Cochrane Library

Cochrane Database of Systematic Reviews

Heated insufflation with or without humidification for laparoscopic abdominal surgery (Review)

Birch DW, Dang JT, Switzer NJ, Manouchehri N, Shi X, Hadi G, Karmali S

Birch DW, Dang JT, Switzer NJ, Manouchehri N, Shi X, Hadi G, Karmali S.
Heated insufflation with or without humidification for laparoscopic abdominal surgery.
Cochrane Database of Systematic Reviews 2016, Issue 10. Art. No.: CD007821.
DOI: 10.1002/14651858.CD007821.pub3.

www.cochranelibrary.com

WILEY

TABLE OF CONTENTS

[Intervention Review]

Heated insufflation with or without humidification for laparoscopic abdominal surgery

Daniel W Birch[1], Jerry T Dang[1], Noah J Switzer[1], Namdar Manouchehri[1], Xinzhe Shi[2], Ghassan Hadi[1], Shahzeer Karmali[1]

[1]Center for the Advancement of Minimally Invasive Surgery, Department of Surgery, University of Alberta, Edmonton, Canada. [2]Center for the Advancement of Minimally Invasive Surgery, Department of Surgery, Royal Alexandra Hospital, Edmonton, Canada

Contact: Xinzhe Shi, Center for the Advancement of Minimally Invasive Surgery, Department of Surgery, Royal Alexandra Hospital, Edmonton, AB, T5H 3V9, Canada. xinzhe@ualberta.ca, Xinzhe.Shi@albertahealthservices.ca.

Editorial group: Cochrane Colorectal Cancer Group.
Publication status and date: Edited (no change to conclusions), published in Issue 10, 2016.

Citation: Birch DW, Dang JT, Switzer NJ, Manouchehri N, Shi X, Hadi G, Karmali S. Heated insufflation with or without humidification for laparoscopic abdominal surgery. *Cochrane Database of Systematic Reviews* 2016, Issue 10. Art. No.: CD007821. DOI: 10.1002/14651858.CD007821.pub3.

ABSTRACT

Background

Intraoperative hypothermia during both open and laparoscopic abdominal surgery may be associated with adverse events. For laparoscopic abdominal surgery, the use of heated insufflation systems for establishing pneumoperitoneum has been described to prevent hypothermia. Humidification of the insufflated gas is also possible. Past studies on heated insufflation have shown inconclusive results with regards to maintenance of core temperature and reduction of postoperative pain and recovery times.

Objectives

To determine the effect of heated gas insufflation compared to cold gas insufflation on maintaining intraoperative normothermia as well as patient outcomes following laparoscopic abdominal surgery.

Search methods

We searched Cochrane Colorectal Cancer Specialised Register (September 2016), the Cochrane Central Register of Controlled Trials (CENTRAL; *The Cochrane Library* 2016, Issue *8*), Ovid MEDLINE (1950 to September 2016), Ovid Embase (1974 to September 2016), International Pharmaceutical Abstracts (IPA) (September 2016), Web of Science (1985 to September 2016), Scopus, www.clinicaltrials.gov and the National Research Register (1956 to September 2016). We also searched grey literature and cross references. Searches were limited to human studies without language restriction.

Selection criteria

Only randomised controlled trials comparing heated (with or without humidification) with cold gas insufflation in adult and paediatric populations undergoing laparoscopic abdominal procedures were included. We assessed study quality in regards to relevance, design, sequence generation, allocation concealment, blinding, possibility of incomplete data and selective reporting. Two review authors independently selected studies for the review, with any disagreement resolved in consensus with a third co-author.

Data collection and analysis

Two review authors independently performed screening of eligible studies, data extraction and methodological quality assessment of the trials. We classified a study as low-risk of bias if all of the first six main criteria indicated in the 'Risk of Bias Assessment' table were assessed as low risk. We used data sheets to collect data from eligible studies. We presented results using mean differences for continuous outcomes and relative risks for dichotomous outcomes, with 95% confidence intervals. We used Review Manager (RevMan) 5.3 software to calculate the estimated effects. We took publication bias into consideration and compiled funnel plots.

Main results

We included 22 studies in this updated analysis, including six new trials with 584 additional participants, resulting in a total of 1428 participants. The risk of bias was low in 11 studies, high in one study and unclear in the remaining studies, due primarily to failure to report methodology for randomisation, and allocation concealment or blinding, or both. Fourteen studies examined intraoperative core temperatures among heated and humidified insufflation cohorts and core temperatures were higher compared to cold gas insufflation (MD 0.31 °C, 95% CI, 0.09 to 0.53, I^2 = 88%, P = 0.005) (low-quality evidence). If the analysis was limited to the eight studies at low risk of bias, this result became non-significant but remained heterogeneous (MD 0.18 °C, 95% CI, -0.04 to 0.39, I^2= 81%, P = 0.10) (moderate-quality evidence).
In comparison to the cold CO_2 group, the meta-analysis of the heated, non-humidified group also showed no statistically significant difference between groups. Core temperature was statistically, significantly higher in the heated, humidified CO_2 with external warming groups (MD 0.29 °C, 95% CI, 0.05 to 0.52, I^2 = 84%, P = 0.02) (moderate-quality evidence). Despite the small difference in temperature of 0.31 °C with heated CO_2, this is unlikely to be of clinical significance.

For postoperative pain scores, there were no statistically significant differences between heated and cold CO_2, either overall, or for any of the subgroups assessed. Interestingly, morphine-equivalent use was homogeneous and higher in heated, non-humidified insufflation compared to cold insufflation for postoperative day one (MD 11.93 mg, 95% CI 0.92 to 22.94, I^2 = 0%, P = 0.03) (low-quality evidence) and day two (MD 9.79 mg, 95% CI 1.58 to 18.00, I^2 = 0%, P = 0.02) *(*low-quality evidence). However, morphine use was not significantly different six hours postoperatively or in any humidified insufflation groups.

There was no apparent effect on length of hospitalisation, lens fogging or length of operation with heated compared to cold gas insufflation, with or without humidification. Recovery room time was shorter in the heated cohort (MD -26.79 minutes, 95% CI -51.34 to -2.25, I^2 = 95%, P = 0.03) (low-quality evidence). When the one and only unclear-risk study was removed from the analysis, the difference in recovery-room time became non-significant and the studies were statistically homogeneous (MD -1.22 minutes, 95% CI, -6.62 to 4.17, I^2 = 12%, P = 0.66) (moderate-quality evidence).

There were also no differences in the frequency of major adverse events that occurred in the cold or heated cohorts.

These results should be interpreted with caution due to some limitations. Heterogeneity of core temperature remained significant despite subgroup analysis, likely due to variations in the study design of the individual trials, as the trials had variations in insufflation gas temperatures (35 °C to 37 °C), humidity ranges (88% to 100%), gas volumes and location of the temperature probes. Additionally, some of the trials lacked specific study design information making evaluation difficult.

Authors' conclusions

While heated, humidified gas leads to mildly smaller decreases in core body temperatures, clinically this does not account for improved patient outcomes, therefore, there is no clear evidence for the use of heated gas insufflation, with or without humidification, compared to cold gas insufflation in laparoscopic abdominal surgery.

PLAIN LANGUAGE SUMMARY

Heated CO_2 for laparoscopic abdominal surgery

Background

In laparoscopic surgery, surgery is performed through small incisions using long instruments and video cameras. To create a working and viewing space in the abdomen, carbon dioxide (CO_2) is insufflated to separate the abdominal wall from internal organs. Traditionally, unheated CO_2 is used but there has been suggestions that heated CO_2 may prevent hypothermia. Hypothermia has been associated with heart attacks, abnormal heart rhythms, increased infections, decreased clotting ability and increased blood loss. We aimed to investigate the role of heated compared with cold CO_2 in laparoscopic abdominal surgery.

Study Characteristics

We searched the medical literature for randomised controlled trials (where people are allocated at random to one of two or more treatment groups) that compared heated and cold CO_2. We analysed data from the trials for changes in core temperature. We also compared post-operative pain scores and pain medication requirements, length of hospital stay, length of surgery and fogging of the surgical video camera lens. Evidence is current to September 2016.

Key results and quality of evidence

We identified and included 22 trials. There was an increase of 0.31 °C in the heated, humidified CO_2 group compared to the cold CO_2 group but the data were heterogeneous (highly variable). However, if the analysis was limited to the eight low-risk-of-bias studies that

reported core temperatures, no significant difference was found. Also, there was no temperature difference for heated and non-humidified gas compared to cold gas.

There was no difference in postoperative pain with heated or cold insufflation. However, pain medication use was higher in only the heated, non-humidified group on postoperative days one and two.

Heated gas apparently did not change length of hospitalisation, lens fogging or length of operation. Recovery room stay was shorter with heated gas but the data was heterogeneous (highly variable). When we only included studies at low risk of bias, the data became homogeneous (less variable) and the recovery room time was not significantly different between the heated and cold gas groups.

Authors' Conclusions

While heated, humidified gas leads to slightly smaller decreases in core body temperatures, this does not account for improvement in any patient outcomes. Therefore, there is no clear evidence for the use of heated gas insufflation, with or without humidification, in laparoscopic abdominal surgery.

Summary of findings for the main comparison. Core temperature

Heated CO_2 with or without humidification for laparoscopic abdominal surgery

Patient or population: Laparoscopic abdominal surgery (core temperature)
Setting: Operating room
Intervention: Heated gas
Comparison: Cold gas

Outcomes	Anticipated absolute effects* (95% CI)		№ of participants (studies)	Quality of the evidence (GRADE)	Comments
	Risk with cold gas	Risk with heated gas			
Change in core temperature (°C)	The mean change in core temperature was -0.22 °C	The mean change in core temperature in the intervention group was 0.21 °C higher (0.06 to 0.36)	1100 (19 RCTs)	⊕⊕◯◯ LOW [1,2]	Negative temperature indicates core temperature dropped during surgery
Change in core temperature: heated, humidified vs cold	The mean change in core temperature: heated, humidified vs cold was -0.25 °C	The mean change in core temperature: heated, humidified vs cold in the intervention group was 0.31 °C higher (0.09 to 0.53)	885 (14 RCTs)	⊕⊕◯◯ LOW [1,2]	
Change in core temperature: heated only vs cold	The mean change in core temperature: heated vs cold was -0.19 °C	The mean change in core temperature: heated vs cold in the intervention group was 0.02 °C higher (-0.16 to 0.20)	215 (7 RCTs)	⊕⊕◯◯ LOW [1,2]	
Change in core temperature for known low risk of bias studies	The mean change in core temperature for low risk of bias studies was -0.10 °C	The mean change in core temperature for low risk of bias studies in the intervention group was 0.16 °C higher (-0.01 to 0.33)	653 (10 RCTs)	⊕⊕⊕◯ MODERATE[4]	
Change in core temperature for known low risk of bias studies: heated, humidified vs cold	The mean change in core temperature for low risk of bias studies: heated, humidified vs cold was -0.09 °C	The mean change in core temperature for low risk of bias studies: heated, humidified vs cold in the intervention group was 0.18 °C higher (-0.04 to 0.39)	561 (8 RCTs)	⊕⊕⊕◯ MODERATE[4]	
Change in core temperature for low risk of bias studies: heated only vs cold	The mean change in core temperature for low risk of bias studies: heated vs cold was -0.10 °C	The mean change in core temperature for low risk of bias studies: heated vs cold in the intervention group was 0.12 °C higher (-0.15 to 0.39)	92 (3 RCTs)	⊕⊕⊕◯ MODERATE [2]	

Change in core temperature with external warming	The mean change in core temperature with external warming was -0.14 °C	The mean change in core temperature with external warming in the intervention group was 0.29 °C higher (0.05 to 0.52)	545 (8 RCTs)	⊕⊕⊕○ MODERATE[1]
Change in core temperature without external warming	The mean change in core temperature without external warming was -0.40 °C	The mean change in core temperature without external warming in the intervention group was 0.32 °C higher (-0.11 to 0.75)	340 (6 RCTs)	⊕⊕⊕○ MODERATE[1]
Change in core temperature for operations > 120 min	The mean change in core temperature for operations > 120 min was -0.74 °C	The mean change in core temperature for operations > 120 min in the intervention group was 0.70 °C higher (0.10 to 1.30)	194 (4 RCTs)	⊕⊕⊕○ MODERATE [1]

*__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; **RR:** Risk ratio; **OR:** Odds ratio;

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: 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 quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

1. Risk of bias not clear
2. Inconsistent effect
3. Low-risk studies only
4. Wide confidence intervals

Summary of findings 2. Pain score

Heated CO_2 with or without humidification for laparoscopic abdominal surgery

Patient or population: Laparoscopic abdominal surgery (pain score)
Setting: Hospital
Intervention: Heated gas
Comparison: Cold gas

Outcomes	Anticipated absolute effects* (95% CI)		№ of participants (studies)	Quality of the evidence (GRADE)	Comments
	Risk with cold gas	Risk with heated gas			

Day 1 pain score (0 to 10-point VAS)	The mean day 1 pain score was 2.8	The mean day 1 pain score in the intervention group was 0.04 fewer (-0.42 to 0.34)	991 (14 RCTs)	⊕⊕◯◯ LOW [1 2]	Higher score indicates more pain for participants
Day 1 pain score: heated, humidified vs cold (abdominal)	The mean day 1 pain score: heated, humidified vs cold (abdominal) was 4	The mean day 1 pain score: heated, humidified vs cold (abdominal) in the intervention group was 0.14 fewer (-0.6 to 0.33)	670 (10 RCTs)	⊕⊕◯◯ LOW [1 2]	
Day 1 pain score: heated, humidified vs cold (shoulder)	The mean day 1 pain score: heated, humidified vs cold (shoulder) was 2	The mean day 1 pain score: heated, humidified vs cold (shoulder) in the intervention group was 0.35 fewer (-1.75 to 1.05)	171 (3 RCTs)	⊕◯◯◯ VERY LOW [1 2 4]	
Day 1 pain score: heated only vs cold	The mean day 1 pain score: heated vs cold was 2.8	The mean day 1 pain score: heated vs cold in the intervention group was 0.5 more (-0.11 to 1.12)	150 (3 RCTs)	⊕⊕⊕◯ MODERATE [1]	
Day 2 pain score	The mean day 2 pain score was 2.2	The mean day 2 pain score in the intervention group was 0.28 fewer (-0.78 to 0.21)	695 (10 RCTs)	⊕⊕◯◯ LOW [1 2]	
Day 2 pain score: heated, humidified vs cold (abdominal)	The mean day 2 pain score: heated, humidified vs cold (abdominal) was 3.2	The mean day 2 pain score: heated, humidified vs cold (abdominal) in the intervention group was 0.4 fewer (-1.07 to 0.28)	442 (7 RCTs)	⊕⊕◯◯ LOW [1 2]	
Day 2 pain score: heated, humidified vs cold (shoulder)	The mean day 2 pain score: heated, humidified vs cold (shoulder) was 1.5	The mean day 2 pain score: heated, humidified vs cold (shoulder) in the intervention group was 0.88 fewer (-2.93 to 1.17)	111 (2 RCTs)	⊕◯◯◯ VERY LOW [1 2 4]	
Day 2 pain score: heated only vs cold	The mean day 2 pain score: heated vs cold was 1.9	The mean day 2 pain score: heated vs cold in the intervention group was 0.41 more (-0.44 to 1.27)	142 (3 RCTs)	⊕⊕◯◯ LOW [1 2]	
Day 1 pain score for low risk of bias studies	The mean day 1 pain score for low risk of bias studies was 2.7	The mean day 1 pain score for low risk of bias studies in the intervention group was 0.17 more (-0.21 to 0.55)	570 (7 RCTs)	⊕⊕⊕⊕ HIGH[3]	
Day 1 pain score for low risk of bias studies: heated, humidified vs cold (abdominal)	The mean day 1 pain score for low risk of bias studies: heated, humidified vs cold (abdominal) was 4.3	The mean day 1 pain score for low risk of bias studies: heated, humidified vs cold (abdominal) in the intervention group was 0.17 more (-0.29 to 0.63)	460 (7 RCTs)	⊕⊕⊕⊕ HIGH[3]	
Day 1 pain score for low risk of bias studies: heated, humidified vs cold (shoulder)	The mean day 1 pain score for low risk of bias studies: heated, humidified vs cold (shoulder) was 1.2	The mean day 1 pain score for low risk of bias studies: heated, humidified vs cold (shoulder) in the intervention group was 0.25 more (-0.81 to 1.31)	110 (2 RCTs)	⊕⊕⊕◯ MODERATE [4]	

Day 2 pain score for low risk of bias studies	The mean day 2 pain score for low risk of bias studies was 3.5	The mean day 2 pain score for low risk of bias studies in the intervention group was 0.29 fewer (-0.65 to 0.07)	380 (5 RCTs)	⊕⊕⊕⊕ HIGH[3]

*__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; **RR:** Risk ratio; **OR:** Odds ratio;

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: 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 quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

1. Risk of bias not clear
2. Inconsistent effect
3. Low-risk studies only
4. Wide confidence intervals

Summary of findings 3. Morphine consumption

Heated CO_2 with or without humidification for laparoscopic abdominal surgery

Patient or population: Laparoscopic abdominal surgery (morphine consumption)
Setting: Post-operative
Intervention: Heated gas
Comparison: Cold gas

Outcomes	Anticipated absolute effects* (95% CI)		№ of participants (studies)	Quality of the evidence (GRADE)	Comments
	Risk with cold gas	Risk with heated gas			
Up to 6 h	The mean up to 6 h morphine consumption was 12.6 mg	The mean up to 6 h in the intervention group was 0.45 mg more (-1.19 to 2.08)	231 (4 RCTs)	⊕⊕⊕◯ MODERATE [1]	Morphine consumption was presented as equivalent daily dose
Day 1 morphine	The mean day 1 morphine consumption was 32.4 mg	The mean day 1 morphine consumption in the intervention group was 0.64 mg less (-4.48 to 3.20)	573 (9 RCTs)	⊕⊕⊕◯ MODERATE [1]	

Day 1 morphine: heated, humidified vs cold	The mean day 1 morphine consumption: heated, humidified vs cold was 31.2 mg	The mean day 1 morphine consumption: heated, humidified vs cold in the intervention group was 1.66 mg less (-4.79 to 1.46)	481 (7 RCTs)	⊕⊕◯◯ LOW [14]
Day 1 morphine: heated only vs cold	The mean day 1 morphine consumption: heated vs cold was 33.6 mg	The mean day 1 morphine consumption: heated vs cold in the intervention group was 11.93 mg more (0.92 to 22.94)	92 (3 RCTs)	⊕⊕◯◯ LOW [12]
Day 2 morphine	The mean day 2 morphine consumption was 22.1 mg	The mean day 2 morphine consumption in the intervention group was 0.61 mg less (-2.79 to 1.57)	532 (7 RCTs)	⊕⊕⊕◯ MODERATE [1]
Day 2 morphine: heated, humidified vs cold	The mean day 2 morphine consumption - Heated, humidified vs cold was 21.3 mg	The mean day 2 morphine consumption: heated, humidified vs cold in the intervention group was 0.94 mg less (-1.9 to 0.01)	410 (6 RCTs)	⊕⊕⊕◯ MODERATE [1]
Day 2 morphine: heated only vs cold	The mean day 2 morphine consumption: heated vs cold was 23 mg	The mean day 2 morphine consumption: heated vs cold in the intervention group was 9.79 mg more (1.58 to 18.00)	122 (2 RCTs)	⊕⊕◯◯ LOW [12]

*__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; **RR:** Risk ratio; **OR:** Odds ratio;

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: 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 quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

1. Risk of bias not clear
2. Wide confidence intervals

Summary of findings 4. Hospital stay

Heated CO_2 with or without humidification for laparoscopic abdominal surgery

Patient or population: Laparoscopic abdominal surgery (hospital stay)
Setting: Hospital
Intervention: Heated gas

Comparison: Cold gas

Outcomes	Anticipated absolute effects* (95% CI)		№ of participants (studies)	Quality of the evidence (GRADE)	Comments
	Risk with cold gas	Risk with heated gas			
Hospital stay (days)	The mean hospital stay was 2.7 days	The mean hospital stay in the intervention group was 0.06 days less (-0.31 to 0.19)	685 (10 RCTs)	⊕⊕⊕○ MODERATE [1]	
Hospital stay: heated, humidified vs cold	The mean hospital stay: heated, humidified vs cold was 2.9 days	The mean hospital stay: heated, humidified vs cold in the intervention group was 0.13 days less (-0.44 to 0.18)	563 (9 RCTs)	⊕⊕⊕○ MODERATE [1]	
Hospital stay: heated only vs cold	The mean hospital stay: heated vs cold was 2.6 days	The mean hospital stay: heated vs cold in the intervention group was 0.20 days more (-0.23 to 0.62)	122 (2 RCTs)	⊕⊕⊕○ MODERATE [1]	

***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; **RR:** Risk ratio; **OR:** Odds ratio;

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: 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 quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

1. Risk of bias not clear

Summary of findings 5. Recovery time

Heated CO_2 with or without humidification for laparoscopic abdominal surgery

Patient or population: Laparoscopic abdominal surgery (recovery time)
Setting: Hospital
Intervention: Heated gas
Comparison: Cold gas

Outcomes	Anticipated absolute effects* (95% CI)	№ of participants (studies)	Quality of the evidence (GRADE)	Comments

	Risk with cold gas	Risk with heated gas		
Recovery time (minutes)	The mean recovery time was 106.8 min	The mean recovery time in the intervention group was 26.79 min less (-51.34 to -2.25)	327 (6 RCTs)	⊕⊕◯◯ LOW [12]
Recovery time for low risk of bias studies	The mean recovery time for low risk of bias studies was 90.1 min	The mean recovery time for low risk of bias studies in the intervention group was 1.22 min less (-6.62 to 4.17)	277 (5 RCTs)	⊕⊕⊕◯ MODERATE[2]

*__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; **RR:** Risk ratio; **OR:** Odds ratio;

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: 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 quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

1. Risk of bias not clear
2. Wide confidence intervals

Summary of findings 6. Lens fogging

Heated CO_2 with or without humidification for laparoscopic abdominal surgery

Patient or population: Laparscopic abdominal surgery (lens fogging)
Setting: Operating room
Intervention: Heated Gas
Comparison: Cold Gas

Outcomes	Anticipated absolute effects* (95% CI)		№ of participants (studies)	Quality of the evidence (GRADE)	Comments
	Risk with cold gas	Risk with heated gas			
Times cleaned	The mean frequency of cleaning was 1.8 times	The mean times cleaned in the intervention group was 0.73 times more (-0.32 to 1.77)	341 (7 RCTs)	⊕⊕◯◯ LOW [1 2]	The frequency of lens cleaning during surgery

*__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; **RR:** Risk ratio; **OR:** Odds ratio;

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: 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 quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

1. Risk of bias not clear
2. Inconsistent effect

Summary of findings 7. Operative time

Heated CO_2 with or without humidification for laparoscopic abdominal surgery

Patient or population: Laparoscopic abdominal surgery (operative time)
Setting: Operating room
Intervention: Heated gas
Comparison: Cold gas

Outcomes	Anticipated absolute effects* (95% CI)		№ of participants (studies)	Quality of the evidence (GRADE)	Comments
	Risk with cold gas	Risk with heated gas			
Operative time (minutes)	The mean operative time was 76.6 min	The mean operative time in the intervention group was 0.44 min less (-3.91 to 3.04)	1318 (20 RCTs)	⊕◯◯◯ VERY LOW [1 2 3]	
Operative time: heated, humidified vs cold	The mean operative time: heated, humidified vs cold was 94.3 min	The mean operative time: heated, humidified vs cold in the intervention group was 2.01 min less (-7.15 to 3.13)	1033 (15 RCTs)	⊕◯◯◯ VERY LOW [1 2 3]	
Operative time: heated only vs cold	The mean operative time: heated vs cold was 58.8 min	The mean operative time: heated vs cold in the intervention group was 0.91 min more (-4.02 to 5.83)	285 (7 RCTs)	⊕⊕◯◯ LOW [1 3]	

*__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; **RR:** Risk ratio; **OR:** Odds ratio;

GRADE Working Group grades of evidence

High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: 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 quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

---

1. Risk of bias not clear
2. Inconsistent effect
3. Wide confidence intervals

BACKGROUND

Description of the condition

Intraoperative hypothermia can occur with open or laparoscopic surgery. General anaesthesia is associated with impaired thermoregulation (Putzu 2007; Qadan 2009) and insufflation of gas at ambient temperature during laparoscopic abdominal surgery may contribute to worsened hypothermia due to prolonged procedure times. Perioperative hypothermia has been associated with myocardial ischaemia and stimulation of cardiac dysrhythmias, such as ventricular tachycardia (Frank 1993; Frank 1997; Putzu 2007). Generalised immunosuppression and increased surgical site infections have also been described in conjunction with hypothermia. Infections are thought to arise because of a reduction in oxygen delivery to healing tissue due to peripheral vasoconstriction, (Beilin 1998; Qadan 2009). Increased blood loss has been associated with intraoperative hypothermia, resulting in greater transfusion requirements (Putzu 2007; Rajagopalan 2008), which may in turn further worsen hypothermia. Certain patient populations, including the elderly, may be at a higher risk of hypothermia (Macario 2002).

