due to differences in anesthetic agents, doses, and study protocols, requiring cautious interpretation. Third, some standard deviations were estimated or extracted from figures rather than directly reported, which could affect the accuracy of the results. Finally, the follow-up periods in most studies were relatively short, with only three reporting outcomes beyond the immediate postoperative period, highlighting the need for more long-term studies to evaluate sustained analgesic effects and recovery.

CONCLUSIONS

This meta-analysis shows that while ISB provides better early pain control and reduces opioid use within 24 hours after shoulder arthroplasty, local infiltration analgesia offers comparable outcomes beyond that period. Given its lower cost, ease of administration, and similar long-term effectiveness, local infiltration analgesia is a practical alternative to ISB, especially in resource-limited settings. More high-quality studies with longer follow-up are needed to confirm these findings.

302 AVAILABILITY OF DATA, CODE, AND OTHER MATERIALS

303 All meta-analytic data and all codebooks and analysis scripts are publicly available on
304 the study's associated page on the Open Science Framework (<https://osf.io/4sme2/>).

305 REFERENCES

- 306 1. Kim SH, Wise BL, Zhang Y, Szabo RM. Increasing incidence of shoulder
307 arthroplasty in the United States. *JBJS*. 2011;93(24):2249–54.
- 308 2. Deshmukh AV, Koris M, Zurakowski D, Thornhill TS. Total shoulder
309 arthroplasty: long-term survivorship, functional outcome, and quality of life. *Journal of*
310 *shoulder and elbow surgery*. 2005;14(5):471–9.
- 311 3. Gohl ML, Moeller RK, Olson RL, Vacchiano CA. The addition of interscalene
312 block to general anesthesia for patients undergoing open shoulder procedures. *AANA*
313 *journal* [Internet]. 2001 [cited 2025 Mar 29];69(2). Available from:
314 <https://search.ebscohost.com/login.aspx?direct=true&profile=ehost&scope=site&auth>
315 [type=crawler&jrnl=00946354&asa=N&AN=6585866&h=jyTv7eOzmGORWSAvakUlw](https://search.ebscohost.com/login.aspx?direct=true&profile=ehost&scope=site&auth)
316 [QiaOWeAFQ4vS1EjOcW92Ka3FtDWdRuxhA1%2ByvmtZj1UKvBC7uwYGSLFYiSB](https://search.ebscohost.com/login.aspx?direct=true&profile=ehost&scope=site&auth)
317 [mUf3w%3D%3D&crl=c](https://search.ebscohost.com/login.aspx?direct=true&profile=ehost&scope=site&auth)
- 318 4. Mahoney A, Bosco III JA, Zuckerman JD. Readmission after shoulder
319 arthroplasty. *Journal of Shoulder and Elbow Surgery*. 2014;23(3):377–81.
- 320 5. Shah A, Nielsen KC, Braga L, Pietrobon R, Klein SM, Steele SM. Interscalene
321 brachial plexus block for outpatient shoulder arthroplasty: postoperative analgesia,
322 patient satisfaction and complications. *Indian Journal of Orthopaedics*.
323 2007;41(3):230.
- 324 6. Bishop JY, Sprague M, Gelber J, Krol M, Rosenblatt MA, Gladstone JN, et al.
325 Interscalene regional anesthesia for arthroscopic shoulder surgery: a safe and
326 effective technique. *Journal of shoulder and elbow surgery*. 2006;15(5):567–70.
- 327 7. Zhang Z, Shen B. Effectiveness and weakness of local infiltration analgesia in
328 total knee arthroplasty: a systematic review. *J Int Med Res*. 2018 Dec;46(12):4874–
329 84.
- 330 8. Sun H, Li S, Wang K, Zhou J, Wu G, Fang S, et al. Do liposomal bupivacaine
331 infiltration and interscalene nerve block provide similar pain relief after total shoulder

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

arthroplasty: a systematic review and meta-analysis. JPR. 2018 Sep;Volume 11:1889–900.

9. Page MJ, Moher D, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. PRISMA 2020 explanation and elaboration: updated guidance and exemplars for reporting systematic reviews. BMJ. 2021 Mar 29;n160.

10. Shea BJ, Reeves BC, Wells G, Thuku M, Hamel C, Moran J, et al. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. BMJ. 2017 Sep 21;j4008.

