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Review Article

# Comparative Efficacy of Different Classes of Antiemetic Medications for the Prevention of Nausea and Vomiting in Cesarean Section: A Network Meta-Analysis

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## Abstract

**Background:** Antiemetic medications have been associated with the prevention of nausea and vomiting in cesarean section, although less is known about the comparative efficacy of different medication classes. **Methods:** We conducted a systematic review with network meta-analyses to compare and rank antiemetic medication classes (5-HT3 receptor antagonists, dopamine receptor antagonists, corticosteroids, antihistamines, anticholinergic agents, sedatives, and opioid antagonists or partial agonists) in terms of preventing intra- and postoperative nausea and vomiting among patients undergoing cesarean section. We included all randomized controlled trials (RCTs) that evaluated any antiemetic medication classes' treatment for target outcomes. Network meta-analysis was conducted with a frequentist approach using the R *netmeta* package. A total of 58 trials were included (6,665 women undergoing cesarean section; mean age, 28.1 years). **Results:** Compared with placebo, all interventions reduced the odds of intraoperative nausea (except antihistamines), intraoperative vomiting (except antihistamines), postoperative nausea (except anticholinergic agents and opioid antagonists), and postoperative vomiting (except opioid antagonists). In terms of intraoperative nausea and both intra- and postoperative vomiting, sedatives ranked first among other medication classes. **Conclusions:** The relative effect sizes for various classes of antiemetic medication in preventing nausea and vomiting in the cesarean section were modeled using the principles of network meta-analysis which may facilitate informed clinical decision-making.

**Keywords:** *Antiemetics, cesarean section, nausea and vomiting, network meta-analysis*

## Introduction

Cesarean section is one of the most frequent surgical procedures performed, comprising about 7% of surgeries worldwide.[1] Despite remarkable advances in different anesthesia techniques,[2] intra- and postoperative nausea and vomiting are still present in a significant number of patients. It is estimated that up to 80% of patients undergoing cesarean section experience nausea and vomiting during and/or after the procedure.[3]

The negative impacts of nausea and vomiting in such surgeries are well-recognized. It can be disturbing and unpleasant to patients and make surgery difficult. In addition, it can complicate the postoperative course in several ways—(i) vomit aspiration, (ii) disturbance of electrolyte and dehydration, (iii) delay in nutrition and fluid intake and oral drug therapy, and (iv) wound dehiscence.[4,5] Moreover, surgery-related nausea and vomiting can result in prolonged or unexpected hospital stays or readmission.[6]

In response to these challenges, it is important for patients undergoing surgery to be provided with sufficient antiemetic prophylaxis.[7] A broad variety of antiemetic medications are available for the prevention of nausea and vomiting among patients undergoing different kinds of surgeries.[4] Many studies have evaluated the effects of the available antiemetics to reduce the likelihood of developing nausea and vomiting in cesarean section procedures.

However, the existent trials investigated different ranges of pharmacological interventions in various ways, creating a wide spectrum of information about their efficacy that is difficult to assess through simple direct comparisons.[8] The lack of

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head-to-head comparisons of various pharmacological interventions renders the choice of treatment a clinical challenge. Therefore, we conducted a network meta-analysis that provided direct, indirect, and mixed evidence[9] to compare multiple medication classes simultaneously regarding their efficacy in terms of preventing nausea and vomiting in cesarean section.

## Methods

We conducted our systematic review in accordance with the PRISMA Extension Statement for Reporting of Systematic Reviews Incorporating Network Meta-analyses of Healthcare Interventions.[10]

### Search strategy

The search strategy was developed in collaboration with a research librarian. Several relevant databases were searched, including Cochrane Central Register of Controlled Trials, CINAHL, Embase, and MEDLINE, from the date of their inception to October 31, 2021 (final search), with no language restrictions. We searched for RCTs on the use of antiemetic medications for nausea and vomiting among women undergoing cesarean section. The initial search was developed in MEDLINE [Supplementary Table 1] and adjusted to other databases. The electronic database searches were supplemented with a manual search of reference lists of all eligible articles as well as relevant reviews.

### Eligibility criteria

**Types of studies**: We included randomized controlled trials (RCTs) of antiemetic drugs in the treatment of nausea and vomiting among patients undergoing cesarean section. We did not restrict the study eligibility by publication status or language. Prospective cohort studies and quasi-randomized studies were excluded.

**Types of participants**: We included pregnant females undergoing elective or emergency cesarean section under regional anesthesia.

**Types of interventions**: In this systematic review, we included studies that participants were females undergoing cesarean section under regional anesthesia (either spinal, epidural, or both) comparing pharmacological interventions for preventing nausea and vomiting against placebo or each other (intervention versus intervention comparisons). We set no restrictions on the drug doses or when treatments were applied (either intraoperatively, postoperatively, or both). In this systematic review, we focused on studies where interventions were given with the specific purpose of preventing nausea and/or vomiting. Thus, interventions of interest were the following drug classifications: (a) serotonin (5-HT3) receptor antagonists, (b) dopamine receptor antagonists, (c) corticosteroids, (d) antihistamines, (e) anticholinergic agents, (f) sedatives, and (g) opioid antagonists or partial agonists.

We excluded studies in which the focus was on non-pharmacological interventions. We also excluded trials with the express purpose of investigating the effects of drugs on other clinical conditions such as aspiration pneumonitis. Studies that investigated the efficacy of interventions for alleviating established nausea and vomiting were also excluded.

**Types of outcomes**: The primary outcomes of this network meta-analysis were the incidence of nausea and vomiting categorized as follows:
1. Intraoperative nausea
2. Intraoperative vomiting
3. Postoperative nausea
4. Postoperative vomiting

We excluded studies that did not provide separate data on nausea or vomiting and presented a combined score. We also excluded studies that reported the number of nausea and vomiting episodes, rather than the number of pregnant women who had nausea and/or vomiting.

### Study selection and data extraction

Two investigators screened titles and abstracts of citations in duplicate and independently. All records judged potentially relevant were evaluated for full-text eligibility by the same two reviewers. Discordances were discussed with a third reviewer and resolved by consensus. We extracted data on study characteristics including first author, publication year, study settings (country), the mean age of participants, anesthesia type, mean operation duration, intervention characteristics, and outcome data using a structured extraction form (Microsoft Access, 2020).

### Risk of bias assessment

The methodological quality of included studies was independently evaluated by two of the reviewers using the Cochrane Collaboration's tool for assessing the risk of bias.[11] Trials were judged as having a "low," "high," or "unclear" risk of bias across the seven specified domains: sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective outcome reporting, and other sources of bias.

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### Statistical analysis

The network meta-analysis was concocted using the R *netmeta* package,[12] applying a frequentist approach.[13] The *netgraph* function was used to generate network plots to describe and present the geometry of different forms of interventions. Nodes were used to represent different medication classes and edges to represent the head-to-head comparisons between interventions. Random effect models were employed because of the between-study heterogeneities. We assessed between-study heterogeneities using Cochran Q (weighted sum of squared differences between individual study effects and the pooled effect across studies) and $I^2$ (percentage of variation across studies due to heterogeneity rather than chance).

We calculated treatment estimates for all outcomes as odds ratios (ORs), together with their 95% confidence intervals (CIs). The relative ranking probability of each pharmacological intervention being among the best intervention was obtained using *P*-score and displayed using a netrank plot.[14] A higher *P*-score meant better treatment. A node-splitting method was used to split network estimates into the contribution of direct and indirect evidence and to test for local inconsistency in network meta-analysis. To assess the global inconsistency in each model, we used *decomp.design* function. A $P$ value $< 0.005$ was considered suggestive of significant inconsistency. Publication bias was assessed using comparison-adjusted funnel plots. $P$ values $< 0.005$ indicated a significant difference.

## Results

We identified a total of 1,613 potentially relevant records through database searching in addition to 25 records retrieved by manual citation search. The results of the literature search and selection process are shown in the PRISMA flowchart [Figure 1].

### Characteristics of included studies

A total of 58 RCTs,[15-69] comprising 6,665 randomized pregnant women, were mostly of small size with a median (IQR [range]) number of 90 (67–149 [40–300]) participants, with a median age of 28.1 years (IQR: 26.3–30.2) and published between 1987 and 2020 (with 80% from 2000 onward). The included studies emanated from 18 separate countries and most of them were from the USA (11 studies), followed by Iran (8 studies) and India (6 studies). In this review, 14 single antiemetic medications under seven classifications were included. Most trials investigated only a single drug (38 studies), and the remaining 20 studies were multi-arm trials with more than one medication agent [Supplementary Table 2].

The risk of bias summary is provided in Figure 2. Of the 55 studies, many were deemed to be of unclear or high risk of bias in three domains as follows: allocation concealment ($n$ = 50 [90%]), blinding ($n$ = 31 [56%]), and selective reporting ($n$ = 55 [100%]). The risk of bias for each study is shown in Supplementary Figure 1

### Assessment of publication bias

Comparison-adjusted funnel plots [Figure 3] were symmetrical, implying evidence of publication bias.