Description of the intervention

A European survey of 8083 surgical cases determined that only 19.4% of patients received intraoperative temperature monitoring (TEMMP). Interventions to prevent hypothermia include passive techniques (such as blankets and covers), and active techniques (such as heated forced air systems, heated mattresses and blankets, warmed humidified ventilator circuits and warmed intravenous and irrigation fluids). These techniques have been suggested to limit perioperative complications due to hypothermia (Putzu 2007; Winkler 2000; Wong 2007). Warm and humidified gas insufflation during laparoscopic surgery has been suggested as another active method to prevent hypothermia. The gas is heated by using a tube with an inline heating coil and water reservoir. The gas may be heated and humidified using such systems. The insufflation gas of choice in laparoscopic surgery is CO_2 but other possibilities include nitrous oxide, helium or argon.

How the intervention might work

Several studies have analysed the impact of using warmed CO_2, with or without humidification, for abdominal insufflation in laparoscopic surgery on patient-centred clinical outcomes. It has been suggested that warming up CO_2 prior to insufflation may prevent hypothermia and peritoneal inflammation (Demco 2001). Other studies concluded that warmed insufflation decreases postoperative pain (Champion 2006; Farley 2004; Hamza 2005; Mouton 1999; Ott 1998) and improves recovery times. These studies typically involved small and specific patient populations. In contradiction, there are a number of studies that show no important clinical benefits of using heated insufflation (Davis 2006; Nguyen 2002) and one in particular showed increased postoperative pain in the heated group (Kissler 2004).

Why it is important to do this review

This systematic review is an update to our previous review (Birch 2011), to further clarify the role of heated CO_2 on core temperature during laparoscopic abdominal surgery and its impact on relevant clinical outcomes.

We repeated our search for eligible trials with updated search strategies, identified additional studies and included them in the meta-analyses.

OBJECTIVES

To determine the effect of heated gas insufflation compared to cold gas insufflation on maintaining intraoperative normothermia as well as patient outcomes following laparoscopic abdominal surgery.

METHODS

Criteria for considering studies for this review

Types of studies

All types of randomised controlled trials (RCT) including parallel-group, crossover, cluster and factorial trials.

Types of participants

Adults and children undergoing laparoscopic abdominal surgery.

Types of interventions

Heated, with or without humidification, gas insufflation versus cold gas insufflation.

Types of outcome measures

Primary outcomes

Change in intra-operative core temperature preferably measured via the tympanic membrane, nasopharynx, oesophagus, bladder or rectum (Cork 1983).

Secondary outcomes

The following clinical outcomes:

- postoperative pain score (10-point visual analogue scale (VAS));
- morphine consumption; preferably reported as morphine equivalent daily doses
- hospital stay;
- recovery room stay;
- lens fogging;
- operative time;
- major adverse events defined as Clavien-Dindo grade III or higher (Dindo 2004).

Search methods for identification of studies

Electronic searches

We conducted a comprehensive literature search to identify all published and unpublished RCTs with no language restrictions in collaboration with the Cochrane Information Specialist (CIS) from Cochrane Colorectal Cancer. We searched the following electronic databases:

- Cochrane Colorectal Cancer Group Specialised Register (September 2016);
- Cochrane Central Register of Controlled Trials (CENTRAL; *The Cochrane Library* 2016, Issue *8*)) (September 2016) (Appendix 1);
- Ovid MEDLINE (1950 to Septermber 2016) (Appendix 2);

- Ovid Embase (1974 to September 2016) (Appendix 3);
- SCOPUS (date to July 2016) (Appendix 4);
- Web of Science (1985 to July 2016) (Appendix 5);
- www.clinicaltrials.gov, International Pharmaceutical Abstracts, the National Research Register and Google Scholar for completed and ongoing trials (Appendix 6).

Searching other resources

We also searched Google Scholar, conference proceedings and reference lists of included studies for relevant studies.

Data collection and analysis

Selection of studies

Two review authors (JD, XS) performed study selection independently, with any subsequent disagreement resolved through discussion with a third co-author (NS). Studies were included in the review irrespective of whether they reported measured outcome data.

Data extraction and management

Two review authors (XS, NS) independently collected data from the included studies into data sheets. We resolved disagreements through discussion with a third co-author (JD). Two studies (Saad 2000; Wills 2001) that did not use standard visual analogue scales (VAS) had their 0 to 100 scores converted to a score from 0 to 10.

Assessment of risk of bias in included studies

We used the Cochrane 'Risk of bias' tool for assessing risk of bias of included trials (Higgins 2011). We assessed risk of bias of the following domains:

- random sequence generation;
- allocation concealment;
- blinding of participants and personnel;
- blinding of outcome assessment;
- incomplete outcome data;
- selective reporting bias;
- other bias (conflicts of interest, reporting of data, reporting and balance of characteristics at baseline).

We judged each domain as low risk, high risk or unclear risk of bias according to criteria used in the Cochrane 'Risk of bias' tool (see Appendix 7) (Higgins 2011). We judged a study as low risk of bias if we assessed all of the first six domains as low risk. Two review authors (JD, XS) independently assessed the risk of bias and disagreements were resolved with a third author (NS).

Measures of treatment effect

We calculated the effect of the intervention for each trial, expressing categorical data as relative risks (RR) with 95% confidence intervals (CI) and continuous data as mean differences (MD) ± 95% CIs.

Unit of analysis issues

For individual trials, the unit of analysis we used was individual participants. There were no cluster-randomised trials or cross-over trials that would be at risk of unit of analysis issues eligible for inclusion in our review. If there are such studies in future updates, we will perform sensitivity analyses to determine the effect of these trials on outcome measures.

Dealing with missing data

If possible, we obtained missing data either from the original study authors or from similar reviews written by others (Lee 2011; Sajid 2008; Sammour 2008). We contacted nine authors, four responded with additional data, two had no further data, and three did not respond. When the original data only provided the mean, we used the largest standard deviation (SD) in the group of trials in the analysis.

Assessment of heterogeneity

We assessed clinical heterogeneity for differences in participant characteristics (paediatric vs adult), intervention characteristics (humidified vs non-humidified, duration of surgery, external warming) and outcome measures (abdominal vs shoulder pain) with subgroup analysis where possible. Heterogeneity was tested using the Chi^2 test with significance set at $P < 0.10$ and the amount of heterogeneity quantified by the I^2 statistic. Heterogeneity was considered as low, moderate, and high based on I^2 values of 25%, 50%, and 75%, respectively (Higgins 2003).

Assessment of reporting biases

We considered publication bias and compiled funnel plots for the studies to reveal this. We then applied Egger's linear regression analysis (Egger 1997) to each funnel plot to detect asymmetry.

Data synthesis

We used meta-analysis to combine the outcomes and determine the estimated effect of intervention, which we calculated using Review Manager (RevMan) software version 5.3 (RevMan 2014). We applied the random-effects method in our analysis, assuming that the true effect estimates varied among studies.

Subgroup analysis and investigation of heterogeneity

When significant heterogeneity was found among studies, we performed subgroup analysis to explore the source. We performed subgroup analysis for humidified vs non-humidified subgroups for the following outcomes: core temperature, pain score, morphine consumption, hospital stay, and operative time. For the core temperature outcome, we also analysed subgroups with longer operative times (more than 120 minutes) and those with external warming. The 120-minute threshold was decided after consulting with surgeons on the research team as there was no clear definition in the literature. Further, for pain scores, we performed subgroup analysis for shoulder and abdominal pain. Shoulder pain occurs in some patients after insufflation due to referred pain from irritation of the diaphragm. Additionally, we performed separate analysis with only low-risk-of-bias studies for core temperature, pain score and recovery time.

Summary of Findings Table

We assessed the quality of evidence of core temperature, pain score, morphine consumption, hospital stay, recovery room stay, lens fogging and operative time for the heated gas group versus cold gas group using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach (Schünemann 2009) in the 'Summary of Findings' table(s).

The GRADE system classifies the quality of evidence in one of four grades:

Grade	Definition
High	Further research is very unlikely to change our confidence in the estimate of effect
Moderate	Further research is likely to have an impact on our confidence in the estimate of effect and may change the estimate
Low	Further research is very likely to have an important impact on our confidence on the estimate of effect and is likely to change the estimate
Very low	Any estimate of effect is very uncertain

Factors that influence the quality of evidence:

Downgrades the evidence	Upgrades the evidence
Study limitation	Large magnitude of effect
Inconsistency of results	All plausible confounding would reduce the demonstrated effect
Indirectness of evidence	Dose-response gradient
Imprecision	
Publication bias	

Sensitivity analysis

Not all studies had adequately reported on sequence generation, allocation concealment, blinding, or number of and reasons for withdrawals, and were therefore at an unclear risk of bias. We therefore performed sensitivity analyses including only those trials with a known low risk of bias.

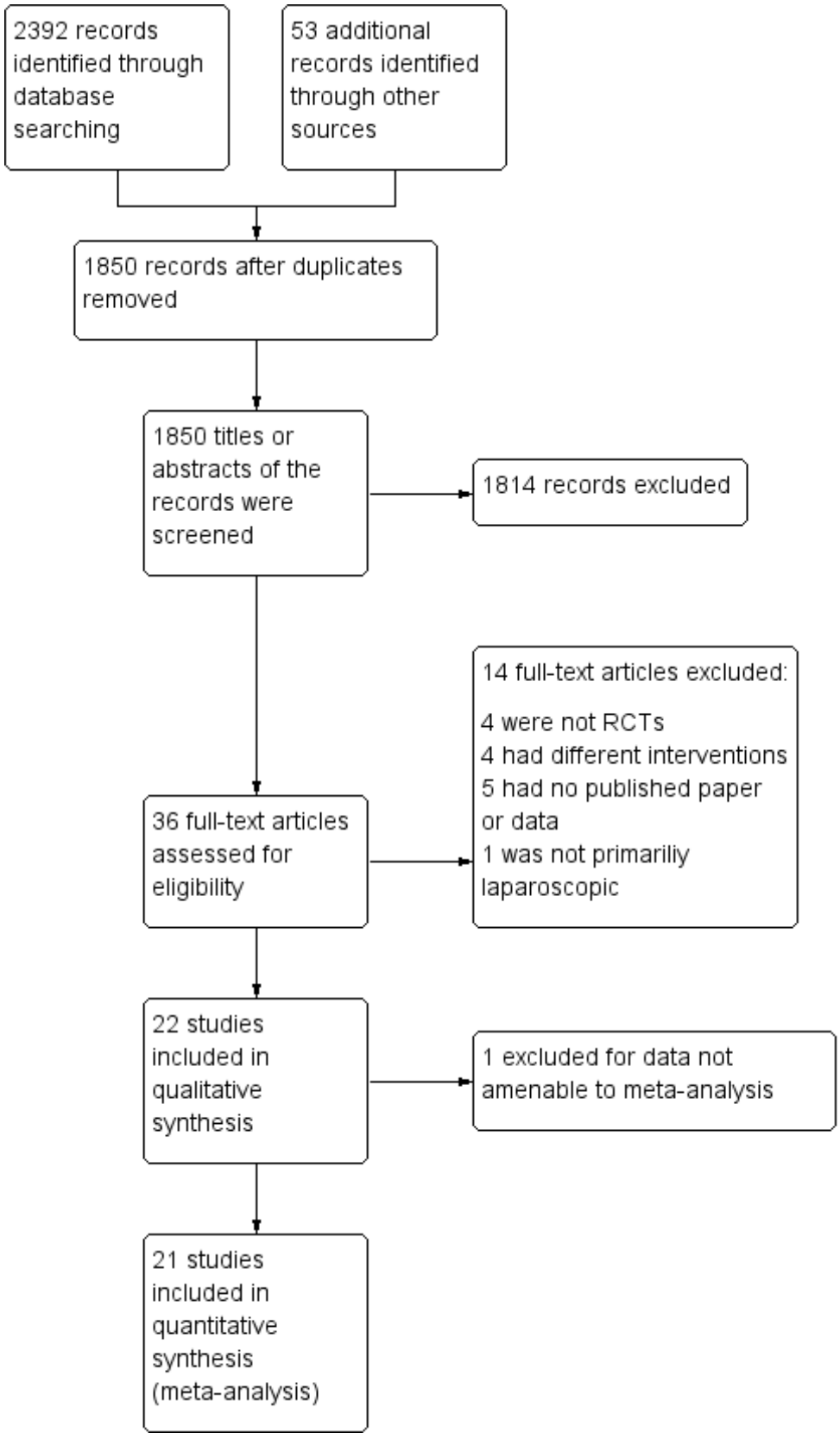
RESULTS

Description of studies

Results of the search

The electronic searches identified a total of 2392 citations. After removing duplicate studies, we reviewed 1850 titles or abstracts, and excluded trials that involved non-abdominal procedures, uncommon laparoscopic procedures, non-human subjects and those not using cold gas as a control. We also excluded duplicated studies and non-randomised controlled trials. Finally, the review authors DB, NS and XS agreed that 22 trials met the inclusion criteria and included them in this review. See PRISMA diagram (Moher 2009) (Figure 1).

Figure 1. Study flow diagram



Included studies

All 22 included studies were RCTs comparing heated CO_2 insufflation (with or without humidification) with standard cold CO_2 insufflation. All the included studies used CO_2 insufflation. We excluded from the review studies examining outcomes that were dissimilar to those relevant to this review and studies where we did not receive a response from the authors. Surgical procedures included in the studies were: gastric bypass (n = 168), gynaecologic surgery (n = 259), cholecystectomy (n = 500), Nissen fundoplication (n = 157), appendicectomy (n = 190), low anterior resection (n = 16), gastrectomy (n = 7), colonic surgery (n = 84), diagnostic laparoscopy (n = 40), hernioplasty (n = 4), myotomy (n = 2) and rectopexy (n = 1).

Primary outcome data were available for 1081 participants as three studies (Demco 2001; Klugsberger 2014; Slim 1999) did not report intraoperative changes in core temperature. Of these, 430 were in the heated, humidified gas group; 105 were in the heated-only gas group; and 546 were in the cold gas group.

Five studies had relatively long operative times (more than 120 minutes) (Backlund 1998; Hamza 2005; Lee 2011; Ott 1991; Sammour 2010). Ten out of 22 studies used a warming blanket for simultaneous warming (Backlund 1998; Farley 2004; Hamza 2005; Lee 2011; Manwaring 2008; Nguyen 2002; Sammour 2010; Savel 2005; Wills 2001; Yu 2013). A heated insufflation company supported 11 of the 22 trials (Backlund 1998; Davis 2006; Farley 2004; Hamza 2005; Kissler 2004; Manwaring 2008; Mouton 1999; Nelskyla 1999; Ott 1998; Savel 2005; Wills 2001). Ten of the 22 studies demonstrated a benefit with the use of heated gas insufflation (Agaev 2013; Backlund 1998; Farley 2004; Hamza 2005; Klugsberger 2014; Lee 2011; Mouton 1999; Nelskyla 1999; Ott 1998; Puttick 1999). See Characteristics of included studies and Table 1; Table 2; Table 3 for full study details.

Agaev 2013: originally published in Russian, this study examined 150 laparoscopic operations (110 cholecystectomies and 40 fundoplications), participants with standard CO_2 vs. warmed, humidified CO_2 during the operations. Their conclusion was warmed, humidified CO_2 had advantages for maintaining a warmer intraoperative core temperature, having less postoperative pain and requiring fewer analgesic prescriptions.

Backlund 1998: examined the effect of 37 °C and room temperature-insufflated CO_2 during and after prolonged laparoscopic surgery (more than 120 minutes). Twenty six participants undergoing fundoplication, hernioplasty, resection of the sigmoid colon and rectopexy were randomly assigned to warm or cold gas groups. Core temperature, cardiac index, urine output and recovery room opioid usage and pain scores were recorded.

Champion 2006: was a trial of heated, humidified versus cold dry CO_2 insufflation for laparoscopic gastric bypass, which examined 50 consecutive obese patients with homogeneous baseline characteristics (gender, age, preoperative weight, body mass index (BMI) and c-reactive protein (CRP)) between groups. The ambient insufflation gas was at a temperature of 35 °C and 95% relative humidity. The sole difference identified in the heated group was a lower postoperative subjective shoulder pain score at 18 hours. There were no differences between groups in intraoperative core temperature, operating room temperature, litres of insufflation, operating time, number of lens cleanings, recovery room temperature, narcotic usage, length of hospitalisation, high-sensitivity CRP at 24 hours or abdominal pain scores.

Davis 2006: with adequate allocation concealment, this study examined 44 laparoscopic Roux-en-Y gastric bypass patients in Ohio State University. There were four study groups with 11 participants in each and similar baseline characteristics across the groups. The groups included the following insufflation techniques: 1) cold dry, 2) cold humidified (97% relative humidity), 3) heated dry (37 °C) and 4) heated humidified (37 °C and 97% relative humidity) CO_2. There were no differences in patient core temperature, intra-abdominal humidity, postoperative narcotic usage, pain scale scores, recovery room time, length of hospitalisation, lens fogging or macrophage activity between groups, though participants in the heated, humidified insufflation group demonstrated increased macrophage activity in biopsies.

Demco 2001: 40 women undergoing diagnostic laparoscopy were randomised to heated, humidified insufflation or cold CO_2. Outcomes were shoulder pain, fentanyl use, percent requiring general anaesthetic, percent requiring intravenous sedation, amount of gas instilled before experiencing pain, operating time, recovery room time and time to recovery of shoulder pain. Outcomes were presented as percentages of participants in various groups (e.g. operative time more than 10 minutes, 10 to 20 minutes, etc.), which could not be included in meta-analysis.

Farley 2004: with adequate allocation concealment, randomised 101 people undergoing laparoscopic cholecystectomy to either cold or heated and humidified CO_2 insufflation. The experimental group showed higher intraoperative core temperatures and decreased postoperative pain scores at day 14; the study authors questioned the clinical relevance of the latter outcome. They identified no differences in the rate of lens fogging, narcotic requirements, length of hospitalisation or time of return to baseline activity levels.

Hamza 2005: randomised 50 people undergoing laparoscopic Roux-en-Y gastric bypass surgery, with no information on allocation concealment, to cold or heated and humidified CO_2 insufflation. Six were excluded. Mean operative times for each group were greater than 120 min. The heated group showed a higher intraoperative core temperature, a reduction in time in the recovery room and narcotic requirements, and a higher quality of recovery at 48 hours postoperatively. There were no differences in postoperative tympanic membrane temperatures, pain scores, shivering, overall morphine usage, nausea scores, Aldrete recovery assessment scores, length of hospital stay or lens fogging.

Kissler 2004: recruited 90 consecutive women scheduled for gynaecologic laparoscopic surgery into this study with randomisation to heated humidified, heated non-humidified and cold gas insufflation groups, each with 30 participants. The trial was stopped following enrolment of 53 participants due to a tendency for less pain and higher postoperative satisfaction in the cold insufflation control group.

Klugsberger 2014: randomised 148 people undergoing laparoscopic cholecystectomy to standard gas or warmed, humidified gas groups. Intraoperative core temperature was significantly higher with less six-hour postoperative pain in the

warmed, humidified gas group. Pain was not significantly different on the first day after operation.