11. CDC. Overdose Prevention. 2024 [cited 2025 Mar 29]. Overdose Prevention. Available from: <https://www.cdc.gov/overdose-prevention/index.html>

12. Sterne JA, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. bmj. 2019;366.

13. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. Bmj. 2003;327(7414):557–60.

14. Egger M, Smith GD, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. Bmj. 1997;315(7109):629–34.

15. Copas J, Shi JQ. Meta-analysis, funnel plots and sensitivity analysis. Biostatistics. 2000;1(3):247–62.

16. Cochrane Handbook for Systematic Reviews of Interventions [Internet]. [cited 2020 Jun 15]. Available from: <https://handbook-5-1.cochrane.org/>

17. Hozo SP, Djulbegovic B, Hozo I. Estimating the mean and variance from the median, range, and the size of a sample. BMC Medical Research Methodology. 2005 Apr 20;5(1):13.

18. Beaudet V, Williams SR, Tétreault P, Perrault MA. Perioperative interscalene block versus intra-articular injection of local anesthetics for postoperative analgesia in shoulder surgery. Regional Anesthesia & Pain Medicine. 2008;33(2):134–8.

19. Namdari S, Nicholson T, Abboud J, Lazarus M, Steinberg D, Williams G. Randomized Controlled Trial of Interscalene Block Compared with Injectable Liposomal Bupivacaine in Shoulder Arthroplasty. The Journal of Bone and Joint Surgery. 2017 Apr 5;99(7):550–6.

20. Weller WJ, Azzam MG, Smith RA, Azar FM, Throckmorton TW. Liposomal bupivacaine mixture has similar pain relief and significantly fewer complications at less

XVII

- cost compared to indwelling interscalene catheter in total shoulder arthroplasty. The Journal of arthroplasty. 2017;32(11):3557–62.
21. Hannan CV, Albrecht MJ, Petersen SA, Srikumaran U. Liposomal bupivacaine vs interscalene nerve block for pain control after shoulder arthroplasty: a retrospective cohort analysis. Am J Orthop. 2016;45(7):424–30.
22. Angerame MR, Ruder JA, Odum SM, Hamid N. Pain and Opioid Use After Total Shoulder Arthroplasty With Injectable Liposomal Bupivacaine Versus Interscalene Block. Orthopedics [Internet]. 2017 Sep [cited 2025 Mar 29];40(5). Available from: <https://journals.healio.com/doi/10.3928/01477447-20170608-01>
23. Stephan BC, Parsa FD. Avoiding opioids and their harmful side effects in the postoperative patient: exogenous opioids, endogenous endorphins, wellness, mood, and their relation to postoperative pain. Hawai'i Journal of Medicine & Public Health. 2016;75(3):63.
24. Surdam JW, Licini DJ, Baynes NT, Arce BR. The use of exparel (liposomal bupivacaine) to manage postoperative pain in unilateral total knee arthroplasty patients. The Journal of arthroplasty. 2015;30(2):325–9.
25. Richard BM, Newton P, Ott LR, Haan D, Brubaker AN, Cole PI, et al. The Safety of EXPAREL ® (Bupivacaine Liposome Injectable Suspension) Administered by Peripheral Nerve Block in Rabbits and Dogs. Journal of Drug Delivery. 2012 Jan 17;2012:1–10.
26. Liu Y, Zeng Y, Zeng J, Li M, Wei W, Shen B. The efficacy of liposomal bupivacaine compared with traditional peri-articular injection for pain control following total knee arthroplasty: an updated meta-analysis of randomized controlled trials. BMC Musculoskelet Disord. 2019 Dec;20(1):306.
27. Kuang M jie, Du Y, Ma J xiong, He W, Fu L, Ma X long. The efficacy of liposomal bupivacaine using periarticular injection in total knee arthroplasty: a systematic review and meta-analysis. The Journal of arthroplasty. 2017;32(4):1395–402.
28. Barrington JW, Halaszynski TM, Sinatra RS. Expert Working Group on Anesthesia and Orthopaedics Critical Issues in Hip and Knee Replacement Arthroplasty FT. Perioperative pain management in hip and knee replacement surgery. Am J Orthop (Belle Mead NJ). 2014;43(4 Suppl):S1–16.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

29. Zhai W, Wang X, Rong Y, Li M, Wang H. Effects of a fixed low-dose ropivacaine with different volume and concentrations on interscalene brachial plexus block: a randomized controlled trial. BMC Anesthesiol. 2015 Dec;16(1):80.