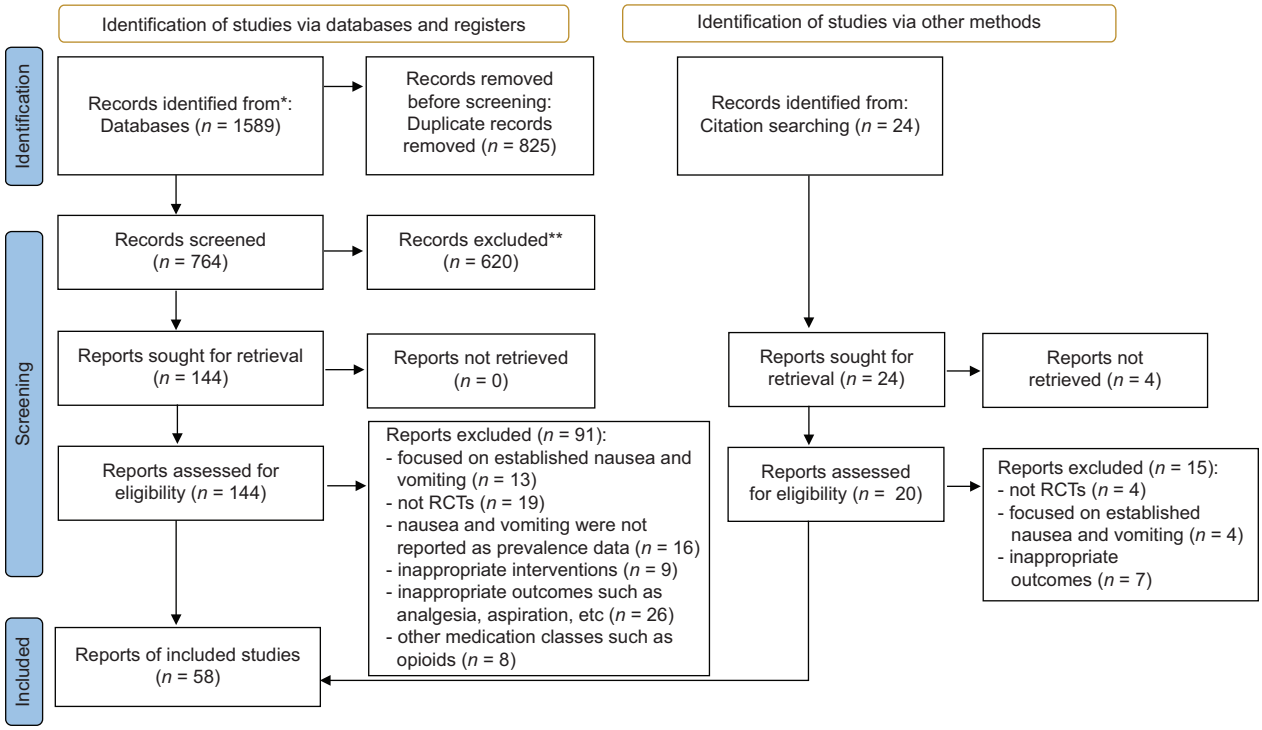


**Figure 1: Study selection for the meta-analysis**

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### Intraoperative nausea

Figure 4 shows the network of eligible comparisons for intraoperative nausea, including 38 RCTs with 4,100 pregnant women and six antiemetic medication classes, and a placebo. Dopamine receptor antagonists ($n$ = 15 studies), 5-HT3 receptor antagonists ($n$ = 12 studies), and sedatives ($n$ = 8 studies), all compared with placebo, were the most common comparisons.

Of the six included pharmacological interventions, five medication classes had significantly greater effects on intraoperative nausea compared with placebo as follows: dopamine receptor antagonists (OR = 0.27, 95% CI: 0.19–0.40), 5-HT3 receptor antagonists (OR = 0.32, 95% CI: 0.23–0.44), anticholinergic agents (OR = 033, 95% CI: 0.19–0.57), and sedatives (OR = 0.44, 95% CI: 0.28–0.70) [Figure 5]. According to the *P*-score for the prevention of intraoperative nausea, dopamine receptor antagonists were ranked the best among all treatments [Figure 5].

### Intraoperative vomiting

Among the eligible trials considered in this review, 34 studies, involving 3,857 patients, reported data on intraoperative vomiting. The network of eligible comparisons for this outcome is shown in Figure 4. Dopamine receptor antagonists ($n$ = 12), 5-HT3 receptor antagonists ($n$ = 11), and sedatives ($n$ = 8), all compared with the placebo, were the most common comparisons.

Figure 5 shows the effects of intraoperative vomiting between active pharmacological interventions and placebo. This ranking plot demonstrated that sedatives (OR = 0.25, 95% CI: 0.15–0.41), dopamine receptor antagonists (OR = 0.34, 95% CI: 0.21–0.54), 5-HT3 receptor antagonists (OR = 0.35, 95% CI: 0.24–0.51), corticosteroids (OR = 0.44, 95% CI: 0.24–0.82), and anticholinergic agents (OR = 0.49, 95% CI: 0.28–0.87) were significantly more efficacious than the placebo. According to the rank-heat plot, sedatives were the most effective pharmacological interventions for preventing early intraoperative vomiting [Figure 5].

### Postoperative nausea

For estimating the drug efficacy against postoperative nausea, we looked at data from 3,251 individuals from 26 studies. The network diagram [Figure 4] presents direct comparisons among classes. 5-HT3 receptor ($n$ = 10), dopamine receptor antagonists ($n$ = 7), and corticosteroids ($n$ = 6), all compared with placebo, were the most common comparisons.

Figure 5 provides the network meta-analysis results with the ranking of all medication classes compared with placebo for intraoperative nausea. This ranking showed that sedatives (OR = 0.17, 95% CI: 0.07–0.40), antihistamines (OR = 0.25, 95% CI: 0.13–0.48), 5-HT3 antagonists (OR = 0.25, 95% CI: 0.17–0.39), corticosteroids (OR = 0.35, 95% CI: 0.21–0.60), and dopamine receptor antagonists (OR = 0.45, 95% CI: 0.26–0.75) were significantly superior for placebo in preventing intraoperative nausea. Two other antiemetics (i.e., anticholinergic agents and opioid antagonists) showed no significant beneficial effect compared with a placebo.

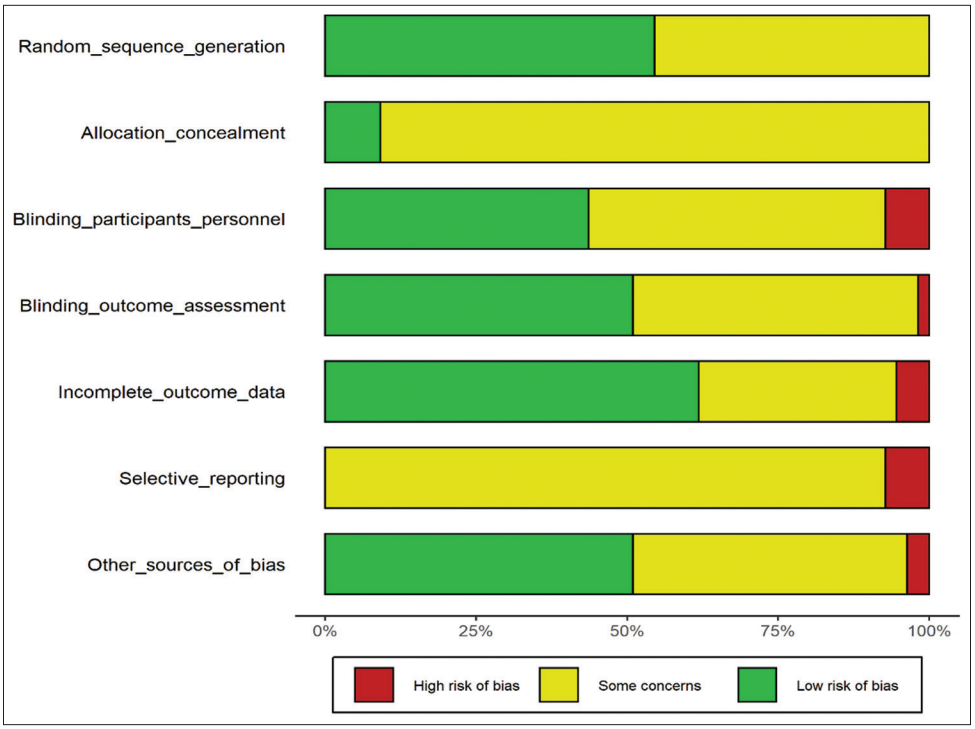


**Figure 2: Risk of bias summary**

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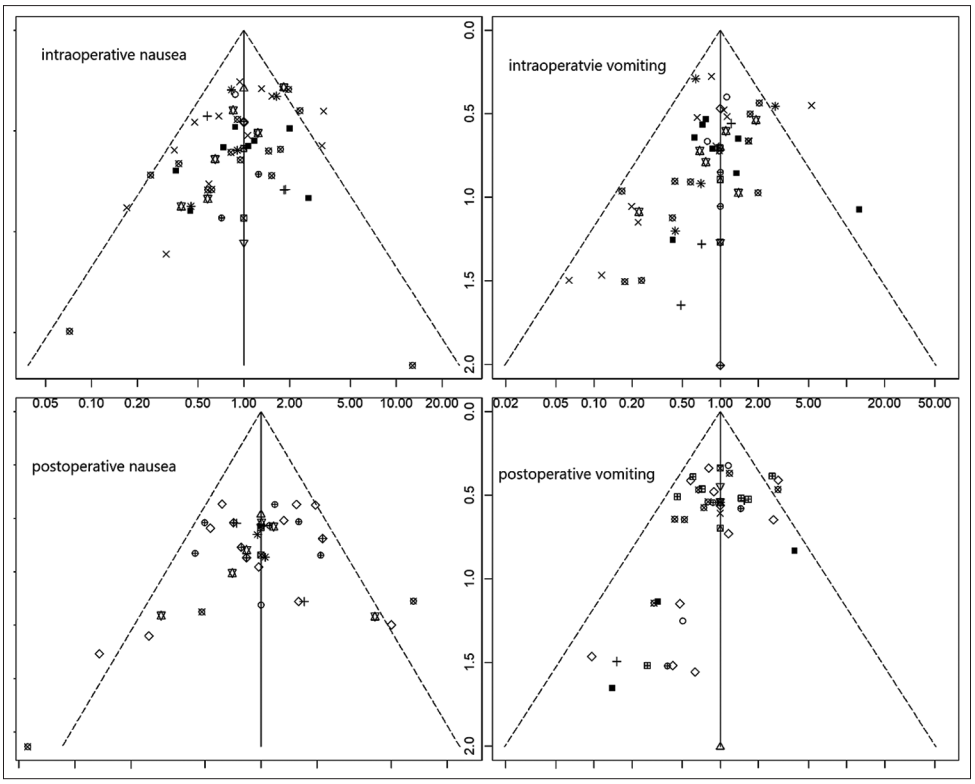