Lee 2011: randomised 30 people undergoing laparoscopic low anterior resection, colectomy or gastrectomy to heated CO_2 or standard CO_2 groups. Mean operative times were greater than 200 minutes for each cohort. They recorded acid-base parameters and core temperature. Heated CO_2 did not significantly change acid-base parameters in participants but reduced the decrease in core body temperature 30 minutes after pneumoperitoneum.

Manwaring 2008: randomised 60 gynaecology patients to heated humidified or cold insufflation groups. Heated and humidified gas insufflation was not associated with any significant benefits as no difference was found in oesophageal temperature, pain scores or narcotic usage.

Mouton 1999): randomised 40 people undergoing cholecystectomy to heated, humidified insufflation or cold gas insufflation. Eight were excluded. Though they found no difference in core temperature during the relatively brief operations, there was significantly less pain compared to the experimental heated and humidified insufflation participants at six hours and on the first to third days postoperatively. Pain was also less on the 14th postoperative day.

Nelskyla 1999: randomised 40 women undergoing laparoscopic hysterectomy to heated or unheated gas insufflation groups. Three were excluded. Tympanic and nasopharyngeal intraoperative temperatures were not different between the groups.

Nguyen 2002: randomised 20 people undergoing laparoscopic Nissen fundoplication, without information on the allocation method, to heated and humidified or cold and dry gas insufflation groups. There were no differences in core temperature, pain scores, narcotic consumption, urine output or lens fogging.

Ott 1998: without stating the number of participants in each group, this study randomised 72 women undergoing laparoscopic gynaecologic surgery to heated and humidified or cold and dry gas insufflation. Most data was extracted from a systematic review (Sammour 2008) and was only available for 50 patients with no reason was given. The experimental heated group showed improved intraoperative normothermia and postoperative pain, and reduced recovery room stay.

Puttick 1999: randomised 30 people undergoing laparoscopic cholecystectomy to heated or cold gas insufflation. The study authors concluded that intraoperative cooling could be prevented by heating the insufflated gas.

Saad 2000: randomised 20 people undergoing laparoscopic cholecystectomy to heated or cold gas insufflation with no effects when comparing core temperature or postoperative pain. VAS pain scores were converted from a 0 to 100 scale to a standard 0 to 10 scale.

Sammour 2010: randomised 82 people undergoing laparoscopic colon surgery to heated, humidified or cold gas insufflation groups, each with 41 participants. Eight patients were excluded. They found no significant effects, including no effect on the early postoperative inflammatory cytokine response. Mean operative times were greater than 170 minutes for both cohorts.

Savel 2005: randomised 30 people undergoing laparoscopic Roux-en-Y gastric bypass to cold or heated and humidified gas insufflation groups. Length of hospitalisation and operative time were reduced in the experimental group but the study found no differences in pain sensation.

Slim 1999: enrolled 100 people undergoing laparoscopic cholecystectomy, fundoplication, or Heller's myotomy and randomised them to cold or heated insufflation. Shoulder and subcostal pain sensation was increased in the heated insufflation group and the study found no difference on core temperature or narcotic consumption.

Wills 2001: randomised 41 people to heated or cold gas insufflation during laparoscopic fundoplication. One was excluded. An increased core temperature was associated with the heated insufflation group, though the control group participants suffered less postoperative pain and required fewer narcotics. VAS pain scores were converted from a 0 to 100 scale to a standard 0 to 10 scale.

Yu 2013: randomised 195 children undergoing laparoscopic appendectomy to warm, humidified CO_2 or standard CO_2 groups. Five were excluded. The study assessed postoperative opioid usage, pain intensity, postoperative recovery and return to normal activities. Warm, humidified CO_2 insufflation had no short-term clinical benefits on postoperative outcomes in children.

Excluded studies

We excluded Beste 2006 and Benavides 2009 from this review because they compared heated, humidified CO_2 with heated, non-humidified CO_2, a comparison not intended for this review. However, they were included in two previously published systematic reviews (Sajid 2008; Sammour 2008). Herrmann 2015 we excluded because it assessed laparoscopic-assisted vaginal hysterectomies which is not primarily an abdominal, laparoscopic surgery. We excluded the remaining studies because they were not RCTs. Excluded studies were excluded from both quantitative and qualitative analyses. See section on Characteristics of excluded studies for details.

Risk of bias in included studies

We assessed risk of bias for all included studies (Figure 2; Figure 3). Eleven studies had an overall low risk of bias (low risk of bias for the six main criteria assessed) in the presentation of their results (Champion 2006; Davis 2006; Farley 2004; Hamza 2005; Lee 2011; Manwaring 2008; Nguyen 2002; Sammour 2010; Slim 1999; Wills 2001; Yu 2013).

Figure 2. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies

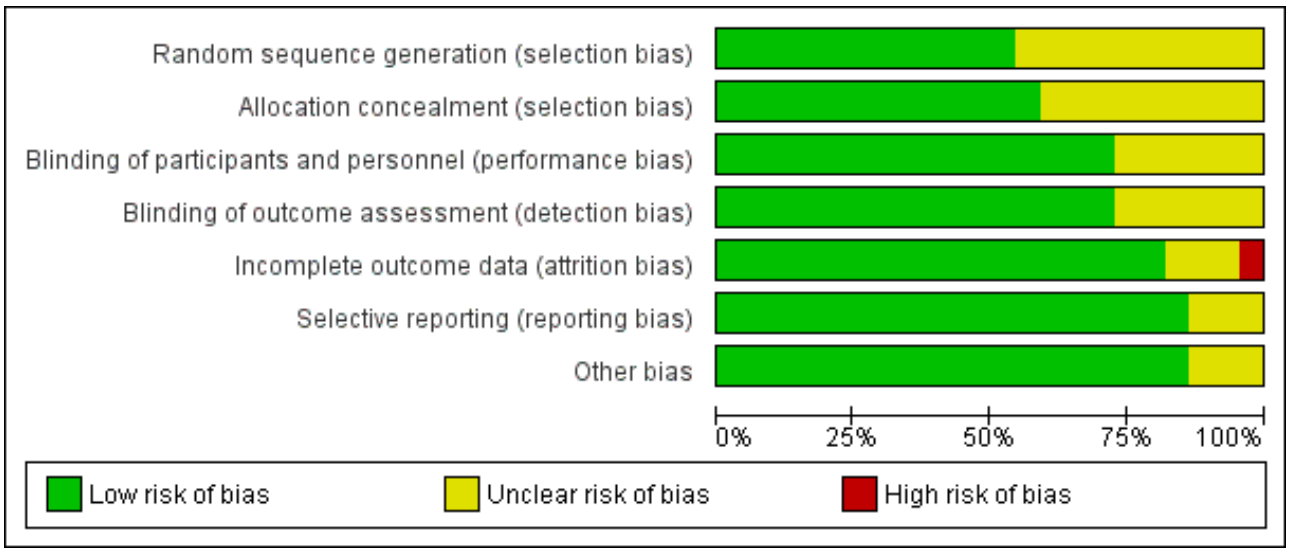


Figure 3. Risk of bias summary: review authors' judgements about each risk of bias item for each included study

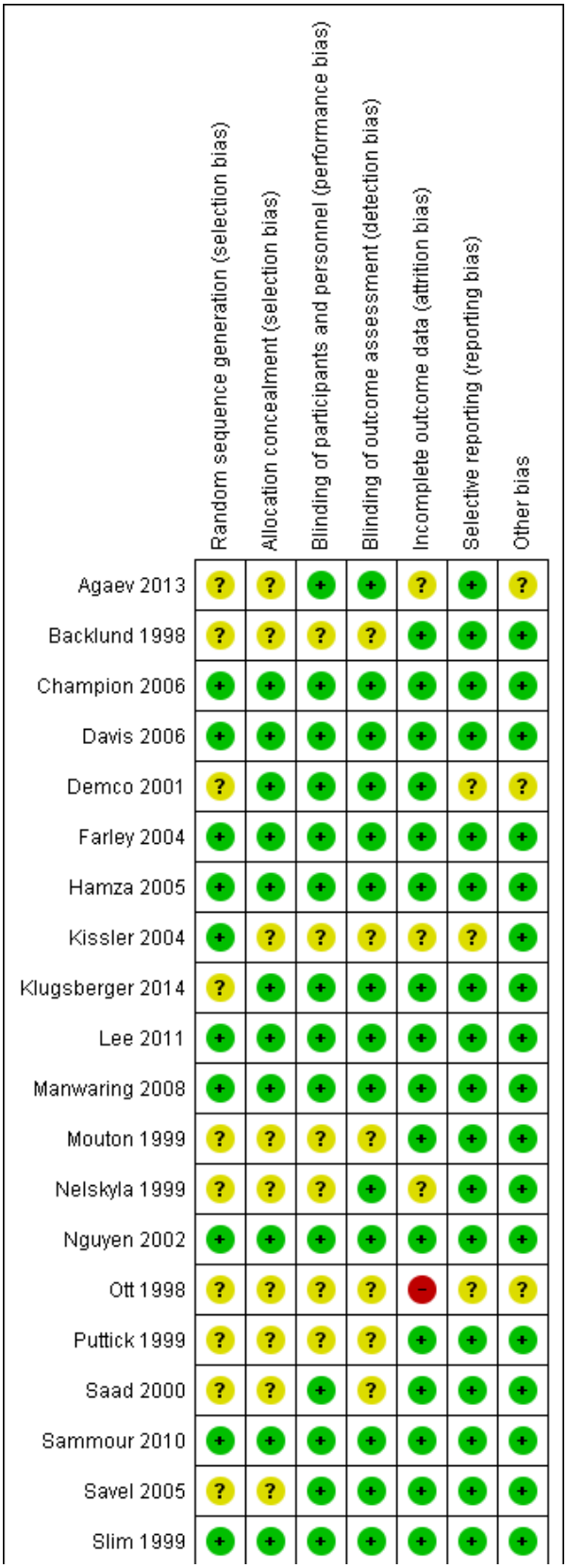
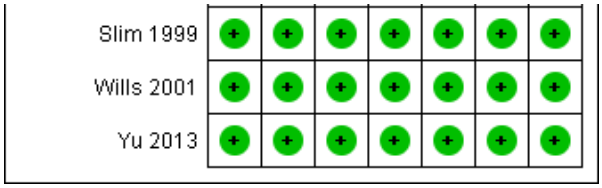


Figure 3. (Continued)



Allocation

We rated 11 studies at unclear risk of bias, with nine of these studies (Backlund 1998; Demco 2001; Kissler 2004; Mouton 1999; Nelskyla 1999; Ott 1998; Puttick 1999; Saad 2000; Savel 2005) failing to report on the methodology for randomisation or allocation concealment. Agaev 2013 stated that randomisation was done with a computer model post-anaesthetic, but comparative groups were very uneven with 84 in the heated group and 66 in non-heated. Klugsberger 2014 was unclear about randomisation and also had uneven groups (67 in heated and 81 in non-heated).

Blinding

We judged five studies (Backlund 1998; Mouton 1999; Ott 1998; Puttick 1999; Saad 2000) at unclear risk of bias because they had no description of blinding. The remaining studies were adequately blinded with only one or two operating-room personnel unblinded to initiate the intervention.

Incomplete outcome data

We deemed three studies an unclear risk of attrition bias. Agaev 2013 did not state the number of participants included in their analysis. Kissler 2004 was stopped early because the control group had less pain and improved satisfaction. Nelskyla 1999 excluded three participants without clear reasoning. Ott 1998 reported data on only 55 of 72 participants and did not state a reason for this missing data. This was assessed a high risk of bias.

Selective reporting

Demco 2001 did not report any core temperatures which would be expected from a study on heated insufflation. Klugsberger 2014 and Slim 1999 reported mean core temperatures but did not report on intraoperative changes in core temperature. However, Slim 1999 only measured subdiaphragmatic core temperatures once during the operation so this is not due to selective reporting.

Other potential sources of bias

Agaev 2013, originally published in Russian, was translated voluntarily by a research scientist employed by a surgical humidification device company. We deemed this an unclear risk of bias due to a possible conflict of interest. Many studies (Agaev 2013; Backlund 1998; Champion 2006; Davis 2006; Hamza 2005; Kissler 2004; Lee 2011; Mouton 1999; Nguyen 2002; Ott 1998; Saad 2000; Savel 2005; Wills 2001) were also missing standard deviations and this potentially distorted the true effects and potentially increased the error.

Demco 2001 did not report any baseline demographics, while Ott 1998 did not separate demographics between groups and potential imbalances in participant characteristics could have contributed to bias.

Industry supported eight trials by providing heated insufflation devices (Backlund 1998; Farley 2004; Kissler 2004; Manwaring 2008; Nelskyla 1999; Savel 2005; Wills 2001). Two trials received educational grants from industry (Davis 2006; Hamza 2005) and one trial reported industry assistance (Mouton 1999). We judged this a low risk of bias as there appeared to be no industry influence in the trials with industry support.

Effects of interventions

See: **Summary of findings for the main comparison** Core temperature; **Summary of findings 2** Pain score; **Summary of findings 3** Morphine consumption; **Summary of findings 4** Hospital stay; **Summary of findings 5** Recovery time; **Summary of findings 6** Lens fogging; **Summary of findings 7** Operative time

Primary outcome

Change in core temperature

(Analysis 1.1; Analysis 1.2; Analysis 1.3)

Nineteen studies reported change in intraoperative core temperatures. Overall, core temperature was slightly higher with heated CO_2 (MD 0.21 °C, 95% CI 0.06 to 0.36, P = 0.007) (Figure 4). Heterogeneity was substantial (I^2 = 86%), therefore subgroup analyses were performed for humidified and non-humidified CO_2. Heated gas with humidification had a small, but positive effect on core temperature intraoperatively compared to cold CO_2 (MD 0.31 °C, 95% CI 0.09 to 0.53, P = 0.005) (Figure 4). When only studies with low risk of bias were assessed, this effect became statistically non-significant (Figure 5). No apparent effect was found in the non-humidified, heated-gas group compared to cold gas, regardless of analysis based on all studies or only low-risk studies. A subgroup analyses for operations lasting less and more than 120 minutes were also performed. There was no difference detected in temperature between heated and cold CO2 for operations lasting less than 120 minutes. However, for operations lasting over 120 minutes (Backlund 1998; Hamza 2005; Ott 1998; Sammour 2010), temperature was significantly higher with warming and humidification, but the studies exhibited significant statistical heterogeneity (I^2 = 91%) (Figure 6). When subgroup analyses of studies using external warming were conducted, core temperatures were significantly higher in the heated, humidified group (MD 0.29 °C, 95% CI 0.05 to 0.52) (Figure 7); but the studies were once again statistically heterogenous (I^2 = 84%). The only trial with a known low risk of bias (Savel 2005) showed no statistically significant difference between groups, however, with only 30 participants, such a small trial would unlikely be adequately powered to detect a difference between groups even if one was present (Figure 7). When only trials not using external warming were analysed, heated, humidified gas had no apparent effect on core temperature compared to cold gas. (Figure 8).

Figure 4. Forest plot of comparison: 2 Core temperature, outcome: 2.1 Change in core temperature

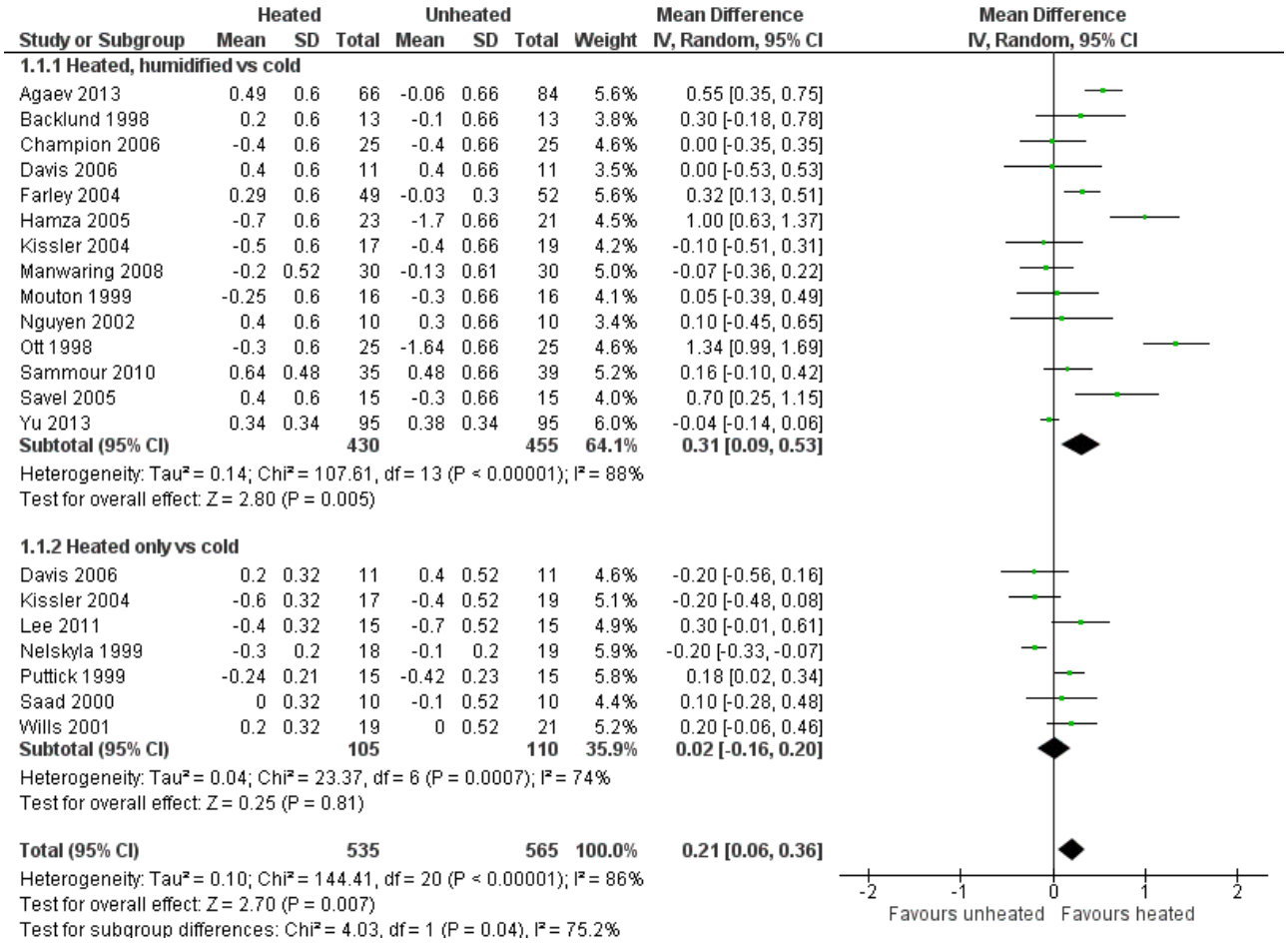


Figure 5. Forest plot of comparison: 2 Core temperature, outcome: 2.2 Change in core temperature for low risk of bias studies

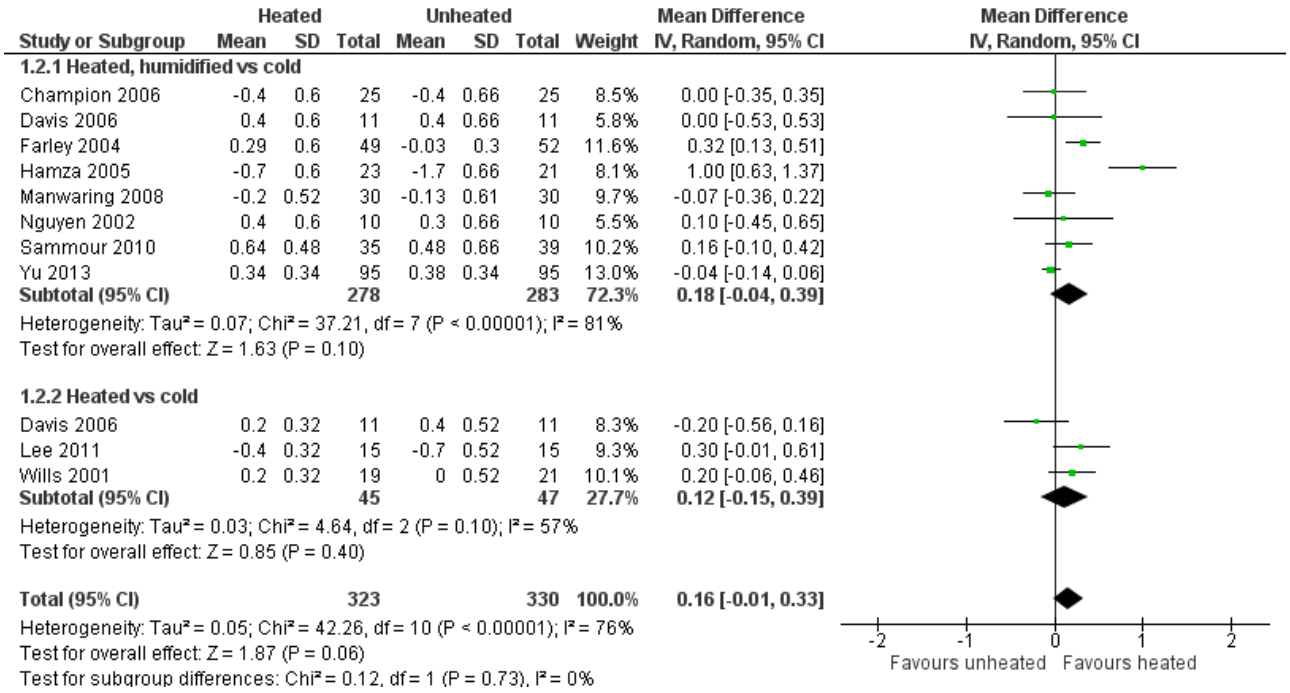


Figure 6. Forest plot of comparison: 1 Core temperature, outcome: 1.5 Change in core temperature in heated, humidified vs cold groups with OR > 120 Minutes