For Peer Review

LIST OF TABLES AND FIGURES

Table 1: General characteristics of the included studies

Table 2: Quality assessment and the risk of bias

Table 3: Summary of the findings table

Figure 1: PRISMA flow diagram of bibliographic research

Figure 2: Forest plot of opioid consumption

Figure 3: Forest plots of the Visual Analgesic scale (H4, H8, H12, H24, and two weeks)

Figure 4: Forest plot of the hospital stay

Figure 5: Forest plot of complications

First author	Year of publication	Country	Age (M/F)	Group Infiltration		Group ISB		Outcomes	Follow-up
				Nb of patients	Drugs and dose	Nb of patients	Drugs		
Abildgaard	2017	USA	68.9 (35/48)	36	20 mL (266 mg) LB	47	Ropivacaine 0.5%, 8mL/h	-VAS score -Opioid consumption	90 days
Ali	2021	USA	66.5±9.1 (61/47)	54	20 mL of liposomal bupivacaine	54	10 to 20 mL of ropivacaine 0.5%	-VAS score -Opioid consumption	96 hours
Bingol	2021	Turkey	52.1±12.7 (32/28)	30	60 mL of local anesthetic	30	20 mL of Bupivacaine 0.5%	-VAS score	90 days
Bjørnholdt	2015	Denmark	65.5 ± 8 (24/37)	30	150 ml ropivacaine 0.2 % with epinephrine	31	Ropivacaine 0.75 %, 7 ml bolus then 5 ml/h	-VAS score -Opioid consumption	90 days
Klag	2020	USA	69.4 ± 8.1 (31/30)	30	200 mg of 0.5% ropivacaine, 1 mg epinephrine, and 30 mg ketorolac	31	40 mL of 0.5% ropivacaine	-VAS score -Opioid consumption	3 days
Michael	2022	Columbia	69 (52/22)	37	-	37	-	-VAS score -Opioid consumption	24 hours
Namdari	2017	USA	69.6 ± 9 (71/85)	78	266 mg of 1.3% bupivacaine diluted in 20 mL of saline solution	78	30 mL of 0.5% ropivacaine	-VAS score -Opioid consumption	24 hours
Okoroha	2016	USA	68.8 (28/29)	26	20 mL of LB (266 mg) mixed in 20 mL of sterile saline	31	40 mL of 0.5% ropivacaine	-VAS score -Opioid consumption	4 days

Panchamia	2019	USA	68.6 ± 11 (45/39)	42	120 mL of ropivacaine 0.5%, epinephrine and ketorolac	42	15-20 ml Bupivacaine 0.5% with epinephrine	-VAS score -Opioid consumption	16 weeks
Sabesan	2017	USA	64 (44/26)	34	20-mL (266-mg) dose of LB was diluted to a total volume of 80 mL with 0.9% normal saline	36	20-mL single bolus with 0.5% bupivacaine then 0.125% bupivacaine at a rate of 6 mL/h	-VAS score -Opioid consumption	30 days
Shumaier	2023	USA	67.5 (42/34)	38	20 mL of liposomal bupivacaine	38	20 to 30 mL of Ropivacaine 0.5%	-VAS score -Opioid consumption	14 days
Sicard	2018	France	72 ± 9.6 (35/64)	50	110 mL of 0.2% ropivacaine, 30 mg of ketoprofen and 0.5 mg of epinephrine	49	20 ml of ropivacaine 0.2% then infusion 5 ml/h	-VAS score -Opioid consumption	30 days

M/F (male/female), ISB (interscalene brachial plexus block), LB (liposomal bupivacaine), VAS (visual analog scale), mL (milliliters), mg (milligrams), h (hours), and USA (United States of America).