**Figure 3: Comparison-adjusted funnel plots of trials included in the network meta-analysis for each outcome**

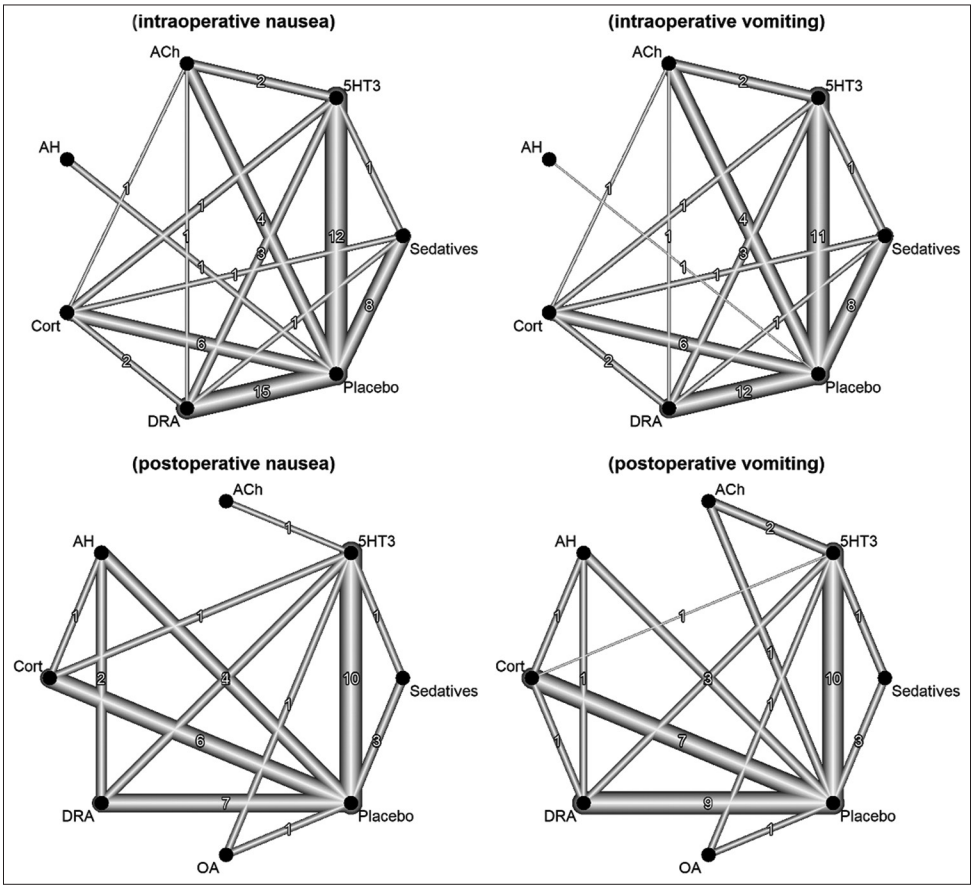


**Figure 4: Network diagram representing direct comparisons among medication classes.** ***The width of lines indicates the number of trials in which each direct comparison is made***

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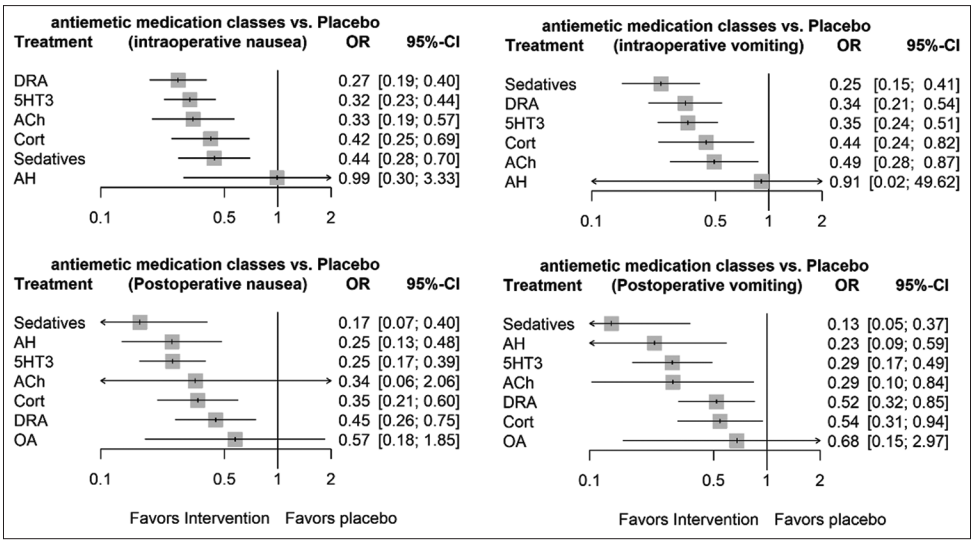


**Figure 5: Treatment efficacy in the prevention of nausea and vomiting among patients undergoing cesarean section.** ***Heterogeneity statistics: intraoperative nausea ($I^2$: 40.2, Q = 51.9); intraoperative vomiting ($I^2$: 23.0, Q = 49.8); postoperative nausea ($I^2$: 51.8.2, Q = 53.9); postoperative vomiting ($I^2$: 47.2, Q = 34.9)***

The rank-heat plot of treatments [Figure 5] showed that sedatives had the most preventive effect among other medication classes in terms of postoperative nausea.

### Postoperative vomiting

Twenty-eight trials were included in the network meta-analysis for postoperative vomiting, with 3,608 pregnant women and seven interventions (6 drug classes and placebo) [Figure 4]. 5-HT3 receptor antagonists ($n$ = 10 studies), dopamine receptor antagonists ($n$ = 9 studies), and corticosteroids ($n$ = 7 studies), all compared with placebo, were the most common comparisons.

For postoperative vomiting, all classes of medications, but opioid antagonists, had significantly beneficial effects compared with the placebo with 46% to 87% relative risk reductions. The specific estimated ORs were as follows: sedatives (OR = 0.13, 95% CI: 0.05–0.37), antihistamines (OR = 0.23, 95% CI: 0.09–0.59), 5-HT3 antagonists (OR = 0.29, 95% CI: 0.17–0.49), anticholinergic agents (OR = 0.29, 95% CI: 0.10–0.84), dopamine receptor antagonists (OR = 0.52, 95% CI: 0.32–0.85), and corticosteroids (OR = 0.54, 95% CI: 0.31–0.94). Opioid antagonists showed no significant beneficial effect compared with the placebo [Figure 5]. According to the *P*-score plot, of all medication classes, sedatives were ranked first for the prevention of postoperative vomiting [Figure 6].

### Heterogeneity and consistency analysis

The evaluation of inconsistency in the contribution of direct and indirect evidence using a node-splitting method showed that there were no inconsistencies among almost all studies ($P$ > 0.05). In addition, the results of the decomp.design function supported the global consistency for all models, indicating the reliability of the results [Supplementary Tables 3 and 4].

## Discussion

Although several systematic reviews on pharmacological interventions for the prevention of post-cesarean nausea and vomiting have been performed,[70,71] they were conducted using traditional meta-analysis. In contrast, we have used network meta-analysis to evaluate the evidence for medication classes' efficacy in preventing these outcomes. Unlike conventional meta-analysis, where only two interventions are compared by applying pooled head-to-head data, network meta-analysis allows not only for comparisons between multiple interventions but also for comparisons between interventions that have not been compared directly in RCTs.[72] These advantages allow clinicians to reach informed treatment decisions based on evidence from network meta-analysis, specifically in the absence of direct comparison of candidate treatments. In this systematic review, we included all antiemetic options for investigating their effect on the prevention of post-cesarean nausea and vomiting.

This network meta-analysis indicates that most of the antiemetic pharmacological classes were statistically superior to placebo in terms of nausea and vomiting among women undergoing cesarean section. For example, In a study conducted by Tkachenko and Pyasetska in 2019, it was found that the addition of 4 mg intrathecal dexamethasone as an adjuvant for spinal anesthesia in the elective cesarean section can significantly decrease the frequency and manifestations of nausea.[23] In another study, 3 mg (3 ml) of Granisetron was injected after intrathecal injection. The results of this study showed that Granisetron is an effective way to prevent shivering, nausea, and vomiting during cesarean delivery under spinal anesthesia with no effect on the Apgar score.[39] However, some investigations showed no significant difference in the number of patients experiencing postoperative nausea and

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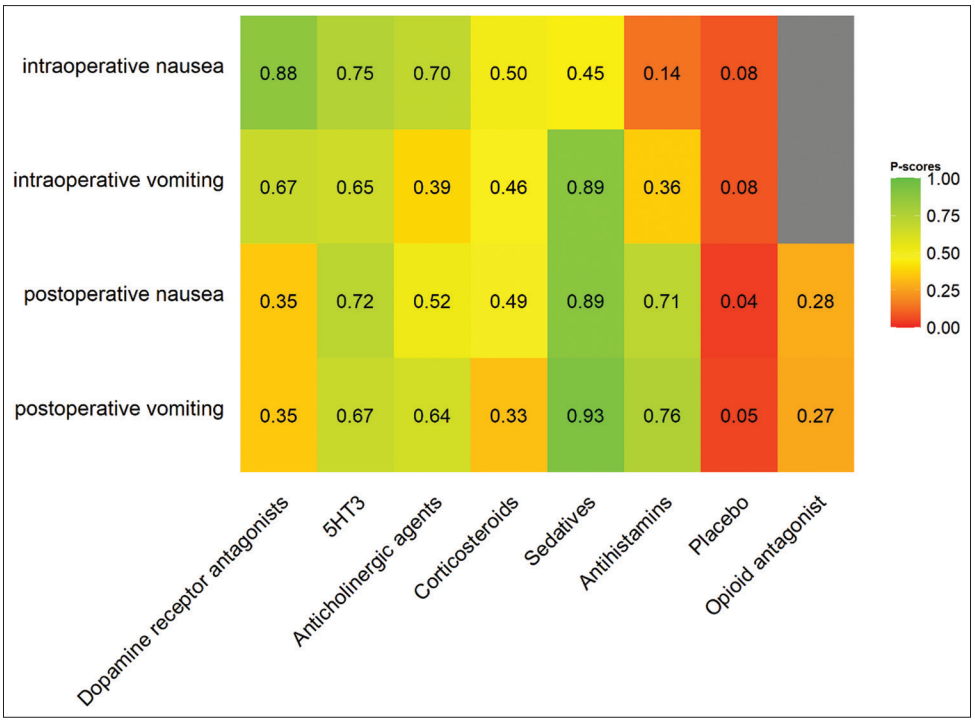


**Figure 6: Results of *P*-score analysis in terms of each outcome**

vomiting between the treatment and control groups.[26] Also, the result of the present network meta-analysis is consistent with results from previous conventional meta-analyses,[70] and a possible explanation for these results may be the multi-factorial pathogenesis of postoperative nausea and vomiting.[73] However, the previous traditional meta-analyses were unable to conclude superiority due to the absence of a direct comparison. In the present network meta-analysis, which included all direct and indirect comparisons, we found that sedatives were significantly better than other medication classes in terms of three of the four selected outcomes, that is, postoperative vomiting, postoperative nausea, and intraoperative vomiting.

The current network meta-analysis showed that different pharmacological classes have different efficacy in terms of nausea and vomiting at different time points (i.e., intraoperatively or postoperatively). These findings further support the idea that drugs with different mechanisms of action (represented as different medication classes in this review) should be used in combination to optimize their efficacy.[74]

The included trials showed that emetic symptoms are very common in both intra- and post-cesarean sections. Non-intervention arms of included studies suggested that the prevalence of nausea during cesarean section ranges between 20 and 60% (data not shown). This finding corroborates the recommendations of available guidelines,[75] suggesting a focus on the treatment of prophylaxis rather than emesis at cesarean section. After the advantages of a single medication, classes had been established in this network meta-analysis, and future research needs to move toward combining antiemetics classes for improved efficacy as these kinds of trials are scarce.