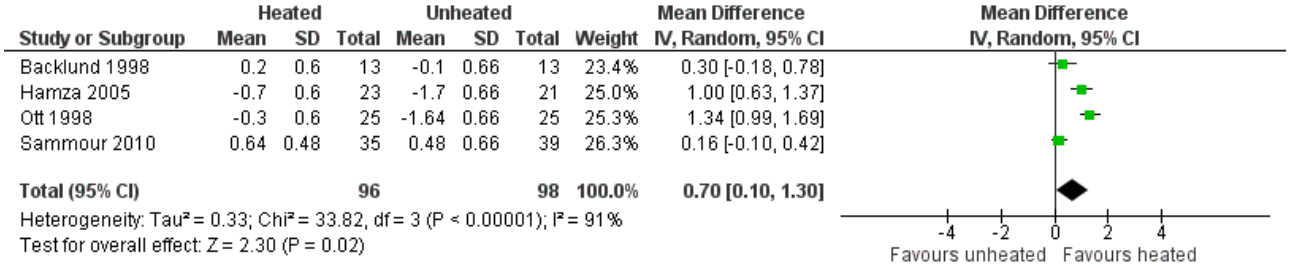


Figure 7. Forest plot of comparison: 2 Core temperature, outcome: 2.3 Change in core temperature in heated, humidified vs cold groups with external warming

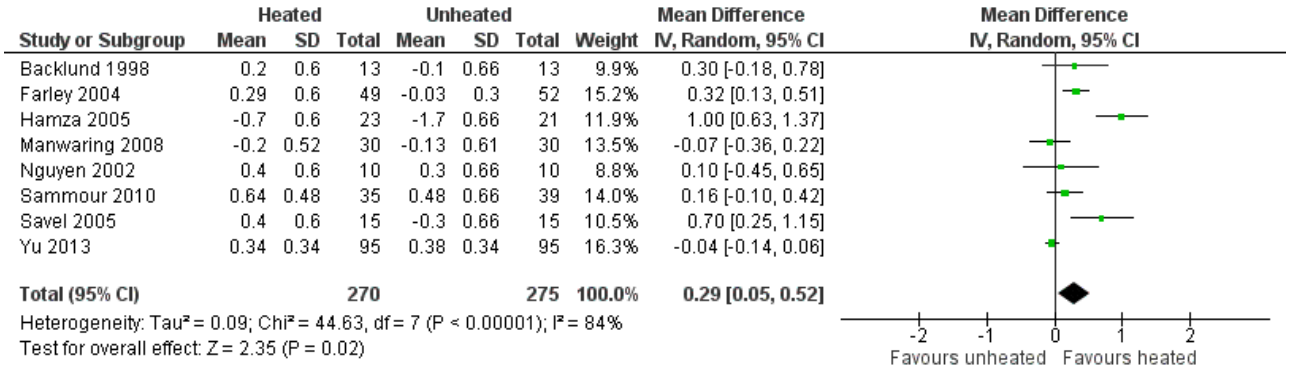
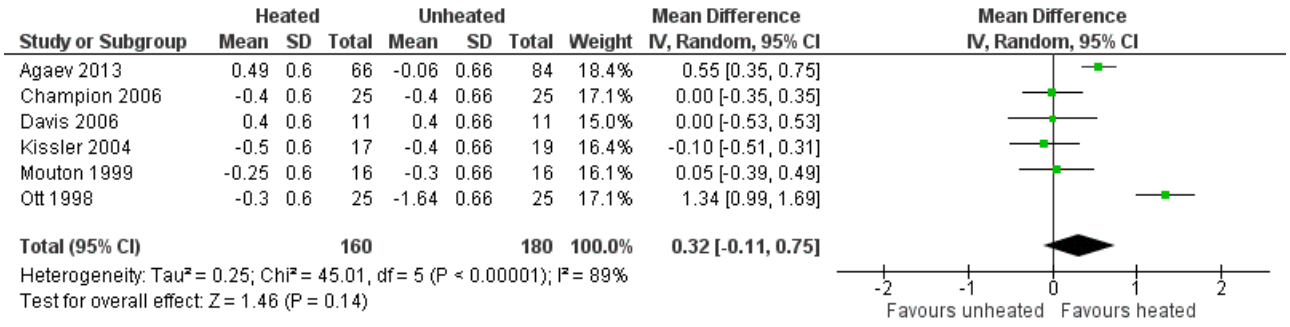


Figure 8. Forest plot of comparison: 1 Core temperature, outcome: 1.4 Change in temperature in heated, humidified vs cold groups without external warming



Secondary outcomes

Pain scores

(Analysis 2.1; Analysis 2.2; Analysis 2.3; Analysis 2.4)

For pain scores (measured using a 0 to 10 visual analogue scale), there was no statistically significant difference detected between groups overall on day 1 (MD -0.04, 95% CI -0.42 to 0.34) or day 2 (MD -0.28, 95% CI -0.78 to 0.21). Subgroup analyses were performed for the effect of humidified CO_2 and non-humidified CO_2, on shoulder and abdominal pain separately, and for heated only versus cold CO2 (not by location of pain).

Day 1

The effect of heated and humidified gas on postoperative day one showed no statistically significant difference compared to cold gas (abdominal pain MD -0.14, 95% CI -0.60 to 0.33, P = 0.57; shoulder pain MD -0.35, 95% CI -1.75 to 1.05, P = 0.62) (Figure 9). Given the significant heterogeneity across studies (abdominal P = 0.02, I^2 = 53%; shoulder P = 0.03, I^2 = 72%), sensitivity analyses were performed and only studies with a known low risk of bias were included. The pain scores were still apparently not different with respect to either abdominal or shoulder pain and the test of heterogeneity was no longer statistically significant (abdominal P = 0.32, I^2 = 15%; shoulder P = 0.22, I^2 = 35%) (Figure 10). When heated only gas was compared to cold gas, the day-one pain scores were not statistically significantly different (Figure 9).

Figure 9. Forest plot of comparison: 1 Pain score, outcome: 1.1 Day 1 pain score

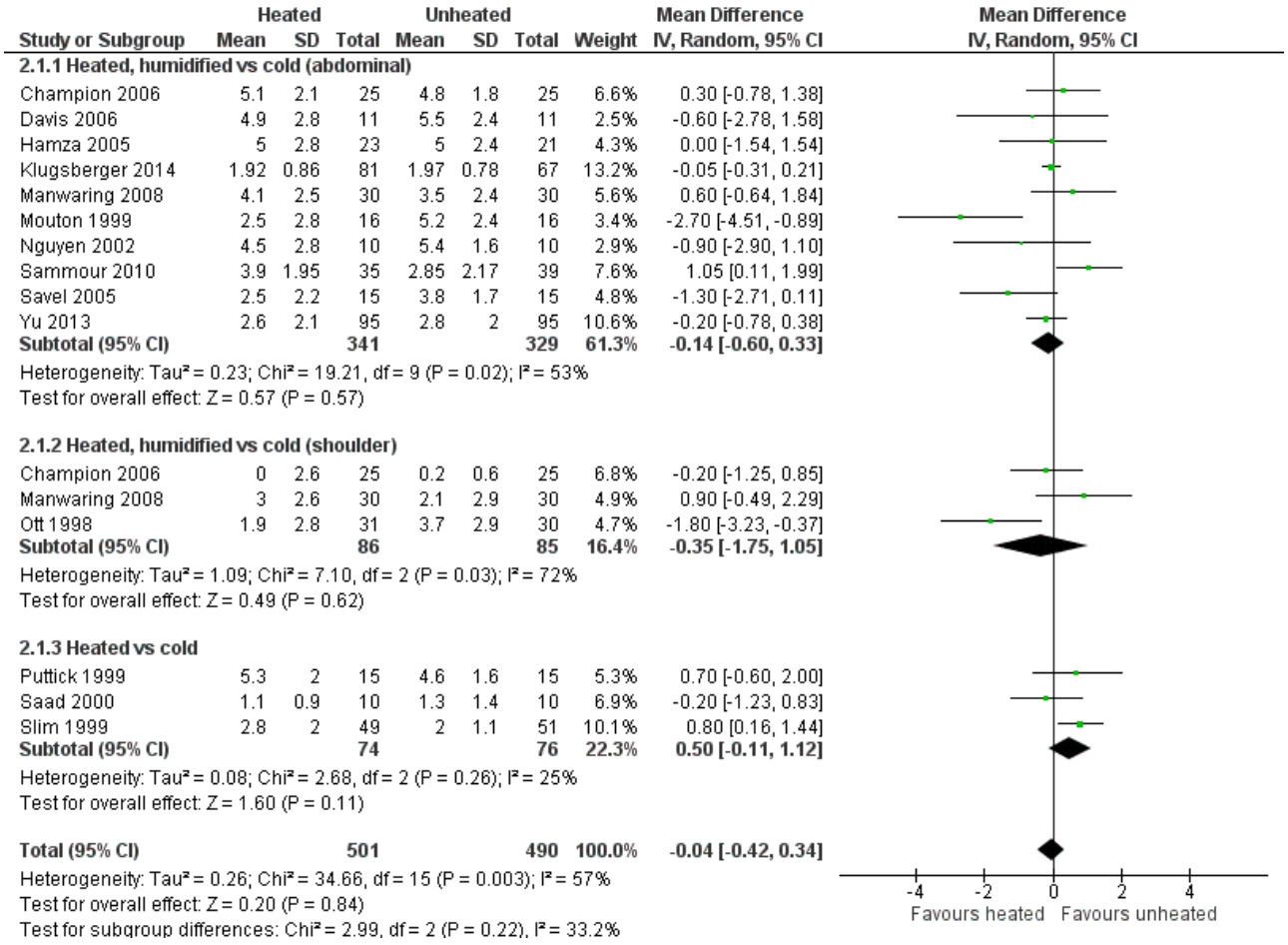
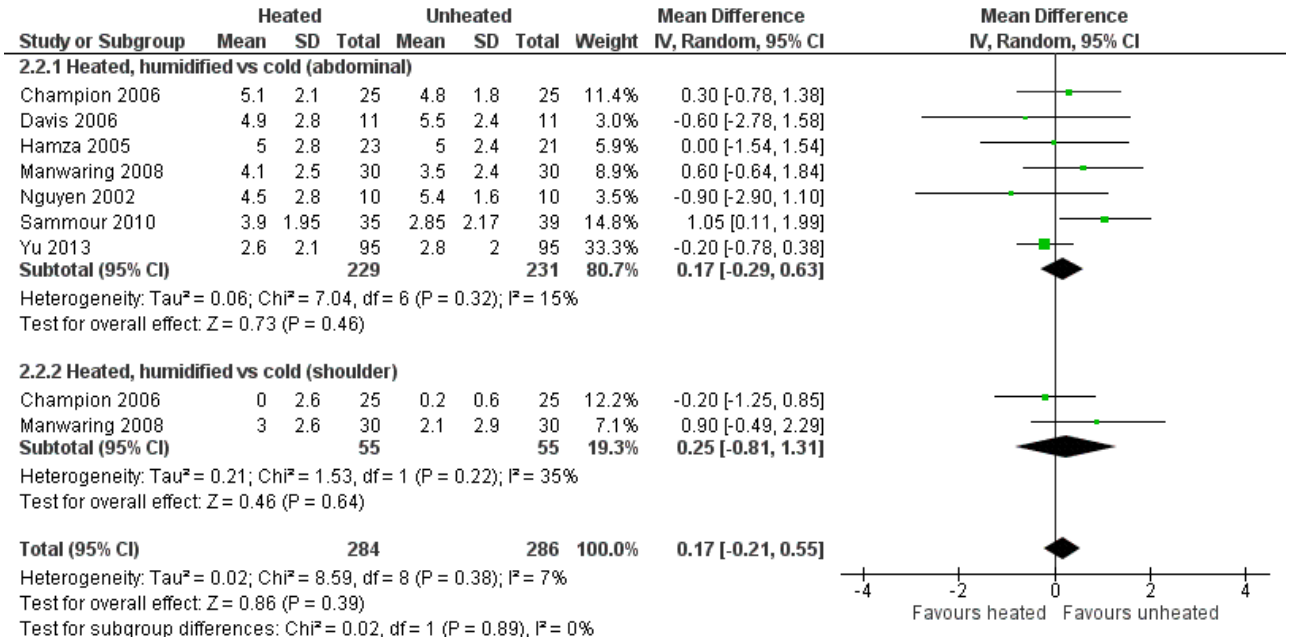


Figure 10. Forest plot of comparison: 1 Pain score, outcome: 1.3 Day 1 pain score for low risk of bias study



Day 2

For pain on the second postoperative day, heated and humidified gas did not apparently improve abdominal or shoulder pain (abdominal MD -0.40, 95% CI -1.07 to 0.28, P = 0.25; shoulder MD -0.88, 95% CI -2.93 to 1.17, P = 0.40), but again, the studies were heterogenous (I^2 62% and 92%, respectively) (Figure 11). When only low risk of bias studies were included, the conclusion remained unchanged (Figure 12) and I^2 decreased to 0%. With heated only gas, the postoperative day-two pain score was similar to the cold gas control (MD 0.41, 95% CI -0.44 to 1.27, P = 0.34) with no statistically significant heterogeneity across trials (P = 0.23, I^2 = 33%).

Figure 11. Forest plot of comparison: 1 Pain score, outcome: 1.2 Day 2 pain score

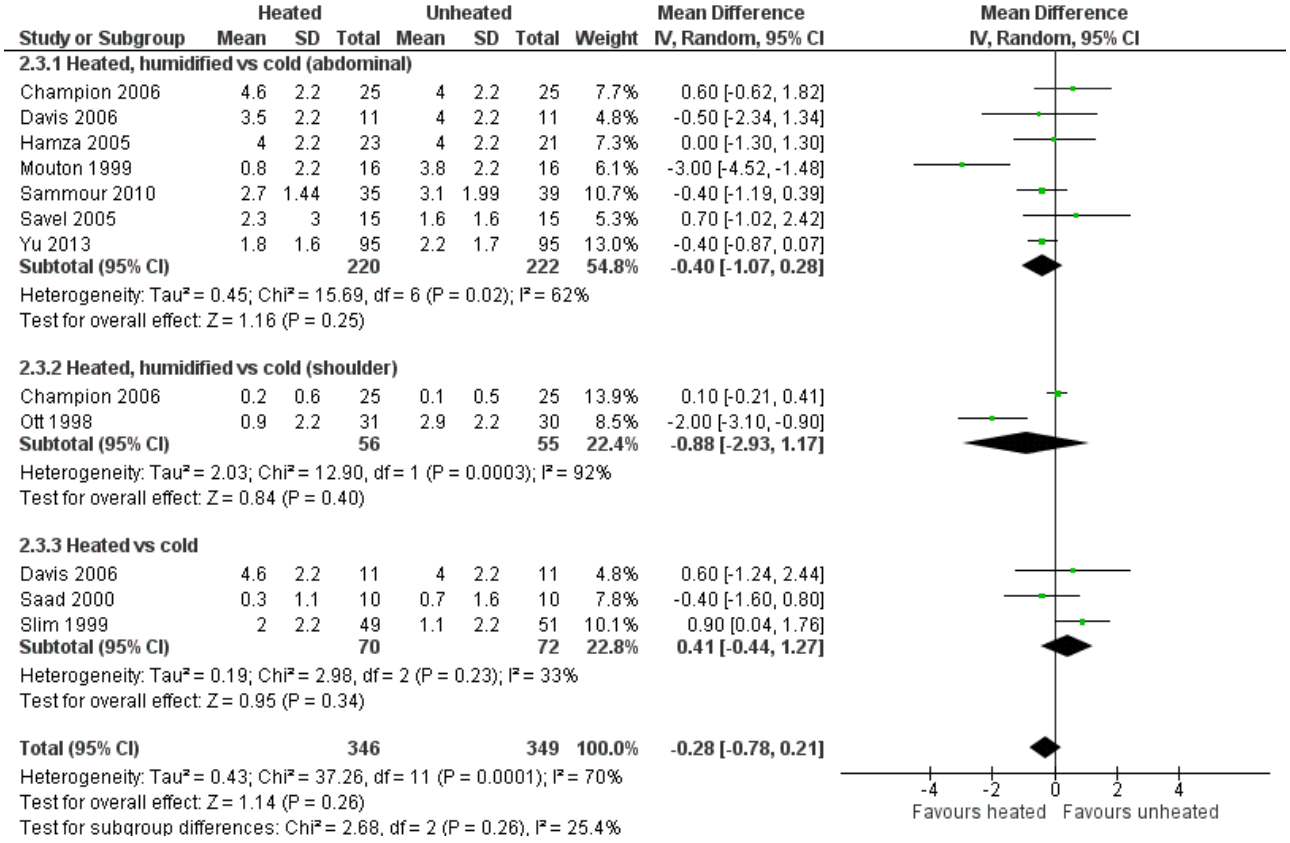
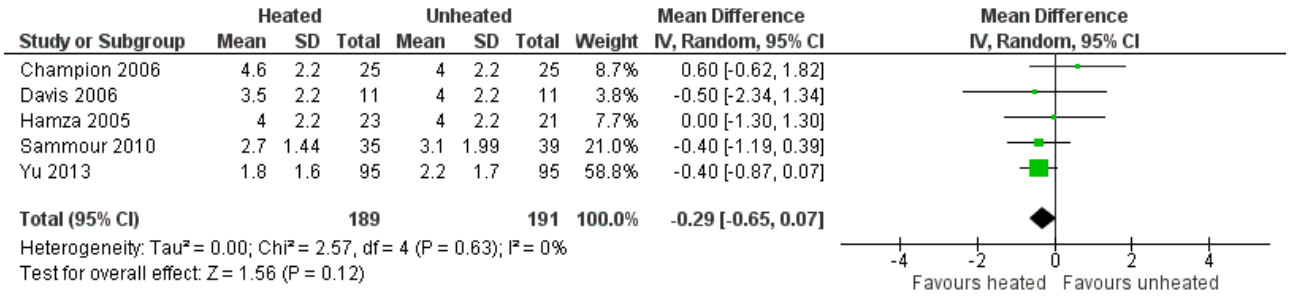


Figure 12. Forest plot of comparison: 1 Pain score, outcome: 1.4 Day 2 pain score of low risk of bias studies



Morphine consumption

(Analysis 3.1; Analysis 3.2; Analysis 3.3)

Four studies comparing heated and humidified CO_2 with cold CO_2 insufflation reported no statistically significant difference in morphine consumption up to six hours post-operatively between groups (MD 0.45 mg, 95% CI -1.19 to 2.08, P = 0.59) (Figure 13). Heterogeneity was not statistically significant across studies (I^2 = 0%). Morphine use on the first postoperative day was not significantly different either overall (MD -0.64 mg, 95% CI -4.48 to 3.20), or when CO_2 was heated and humidified (MD -1.66 mg, 95% CI -4.79 to 1.46, P = 0.30), but was higher when CO_2 was heated without humidification (MD 11.93 mg, 95% CI 0.92 to 22.94, P = 0.03) (Figure 14). A similar pattern was observed for the second postoperative

day, where there was no difference overall or with humidification, but was higher with heated, non-humidified CO_2 (MD 9.79 mg, 95% CI 1.58 to 18.00, P = 0.02) (Figure 15).