First author	Cochrane risk of bias 2					
	Bias arising from the randomization process	Bias due to deviations from intended interventions	Bias due to missing outcome data	Bias in the measurement of the outcome	Bias in the selection of the reported results	Overall bias
Abildgaard	Low risk	Some concerns	Low risk	Low risk	Low risk	Some concerns
Ali	Low risk	Some concerns	Low risk	Low risk	Low risk	Some concerns
Bingol	Low risk	Some concerns	Low risk	Some concerns	Low risk	Some concerns
Bjørnholdt	Low risk	High risk	Low risk	Some concerns	Low risk	
Klag	Low risk	Some concerns	Low risk	Low risk	Low risk	Some concerns
Michael	Some concerns	High risk	Low risk	Some concerns	Some concerns	High risk
Namdari	Low risk	Some concerns	Low risk	Some concerns	Low risk	Some concerns
Okoroha	Some concerns	High risk	Low risk	Some concerns	Low risk	High risk
Panchamia	Low risk	Some concerns	Low risk	Low risk	Low risk	Some concerns
Sabesan	Low risk	Some concerns	Low risk	Low risk	Low risk	Some concerns
Shumaier	Low risk	Some concerns	Low risk	Low risk	Low risk	Some concerns
Sicard	Low risk	High risk	Low risk	Some concerns	Low risk	High risk

Outcomes	№ of participants (studies) Follow-up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with ISB	Risk difference with Infiltration
Complications	763 (9 RCTs)	⊕⊕⊕○ Moderate ^a	OR 0.60 (0.25 to 1.42)	41 per 1 000	16 fewer per 1 000 (31 fewer to 16 more)
VAS H4	839 (10 RCTs)	⊕⊕⊕○ Moderate ^b	-	-	MD 1.96 higher (1.14 higher to 2.77 higher)
VAS H8	588 (7 RCTs)	⊕⊕⊕○ Moderate ^b	-	-	MD 1.33 higher (0.02 higher to 2.64 higher)
VAS H12	635 (7 RCTs)	⊕⊕⊕○ Moderate ^b	-	-	MD 0.32 higher (0.82 lower to 1.47 higher)
VAS H24	855 (10 RCTs)	⊕⊕⊕○ Moderate ^b	-	-	MD 0.13 higher (0.84 lower to 1.1 higher)
VAS 2 weeks	229 (3 RCTs)	⊕⊕○○ Low ^{a,b}	-	-	MD 0.6 higher (0.87 lower to 2.08 higher)
Opioids H24	855 (10 RCTs)	⊕⊕⊕⊕ High ^b	-	-	MD 7.68 higher (0.96 higher to 14.4 higher)
Hospital stay	756 (9 RCTs)	⊕⊕○○ Low ^{a,b}	-	-	MD 0 (0.13 lower to 0.12 higher)

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI). CI: confidence interval; MD: mean difference; OR: odds ratio

GRADE Working Group grades of evidence

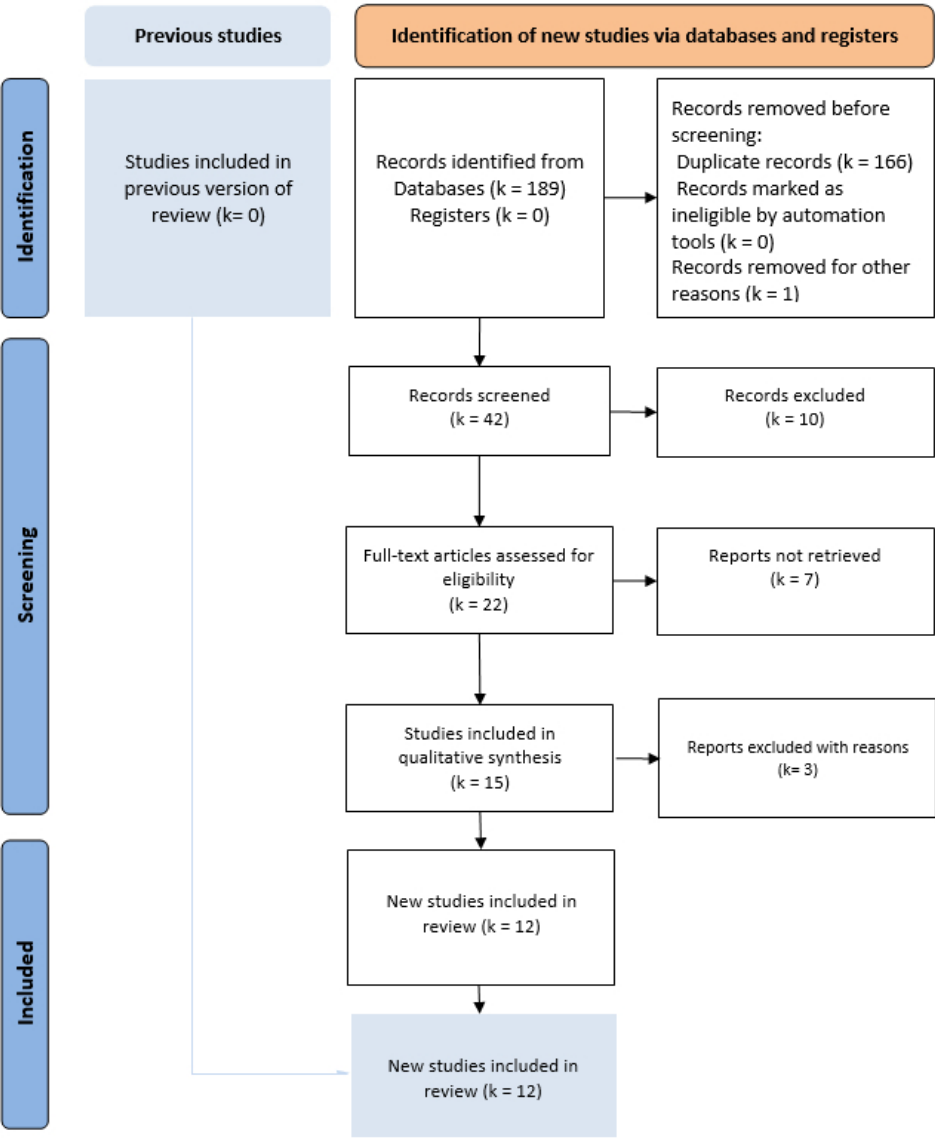
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect. **Moderate certainty:** we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different. **Low certainty:** our confidence in the effect estimate is limited: the true effect may be substantially different