### Limitations of the study

This study has limitations that should be considered when interpreting the results. First, most of the included trials in our network meta-analysis had an unclear or high risk of bias for most domains, which decreased this study's overall evidence level. Second, there were potential heterogeneities in patients' characteristics as well as surgical procedures or postoperative care that could have confounded or affected findings for the target outcomes. Third, we could not retrieve additional unpublished reports and are aware that a substantial amount of information is not publicly available. Finally, differences in the time frame outcome evaluation also could not be assessed due to a limited number of studies in certain time frames.

## Conclusion

In conclusion, all topically applied medication classes included in this network meta-analysis were efficacious in terms of most of the targeted outcomes. Sedative agents were highly efficacious in preventing nausea and vomiting among women undergoing cesarean section surgery. However, a similar network meta-analysis is required to rank each treatment option in terms of potential adverse effects.

### Ethical considerations

Ethical issues (including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double

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publication and/or submission, redundancy, etc.) have been completely observed by the authors.

### Authors' contributions

ZA and SA contributed to the concept and design of the study. ZA and SH contributed to the analysis and interpretation of the data. EDM, SGS, AM, MM, and SA contributed to the critical revision of the article and writing of the manuscript. All authors reviewed the manuscript.

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### Conflicts of interest

There are no conflicts of interest.

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# Comparative efficacy of different classes of antiemetic medications for the prevention of nausea and vomiting in cesarean section: a network meta-analysis

## Supplementary File

Supplementary Table 1: Search Strategy

| Data source: MEDLINE | |
|---|---|
| 1 | Delivery, Obstetric/ |
| 2 | exp Cesarean Section/ |
| 3 | exp Extraction, Obstetrical/ |
| 4 | Obstetrical Forceps/ |
| 5 | ("c section*" or c-section* or cesar* or caesar* or delivery mode or delivery modes or elective cs or "mode of delivery" or obstetric* forcep* or planned cs* or ventouse*).ti,ab,kf |
| **6** | **1 OR 2 OR 3 OR 4 OR 5** |
| 7 | exp "Postoperative Nausea and Vomiting" |
| 8 | exp Anesthesia Recovery Period |
| 9 | postoperative adj3 (care or nausea or vomit*)).mp. |
| 10 | (recovery adj3 (room or an?esthesia or period)).mp |
| 11 | PONV |
| **12** | **7 OR 8 OR 9 OR 10 OR 11** |
| 13 | (randomized controlled trial).pt |
| 14 | (controlled clinical trial).pt |
| 15 | randomized.ab |
| 16 | clinical trials as topic.sh |
| 17 | placebo.ab |
| 18 | randomly.ab |
| **21** | **13 OR 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20** |
| **22** | **6 AND 12 AND 21** |

**Supplementary Table 2: characteristics of included studies**

| study | country | anesthesia | surgery duration (min) | mean age (yrs) | outcome | drug1 | No. of Patients in group 1 | No. of events in group 1 | drug2 | No. of Patients in group 2 | No. of events in group 2 | drug3 | No. of Patients in group 3 | No. of events in group 3 | drug4 | No. of Patients in group 4 | No. of events in group 4 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Abdel-Aleem 2012 | Egypt | Spinal | | 24.9 | Nausea postoperatively | Corticos-Dexamethasone - 8 mg | 60 | 25 | Placebo | 60 | 48 | | | | | | |
| Abdel-Aleem 2012 | Egypt | Spinal | | 24.9 | Vomiting (and/or retching) postoperatively | Corticos-Dexamethasone - 8 mg | 60 | 16 | Placebo | 60 | 32 | | | | | | |
| Abdollahpour 2015 | Iran | Spinal | | 28.3 | Nausea postoperatively | Sedatives-Midazolam - 0.2 mg/kg | 25 | 3 | Placebo | 25 | 8 | | | | | | |
| Abdollahpour 2012 | Iran | Spinal | | 28.3 | Vomiting (and/or retching) postoperatively | Sedatives-Midazolam - 0.2 mg/kg | 25 | 1 | Placebo | 25 | 5 | | | | | | |
| Abouleish 1999 | UK | Spinal | 47.5 | 26.7 | Nausea intraoperatively | 5-HT3-Ondansetron - 4 mg | 36 | 21 | Placebo | 38 | 30 | | | | | | |
| Abouleish 1999 | UK | Spinal | 47.5 | 26.7 | Vomiting (and/or retching) intraoperatively | 5-HT3-Ondansetron - 4 mg | 36 | 13 | Placebo | 38 | 22 | | | | | | |
| Apiliogullari 2007 | Turkey | unclear | | | Nausea postoperatively | D2-Metoclopramide - 10 mg | 58 | 11 | Placebo | 63 | 20 | Antihist-Dimenhydrate - 50 mg | 62 | 8 | Antihist-Dimenhydrate - 100 mg | 60 | 3 |
| Apiliogullari 2007 | Turkey | unclear | | | Vomiting (and/or retching) postoperatively | D2-Metoclopramide - 10 mg | 58 | 13 | Placebo | 63 | 10 | | | | | | |
| Baciarello 2011 | Italy | Spinal | | 34.3 | N+V Postopetarively | Antichol-Atropine - 100 mcg | 139 | 34 | Placebo | 65 | 33 | | | | | | |
| Biswas 2003 | India | Spinal | 67.2 | 24.2 | Nausea intraoperatively | D2-Metoclopramide - 10 mg | 20 | 4 | Placebo | 20 | 8 | Corticos-Dexamethasone - 8 mg | 20 | 2 | Antichol-Glycopyrrolate - 0.2 mg | 20 | 2 |
| Biswas 2003 | India | Spinal | 67.2 | 24.2 | Vomiting (and/or retching) intraoperatively | D2-Metoclopramide - 10 mg | 20 | 2 | Placebo | 20 | 3 | Corticos-Dexamethasone - 8 mg | 20 | 2 | Antichol-Glycopyrrolate - 0.2 mg | 20 | 1 |
| Caba 1997 | Spain | Intradural | | | Nausea intraoperatively | Sedatives-Propofol - 10 mg | 26 | 5 | Placebo | 31 | 5 | | | | | | |
| Caba 1997 | Spain | Intradural | | | Vomiting (and/or retching) intraoperatively | Sedatives-Propofol - 10 mg | 26 | 1 | Placebo | 31 | 2 | | | | | | |
| Caba 1997 | Spain | Intradural | | | Nausea postoperatively | Sedatives-Propofol - 10 mg | 26 | 2 | Placebo | 31 | 1 | | | | | | |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Caba 1997 | Spain | Intradural | | | Vomiting (and/or retching) postoperatively | Sedatives-Propofol - 10 mg | 26 | 0 | Placebo | 31 | 1 | | | | | | |
| Cardoso 2013 | Brazil | Spinal | | 27.1 | Nausea postoperatively | Corticos-Dexamethasone - 10 mg | 35 | 11 | Placebo | 35 | 26 | | | | | | |
| Cardoso 2013 | Brazil | Spinal | | 27.1 | Vomiting (and/or retching) postoperatively | Corticos-Dexamethasone - 10 mg | 35 | 11 | Placebo | 35 | 23 | | | | | | |
| Carvalho 2010 | Canada | Spinal | | | Nausea intraoperatively | Antihist-Dimenhydrinate - 25 mg | 78 | 12 | Placebo | 71 | 11 | | | | | | |
| Carvalho 2010 | Canada | Spinal | | | Nausea postoperatively | Antihist-Dimenhydrinate - 25 mg | 78 | 9 | Placebo | 71 | 12 | | | | | | |
| Carvalho 2010 | Canada | Spinal | | | Vomiting (and/or retching) intraoperatively | Antihist-Dimenhydrinate - 25 mg | 78 | 0 | Placebo | 71 | 0 | | | | | | |
| Carvalho 2010 | Canada | Spinal | | | Vomiting (and/or retching) postoperatively | Antihist-Dimenhydrinate - 25 mg | 78 | 0 | Placebo | 71 | 3 | | | | | | |
| Charuluxananan 2003 | Thailand | Spinal | | | Nausea postoperatively | Opioid antagonist-Nalbuphine - 4 mg | 60 | 12 | Placebo | 60 | 16 | 5-HT3-Ondansetron - 4 mg | 60 | 7 | 5-HT3-Ondansetron - 8 mg | 60 | 7 |
| Charuluxananan 2003 | Thailand | Spinal | | | Vomiting (and/or retching) postoperatively | Opioid antagonist-Nalbuphine - 4 mg | 60 | 5 | Placebo | 60 | 4 | 5-HT3-Ondansetron - 4 mg | 60 | 3 | 5-HT3-Ondansetron - 8 mg | 60 | 4 |
| Cherian 2001 | UK | Spinal | | | Nausea intraoperatively | 5-HT3-Ondansetron - 4 mg | 41 | 8 | Placebo | 40 | 7 | | | | | | |
| Cherian 2001 | UK | Spinal | | | Vomiting (and/or retching) intraoperatively | 5-HT3-Ondansetron - 4 mg | 41 | 7 | Placebo | 40 | 18 | | | | | | |
| Chestnut 1987 | USA | lumbar epidural | | | Nausea intraoperatively | D2-Metoclopramide - 0.15 mg/kg | 34 | 4 | Placebo | 33 | 12 | | | | | | |
| Chestnut 1987 | USA | lumbar epidural | | | Vomiting (and/or retching) intraoperatively | D2-Metoclopramide - 0.15 mg/kg | 34 | 0 | Placebo | 33 | 5 | | | | | | |
| Chestnut 1987 | USA | lumbar epidural | | | Nausea postoperatively | D2-Metoclopramide - 0.15 mg/kg | 34 | 5 | Placebo | 33 | 12 | | | | | | |
| Chestnut 1987 | USA | lumbar epidural | | | Vomiting (and/or retching) postoperatively | D2-Metoclopramide - 0.15 | 34 | 4 | Placebo | 33 | 12 | | | | | | |