Figure 13. Forest plot of comparison: 3 Morphine consumption, outcome: 3.1 Up to 6 hours

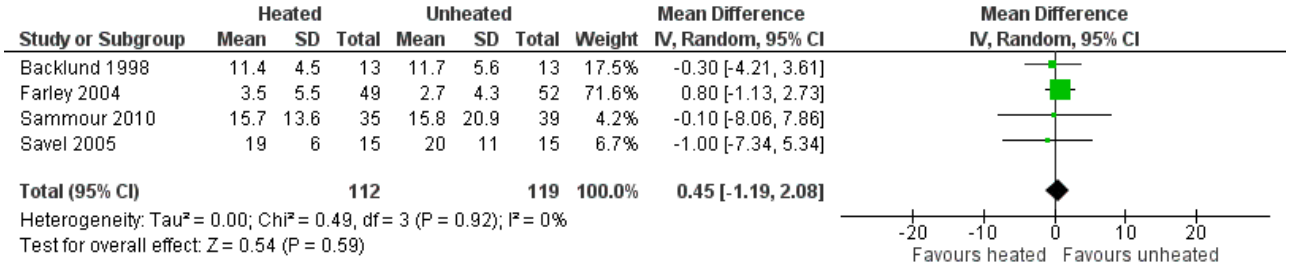


Figure 14. Forest plot of comparison: 3 Morphine consumption, outcome: 3.2 Day 1 morphine

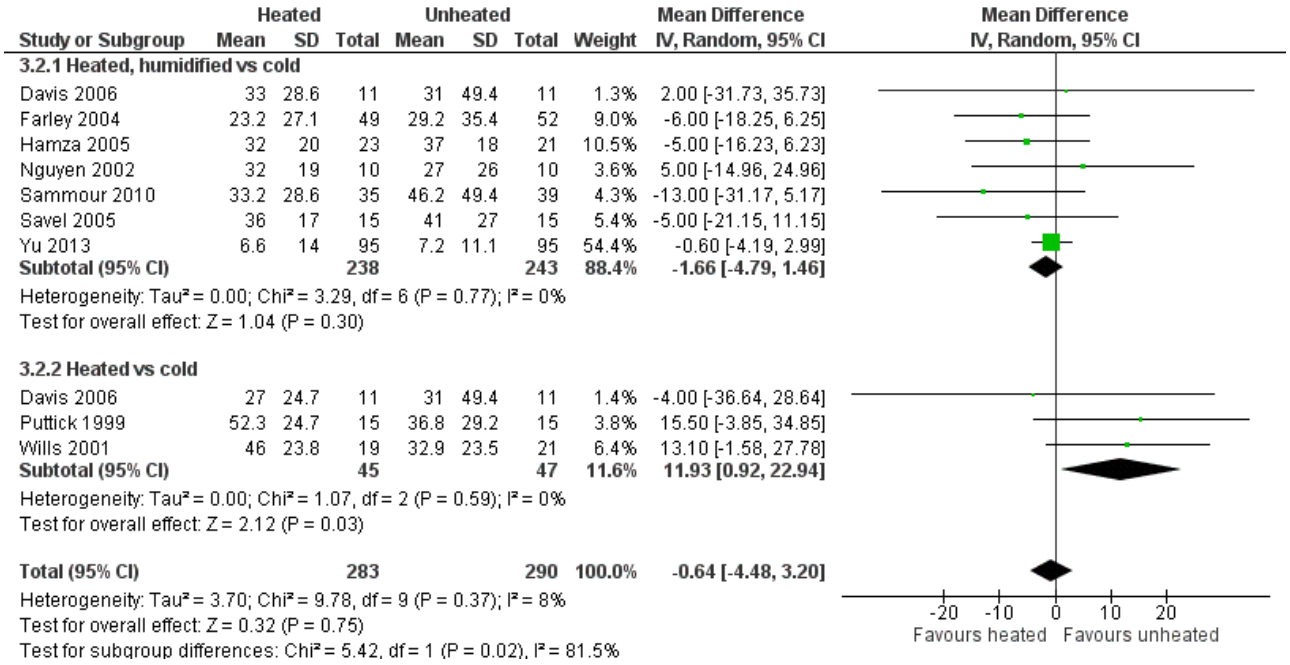
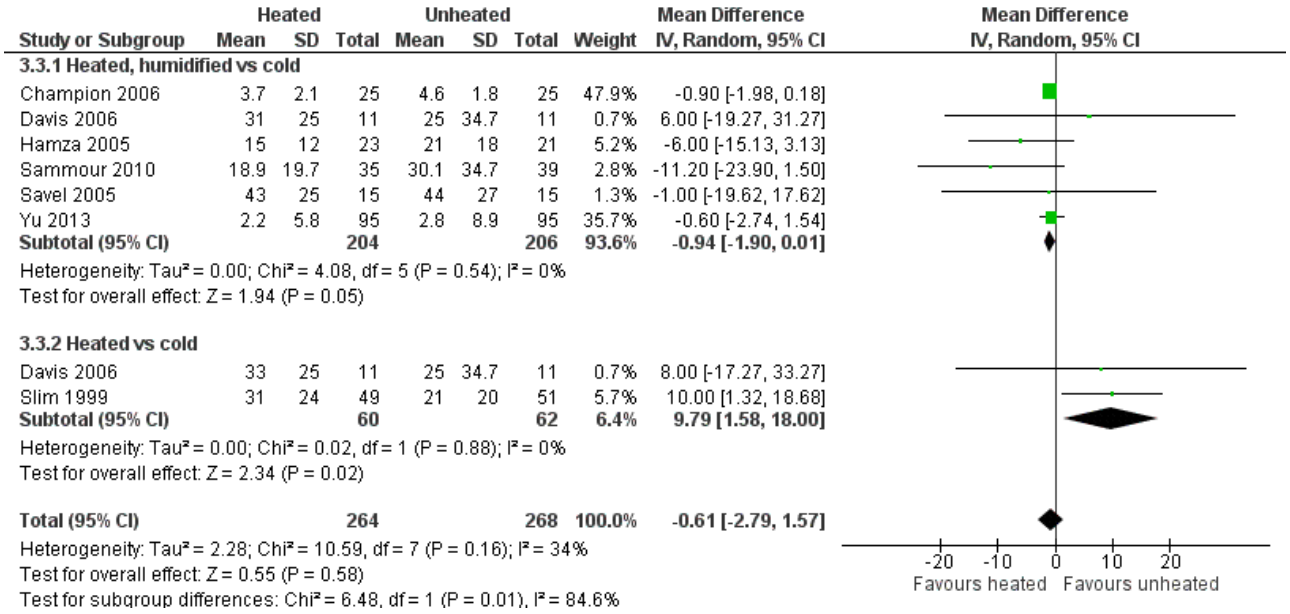


Figure 15. Forest plot of comparison: 3 Morphine consumption, outcome: 3.3 Day 2 morphine

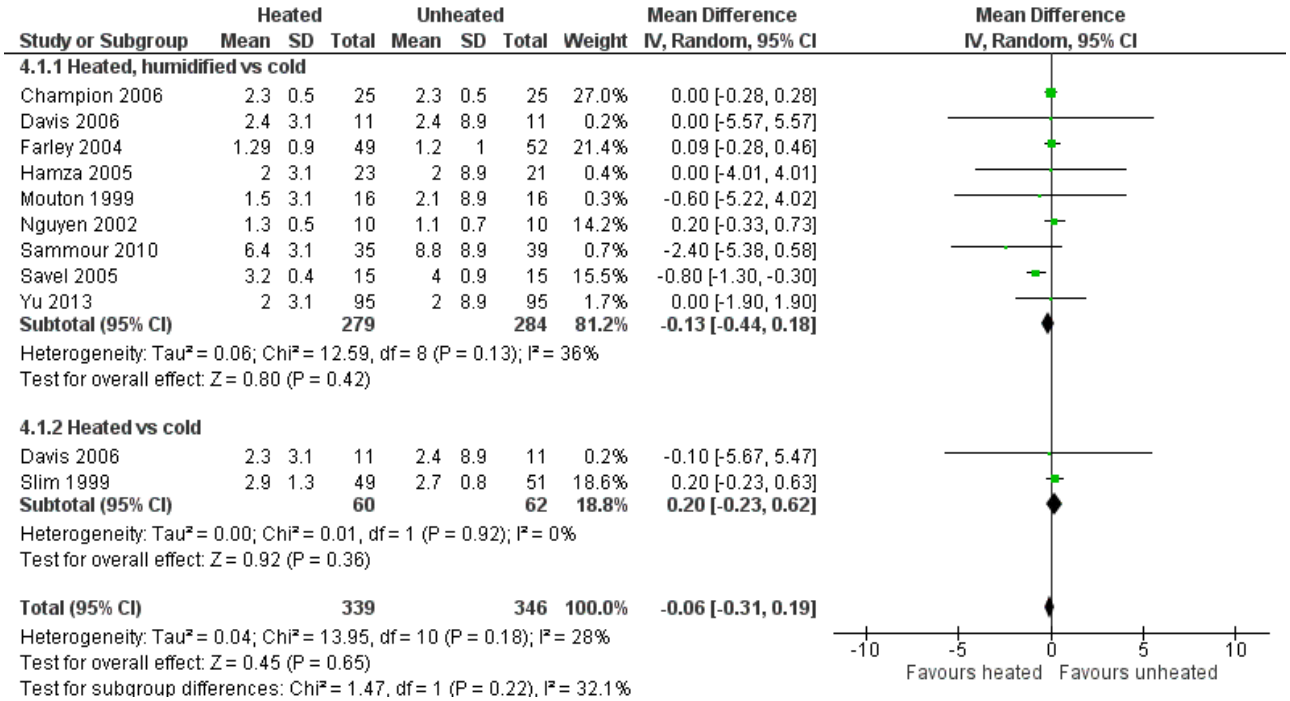


Hospital stay

(Analysis 4.1)

Length of stay in hospital was not different between the heated (with or without humidification) and cold gas insufflation groups (MD -0.06 days, 95% CI -0.31 to 0.19, P = 0.65) (Figure 16). There was no statistically significant heterogeneity across studies (I^2 = 28%).

Figure 16. Forest plot of comparison: 4 Hospital stay, outcome: 4.1 Hospital stay



Recovery room stay

(Analysis 5.1; Analysis 5.2)

Recovery room time was documented in six studies and there was substantial heterogeneity among them (I^2 = 95%). Shorter recovery time (MD -26.79 minutes, 95% CI -51.34 to -2.25, P = 0.03) was found with heated insufflation (Figure 17). With exclusion of the only high risk study (Ott 1998), the studies were statistically homogenous (I^2 =12%) but the difference in recovery room stay was statistically not

significant (MD -1.22 minutes, 95% CI -6.62 to 4.17, P = 0.44) (Figure 18).

Figure 17. Forest plot of comparison: 7 Recovery room stay, outcome: 7.1 Recovery time

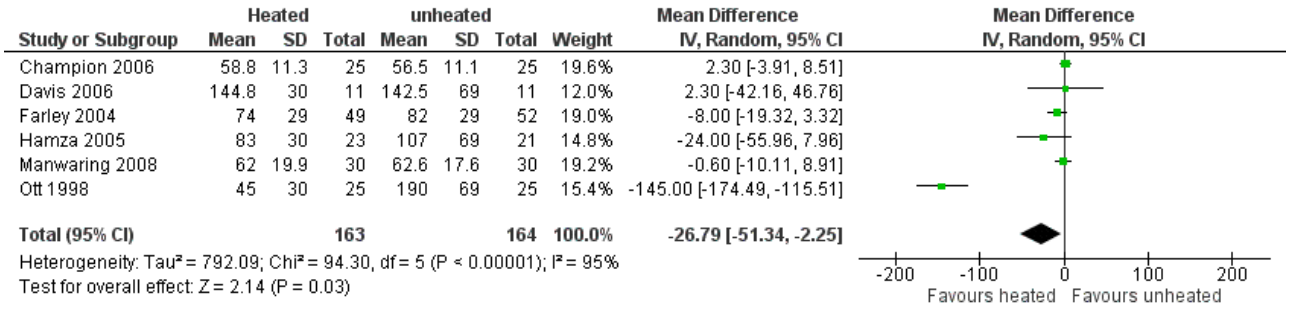
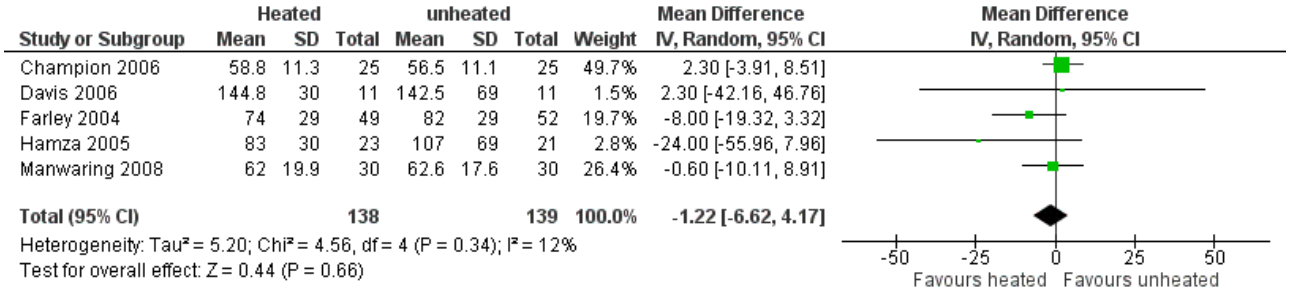


Figure 18. Forest plot of comparison: 7 Recovery room stay, outcome: 7.2 Recovery time for low risk of bias studies

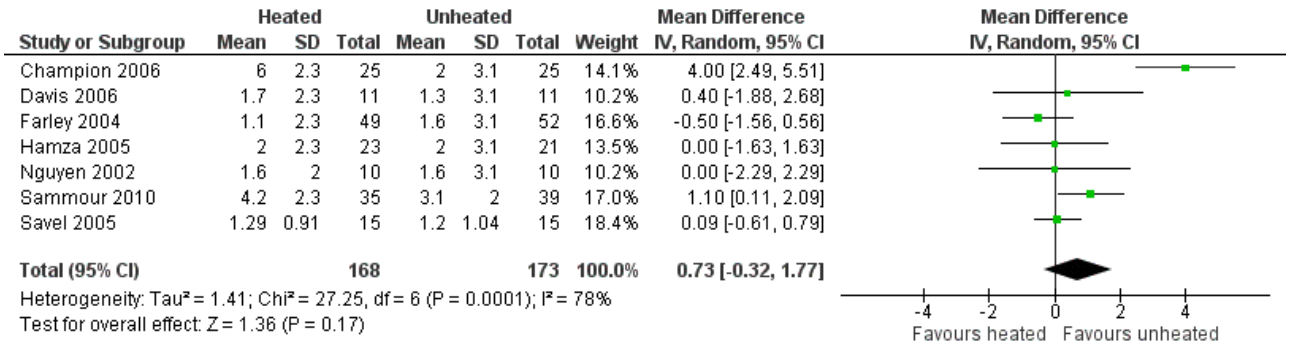


Lens fogging

(Analysis 6.1)

Evidence of substantial heterogeneity was present (I^2 = 78%) and no significant difference in the lens fogging scores was shown (MD 0.73, 95% CI -0.32 to 1.77, P = 0.17) (Figure 19).

Figure 19. Forest plot of comparison: 5 Lens fogging, outcome: 5.1 Lens fogging

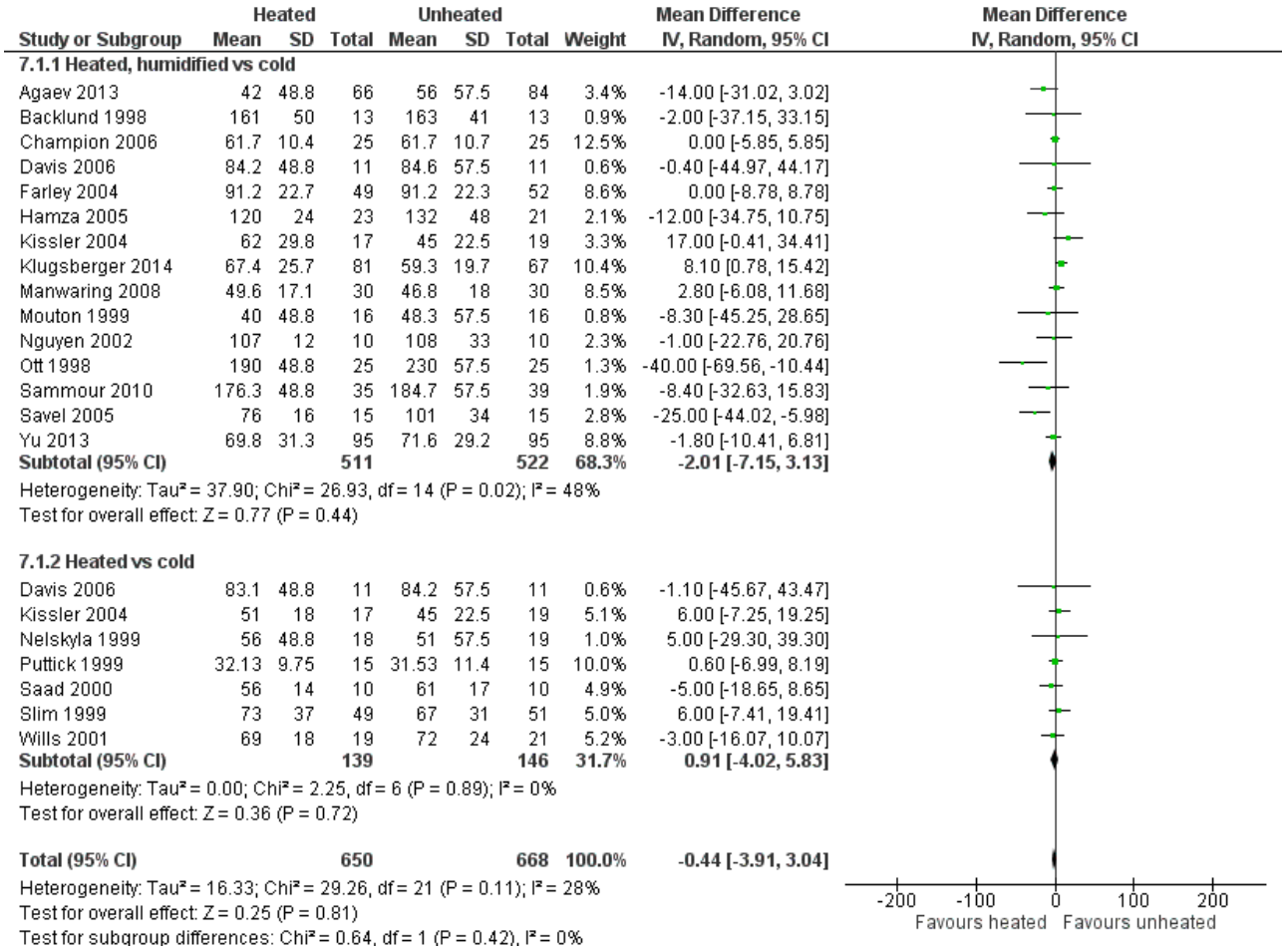


Operative time

(Analysis 7.1)

Twenty studies reported their mean operative time; no evidence of statistically significant heterogeneity was found (I^2 = 28%). The mean operative time was similar across groups (MD -0.44 minutes, 95% CI -3.91 to 3.04, P = 0.81) (Figure 20). Subgroup analyses on humidified and non-humidified subgroups did not change the results.

Figure 20. Forest plot of comparison: 6 Operative time, outcome: 6.1 Operative time



Adverse events

The majority of included studies did not report on adverse events (Table 3). There were a total of twelve major adverse events with six in the heated group and six in the cold group.

DISCUSSION

Controversy exists on the use of heated CO_2 insufflation during laparoscopic surgery. Laparoscopic procedures already demand higher operating expenses than conventional open techniques (Janson 2004) and the addition of further complex equipment only increases this limitation. In 2002, the European Association for Endoscopic Surgery published consensus guidelines for laparoscopic pneumoperitoneum and stated that, "the clinical benefits of warmed humidified insufflation gas are minor and contradictory" (Neudecker 2002).

Summary of main results

Evidence based on the 22 RCTs in this systematic review failed to demonstrate definitive evidence for the use of heated CO_2 insufflation during laparoscopic abdominal surgery. While heated and humidified gas insufflation leads to slightly higher core body temperatures, these studies are quite heterogeneous and patient outcomes were not improved with respect to pain scores, morphine consumption and hospital length of stay. For longer operative cases (more than 120 minutes), heated gas is associated with improved core temperatures during surgery. However, these benefits disappeared when the analysis only included trials with a known low risk of bias.

Among the 11 trials at a known low risk of bias included in the review, only one study demonstrated both improved maintenance of normothermia, as well as a reduction in analgesic use in the early postoperative period (Hamza 2005). In this study, external warming blankets were used solely as a 'rescue' treatment, potentially confounding the effect of the experimental intervention. Another study reported higher intraoperative core temperatures (Farley 2004) and improved postoperative pain but no differences in other outcomes. One heated, non-humidified gas insufflation study reported increased core temperatures but with higher operative pain scores and narcotics usage (Wills 2001). The remaining eight known low risk of bias studies did not find any beneficial effect for the intervention in terms of maintaining normothermia. The heterogeneity in core temperature outcomes across studies may be secondary to minor protocol differences between studies such as different insufflation gas temperatures (35 °C to 37 °C), humidity ranges (88% to 100%), gas volumes and location of the temperature probe.

Overall completeness and applicability of evidence

All 22 RCTs included in this review compared heated CO_2 with cold CO_2 insufflation. The majority (19 RCTs, n = 1100) reported the primary outcome, change in core temperature. Fifteen studies (n = 925) included humidified insufflation and ten studies (n = 617) used external warming. This allowed for various subgroup analyses on different modalities of heated insufflation and helps to determine whether changes such as humidification and external warming have any effect. The review also included a broad range of laparoscopic surgeries including cholecystectomy, gastric bypass, gynaecological, gastrectomy, colectomy, low anterior resection and fundoplication, proving its applicability to many different laparoscopic abdominal surgeries. However, this variability may have contributed to the heterogeneity of the results.

The majority of participants were 30 to 60 years old and were female, as some studies only included women. Few of the studies included participants more than 60 years old and results may not be generalisable to an older population, who may be at higher risk of hypothermia (Macario 2002). Additionally, only one study (Yu 2013) enrolled primarily adolescents, who are at higher risk of intraoperative hypothermia given their higher surface area to body mass. This risk is particularly high in neonatal populations (Macario 2002), who were not studied in any trial included in this review.

Quality of the evidence

The results of this review should be interpreted cautiously due to some limitations. Although the studies were all randomised controlled trials and applicable to the research question, some lacked design information making evaluation of study quality difficult. Many of the studies included small sample sizes, which made individual inferences difficult regarding the attribution of effects to random error or the heated insufflation intervention. This also affects precision of the results. The standard deviations used for meta-analysis were missing from some studies and the largest standard deviation from that group was used instead. This potentially distorts the true effects and potentially increases error. Finally, some heterogeneity across studies could not be explained through subgroup analysis, and the results from studies were often inconsistent. Specifically, conclusions on the effectiveness of heated CO_2 on core temperature is downgraded as heterogeneity remained significant despite subgroup analysis. See Summary of findings for the main comparison.

We also assessed publication bias for each outcome with funnel plots and Egger's linear regression test (Egger 1997) and we found no publication bias (Figure 21; Figure 22; Figure 23; Figure 24; Figure 25). We performed Egger's test on outcomes that included data from at least 10 trials: core temperature change (P = 0.697, 95% CI -4.26 to 2.94), day one pain score (P = 0.347, 95% CI -3.98 to 1.57), operating time (P = 0.662, 95% CI -0.41 to 0.63), day one morphine (P = 0.917, 95% CI -1.58 to 1.72) and length of stay (P = 0.477, 95% CI -3.38 to 1.75).