from the estimate of the effect. **Very low certainty:** we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

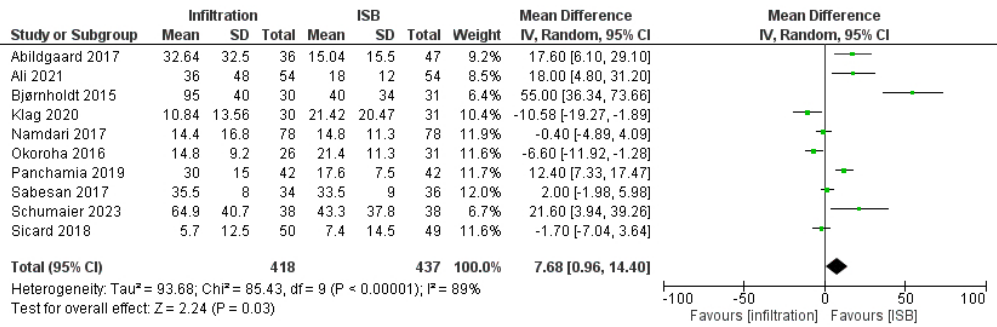
Explanations

- a. Small incidence of the effect
- b. Existence of heterogeneity among the studies

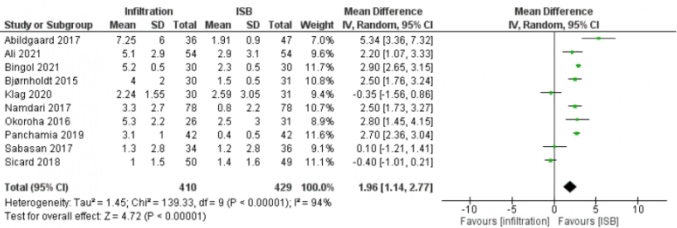
For Peer Review



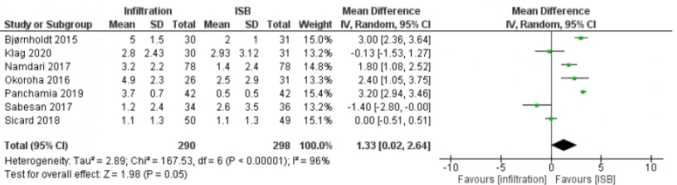
451x524mm (38 x 38 DPI)



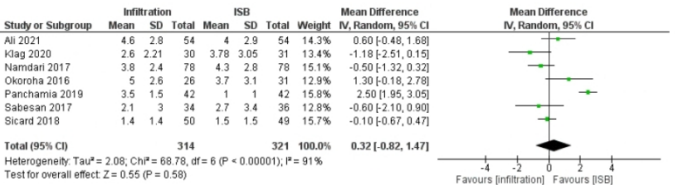
291x95mm (72 x 72 DPI)