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| | | | | | | mg/kg | | | | | | | | | | | |
| Dasgupta 2012 | India | Spinal | 47 | 25 | Nausea postoperatively | 5-HT3-Granisetron - 40 mcg/kg | 40 | 5 | Placebo | 40 | 14 | | | | | | |
| Dasgupta 2012 | India | Spinal | 47 | 25 | Vomiting (and/or retching) postoperatively | 5-HT3-Granisetron - 40 mcg/kg | 40 | 3 | Placebo | 40 | 7 | | | | | | |
| Direkvand-Moghadam 2013 | Iran | Spinal | 55.2 | 26.6 | Nausea postoperatively | D2-Metoclopramide - 10 mg | 34 | 9 | Placebo | 34 | 17 | | | | | | |
| Direkvand-Moghadam 2013 | Iran | Spinal | 55.2 | 26.6 | Vomiting (and/or retching) postoperatively | D2-Metoclopramide - 10 mg | 34 | 4 | Placebo | 34 | 11 | | | | | | |
| Duman 2010 | Turkey | Spinal | | | Vomiting (and/or retching) postoperatively | D2-Metoclopramide - 10 mg | 58 | 13 | Placebo | 63 | 10 | Antihist-Dimenhydrate - 50 mg | 61 | 5 | | | |
| Duman 2010 | Turkey | Spinal | | | Nausea postoperatively | Antihist-Dimenhydrate - 50 mg | 61 | 6 | Placebo | 63 | 20 | D2-Metoclopramide - 10 mg | 58 | 11 | | | |
| El-Deeb 2011 | Egypt | Spinal | 69.7 | 26.1 | Nausea intraoperatively | 5-HT3-Ondansetron - 4 mg | 150 | 33 | Placebo | 150 | 69 | | | | | | |
| El-Deeb 2011 | Egypt | Spinal | 69.7 | 26.1 | Vomiting (and/or retching) intraoperatively | 5-HT3-Ondansetron - 4 mg | 150 | 25 | Placebo | 150 | 57 | | | | | | |
| El-Deeb 2011 | Egypt | Spinal | 69.7 | 26.1 | Nausea postoperatively | 5-HT3-Ondansetron - 4 mg | 150 | 12 | Placebo | 150 | 51 | | | | | | |
| El-Deeb 2011 | Egypt | Spinal | 69.7 | 26.1 | Vomiting (and/or retching) postoperatively | 5-HT3-Ondansetron - 4 mg | 150 | 8 | Placebo | 150 | 34 | | | | | | |
| Garcia-Miguel 2000 | Spain | Spinal | | | Nausea intraoperatively | D2-Metoclopramide - 10 mg | 48 | 3 | Placebo | 50 | 21 | 5-HT3-Ondansetron - 4 mg | 49 | 4 | | | |
| Garcia-Miguel 2000 | Spain | Spinal | | | Vomiting (and/or retching) intraoperatively | D2-Metoclopramide - 10 mg | 48 | 1 | Placebo | 50 | 9 | 5-HT3-Ondansetron - 4 mg | 49 | 0 | | | |
| Habib 2013 | Canada | Spinal | | | Nausea intraoperatively | D2-Metoclopramide - 10 mg | 99 | 31 | Placebo | 101 | 49 | | | | | | |
| Habib 2013 | Canada | Spinal | | | Vomiting (and/or retching) intraoperatively | D2-Metoclopramide - 10 mg | 99 | 10 | Placebo | 101 | 15 | | | | | | |
| Harnett 2007 | USA | Spinal | | | Nausea intraoperatively | Antichol-Scopolamine patch | 80 | 45 | Placebo | 81 | 55 | 5-HT3-Ondansetron - 4 mg | 79 | 42 | | | |

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| Harnett 2007 | USA | Spinal | | | Vomiting (and/or retching) intraoperatively | Antichol-Scopolamine patch | 80 | 15 | Placebo | 81 | 9 | 5-HT3-Ondansetron - 4 mg | 79 | 16 | | | |
| Harnett 2007 | USA | Spinal | | | Vomiting (and/or retching) postoperatively | Antichol-Scopolamine patch | 80 | 32 | Placebo | 81 | 59 | 5-HT3-Ondansetron - 4 mg | 79 | 33 | | | |
| Hassanein 2015 | Egypt | Spinal | 53.6 | 29.3 | Nausea intraoperatively | Corticos-Dexamethasone - 8 mg | 45 | 8 | Placebo | 45 | 13 | Sedatives-Ketamine 0.4.mg/kg | 45 | 6 | | | |
| Hassanein 2015 | Egypt | Spinal | 53.6 | 29.3 | Vomiting (and/or retching) intraoperatively | Corticos-Dexamethasone - 8 mg | 45 | 5 | Placebo | 45 | 9 | Sedatives-Ketamine 0.4.mg/kg | 45 | 4 | | | |
| Huang 1992 | | Regional | | | Nausea intraoperatively | D2-Metoclopramide - 20 mg | 50 | 4 | Placebo | 50 | 15 | | | | | | |
| Jaafarpour 2008 | Iran | Spinal | | | Nausea intraoperatively | Corticos-Dexamethasone - 8 mg | 40 | 2 | Placebo | 40 | 7 | | | | | | |
| Jaafarpour 2008 | Iran | Spinal | | | Vomiting (and/or retching) intraoperatively | Corticos-Dexamethasone - 8 mg | 40 | 1 | Placebo | 40 | 8 | | | | | | |
| Kasodekar 2006 | Egypt | Spinal | | | Nausea intraoperatively | 5-HT3-Granisetron - 1 mg | 88 | 16 | Placebo | 88 | 14 | | | | | | |
| Kasodekar 2006 | Egypt | Spinal | | | Vomiting (and/or retching) intraoperatively | 5-HT3-Granisetron - 1 mg | 88 | 4 | Placebo | 88 | 6 | | | | | | |
| Khalayleh 2005 | Iran | Spinal | | | Nausea intraoperatively | D2-Metoclopramide - 10 mg | 48 | 3 | Placebo | 50 | 21 | | | | | | |
| Kim 1999 | South Korea | combinde spinal & epidural | | | Nausea intraoperatively | D2-Metoclopramide - 10 mg | 20 | 1 | Placebo | 20 | 0 | | | | | | |
| Koju 2015 | Nepal | Spinal | | | Nausea postoperatively | 5-HT3-Ondansetron - 4 mg | 25 | 2 | Placebo | 25 | 14 | | | | | | |
| Kotelko 1989 | USA | epidural | | | Nausea intraoperatively | Antichol-Scopolamine patch | 102 | 43 | Placebo | 101 | 71 | | | | | | |
| Kotelko 1989 | USA | epidural | | | Vomiting (and/or retching) intraoperatively | Antichol-Scopolamine patch | 102 | 33 | Placebo | 101 | 53 | | | | | | |
| Lussos 1992 | USA | Spinal | | | Nausea intraoperatively | D2-Metoclopramide - 10 mg | 21 | 0 | Placebo | 21 | 12 | | | | | | |