Figure 21. Funnel plot of comparison: 2 Core temperature, outcome: 2.1 Change in core temperature

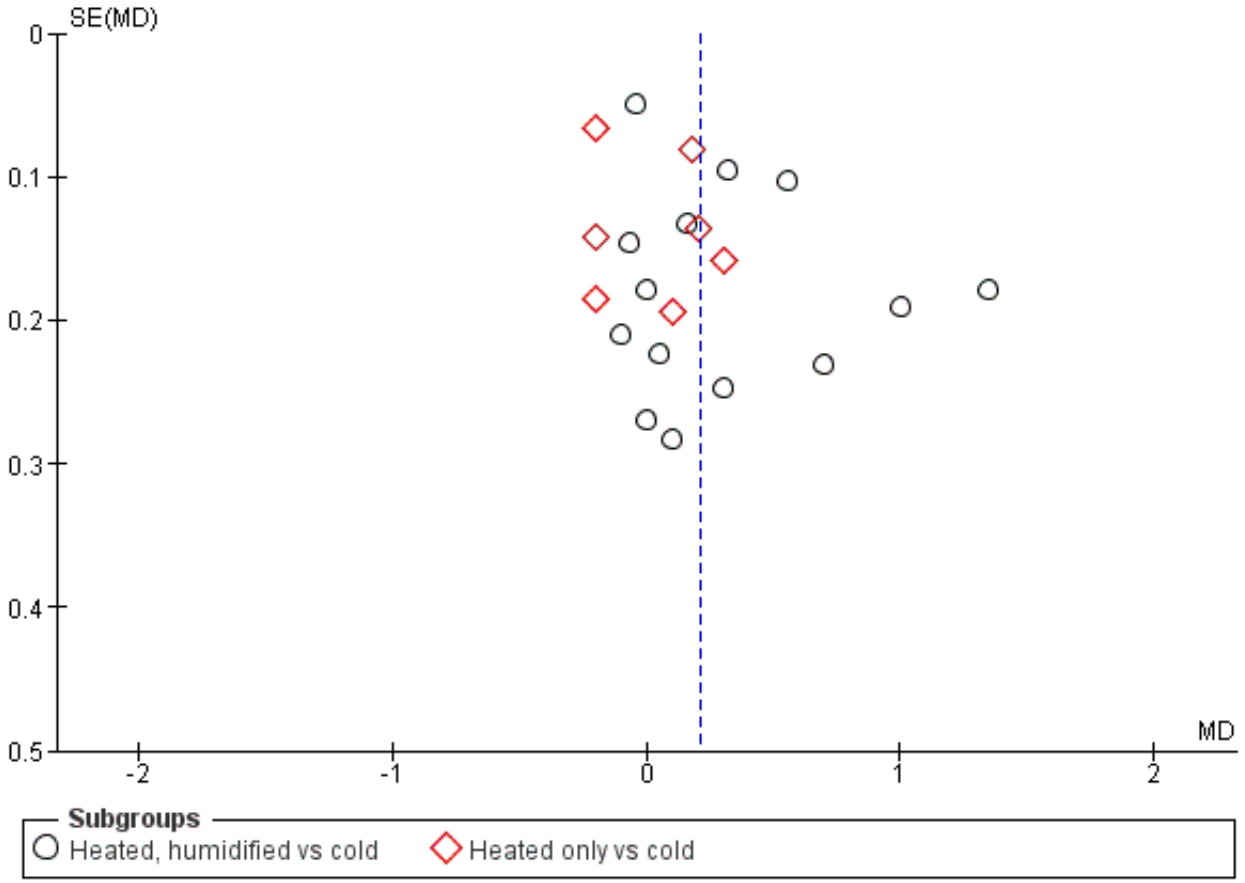


Figure 22. Funnel plot of comparison: 1 Pain Score, outcome: 1.1 Day 1 pain score

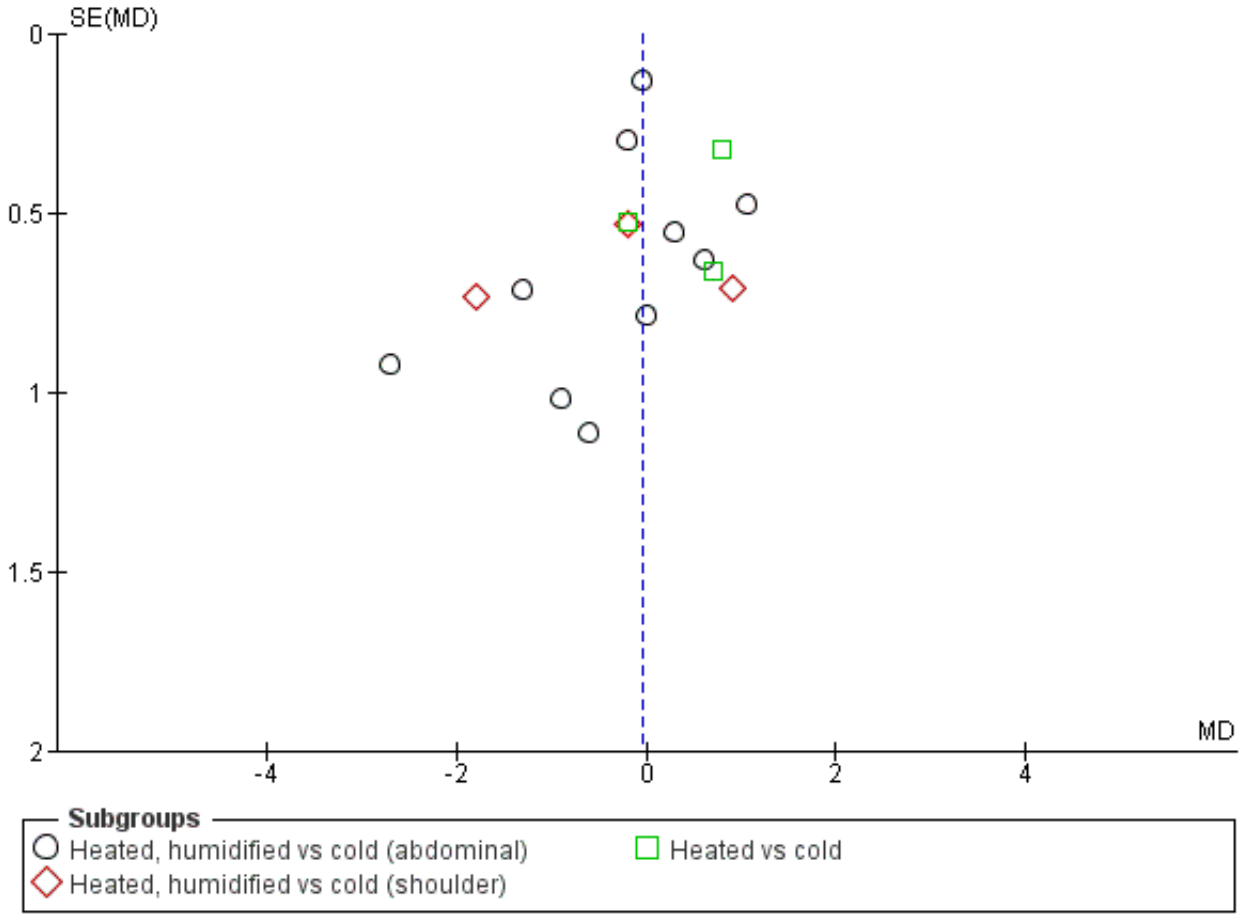


Figure 23. Funnel plot of comparison: 3 Morphine consumption, outcome: 3.2 Day 1 morphine

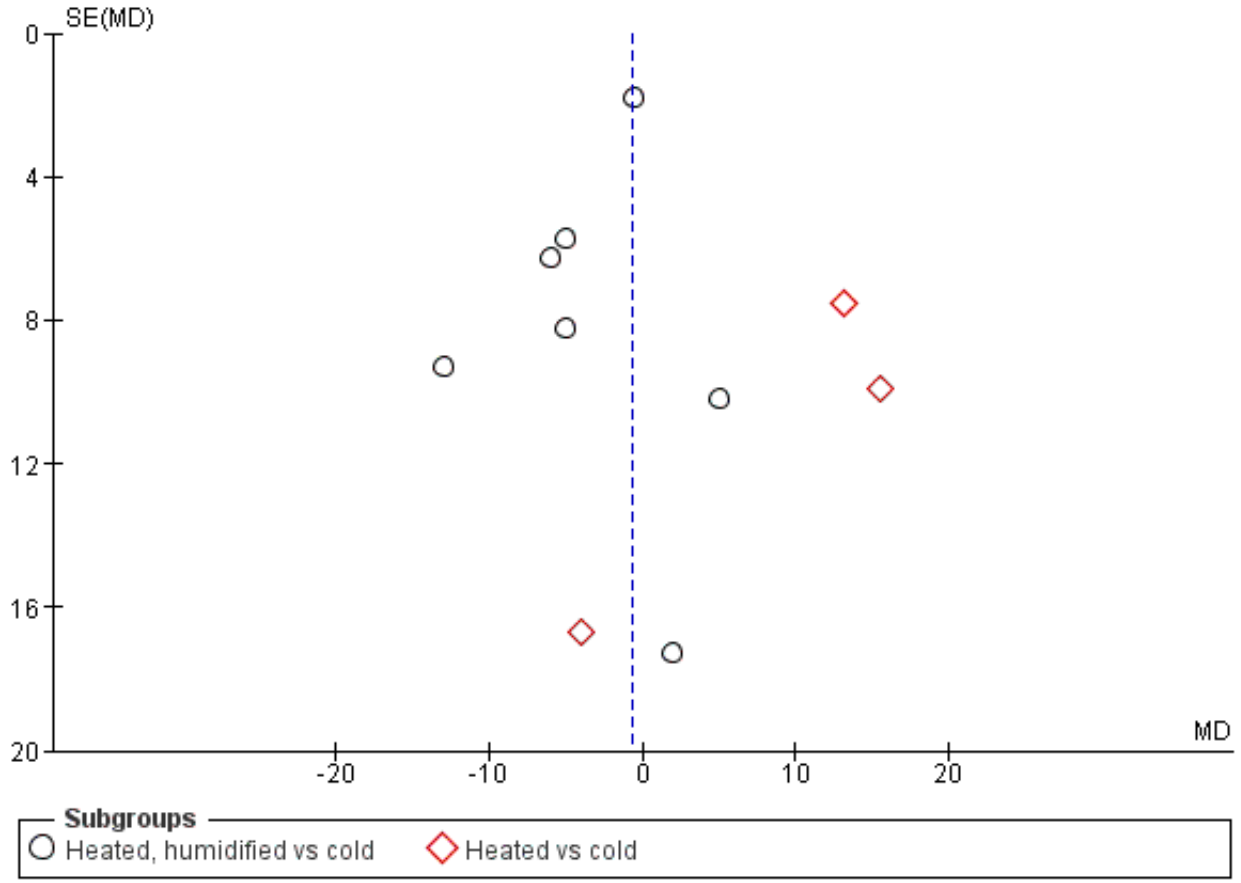


Figure 24. Funnel plot of comparison: 4 Hospital stay, outcome: 4.1 Hospital stay

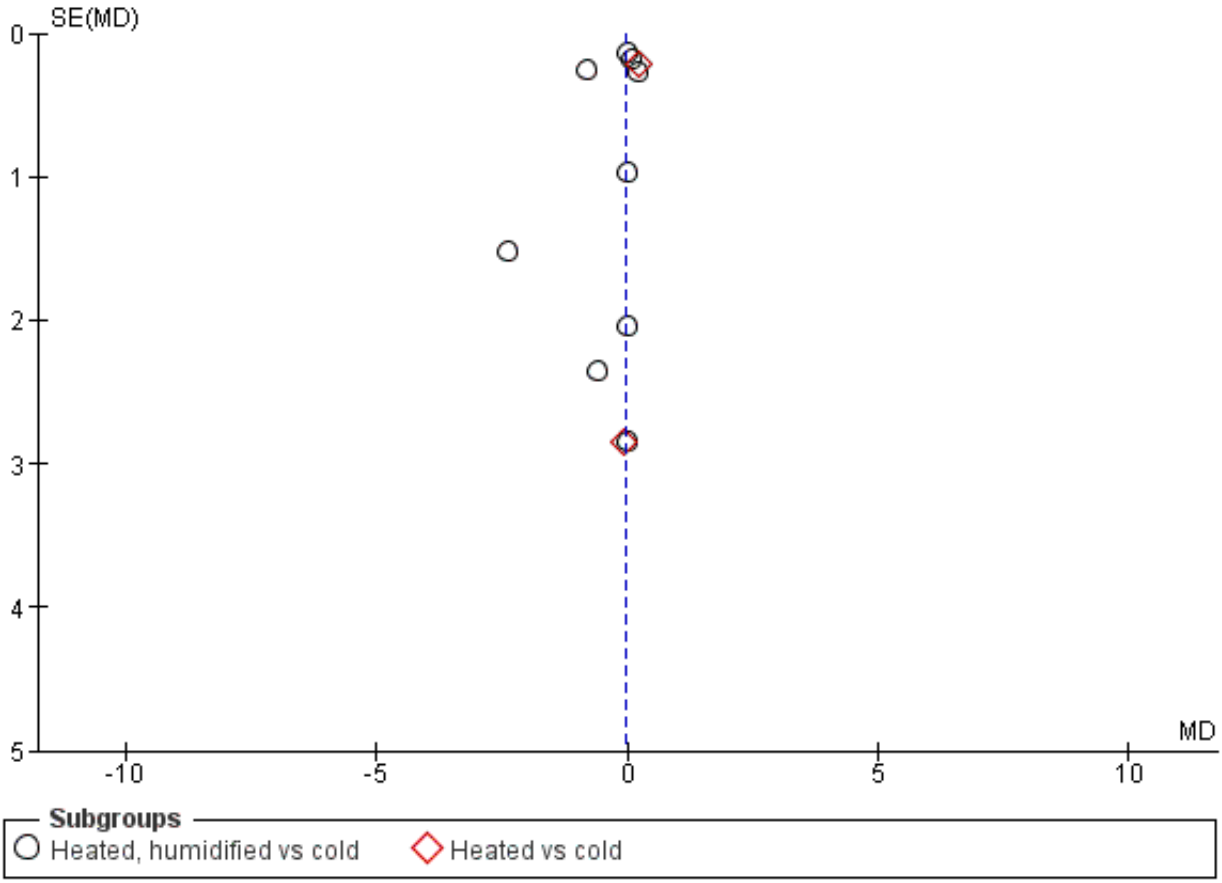
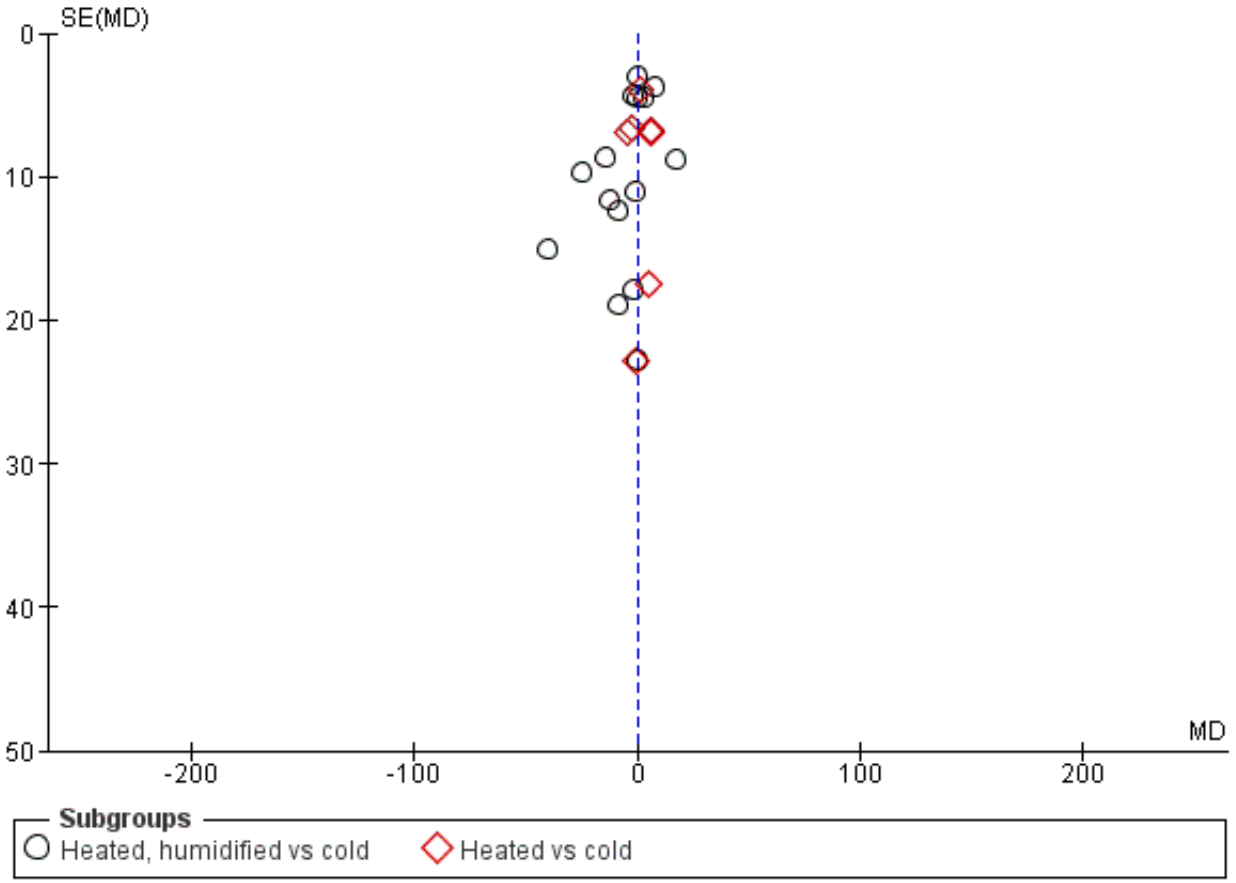


Figure 25. Funnel plot of comparison: 6 Operative time, outcome: 6.1 Operative time



Potential biases in the review process

We could not identify any potential biases in the review process.

Agreements and disagreements with other studies or reviews

Two previously published meta-analyses revealed different conclusions from the current review (Sajid 2008; Sammour 2008). Both provided evidence for a reduction in postoperative pain and Sajid 2008 also demonstrated improved maintenance of core temperature and decreased narcotic requirements. The current review incorporates a greater number of studies in the analysis, including six recent trials showing equivocal results with heated insufflation compared to cold gas insufflation (Agaev 2013; Klugsberger 2014; Lee 2011; Manwaring 2008; Sammour 2010; Yu 2013). Finally, one study (Beste 2006) included in the previous reviews compared heated insufflation with humidification to heated insufflation without humidification, a comparison not in keeping with the aims of the current review and therefore excluded.

AUTHORS' CONCLUSIONS

Implications for practice

Based on our review, heated CO_2 insufflation with humidification leads to a small improvement in maintenance of core temperatures in people undergoing laparoscopic abdominal surgery. The clinical significance of a 0.31 °C difference in core temperature is unclear. One systematic review (Rajagopalan 2008) analysed the effect of mild hypothermia and found increased blood loss and transfusion requirements in hypothermia with a median temperature difference of 0.85 °C between hypothermic and normothermic groups. Whether this still applies for a smaller temperature difference has not been studied. However, heated insufflation did not reduce postoperative pain or analgesic requirements overall. There were also no differences in serious adverse events that occurred in the cold or heated cohorts to support the use of heated CO_2 in preventing hypothermia-associated complications. Additionally, heated insufflation did not seem to reduce hospital stay, recovery room stay, lens fogging, or operative time. If the maintenance of normothermia can be achieved through the use of warmed irrigation and external warming devices, perhaps less consideration can be given to the use of heated insufflation systems which adds expenses to procedures already more costly than open surgical approaches.

Implications for research

Good quality studies of how heated and humidified CO_2 affects patient outcomes have been completed. However, the studies have relatively small sample sizes making detection of differences between groups difficult due to low statistical power. In order to further clarify the effect of heated insufflation on patient outcomes, at least one large multi-centre RCT with adequate power should

be performed. Though some change in core temperature may be noted during intraoperative monitoring, one must question the clinical relevance of such findings and, therefore, other useful outcomes such as postoperative pain and adverse events may be more appropriate to use to calculate the size of an adequately powered study.

ACKNOWLEDGEMENTS

Cochrane Colorectal Cancer editorial office for advice and careful copy editing.

REFERENCES

References to studies included in this review

Agaev 2013 *{published data only}*

Agaev BA, Muslimov GF, Ibragimov TR, Alieva GR. The efficacy of the moisture and warmed CO(2) for laparoscopic surgery. *Khirurgiia (Mosk)* 2013;**11**:35-9.

Backlund 1998 *{published data only}*

Backlund M, Kellokumpu I, Scheinin T, von Smitten K, Tikkanen I, Lindgren L. Effect of temperature of insufflated CO_2 during and after prolonged laparoscopic surgery. *Surgical Endoscopy* 1998;**12**(9):1126-30.

Champion 2006 *{published data only}*

Champion JK, Williams M. Prospective randomized trial of heated humidified versus cold dry carbon dioxide insufflation during laparoscopic gastric bypass. *Surgery for Obesity and Related Diseases* 2006;**2**(4):445-9; discussion 449-50.

Davis 2006 *{published data only}*

Davis SS, Mikami DJ, Newlin M, Needleman BJ, Barett MS, Fries R, et al. Heating and humidifying of carbon dioxide during pneumoperitoneum is not indicated: a prospective randomized trial. *Surgical Endoscopy* 2006;**20**(1):153-8.

Demco 2001 *{published data only}*

Demco L. Effect of heating and humidifying gas on patients undergoing awake laparoscopy. *The Journal of the American Association of Gynecologic Laparoscopists* 2001;**8**(2):247-51.

Farley 2004 *{published data only}*

Farley DR, Greenlee SM, Larson DR, Harrington JR. Double-blind, prospective, randomized study of warmed, humidified carbon dioxide insufflation vs standard carbon dioxide for patients undergoing laparoscopic cholecystectomy. *Archives of Surgery (Chicago, Ill: 1960)* 2004;**139**(7):739-4.

Hamza 2005 *{published data only}*

Hamza MA, Schneider BE, White PF, Recart A, Villegas L, Ogunnaike B, et al. Heated and humidified insufflation during laparoscopic gastric bypass surgery: effect on temperature, postoperative pain, and recovery outcomes. *Journal of Laparoendoscopic & Advanced Surgical Techniques. Part A* 2005;**15**(1):6-12.

Kissler 2004 *{published data only}*

Kissler S, Haas M, Strohmeier R, Schmitt H, Rody A, Kaufmann M, et al. Effect of humidified and heated CO2 during gynecologic laparoscopic surgery on analgesic requirements and postoperative pain. *The Journal of the American Association of Gynecologic Laparoscopists* 2004;**11**(4):473-7.

Klugsberger 2014 *{published data only}*

Klugsberger B, Schreiner M, Rothe A, Haas D, Oppelt P, Shamiyeh A. Warmed, humidified carbon dioxide insufflation versus standard carbon dioxide in laparoscopic cholecystectomy: a double-blinded randomized controlled trial. *Surgical Endoscopy* 2014;**28.9**:2656-60.

Lee 2011 *{published data only}*

Lee KC, Kim JY, Kwak HJ, Lee HD, Kwon IW. The effect of heating insufflation gas on acid-base alterations and core temperature during laparoscopic major abdominal surgery. *Korean Journal of Anesthesiology* 2011;**61**(4):275-80.