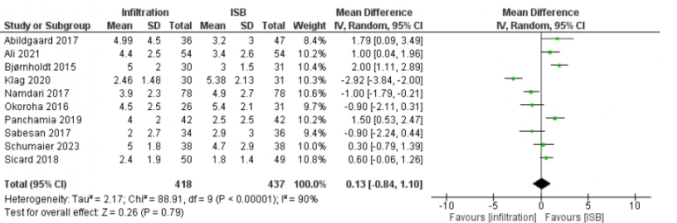
A. Forest plot of VAS H4



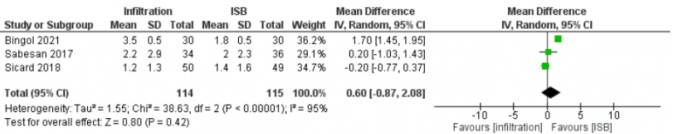
B. Forest plot of VAS H8



C. Forest plot of VAS H12



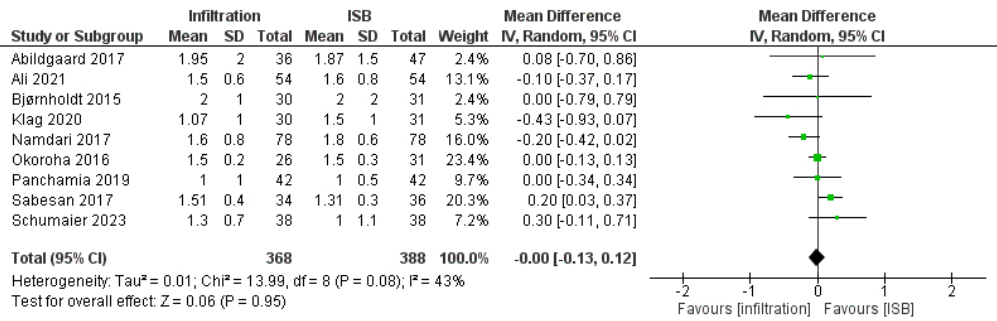
D. Forest plot of VAS H24



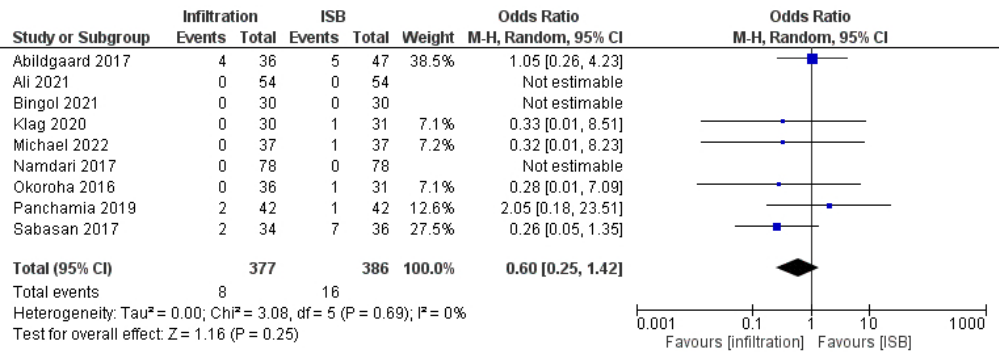
E. Forest plot of 2 Week

159x273mm (150 x 150 DPI)

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60



279x90mm (72 x 72 DPI)



268x95mm (72 x 72 DPI)



PRISMA 2020 Checklist

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	1
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	2
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	2
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	3
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	3
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	3
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	3
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	3
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	4
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	4
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	4
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	4
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	4-5
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	4-5
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	4-5
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	4
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	3
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	3
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	3
Certainty	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	4-5



PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
assessment			
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	5
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	5
Study characteristics	17	Cite each included study and present its characteristics.	5
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	7
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	6
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	6
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	6
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	8
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	8
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	8
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	9
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	10
	23b	Discuss any limitations of the evidence included in the review.	10
	23c	Discuss any limitations of the review processes used.	10
	23d	Discuss implications of the results for practice, policy, and future research.	10-11
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	3
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	3
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	3
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	12
Competing interests	26	Declare any competing interests of review authors.	12
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	12



PRISMA 2020 Checklist

10.1136/bmj.n71

For more information, visit: <http://www.prisma-statement.org/>

For Peer Review