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| Lussos 1992 | USA | Spinal | | | Vomiting (and/or retching) intraoperatively | D2-Metoclopramide - 10 mg | 21 | 0 | Placebo | 21 | 6 | | | | | | |
| Lussos 1992 | USA | Spinal | | | Nausea postoperatively | D2-Metoclopramide - 10 mg | 21 | 3 | Placebo | 21 | 12 | | | | | | |
| Lussos 1992 | USA | Spinal | | | Vomiting (and/or retching) postoperatively | D2-Metoclopramide - 10 mg | 21 | 1 | Placebo | 21 | 5 | | | | | | |
| Habib 2013 | Canada | Spinal | | | Vomiting (and/or retching) postoperatively | D2-Metoclopramide - 10 mg | 99 | 15 | Placebo | 100 | 22 | | | | | | |
| Mandell 1992 | USA | Regional | | 28 | Nausea intraoperatively | D2-Droperidol - 0.5 mg | 67 | 9 | Placebo | 61 | 25 | | | | | | |
| Mandell 1992 | USA | Regional | | 28 | Vomiting (and/or retching) intraoperatively | D2-Droperidol - 0.5 mg | 67 | 3 | Placebo | 61 | 8 | | | | | | |
| Maranhao 1988 | | subarachnoid block | | | Vomiting (and/or retching) intraoperatively | D2-Metoclopramide - 10 mg | 20 | 1 | Placebo | 10 | 5 | D2-Droperidol - 5 mg | 20 | 1 | | | |
| Maranhao 1988 | | subarachnoid block | | | Nausea intraoperatively | D2-Metoclopramide - 10 mg | 20 | 2 | Placebo | 10 | 5 | D2-Droperidol - 5 mg | 20 | 3 | | | |
| Mohammadi 2015 | Iran | Spinal | | 30.5 | Nausea intraoperatively | 5-HT3-Granisetron - 3 mg | 50 | 10 | Placebo | 50 | 30 | | | | | | |
| Mokini 2014 | Italy | Regional | | | Nausea intraoperatively | D2-Metoclopramide - 10 mg | 24 | 9 | Placebo | 24 | 14 | Sedatives-Propofol - 1.0 mg/kg/hr | 24 | 11 | | | |
| Mokini 2014 | Italy | Regional | | | Vomiting (and/or retching) intraoperatively | D2-Metoclopramide - 10 mg | 24 | 5 | Placebo | 24 | 8 | Sedatives-Propofol - 1.0 mg/kg/hr | 24 | 2 | | | |
| Mukherjee 2006 | India | Spinal | | | Vomiting (and/or retching) intraoperatively | Sedatives-Propofol - 0.5 mg/kg/hr | 20 | 6 | Placebo | 20 | 8 | Sedatives-Propofol - 1.0 mg/kg/hr | 20 | 3 | Sedatives-Propofol - 1.5 mg/kg/hr | 20 | 2 |
| Mukherjee 2006 | India | Spinal | | | Nausea intraoperatively | Sedatives-Propofol - 0.5 mg/kg/hr | 20 | 5 | Placebo | 20 | 7 | Sedatives-Propofol - 1.0 mg/kg/hr | 20 | 3 | Sedatives-Propofol - 1.5 mg/kg/hr | 20 | 3 |
| Niu 2018 | China | Spinal | | | Nausea intraoperatively | Sedatives-Propofol TCI target 1 ug/ml | 40 | 10 | Placebo | 40 | 24 | | | | | | |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Niu 2018 | China | Spinal | | | Vomiting (and/or retching) intraoperatively | Sedatives-Propofol TCI target 1 ug/ml | 40 | 3 | Placebo | 40 | 9 | | | | | | |
| Nortcliffe 2003 | UK | Spinal | | | Nausea postoperatively | Corticos-Dexamethasone - 8 mg | 30 | 18 | Placebo | 30 | 20 | Antihist-Cyclizine - 50 mg | 30 | 10 | | | |
| Nortcliffe 2003 | UK | Spinal | | | Vomiting (and/or retching) postoperatively | Corticos-Dexamethasone - 8 mg | 30 | 17 | Placebo | 30 | 18 | Antihist-Cyclizine - 50 mg | 30 | 9 | | | |
| Pan 1996 | USA | epidural | 58.6 | 28 | Nausea intraoperatively | 5-HT3-Ondansetron - 8 mg | 16 | 5 | Placebo | 16 | 11 | D2-Droperidol - 0.625 mg | 16 | 4 | | | |
| Pan 1996 | USA | epidural | 58.6 | 28 | Vomiting (and/or retching) intraoperatively | 5-HT3-Ondansetron - 8 mg | 16 | 1 | Placebo | 16 | 7 | D2-Droperidol - 0.625 mg | 16 | 2 | | | |
| Pan 2001 | USA | epidural | | | Vomiting (and/or retching) intraoperatively | D2-Metoclopramide - 10 mg | 51 | 8 | Placebo | 51 | 13 | 5-HT3-Ondansetron - 4 mg | 54 | 7 | | | |
| Pan 2001 | USA | epidural | | | Nausea postoperatively | D2-Metoclopramide - 10 mg | 51 | 26 | Placebo | 51 | 36 | 5-HT3-Ondansetron - 4 mg | 54 | 14 | | | |
| Pan 2001 | USA | epidural | | | Vomiting (and/or retching) postoperatively | D2-Metoclopramide - 10 mg | 51 | 9 | Placebo | 51 | 19 | 5-HT3-Ondansetron - 4 mg | 54 | 8 | | | |
| Pan 2001 | USA | epidural | | | Nausea intraoperatively | 5-HT3-Ondansetron - 4 mg | 54 | 13 | Placebo | 51 | 29 | D2-Metoclopramide - 10 mg | 51 | 22 | | | |
| Pan 2003 | USA | epidural | | 26.5 | Nausea intraoperatively | 5-HT3-Ondansetron - 4 mg | 20 | 2 | Placebo | 20 | 13 | | | | | | |
| Pan 2003 | USA | epidural | | 26.5 | Vomiting (and/or retching) intraoperatively | 5-HT3-Ondansetron - 4 mg | 20 | 0 | Placebo | 20 | 10 | | | | | | |
| Pan 2003 | USA | epidural | | 26.5 | Nausea postoperatively | 5-HT3-Ondansetron - 4 mg | 20 | 2 | Placebo | 20 | 15 | | | | | | |
| Pan 2003 | USA | epidural | | 26.5 | Vomiting (and/or retching) postoperatively | 5-HT3-Ondansetron - 4 mg | 20 | 1 | Placebo | 20 | 5 | | | | | | |
| Parra-Guiza 2018 | Columbia | Spinal | | | Vomiting (and/or retching) postoperatively | 5-HT3-Ondansetron - 4 mg | 100 | 0 | Placebo | 100 | 3 | Corticos-Dexamethasone - 4 mg | 100 | 0 | | | |
| Parra-Guiza 2018 | Columbia | Spinal | | | Nausea postoperatively | Corticos-Dexamethasone - 4 mg | 100 | 16 | Placebo | 100 | 31 | 5-HT3-Ondansetron - 4 mg | 100 | 16 | | | |
| Parra-Guiza 2018 | Columbia | Spinal | | | Nausea intraoperatively | Corticos-Dexamethasone - 4 mg | 100 | 48 | Placebo | 100 | 54 | 5-HT3-Ondansetron - 4 mg | 100 | 35 | | | |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Parra-Guiza 2018 | Columbia | Spinal | | | Vomiting (and/or retching) intraoperatively | Corticos-Dexamethasone - 4 mg | 100 | 7 | Placebo | 100 | 8 | 5-HT3-Ondansetron - 4 mg | 100 | 3 | | | |
| Peixoto 2006 | USA | Spinal | | 30 | Nausea postoperatively | 5-HT3-Ondansetron - 4 mg | 40 | 4 | Placebo | 40 | 3 | D2-Droperidol - 1.25 mg | 40 | 5 | | | |
| Peixoto 2006 | USA | Spinal | | 30 | Vomiting (and/or retching) postoperatively | 5-HT3-Ondansetron - 4 mg | 40 | 0 | Placebo | 40 | 11 | D2-Droperidol - 1.25 mg | 40 | 5 | | | |
| Rasooli 2014 | Iran | Spinal | 49.2 | 28.9 | Vomiting (and/or retching) intraoperatively | Sedatives-Propofol - 20 mg + 1.0 m | 30 | 1 | Placebo | 30 | 14 | Sedatives-Midazolam - 1.0 mg | 30 | 0 | | | |
| Rasooli 2014 | Iran | Spinal | 49.2 | 28.9 | Nausea intraoperatively | Sedatives-Propofol - 20 mg + 1.0 m | 30 | 2 | Placebo | 30 | 2 | Sedatives-Midazolam - 1.0 mg | 30 | 2 | | | |
| Rudra 2004 | India | Spinal | 53 | 24.5 | Vomiting (and/or retching) intraoperatively | Sedatives-Propofol - 1.0 mg/kg/hr | 30 | 4 | Placebo | 30 | 14 | | | | | | |
| Rudra 2004 | India | Spinal | 53 | 24.5 | Nausea intraoperatively | Sedatives-Propofol - 1.0 mg/kg/hr | 30 | 2 | Placebo | 30 | 9 | | | | | | |
| Sahoo 2012 | India | Spinal | | 25.8 | Nausea intraoperatively | 5-HT3-Ondansetron - 4 mg | 26 | 1 | Placebo | 26 | 7 | | | | | | |
| Selzer 2020 | USA | Spinal | 43.5 | 35.5 | Nausea postoperatively | Corticos-Dexamethasone - 8 mg | 55 | 15 | Placebo | 53 | 21 | | | | | | |
| Selzer 2020 | USA | Spinal | 43.5 | 35.5 | Vomiting (and/or retching) postoperatively | Corticos-Dexamethasone - 8 mg | 55 | 29 | Placebo | 53 | 24 | | | | | | |
| Stein 1997 | USA | Spinal | | | Nausea intraoperatively | D2-Metoclopramide - 10 mg | 25 | 4 | Placebo | 25 | 19 | | | | | | |
| Stein 1997 | USA | Spinal | | | Vomiting (and/or retching) intraoperatively | D2-Metoclopramide - 10 mg | 25 | 1 | Placebo | 25 | 6 | | | | | | |
| Tarhan 2007 | Turkey | Spinal | | | Nausea intraoperatively | Sedatives-Propofol - 20 mg + 1.0 m | 30 | 15 | Placebo | 28 | 19 | Sedatives-Midazolam - 1.0 mg | 30 | 16 | | | |
| Tarhan 2007 | Turkey | Spinal | | | Vomiting (and/or retching) intraoperatively | Sedatives-Propofol - 20 mg + 1.0 m | 30 | 3 | Placebo | 28 | 10 | Sedatives-Midazolam - 1.0 mg | 30 | 6 | | | |
| Tarhan 2007 | Turkey | Spinal | | | Nausea postoperatively | Sedatives-Propofol - 20 mg + 1.0 m | 30 | 4 | Placebo | 28 | 25 | Sedatives-Midazolam - 1.0 mg | 30 | 5 | | | |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Tarhan 2007 | Turkey | Spinal | | | Vomiting (and/or retching) postoperatively | Sedatives-Propofol - 20 mg + 1.0 m | 30 | 0 | Placebo | 28 | 20 | Sedatives-Midazolam - 1.0 mg | 30 | 2 | | | |
| Tkachenko 2019 | Ukraine | Spinal | | | Nausea intraoperatively | Corticos-Dexamethasone - 4 mg | 42 | 7 | Placebo | 41 | 21 | Corticos-Dexamethasone - 8 mg | 41 | 16 | | | |
| Tkachenko 2019 | Ukraine | Spinal | | | Vomiting (and/or retching) intraoperatively | Corticos-Dexamethasone - 4 mg | 42 | 1 | Placebo | 41 | 4 | Corticos-Dexamethasone - 8 mg | 41 | 2 | | | |
| Tzeng 2000 | Taiwn | epidural | | | Nausea intraoperatively | D2-Droperidol - 1.25 mg | 38 | 5 | Placebo | 37 | 11 | Corticos-Dexamethasone - 8 mg | 38 | 4 | | | |
| Tzeng 2000 | Taiwn | epidural | | | Vomiting (and/or retching) intraoperatively | D2-Droperidol - 1.25 mg | 38 | 3 | Placebo | 37 | 8 | Corticos-Dexamethasone - 8 mg | 38 | 3 | | | |
| Uerpairojkit 2017 | Thailand | Spinal | | 31.2 | Vomiting (and/or retching) postoperatively | 5-HT3-Ondansetron - 4 mg | 78 | 14 | Placebo | 80 | 15 | | | | | | |
| Uerpairojkit 2017 | Thailand | Spinal | | 31.2 | Nausea postoperatively | 5-HT3-Ondansetron - 4 mg | 78 | 19 | Placebo | 80 | 30 | | | | | | |
| Ure 1999 | UK | Spinal | | | Nausea intraoperatively | Antichol-Glycopyrrolate - 0.2 mg | 24 | 10 | Placebo | 25 | 17 | | | | | | |
| Ure 1999 | UK | Spinal | | | Vomiting (and/or retching) intraoperatively | Antichol-Glycopyrrolate - 0.2 mg | 24 | 2 | Placebo | 25 | 4 | | | | | | |
| Voigt 2013 | Germany | Spinal | 26.3 | 32.6 | Vomiting (and/or retching) postoperatively | 5-HT3-Tropisotron-2 mg | 71 | 0 | Placebo | 76 | 2 | | | | | | |
| Voigt 2013 | Germany | Spinal | 26.3 | 32.6 | Vomiting (and/or retching) intraoperatively | 5-HT3-Tropisotron-2 mg | 71 | 1 | Placebo | 76 | 12 | | | | | | |
| Voigt 2013 | Germany | Spinal | 26.3 | 32.6 | Nausea postoperatively | 5-HT3-Tropisotron-2 mg | 71 | 3 | Placebo | 76 | 7 | | | | | | |
| Wang 2001 | Taiwn | epidural | 51.3 | 27.5 | Nausea postoperatively | Corticos-Dexamethasone - 2.5 mg | 44 | 7 | Placebo | 44 | 12 | Corticos-Dexamethasone - 5 mg | 44 | 5 | Corticos-Dexamethasone - 10 mg | 43 | 5 |
| Wang 2001 | Taiwn | epidural | 51.3 | 27.5 | Vomiting (and/or retching) postoperatively | Corticos-Dexamethasone - 2.5 mg | 44 | 7 | Placebo | 44 | 10 | Corticos-Dexamethasone - 5 mg | 44 | 3 | Corticos-Dexamethasone - 10 mg | 43 | 3 |
| Wu 2007 | Taiwn | Spinal | 51.8 | 29 | Vomiting (and/or retching) postoperatively | D2-Droperidol - 1.25 mg | 30 | 9 | Placebo | 30 | 15 | Corticos-Dexamethasone - 8 mg | 30 | 13 | | | |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Jabalameli 2012 | Iran | Spinal | 65.3 | 29.6 | Vomiting (and/or retching) postoperatively | Sedatives-Midazolam 30 µg/kg | 44 | 16 | 5-HT3-Ondansetron - 8 mg | 44 | 15 | | | | | | |
| Jabalameli 2012 | Iran | Spinal | 65.3 | 29.6 | Nausea postoperatively | Sedatives-Midazolam 30 µg/kg | 44 | 18 | 5-HT3-Ondansetron - 8 mg | 44 | 20 | | | | | | |
| Jabalameli 2012 | Iran | Spinal | 65.3 | 29.6 | Nausea intraoperatively | Sedatives-Midazolam 30 µg/kg | 44 | 32 | 5-HT3-Ondansetron - 8 mg | 44 | 27 | | | | | | |
| Jabalameli 2012 | Iran | Spinal | 65.3 | 29.6 | Vomiting (and/or retching) intraoperatively | Sedatives-Midazolam 30 µg/kg | 44 | 30 | 5-HT3-Ondansetron - 8 mg | 44 | 32 | | | | | | |
| Jain 2015 | India | Spinal | | 30.4 | Nausea intraoperatively | 5-HT3-Ondansetron - 4 mg | 32 | 15 | Antichol-Glycopyrrolate - 0.2 mg | 31 | 13 | | | | | | |
| Jain 2015 | India | Spinal | | 30.4 | Vomiting (and/or retching) intraoperatively | 5-HT3-Ondansetron - 4 mg | 32 | 5 | Antichol-Glycopyrrolate - 0.2 mg | 31 | 6 | | | | | | |
| Jain 2015 | India | Spinal | | 30.4 | Nausea postoperatively | 5-HT3-Ondansetron - 4 mg | 32 | 4 | Antichol-Glycopyrrolate - 0.2 mg | 31 | 5 | | | | | | |
| Jain 2015 | India | Spinal | | 30.4 | Vomiting (and/or retching) postoperatively | 5-HT3-Ondansetron - 4 mg | 32 | 1 | Antichol-Glycopyrrolate - 0.2 mg | 31 | 2 | | | | | | |