Manwaring 2008 *{published data only}*

Manwaring JM, Readman E, Maher PJ. The effect of heated humidified carbon dioxide on postoperative pain, core temperature, and recovery times in patients having laparoscopic surgery: A randomized controlled trial. *Journal of Minimally Invasive Gynecology* 2008;**15**(2):161-5. [DOI: 10.1016/j.jmig.2007.09.007]

Mouton 1999 *{published data only}*

Mouton WG, Bessell JR, Millard SH, Baxter PS, Maddern GJ. A randomized controlled trial assessing the benefit of humidified insufflation gas during laparoscopic surgery. *Surgical Endoscopy* 1999;**13**(2):106-8.

Nelskyla 1999 *{published data only}*

Nelskyla K, Yli-Hankala A, Sjoberg J, Korhonen I, Korttila K. Warming of insufflation gas during laparoscopic hysterectomy: effect on body temperature and the autonomic nervous system. *Acta Anaesthesiological Scandinavica* 1999;**43**(10):974-8.

Nguyen 2002 *{published data only}*

Nguyen NT, Furdui G, Fleming NW, Lee SJ, Goldman CD, Singh A, et al. Effect of heated and humidified carbon dioxide gas on core temperature and postoperative pain: a randomized trial. *Surgical Endoscopy* 2002;**16**(7):1050-4.

Ott 1998 *{published data only}*

Ott DE, Reich H, Love B, McCorvey R, Toledo A, Liu CY, et al. Reduction of laparoscopic-induced hypothermia, postoperative pain and recovery room length of stay by pre-conditioning gas with the Insuflow device: a prospective randomized controlled multi-center study. *Journal of the Society of Laparoendoscopic Surgeons* 1998;**2**(4):321-9.

Puttick 1999 *{published data only}*

Puttick MI, Scott-Coombes DM, Dye J, Nduka CC, Menzies-Gow NM, Mansfield AO, et al. Comparison of immunologic and physiologic effects of CO_2 pneumoperitoneum at room and body temperatures. *Surgical Endoscopy* 1999;**13**(6):572-5.

Saad 2000 *{published data only}*

Saad S, Minor I, Mohri T, Nagelschmidt M. The clinical impact of warmed insufflation carbon dioxide gas for laparoscopic cholecystectomy. *Surgical Endoscopy* 2000;**14**(9):787-90.

Sammour 2010 *{published data only}*

Sammour T, Kahokehr A, Hayes J, Hulme-Moir M, Hill AG. Warming and humidification of insufflation carbon dioxide in laparoscopic colonic surgery. *Annals of Surgery* 2010;**251**(6):1024-33. [DOI: 10.1097/SLA.0b013e3181d77a25]

Savel 2005 *{published data only}*

Savel RH, Balasubramanya S, Lasheen S, Gaprindashvili T, Arabov E, Fazylov RM, et al. Beneficial effects of humidified, warmed carbon dioxide insufflation during laparoscopic bariatric surgery: a randomized clinical trial. *Obesity Surgery* 2005;**15**(1):64-9.

Slim 1999 *{published data only}*

Slim K, Bousquet J, Kwiatkowski F, Lescure G, Pezet D, Chipponi J. Effect of CO(2) gas warming on pain after laparoscopic surgery: a randomized double-blind controlled trial. *Surgical Endoscopy* 1999;**13**(11):1110-4.

Wills 2001 *{published data only}*

Wills VL, Hunt DR, Armstrong A. A randomized controlled trial assessing the effect of heated carbon dioxide for insufflation on pain and recovery after laparoscopic fundoplication. *Surgical Endoscopy* 2001;**15**(2):166-70.

Yu 2013 *{published data only}*

Yu TC, Hamill JK, Liley A, Hill AG. Warm, humidified carbon dioxide gas insufflation for laparoscopic appendicectomy in children: a double-blinded randomized controlled trial. *Annals of Surgery* 2013;**257**(1):44-53.

References to studies excluded from this review

Barragan 2005 *{published data only}*

Barragan AB, Frezza EE. Impact of a warm gas insufflation on operating-room ergonometrics during laparoscopic gastric bypass: a pilot study. *Obesity Surgery* 2005;**15**(1):70-2.

Benavides 2009 *{published data only}*

Benavides R, Wong A, Nguyen H. Improved outcomes for lap-banding using the Insuflow device compared with heated-only gas.. *Journal of the Society of Laparoendoscopic Surgeons* 2009;**13**(3):302-5.

Beste 2006 *{published data only}*

Beste TM, Daucher JA, Holbert D. Humidified compared with dry, heated carbon dioxide at laparoscopy to reduce pain. *Obstetrics and Gynecology* 2006;**107**(2 pt 1):263-8.

Herrmann 2015 *{published data only}*

Herrmann A, De Wilde RL. Insufflation with humidified and heated carbon dioxide in short-term laparoscopy: a double-blinded randomized controlled trial. *BioMed Research International* 2015;**Epub 2015**:Jan 28.

Monagle 1993 *{published data only}*

Monagle J, Bradfield S, Nottle P. Carbon dioxide, temperature and laparoscopic cholecystectomy. *The Australian and New Zealand Journal of Surgery* 1993;**63**(3):186-9.

Mouton 2001 *{published data only}*

Mouton WG, Naef M, Bessell JR, Otten KT, Wagner HE, Maddern GJ. A randomized controlled trial to determine the effect of humidified carbon dioxide (CO_2) insufflation on postoperative pain following thoracoscopic procedures. *Surgical Endoscopy* 2001;**15**(6):579-81.

Ott 1991 *{published data only}*

Ott DE. Correction of laparoscopic insufflation hypothermia. *Journal of Laparoendoscopic Surgery* 1991;**1**(4):183-6.

Pu 2014 *{published data only}*

Pu Y, Cen G, Sun J, Gong J, Zhang Y, Zhang M, et al. Warming with an underbody warming system reduces intraoperative hypothermia in patients undergoing laparoscopic gastrointestinal surgery: a randomized controlled study. *International Journal of Nursing Studies* 2014;**51**(2):181-9.

Siebzehnrubl 2001 *{published data only}*

Siebzehnruebl E, Haas M, Schmidt H, Lang N. Warm and humidified CO2 does not improve the postoperative pain score after laparoscopy-a prospective, randomized and double blinded study. *Human Reproduction* June 2001;**Abstracts of the 17th Annual Meeting of the ESHRE**:216-7.

Tohme 2010 *{published data only}*

Tohme S, Shantha Kumara M, Yan CX, Nasar A, Cekic V, Whelan R. Effect of warmed, humidified CO2 gas on cytokine response to minimally invasive colorectal surgery: a randomized trial. *Diseases of the Colon & Rectum* 2010;**53**:4.

Trevelyan 2011 *{published data only}*

Trevelyan S, Mason C, Chan A, Baird D, Flook D. Does humidified warmed CO2 insufflation gas improve post-operative pain control in laparoscopic cholecystectomy? A randomized controlled trial. *British Journal of Surgery* 2011;**98**(s3):1-79.

Yeh 2007 *{published data only}*

Yeh CH, Kwok SY, Chan MK, Tjandra JJ. Prospective, case-matched study of heated and humidified carbon dioxide insufflation in laparoscopic colorectal surgery. *Colorectal Disease* 2007;**9**(8):695-700.

References to studies awaiting assessment

Sutton 2016 *{published data only}*

Sutton E, Bellini G, Kumara HS, Yan X, Njoh L, Cekic V, et al. Warm and humidified vs cold and dry CO2 pneumoperitoneum in minimally invasive colon resection: a randomized controlled trial. *Surgical Endoscopy* 2016;**30**(S1):317.

Additional references

Beilin 1998

Beilin B, Shavit Y, Razumovsky J, Wolloch Y, Zeidel A, Bessler H. Effects of mild perioperative hypothermia on cellular immune responses. *Anesthesiology* 1998;**89**(5):1133-40. [9822001]

Cork 1983

Cork RC, Vaughan RW, Humphrey LS. Precision and accuracy of intraoperative temperature monitoring . *Anesthesia & Analgesia* 1983;**62**:211-4.

Dindo 2004

Dindo D, Demartines N, Clavien P. Classification of surgical complications: a new proposal with evaluation in a cohort

of 6336 patients and results of a survey. *Annals of Surgery* 2004;**240**(2):205-13.

Egger 1997

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

Frank 1993

Frank SM, Beattie C, Christopherson R, Norris EJ, Perler BA, Williams GM, et al. Unintentional hypothermia is associated with postoperative myocardial ischemia. The Perioperative Ischemia Randomized Anesthesia Trial Study Group. *Anesthesiology* 1993;**78**(3):468-76. [8457047]

Frank 1997

Frank SM, Fleisher LA, Breslow MJ, Higgins MS, Olson KF, Kelly S, et al. Perioperative maintenance of normothermia reduces the incidence of morbid cardiac events. A randomized clinical trial. *JAMA* 1997;**277**(14):1127-34. [PUBMED: 9087467]

Higgins 2003

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

Higgins 2011

Higgins JPT, Altman DG, Sterne JAC (editors). Chapter 8: Assessing risk of bias in included studies. In: Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from www.handbook.cochrane.org.

Janson 2004

Janson M, Bjorholt I, Carlsson P, Haglind E, Henriksson M, Lindholm E, et al. Randomized clinical trial of the costs of open and laparoscopic surgery for colonic cancer. *British Journal of Surgery* 2004;**91**(4):409-17. [DOI: 10.1002/bjs.4469]

Macario 2002

Macario A. What are the most important risk factors for a patient's developing intraoperative hypothermia?. *Anesthesia and Analgesia* 2002;**94**(1):215-20. [11772832]

Moher 2009

Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. *PLoS Medicine* 2009;**6**(7):e 1000097. [DOI: 10.1371/journal.pmed.1000097]

Neudecker 2002

Neudecker J, Sauerland S, Neugebauer E, Bergamaschi R, Bonjer HJ, Cuschieri A, et al. The European Association for Endoscopic Surgery clinical practice guideline on the pneumoperitoneum for laparoscopic surgery. *Surgical Endoscopy* 2002;**16**(7):1121-43. [PUBMED: 12015619]

Putzu 2007

Putzu M, Casati A, Berti M, Pagliarini G, Fanelli G. Clinical complications, monitoring and management of perioperative mild hypothermia: anesthesiological features. *Acta Bio-Medica de l Ateneo Parmense* 2007;**78**(3):163-9. [PUBMED: 18330074]

Qadan 2009

Qadan M, Gardner SA, Vitale DS, Lominadze D, Joshua IG, Polk HC Jr. Hypothermia and surgery: immunologic mechanisms for current practice. *Annals of Surgery* 2009;**250**(1):134-40. [PUBMED: 19561472]

Rajagopalan 2008

Rajagopalan S, Mascha E, Na J, Sessler DI. The effects of mild perioperative hypothermia on blood loss and transfusion requirement. *Anesthesiology* 2008;**108**(1):71-7.

RevMan 2014 [Computer program]

Nordic Cochrane Centre, The Cochrane Collaboration. Review Manager 5 (RevMan 5). Version 5.3. Copenhagen: Nordic Cochrane Centre, The Cochrane Collaboration, 2014.

Sajid 2008

Sajid MS, Mallick AS, Rimpel J, Bokari SA, Cheek E, Baig MK. Effect of heated and humidified carbon dioxide on patients after laparoscopic procedures: a meta-analysis. *Surgical Laparoscopy, Endoscopy & Percutaneous Techniques* 2008;**18**(6):539-46. [DOI: 10.1097/SLE.0b013e3181886ff4; 00129689-200812000-00001; Sajid:2008p530; PUBMED: 19098656]

Sammour 2008

Sammour T, Kahokehr A, Hill AG. Meta-analysis of the effect of warm humidified insufflation on pain after laparoscopy. *The British Journal of Surgery* 2008;**95**(8):950-6. [DOI: 10.1002/bjs.6304; Sammour:2008p528; PUBMED: 18618870]

Schünemann 2009

Schünemann H, Brozek J, Oxman A, editors. The GRADE Working Group 2009. GRADE handbook for grading quality of evidence and strength of recommendation. Available from http://www.cc-ims/gradepro [updated March 2009]; Vol. version 3.2.

Winkler 2000

Winkler M, Akca O, Birkenberg B, Hetz H, Scheck T, Arkiliç CF, et al. Aggressive warming reduces blood loss during hip arthroplasty. *Anesthesia and Analgesia* 2000;**91**:978-84.

Wong 2007

Wong PF, Kumar S, Bohra A, Whetter D, Leaper DJ. Randomized clinical trial of perioperative systemic warming in major elective abdominal surgery. *The British Journal of Surgery* 2007;**94**(4):421-6. [MEDLINE: 10.1002/bjs.5631; 17380549]

References to other published versions of this review

Birch 2011

Birch DW, Manouchehri N, Shi X, Hadi G, Karmali S. Heated CO2 with or without humidification for minimally invasive abdominal surgery. *Cochrane Database of Systematic Reviews* 2011, Issue 1. [DOI: 10.1002/14651858.CD007821.pub2]

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Agaev 2013

Methods	Double-blinded RCT
Participants	n = 110, laparoscopic cholecystectomy; n = 40, laparoscopic fundoplication
Interventions	Warmed, humidified CO_2 vs standard CO_2
Outcomes	Core temperature, postoperative pain, analgesic requirements, lens fogging, postoperative pain and the need for anaesthesia. In addition , OR time, hospitalisation, complications
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Participants were assigned to 2 groups using a computer model post-anaesthesia but the groups were 84 in standard CO_2 and 66 in heated, humidified CO_2 Comment: with computer-generated randomisation, it would be unlikely for the groups to be this uneven
Allocation concealment (selection bias)	Unclear risk	Allocation concealment was not clearly stated
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Only the surgical nurse knew the temperature of the CO_2 feed." Comment: adequate blinding
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "Only the surgical nurse knew the temperature of the CO_2 feed." Comment: adequate blinding
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Outcome data was unclear, number of participants included in analysis was not reported
Selective reporting (reporting bias)	Low risk	We judged this trial free of selective reporting.
Other bias	Unclear risk	Originally published in Russian, the study authors had a certified translator translate it into English. However, the translation and the qualification certificate of the translator were provided voluntarily by a research scientist from a surgical humidification device company

Backlund 1998

Methods	RCT

Backlund 1998 *(Continued)*

Participants	n = 26, prolonged (> 120 min) fundoplication, hernioplasty, resection of the sigmoid colon and rectopexy
Interventions	Warmed, humidified CO_2 vs standard CO_2
Outcomes	Core temperature, cardiac index, urine output, recovery room opioid usage and pain score
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No description
Allocation concealment (selection bias)	Unclear risk	No description
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No description
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Only stated that the pain score was recorded by a trained nurse unaware of the temperature of the pneumoperitoneum
Incomplete outcome data (attrition bias) All outcomes	Low risk	All participants completed the study and there were no treatment withdrawals, no trial group changes and no major adverse events.
Selective reporting (reporting bias)	Low risk	We judged this trial free of selective reporting.
Other bias	Low risk	Industry provided heating device

Champion 2006

Methods	RCT
Participants	n = 50, consecutive, morbidly obese, laparoscopic antecolic proximal Roux-en-Y gastric bypass surgery
Interventions	Heated and humidified CO_2 vs cold and dry CO_2
Outcomes	Intraoperative core temperature, room temperature, litres of CO_2 insufflation, operating time, number of lens cleanings, recovery room temperature, narcotics usage, length of hospitalisation, high-sensitivity CRP at 24 h, abdominal and shoulder pain scores
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement

Champion 2006 *(Continued)*

Random sequence generation (selection bias)	Low risk	A blind draw by an impartial third party
Allocation concealment (selection bias)	Low risk	A draw was held to determine which type of insufflation was to be used on the first case, after which the insufflation method was alternated for the next 49 cases consecutively, with no interruption or exclusions.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Single-blind study where participants were blinded as they were anaesthetized but personnel were not blinded
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Quote: "The nursing personnel, who were unaware of the study, recorded the subjective pain score." Comment: adequate blinding of outcome assessment
Incomplete outcome data (attrition bias) All outcomes	Low risk	All participants completed the study and there were no treatment withdrawals, no trial group changes and no major adverse events.
Selective reporting (reporting bias)	Low risk	We judged this trial free of selective reporting.
Other bias	Low risk	We did not detect any other potential bias.

Davis 2006

Methods	Blinded RCT
Participants	n = 44, laparoscopic gastric bypass
Interventions	Cold CO_2 vs cold humidified CO_2 vs heated CO_2 vs heated humidified CO_2
Outcomes	Core temperature, humidity, intraoperative urine output, lens fogging, recovery room time, length of hospital stay, postoperative pain, total morphine sulphate equivalent
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Block fashion randomisation
Allocation concealment (selection bias)	Low risk	Results in sealed envelopes
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Single-blind study where participants were blinded as they were anaesthetised but study personnel were not blinded

Davis 2006 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Low risk	Intraoperative outcomes were not blinded but they are objective measurements. Participants recorded postoperative pain and they remained blinded to their intervention.
Incomplete outcome data (attrition bias) All outcomes	Low risk	All participants completed the study and there were no treatment withdrawals, no trial group changes and no major adverse events.
Selective reporting (reporting bias)	Low risk	We judged this trial free of selective reporting.
Other bias	Low risk	Industry funded research grant.

Demco 2001

Methods	Double-blinded RCT
Participants	n = 40 women, diagnostic laparoscopy
Interventions	Heated, humidified vs cold CO_2
Outcomes	Shoulder pain, fentanyl use, percent requiring general anaesthetic, percent requiring intravenous sedation, amount of gas instilled before experiencing pain, operating time, recovery room time, time to recovery of shoulder pain
Notes	This study presented outcomes as percentages of participants in each group (e.g. for operative time, percentage of participants in groups 0-10 min, 10-20 min, 20-30 min, and 30-40 min)

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Unclear
Allocation concealment (selection bias)	Low risk	Sealed envelope: "The circulating nurse opened a sealed envelope directing her to have the unit turned on or off during the procedure."
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Only the circulating nurse was not blinded: "To blind the surgeon further, the light on the unit could not be seen, and the plastic tubing was taped so the surgeon could not see condensation there."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Only the circulating nurse was not blinded: "To blind the surgeon further, the light on the unit could not be seen, and the plastic tubing was taped so the surgeon could not see condensation there."
Incomplete outcome data (attrition bias) All outcomes	Low risk	All participants completed the study and there were no treatment withdrawals, no trial group changes and no major adverse events.
Selective reporting (reporting bias)	Unclear risk	This study did not report any temperatures.
Other bias	Unclear risk	This study did not report any baseline demographics.

Farley 2004

Methods	Double-blinded RCT
Participants	n = 117, laparoscopic cholecystectomy (16 excluded)
Interventions	Heated, humidified CO_2 vs cold CO_2
Outcomes	Core temperature, lens fogging, postoperative pain, total morphine equivalents, hospital stay, return to baseline activity level
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer model randomisation
Allocation concealment (selection bias)	Low risk	Randomisation was done by surgical scrub nurse at the time of anaesthetic induction
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Participants, surgeons, operative and floor nurses, study co-ordinators were blinded
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome assessors were blinded when measuring intraoperative outcomes. Participants remained blinded when completing their pain scores.
Incomplete outcome data (attrition bias) All outcomes	Low risk	16 participants excluded from analysis due to 11 conversions to open, 3 requiring additional operations and 2 had the insufflation removed for technical reasons Comment: all excluded participants properly reported and not included in the analysis
Selective reporting (reporting bias)	Low risk	We judged this trial free of selective reporting.
Other bias	Low risk	Industry provided heating device.

Hamza 2005

Methods	Double-blinded RCT
Participants	n = 50, laparoscopic gastric bypass (6 excluded)
Interventions	Heated and humidified CO_2 vs cold CO_2
Outcomes	Core temperature, postoperatively tympanic temperature, pain score, shivering, morphine, nausea score, Aldrete recovery assessment score, hospital stay, lens fogging

Hamza 2005 *(Continued)*

Notes	Warm blankets were used to cover the upper chest and arms in all control group participants for ethical considerations

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated randomisation
Allocation concealment (selection bias)	Low risk	An OR nurse was responsible for connecting the device
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Participants, surgeons, anaesthesiologist, data-collecting personnel, recovery nurses were blinded
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Personnel collecting data were blinded and participants remained blinded when completing their verbal rating scales
Incomplete outcome data (attrition bias) All outcomes	Low risk	6 participants excluded from analysis (4 converted to open, 2 required rescuing with active warming for temperature < 34 °C) Comment: all excluded participants properly reported and not included in analysis
Selective reporting (reporting bias)	Low risk	We judged this trial free of selective reporting.
Other bias	Low risk	Industry funded research grant.

Kissler 2004

Methods	Double-blinded RCT
Participants	n = 90 women, gynaecologic laparoscopic surgery (53 with data)
Interventions	Humidified heated CO_2 vs heated dry CO_2 vs cold dry CO_2
Outcomes	Analgesic requirements and postoperative pain
Notes	The trial was stopped following enrolment of 53 participants because of a tendency toward less pain and higher postoperative satisfaction in control group

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated randomisation
Allocation concealment (selection bias)	Unclear risk	No description

Kissler 2004 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Participants, data analyst and interviewer were blinded to randomisation. However, no description of blinding of other participants (surgeon and nurses)
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No description of blinding of outcomes assessors
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Trial was stopped early for there was a tendency toward less pain and higher postoperative satisfaction in participants in the control group
Selective reporting (reporting bias)	Unclear risk	Out of 90 participants, data only available on 53 participants
Other bias	Low risk	Industry provided heating device.

Klugsberger 2014

Methods	Double-blinded RCT
Participants	n = 148, laparoscopic cholecystectomy
Interventions	Warmed, humidified CO_2 vs standard CO_2
Outcomes	Core temperature, postoperative pain, time of first bowel movement after surgery
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomisation was unclear and treatment groups were uneven (67 received heated, humidified CO_2 and 81 received standard CO_2) Comment: randomisation likely not properly done
Allocation concealment (selection bias)	Low risk	Quote: "The secretary was privy to which method of gas was being used. The secretary opened a sealed opaque envelope to randomly allocate the procedure."
Blinding of participants and personnel (performance bias) All outcomes	Low risk	The participants, surgeons, nurses, and study co-ordinator were blinded
Blinding of outcome assessment (detection bias) All outcomes	Low risk	The nurses recording intraoperative outcomes were blinded. Participants remained blinded when recording their visual analogue pain scales.
Incomplete outcome data (attrition bias) All outcomes	Low risk	All participants completed the study and there were no treatment withdrawals, no trial group changes and no major adverse events.