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Supplementary Table 3: Q statistic to assess consistency under the assumption of a full design-by-treatment interaction random effects model:

**1. intraoperative nausea**

| | Q | d.f. | *P* value |
|---|---|---|---|
| Between-designs | 7.9 | 17 | 0.96 |

**2. intraoperative vomiting**

| | Q | d.f. | *P* value |
|---|---|---|---|
| Between-designs | 14.7 | 17 | 0.61 |

**3. postoperative nausea**

| | Q | d.f. | *P* value |
|---|---|---|---|
| Between-designs | 5.6 | 10 | 0.84 |

**4. postoperative vomiting**

| | Q | d.f. | *P* value |
|---|---|---|---|
| Between-designs | 8.4 | 14.0 | 0.86 |

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**Supplementary Table 4: Results of direct, indirect, and network meta-analyses**

**Supplementary Table 4-1 Results of *netsplit* on intraoperative nausea**

| Comparisons | Number of RCTs | Direct Evidence proportion | NMA | OR derived from direct evidence | OR derived from indirect evidence | Ratio of Ratios | p-value |
|---|---|---|---|---|---|---|---|
| 5HT3 vs Anticholinergic agents | 2 | 0.49 | 0.95 | 1.00 | 0.91 | 1.09 | 0.87 |
| 5HT3 vs Antihistamines | 0 | 0.00 | 0.32 | . | 0.32 | . | . |
| 5HT3 vs Corticosteroids | 1 | 0.32 | 0.76 | 0.58 | 0.86 | 0.64 | 0.52 |
| 5HT3 vs Dopamine receptor antagonists | 3 | 0.30 | 1.16 | 0.72 | 1.42 | 0.51 | 0.19 |
| 5HT3 vs Placebo | 12 | 0.83 | 0.31 | 0.35 | 0.19 | 1.76 | 0.21 |
| 5HT3 vs Sedatives | 1 | 0.19 | 0.72 | 0.59 | 0.76 | 0.78 | 0.72 |
| Anticholinergic agents vs Antihistamines | 0 | 0.00 | 0.33 | . | 0.33 | . | . |
| Anticholinergic agents vs Corticosteroids | 1 | 0.10 | 0.79 | 1.00 | 0.77 | 1.29 | 0.83 |
| Anticholinergic agents vs Dopamine receptor antagonists | 1 | 0.10 | 1.21 | 0.44 | 1.35 | 0.32 | 0.29 |
| Anticholinergic agents vs Placebo | 4 | 0.77 | 0.33 | 0.37 | 0.23 | 1.59 | 046 |
| Anticholinergic agents vs Sedatives | 0 | 0.00 | 0.75 | . | 0.75 | . | . |
| Antihistamines vs Corticosteroids | 0 | 0.00 | 2.36 | . | 2.36 | . | . |
| Antihistamines vs Dopamine receptor antagonists | 0 | 0.00 | 3.61 | . | 3.61 | . | . |
| Antihistamines vs Placebo | 1 | 1.00 | 0.99 | 0.99 | . | . | . |
| Antihistamines vs Sedatives | 0 | 0.00 | 2.25 | . | 2.25 | . | . |
| Corticosteroids vs Dopamine receptor antagonists | 2 | 0.23 | 1.52 | 0.62 | 1.99 | 0.31 | 0.11 |
| Corticosteroids vs Placebo | 6 | 0.87 | 0.41 | 0.42 | 0.35 | 1.21 | 0.80 |
| Corticosteroids vs Sedatives | 1 | 0.22 | 0.95 | 1.40 | 0.85 | 1.63 | 0.54 |
| **Dopamine receptor antagonists vs Placebo** | **15** | **0.92** | **0.27** | **0.24** | **1.00** | **0.24** | **0.04** |
| Dopamine receptor antagonists vs Sedatives | 1 | 0.16 | 0.62 | 0.70 | 0.60 | 1.16 | 0.84 |
| Sedatives vs Placebo | 8 | 0.81 | 0.43 | 0.44 | 0.41 | 1.07 | 0.90 |

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**Supplementary Table 4-2 Results of *netsplit* on intraoperative vomiting**

| Comparisons | Number of RCTs | Direct Evidence proportion | NMA | OR derived from direct evidence | OR derived from indirect evidence | Ratio of Ratios | p-value |
|---|---|---|---|---|---|---|---|
| 5HT3 vs Anticholinergic agents | 2 | 0.50 | 0.70 | 0.97 | 0.51 | 1.89 | 0.30 |
| 5HT3 vs Antihistamines | 0 | 0.00 | 0.38 | . | 0.38 | . | . |
| 5HT3 vs Corticosteroids | 1 | 0.20 | 0.78 | 0.41 | 0.92 | 0.44 | 0.35 |
| 5HT3 vs Dopamine receptor antagonists | 3 | 0.28 | 1.03 | 0.65 | 1.22 | 0.53 | 0.34 |
| 5HT3 vs Placebo | 11 | 0.82 | 0.34 | 0.38 | 0.22 | 1.69 | 0.30 |
| 5HT3 vs Sedatives | 1 | 0.25 | 1.41 | 1.24 | 1.48 | 0.84 | 0.79 |
| Anticholinergic agents vs Antihistamines | 0 | 0.00 | 0.54 | . | 0.54 | . | . |
| Anticholinergic agents vs Corticosteroids | 1 | 0.10 | 1.11 | 0.47 | 1.22 | 0.38 | 0.49 |
| Anticholinergic agents vs Dopamine receptor antagonists | 1 | 0.08 | 1.45 | 0.47 | 1.60 | 0.29 | 0.37 |
| **Anticholinergic agents vs Placebo** | **4** | **0.78** | **0.49** | **0.67** | **0.15** | **4.29** | **0.03** |
| Anticholinergic agents vs Sedatives | 0 | 0.00 | 1.99 | . | 1.99 | . | . |
| Antihistamines vs Corticosteroids | 0 | 0.00 | 2.05 | . | 2.05 | . | . |
| Antihistamines vs Dopamine receptor antagonists | 0 | 0.00 | 2.69 | . | 2.69 | . | . |
| Antihistamines vs Placebo | 1 | 1.00 | 0.91 | 0.91 | . | . | . |
| Antihistamines vs Sedatives | 0 | 0.00 | 3.69 | . | 3.69 | . | . |
| Corticosteroids vs Dopamine receptor antagonists | 2 | 0.29 | 1.31 | 1.00 | 1.46 | 0.68 | 0.65 |
| Corticosteroids vs Placebo | 6 | 0.89 | 0.44 | 0.45 | 0.38 | 1.17 | 0.87 |
| Corticosteroids vs Sedatives | 1 | 0.24 | 1.80 | 1.28 | 2.0 | 0.63 | 0.62 |
| Dopamine receptor antagonists vs Placebo | 12 | 0.93 | 0.33 | 0.31 | 0.86 | 0.36 | 0.29 |
| Dopamine receptor antagonists vs Sedatives | 1 | 0.13 | 1.37 | 2.89 | 1.23 | 0.83 | 0.40 |
| Sedatives vs Placebo | 8 | 0.81 | 0.24 | 0.24 | 0.25 | 0.95 | 0.94 |

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**Supplementary Table 4-3 Results of *netsplit* on postoperative nausea**

| Comparisons | Number of RCTs | Direct Evidence proportion | NMA | OR derived from direct evidence | OR derived from indirect evidence | Ratio of Ratios | p-value |
|---|---|---|---|---|---|---|---|
| 5HT3 vs Anticholinergic agents | 1 | 1.00 | 0.74 | 0.74 | . | . | . |
| 5HT3 vs Antihistamines | 0 | 0.00 | 1.00 | 0.00 | 1.00 | . | . |
| 5HT3 vs Corticosteroids | 1 | 0.26 | 0.72 | 1.00 | 0.64 | 1.55 | 0.55 |
| 5HT3 vs Dopamine receptor antagonists | 2 | 0.36 | 0.57 | 0.45 | 0.65 | 0.70 | 0.59 |
| 5HT3 vs Opioid antagonist | 1 | 0.79 | 0.44 | 0.52 | 0.22 | 2.31 | 0.56 |
| 5HT3 vs Placebo | 10 | 0.87 | 0.25 | 0.27 | 0.15 | 1.71 | 0.40 |
| 5HT3 vs Sedatives | 1 | 0.46 | 1.53 | 1.20 | 1.87 | 0.64 | 0.62 |
| Anticholinergic agents vs Antihistamines | 0 | 0.00 | 1.35 | . | 1.35 | . | . |
| Anticholinergic agents vs Corticosteroids | 0 | 0.00 | 0.97 | . | 0.97 | . | . |
| Anticholinergic agents vs Dopamine receptor antagonists | 0 | 0.00 | 0.76 | . | 0.76 | . | . |
| Anticholinergic agents vs Opioid antagonist | 0 | 0.00 | 0.59 | . | 0.59 | . | . |
| Anticholinergic agents vs Placebo | 0 | 0.00 | 0.34 | . | 0.34 | . | . |
| Anticholinergic agents vs Sedatives | 0 | 0.00 | 2.06 | . | 2.06 | . | . |
| Antihistamines vs Corticosteroids | 1 | 0.29 | 0.71 | 0.33 | 0.97 | 0.34 | 0.22 |
| Antihistamines vs Dopamine receptor antagonists | 2 | 0.56 | 0.56 | 0.44 | 0.77 | 0.56 | 0.46 |
| Antihistamins vs Opioid antagonist | 0 | 0.00 | 0.43 | . | 0.43 | . | . |
| Antihistamines vs Placebo | 4 | 0.87 | 0.25 | 0.29 | 0.07 | 3.80 | 0.17 |
| Antihistamines vs Sedatives | 0 | 0.00 | 1.51 | . | 1.51 | . | . |
| Corticosteroids vs Dopamine receptor antagonists | 0 | 0.00 | 0.79 | . | 0.79 | . | . |
| Corticosteroids vs Opioid antagonist | 0 | 0.00 | 0.61 | . | 0.61 | . | . |
| Corticosteroids vs Placebo | 6 | 0.93 | 0.35 | 0.35 | 0.30 | 1.19 | 0.86 |
| Corticosteroids vs Sedatives | 0 | 0.00 | 2.12 | . | 2.12 | . | . |
| Dopamine receptor antagonists vs Opioid antagonist | 0 | 0.00 | 0.77 | . | 0.77 | . | . |
| Dopamine receptor antagonists vs Placebo | 7 | 0.89 | 0.44 | 0.43 | 0.59 | 0.72 | 0.70 |
| Dopamine receptor antagonists vs Sedatives | 0 | 0.00 | 2.68 | . | 2.68 | . | . |
| Opioid antagonist vs Placebo | 1 | 0.78 | 0.57 | 0.68 | 0.29 | 2.29 | 0.56 |
| Opioid antagonist vs Sedatives | 0 | 0.00 | 3.45 | . | 3.45 | . | . |
| Sedatives vs Placebo | 3 | 0.60 | 0.16 | 0.13 | 0.21 | 0.64 | 0.62 |

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**Supplementary Table 4-4 Results of *netsplit* on postoperative vomiting**

| Comparisons | Number of RCTs | Direct Evidence proportion | NMA | OR derived from direct evidence | OR derived from indirect evidence | Ratio of Ratios | p-value |
|---|---|---|---|---|---|---|---|
| 5HT3 vs Anticholinergic agents | 2 | 0.83 | 0.99 | 0.92 | 1.38 | 0.67 | 0.77 |
| 5HT3 vs Antihistamines | 0 | 0.00 | 1.26 | . | 1.26 | . | . |
| 5HT3 vs Corticosteroids | 1 | 0.03 | 0.53 | 1.00 | 0.53 | 1.89 | 0.76 |
| 5HT3 vs Dopamine receptor antagonists | 2 | 0.26 | 0.56 | 0.52 | 0.57 | 0.91 | 0.90 |
| 5HT3 vs Opioid antagonist | 1 | 0.83 | 0.43 | 0.68 | 0.04 | 14.38 | 0.17 |
| 5HT3 vs Placebo | 10 | 0.90 | 0.29 | 0.32 | 0.10 | 3.06 | 0.19 |
| 5HT3 vs Sedatives | 1 | 0.54 | 2.21 | 0.90 | 3.25 | 0.14 | 0.06 |
| Anticholinergic agents vs Antihistamines | 0 | 0.00 | 1.26 | . | 1.26 | . | . |
| Anticholinergic agents vs Corticosteroids | 0 | 0.00 | 0.54 | . | 0.54 | . | . |
| Anticholinergic agents vs Dopamine receptor antagonists | 0 | 0.00 | 0.56 | . | 0.56 | . | . |
| Anticholinergic agents vs Opioid antagonist | 0 | 0.00 | 0.43 | . | 0.43 | . | . |
| Anticholinergic agents vs Placebo | 1 | 0.69 | 0.29 | 0.24 | 0.43 | 0.57 | 0.63 |
| Anticholinergic agents vs Sedatives | 0 | 0.00 | 2.22 | . | 2.22 | . | . |
| Antihistamines vs Corticosteroids | 1 | 0.44 | 0.42 | 0.32 | 0.52 | 0.62 | 0.64 |
| Antihistamines vs Dopamine receptor antagonists | 1 | 0.42 | 0.44 | 0.30 | 0.57 | 0.53 | 0.54 |
| Antihistamins vs Opioid antagonist | 0 | 0.00 | 0.34 | . | 0.34 | . | . |
| Antihistamines vs Placebo | 3 | 0.82 | 0.23 | 0.32 | 0.05 | 6.42 | 0.13 |
| Antihistamines vs Sedatives | 0 | 0.00 | 1.75 | . | 1.75 | . | . |
| Corticosteroids vs Dopamine receptor antagonists | 1 | 0.22 | 1.04 | 1.78 | 0.90 | 1.97 | 0.43 |
| Corticosteroids vs Opioid antagonist | 0 | 0.00 | 0.80 | . | 0.80 | . | . |
| Corticosteroids vs Placebo | 7 | 0.94 | 0.54 | 0.52 | 1.03 | 0.50 | 0.57 |
| Corticosteroids vs Sedatives | 0 | 0.00 | 4.10 | . | 4.10 | . | . |
| Dopamine receptor antagonists vs Opioid antagonist | 0 | 0.00 | 0.76 | . | 0.76 | . | . |
| Dopamine receptor antagonists vs Placebo | 9 | 0.93 | 0.52 | 0.53 | 0.35 | 1.48 | 0.68 |
| Dopamine receptor antagonists vs Sedatives | 0 | 0.00 | 3.93 | . | 3.93 | . | . |
| Opioid antagonist vs Placebo | 1 | 0.72 | 0.67 | 1.27 | 0.13 | 9.58 | 0.17 |
| Opioid antagonist vs Sedatives | 0 | 0.00 | 5.11 | . | 5.11 | . | . |
| Sedatives vs Placebo | 3 | 0.53 | 0.13 | 0.05 | 0.36 | 0.14 | 0.06 |

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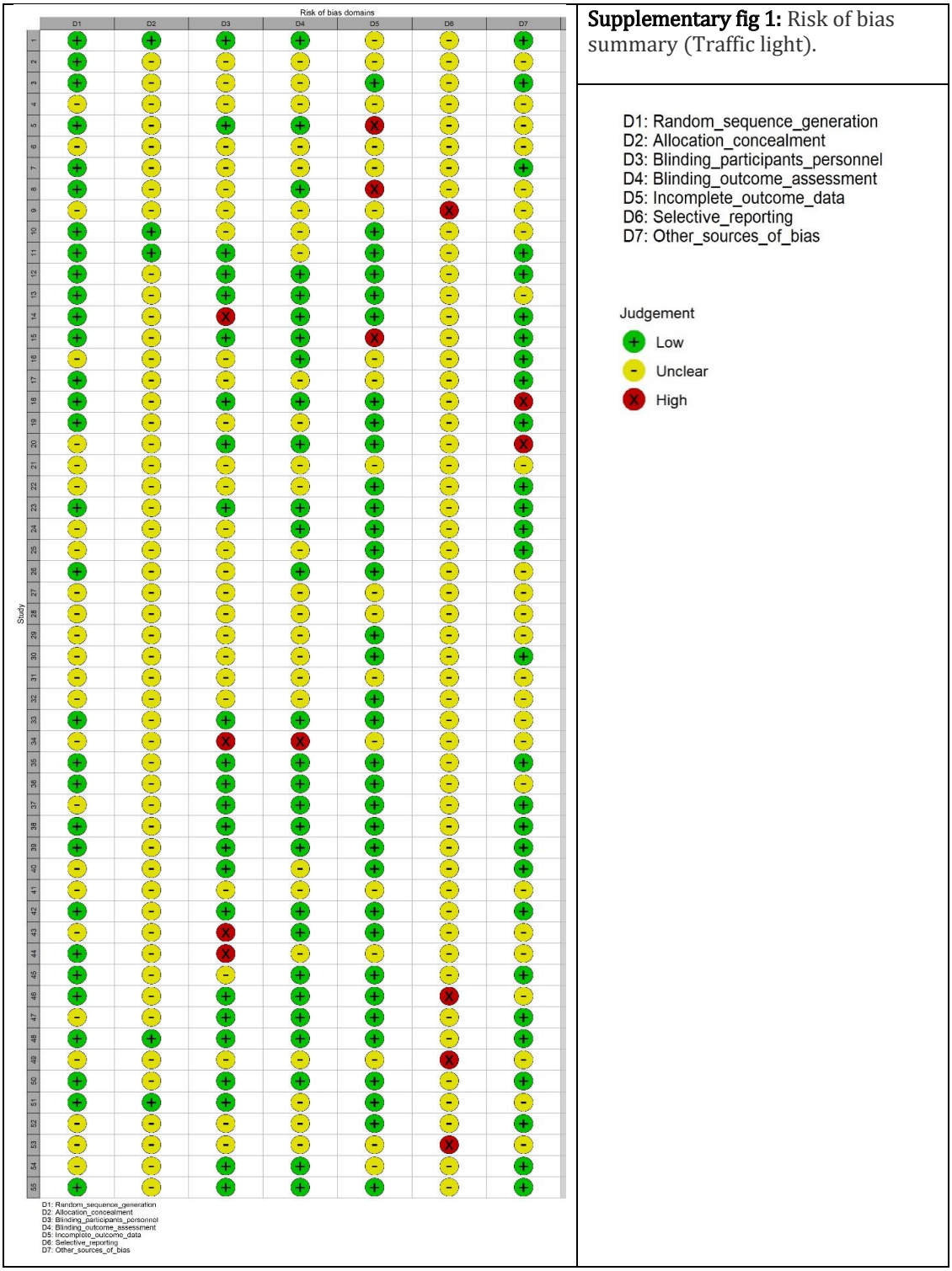


**Supplementary fig 1:** Risk of bias summary (Traffic light).