Klugsberger 2014 *(Continued)*

Selective reporting (reporting bias)	Low risk	We judged this trial free of selective reporting.
Other bias	Low risk	We did not detect any other potential bias.

Lee 2011

Methods	RCT
Participants	n = 30, gastrectomy, colectomy or low-anterior resection
Interventions	Heated CO_2 vs room temperature CO_2
Outcomes	Acid-base parameters, $ETCO_2$, and core temperature
Notes	An upper body blanket was applied to all participants and if their temperature fell below 35 °C, a Bair Hugger forced air warmer and a warming mattress with circulating water at 38 °C were applied

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	No description in the article. Contacted study authors and they indicated that a random number table was used
Allocation concealment (selection bias)	Low risk	Sealed envelopes were used
Blinding of participants and personnel (performance bias) All outcomes	Low risk	No description but contacted study authors and they indicated that this was a blinded study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	No description but contacted study authors and they indicated that this was a blinded study
Incomplete outcome data (attrition bias) All outcomes	Low risk	All participants completed the study and there were no treatment withdrawals, no trial group changes and no major adverse events.
Selective reporting (reporting bias)	Low risk	We judged this trial free of selective reporting.
Other bias	Low risk	We did not detect any other potential bias.

Manwaring 2008

Methods	RCT
Participants	n = 60 women, gynaecologic laparoscopic surgery

Manwaring 2008 *(Continued)*

Interventions	Heated humidified CO_2 vs cold dry CO_2
Outcomes	Core temperature, analgesic usage, postoperative pain, postoperative nausea and recovery room time
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random number generator
Allocation concealment (selection bias)	Low risk	Sealed in sequential opaque envelopes
Blinding of participants and personnel (performance bias) All outcomes	Low risk	All nursing staff were blinded and patient was blinded as they were anaesthetised
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Nurses recording outcome data were blinded. Participants remained blinded when nurses administered visual analogue scales.
Incomplete outcome data (attrition bias) All outcomes	Low risk	All participants completed the study and there were no treatment withdrawals, no trial group changes and no major adverse events.
Selective reporting (reporting bias)	Low risk	We judged this trial free of selective reporting.
Other bias	Low risk	Industry provided heating device.

Mouton 1999

Methods	RCT
Participants	n = 40, laparoscopic cholecystectomy (8 excluded)
Interventions	Heated, humidified CO_2 vs cold CO_2
Outcomes	Core temperature change, postoperative pain score, morphine usage
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No description

Mouton 1999 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	No description
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No description
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No description
Incomplete outcome data (attrition bias) All outcomes	Low risk	8 participants excluded due to conversion to open, pancreatitis or postoperative haematoma Comment: all excluded participants properly reported and not included in the analysis
Selective reporting (reporting bias)	Low risk	Data were available on 32 out of 40 participants and the reason was given by the study author.
Other bias	Low risk	Industry offered assistance for research.

Nelskyla 1999

Methods	Double-blinded RCT
Participants	n = 40 women, laparoscopic hysterectomy (3 excluded)
Interventions	Heated CO_2 vs cold CO_2
Outcomes	Tympanic temperature, heart rate variability
Notes	Data on 37 women were analysed

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No description
Allocation concealment (selection bias)	Unclear risk	No description
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No description on which personnel were blinded during operation
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Participants and staff in the postoperation care unit and ward were blinded. Intraoperative outcomes are objective so non-blinding likely has less effect
Incomplete outcome data (attrition bias)	Unclear risk	3 excluded participants, 2 "did not fulfil the study protocol" and 1 "because of surgical problems."

Nelskyla 1999 *(Continued)*

All outcomes		Comment: unclear reasons for exclusion
Selective reporting (reporting bias)	Low risk	We judged this trial free of selective reporting.
Other bias	Low risk	Industry provided heating device.

Nguyen 2002

Methods	RCT
Participants	n = 20, laparoscopic Nissen fundoplication
Interventions	Heated and humidified CO_2 vs cold CO_2
Outcomes	Core temperature, pain score, morphine consumption, urine output, lens fogging
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Sealed envelopes
Allocation concealment (selection bias)	Low risk	Intraoperative randomisation
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Single-blinded study where the participants were blinded
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Intraoperative outcomes were not blinded but they are objective measurements. Participants recorded postoperative pain and they remained blinded to their intervention
Incomplete outcome data (attrition bias) All outcomes	Low risk	All participants completed the study and there were no treatment withdrawals, no trial group changes and no major adverse events.
Selective reporting (reporting bias)	Low risk	We judged this trial free of selective reporting.
Other bias	Low risk	We did not detect any other potential bias.

Ott 1998

Methods	Multi-centre RCT
Participants	n = 72 women, laparoscopic gynaecologic surgery (50 with data)

Ott 1998 *(Continued)*

Interventions	Heated and humidified CO_2 vs cold CO_2
Outcomes	Postoperative pain and recovery room length of stay
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No description
Allocation concealment (selection bias)	Unclear risk	No description
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No description
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No description
Incomplete outcome data (attrition bias) All outcomes	High risk	Data were only available on 50 out of 72 participants and no reason was given. Some data was extracted from a different systematic review (Sammour 2008) as the original trial did not present all data.
Selective reporting (reporting bias)	Unclear risk	Data were only available on 50 out of 72 participants and no reason was given.
Other bias	Unclear risk	This study did not separate baseline demographics between groups. Industry provided heating device.

Puttick 1999

Methods	RCT
Participants	n = 30, laparoscopic cholecystectomy
Interventions	Warmed CO_2 vs cold CO_2
Outcomes	Core temperature, intraperitoneal cytokines, pain score
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No description

Puttick 1999 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	No description
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No description
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No description
Incomplete outcome data (attrition bias) All outcomes	Low risk	All participants completed the study and there were no treatment withdrawals, no trial group changes and no major adverse events.
Selective reporting (reporting bias)	Low risk	We judged this trial free of selective reporting.
Other bias	Low risk	We did not detect any other potential bias.

Saad 2000

Methods	RCT
Participants	n = 20, laparoscopic cholecystectomy
Interventions	Heated CO_2 vs cold CO_2
Outcomes	Core temperature, intra-abdominal temperature, postoperative pain, analgesics consumption
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No description
Allocation concealment (selection bias)	Unclear risk	No description
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Participants and ward nurses were blinded.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Participants remained blinded when assessing postoperative pain. Unclear if operating room nurses were blinded during measurement of outcomes
Incomplete outcome data (attrition bias) All outcomes	Low risk	All participants completed the study and there were no treatment withdrawals, no trial group changes and no major adverse events.

Saad 2000 *(Continued)*

Selective reporting (reporting bias)	Low risk	We judged this trial free of selective reporting.
Other bias	Low risk	Industry provided heating device.

Sammour 2010

Methods	Multi-centre RCT
Participants	n = 82, laparoscopic colonic surgery (8 excluded)
Interventions	Heated humidified CO_2 vs cold CO_2
Outcomes	Postoperative pain, intraoperative core temperature, camera fogging, morphine-equivalent usage, postoperative parameters
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer generated
Allocation concealment (selection bias)	Low risk	Allocations were concealed in opaque numbered envelopes
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Participants, investigators, surgeon and medical care staff were all blinded.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Participants, investigators, surgeon and medical care staff were all blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Eight excluded after randomisation with clearly stated rationale Comment: all excluded participants properly reported and not included in the analysis
Selective reporting (reporting bias)	Low risk	We judged this trial free of selective reporting.
Other bias	Low risk	We did not detect any other potential bias.

Savel 2005

Methods	Blinded RCT
Participants	n = 30, laparoscopic gastric bypass

Savel 2005 *(Continued)*

Interventions	Heated humidified CO_2 vs cold CO_2
Outcomes	Postoperative pain score, morphine consumption, OR time, core temperature, hospital stay
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No description
Allocation concealment (selection bias)	Unclear risk	Participants randomised at the time of enrolment
Blinding of participants and personnel (performance bias) All outcomes	Low risk	All clinicians except 1 author were blinded.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	All clinicians except 1 author were blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	All participants completed the study and there were no treatment withdrawals, no trial group changes and no major adverse events.
Selective reporting (reporting bias)	Low risk	We judged this trial free of selective reporting.
Other bias	Low risk	We did not detect any other potential bias.

Slim 1999

Methods	Double-blinded RCT
Participants	n = 108, laparoscopic cholecystectomy, fundoplication or Heller's myotomy (8 excluded)
Interventions	Heated CO_2 vs unheated CO_2
Outcomes	Postoperative pain, core temperature, morphine consumption, nausea and vomiting, hospital stay, length of postoperative Ileus
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random number table in sealed envelopes

Slim 1999 *(Continued)*

Allocation concealment (selection bias)	Low risk	Sealed envelopes opened in the operating room
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Participants and nurses were blinded
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Nurses were blinded when collecting outcome data. Participants remained blinded when assessing postoperative pain.
Incomplete outcome data (attrition bias) All outcomes	Low risk	8 participants excluded (4 conversion to open, 2 postoperative biliary collections, 1 technical problems with insufflator, 1 refused) Comment: all excluded participants properly reported and not included in the analysis
Selective reporting (reporting bias)	Low risk	We judged this trial free of selective reporting.
Other bias	Low risk	We did not detect any other potential bias.

Wills 2001

Methods	Blinded RCT
Participants	n = 41, laparoscopic fundoplication (1 excluded)
Interventions	Heated CO_2 vs cold CO_2
Outcomes	Core temperature, postoperative pain, analgesic requirement, postoperative recovery
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random number table
Allocation concealment (selection bias)	Low risk	Sequentially numbered opaque, sealed envelopes
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Surgeons, anaesthetist, data analyst, participants and ward nurses were blinded.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Surgeons, anaesthetist, data analyst, participants and ward nurses were blinded.
Incomplete outcome data (attrition bias)	Low risk	One participant excluded for missing postoperative pain scores and one underwent repeat laparotomy.

Wills 2001 *(Continued)*

All outcomes		Comment: all excluded participants properly reported and not included in the analysis
Selective reporting (reporting bias)	Low risk	We judged this trial free of selective reporting.
Other bias	Low risk	Industry provided heating device.

Yu 2013

Methods	Double-blinded RCT
Participants	n = 195 adolescents, laparoscopic appendectomy (5 excluded)
Interventions	Warm, humidified CO_2 vs standard CO_2
Outcomes	Opioid usage, pain score, core temperature, postoperative recovery and return to normal activities
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Online random number programme
Allocation concealment (selection bias)	Low risk	Sealed, opaque, numbered envelopes were used
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Only one rotating scrub nurse assisted with randomisation. All other participants were blinded
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Only one rotating scrub nurse assisted with randomisation. All other participants were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	5 participants excluded after randomisation for major protocol violation Comment: all excluded participants properly reported and not included in the analysis
Selective reporting (reporting bias)	Low risk	We judged this trial free of selective reporting.
Other bias	Low risk	We did not detect any other potential bias.

CO2: carbon dioxide
ETCO2: end tidal carbon dioxide
VAS: visual analogue scale

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Barragan 2005	Not a RCT
Benavides 2009	Intervention was heated dry CO_2 vs heated humidified CO_2
Beste 2006	Intervention was heated dry CO_2 vs heated humidified CO_2
Herrmann 2015	Not primarily a laparoscopic abdominal surgery (laparoscopic-assisted vaginal hysterectomy)
Monagle 1993	Not a RCT
Mouton 2001	Not a laparoscopic abdominal procedure (thoracoscopic)
Ott 1991	Not a RCT
Pu 2014	Different intervention: underbody warming system
Siebzehnrubl 2001	This study was only presented as a poster and no published paper was found
Tohme 2010	Published as an abstract only, study authors contacted for data. No response
Trevelyan 2011	Published as an abstract only, authors contacted for data. No response
Yeh 2007	Not a RCT

Characteristics of studies awaiting assessment *[ordered by study ID]*

Sutton 2016

Methods	RCT
Participants	n = 101, minimally-invasive colon resection
Interventions	Warmed, humidified CO_2 vs standard CO_2
Outcomes	Core temperature, postoperative pain, analgesic requirements, length of stay, time to first flatus, and tolerance of solids
Notes	Recently published abstract awaiting classification

DATA AND ANALYSES

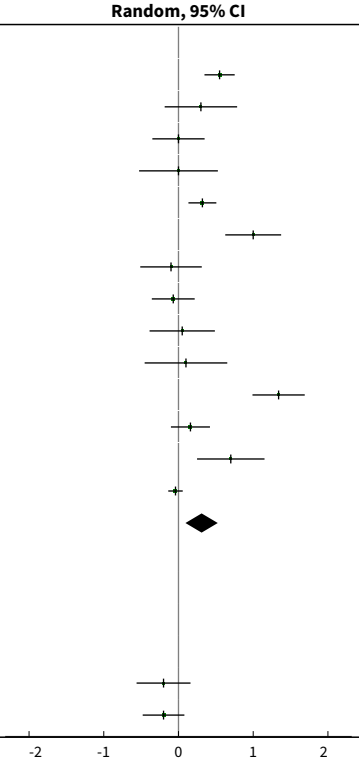
Comparison 1. Core temperature (°C)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Change in core temperature	19	1100	Mean Difference (IV, Random, 95% CI)	0.21 [0.06, 0.36]

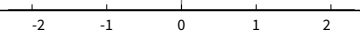
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 Heated, humidified vs cold	14	885	Mean Difference (IV, Random, 95% CI)	0.31 [0.09, 0.53]
1.2 Heated only vs cold	7	215	Mean Difference (IV, Random, 95% CI)	0.02 [-0.16, 0.20]
2 Change in core temperature for low risk of bias studies	10	653	Mean Difference (IV, Random, 95% CI)	0.16 [-0.01, 0.33]
2.1 Heated, humidified vs cold	8	561	Mean Difference (IV, Random, 95% CI)	0.18 [-0.04, 0.39]
2.2 Heated vs cold	3	92	Mean Difference (IV, Random, 95% CI)	0.12 [-0.15, 0.39]
3 Change in core temperature for operations > 120 Minutes	4	194	Mean Difference (IV, Random, 95% CI)	0.70 [0.10, 1.30]
4 Change in core temperature with external warming	8	545	Mean Difference (IV, Random, 95% CI)	0.29 [0.05, 0.52]
5 Change in temperature without external warming	6	340	Mean Difference (IV, Random, 95% CI)	0.32 [-0.11, 0.75]

Analysis 1.1. Comparison 1 Core temperature (°C), Outcome 1 Change in core temperature.

Study or subgroup	Heated N	Heated Mean(SD)	Unheated N	Unheated Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
1.1.1 Heated, humidified vs cold							
Agaev 2013	66	0.5 (0.6)	84	-0.1 (0.7)		5.56%	0.55[0.35,0.75]
Backlund 1998	13	0.2 (0.6)	13	-0.1 (0.7)		3.76%	0.3[-0.18,0.78]
Champion 2006	25	-0.4 (0.6)	25	-0.4 (0.7)		4.63%	0[-0.35,0.35]
Davis 2006	11	0.4 (0.6)	11	0.4 (0.7)		3.51%	0[-0.53,0.53]
Farley 2004	49	0.3 (0.6)	52	-0 (0.3)		5.64%	0.32[0.13,0.51]
Hamza 2005	23	-0.7 (0.6)	21	-1.7 (0.7)		4.47%	1[0.63,1.37]
Kissler 2004	17	-0.5 (0.6)	19	-0.4 (0.7)		4.22%	-0.1[-0.51,0.31]
Manwaring 2008	30	-0.2 (0.5)	30	-0.1 (0.6)		5.05%	-0.07[-0.36,0.22]
Mouton 1999	16	-0.2 (0.6)	16	-0.3 (0.7)		4.06%	0.05[-0.39,0.49]
Nguyen 2002	10	0.4 (0.6)	10	0.3 (0.7)		3.37%	0.1[-0.45,0.65]
Ott 1998	25	-0.3 (0.6)	25	-1.6 (0.7)		4.63%	1.34[0.99,1.69]
Sammour 2010	35	0.6 (0.5)	39	0.5 (0.7)		5.21%	0.16[-0.1,0.42]
Savel 2005	15	0.4 (0.6)	15	-0.3 (0.7)		3.97%	0.7[0.25,1.15]
Yu 2013	95	0.3 (0.3)	95	0.4 (0.3)		6.03%	-0.04[-0.14,0.06]
Subtotal ***	**430**		**455**			**64.11%**	**0.31[0.09,0.53]**
Heterogeneity: Tau²=0.14; Chi²=107.61, df=13(P<0.0001); I²=87.92%							
Test for overall effect: Z=2.8(P=0.01)							
1.1.2 Heated only vs cold							
Davis 2006	11	0.2 (0.3)	11	0.4 (0.5)		4.56%	-0.2[-0.56,0.16]
Kissler 2004	17	-0.6 (0.3)	19	-0.4 (0.5)		5.1%	-0.2[-0.48,0.08]



Study or subgroup	Heated N	Heated Mean(SD)	Unheated N	Unheated Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Lee 2011	15	-0.4 (0.3)	15	-0.7 (0.5)		4.9%	0.3[-0.01,0.61]
Nelskyla 1999	18	-0.3 (0.2)	19	-0.1 (0.2)		5.91%	-0.2[-0.33,-0.07]
Puttick 1999	15	-0.2 (0.2)	15	-0.4 (0.2)		5.79%	0.18[0.02,0.34]
Saad 2000	10	0 (0.3)	10	-0.1 (0.5)		4.44%	0.1[-0.28,0.48]
Wills 2001	19	0.2 (0.3)	21	0 (0.5)		5.19%	0.2[-0.06,0.46]
Subtotal ***	**105**		**110**			**35.89%**	**0.02[-0.16,0.2]**
Heterogeneity: Tau^2=0.04; Chi^2=23.37, df=6(P=0); I^2=74.32%							
Test for overall effect: Z=0.25(P=0.81)							
Total ***	**535**		**565**			**100%**	**0.21[0.06,0.36]**
Heterogeneity: Tau^2=0.1; Chi^2=144.41, df=20(P<0.0001); I^2=86.15%							
Test for overall effect: Z=2.7(P=0.01)							
Test for subgroup differences: Chi^2=4.03, df=1 (P=0.04), I^2=75.17%							

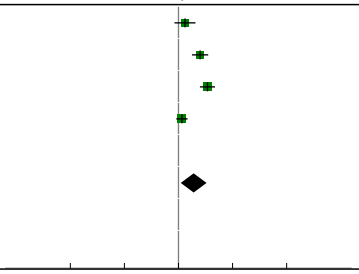


Analysis 1.2. Comparison 1 Core temperature (°C), Outcome 2 Change in core temperature for low risk of bias studies.

Study or subgroup	Heated N	Heated Mean(SD)	Unheated N	Unheated Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
1.2.1 Heated, humidified vs cold							
Champion 2006	25	-0.4 (0.6)	25	-0.4 (0.7)		8.51%	0[-0.35,0.35]
Davis 2006	11	0.4 (0.6)	11	0.4 (0.7)		5.78%	0[-0.53,0.53]
Farley 2004	49	0.3 (0.6)	52	-0 (0.3)		11.6%	0.32[0.13,0.51]
Hamza 2005	23	-0.7 (0.6)	21	-1.7 (0.7)		8.08%	1[0.63,1.37]
Manwaring 2008	30	-0.2 (0.5)	30	-0.1 (0.6)		9.69%	-0.07[-0.36,0.22]
Nguyen 2002	10	0.4 (0.6)	10	0.3 (0.7)		5.46%	0.1[-0.45,0.65]
Sammour 2010	35	0.6 (0.5)	39	0.5 (0.7)		10.19%	0.16[-0.1,0.42]
Yu 2013	95	0.3 (0.3)	95	0.4 (0.3)		12.98%	-0.04[-0.14,0.06]
Subtotal ***	**278**		**283**			**72.3%**	**0.18[-0.04,0.39]**
Heterogeneity: Tau^2=0.07; Chi^2=37.21, df=7(P<0.0001); I^2=81.19%							
Test for overall effect: Z=1.63(P=0.1)							
1.2.2 Heated vs cold							
Davis 2006	11	0.2 (0.3)	11	0.4 (0.5)		8.31%	-0.2[-0.56,0.16]
Lee 2011	15	-0.4 (0.3)	15	-0.7 (0.5)		9.27%	0.3[-0.01,0.61]
Wills 2001	19	0.2 (0.3)	21	0 (0.5)		10.12%	0.2[-0.06,0.46]
Subtotal ***	**45**		**47**			**27.7%**	**0.12[-0.15,0.39]**
Heterogeneity: Tau^2=0.03; Chi^2=4.64, df=2(P=0.1); I^2=56.87%							
Test for overall effect: Z=0.85(P=0.4)							
Total ***	**323**		**330**			**100%**	**0.16[-0.01,0.33]**
Heterogeneity: Tau^2=0.05; Chi^2=42.26, df=10(P<0.0001); I^2=76.33%							
Test for overall effect: Z=1.87(P=0.06)							
Test for subgroup differences: Chi^2=0.12, df=1 (P=0.73), I^2=0%							

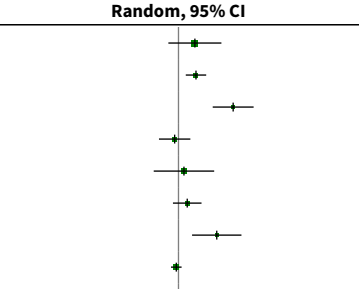
Analysis 1.3. Comparison 1 Core temperature (°C), Outcome 3 Change in core temperature for operations > 120 Minutes.

Study or subgroup	Heated N	Heated Mean(SD)	Unheated N	Unheated Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Backlund 1998	13	0.2 (0.6)	13	-0.1 (0.7)		23.42%	0.3[-0.18,0.78]
Hamza 2005	23	-0.7 (0.6)	21	-1.7 (0.7)		24.98%	1[0.63,1.37]
Ott 1998	25	-0.3 (0.6)	25	-1.6 (0.7)		25.29%	1.34[0.99,1.69]
Sammour 2010	35	0.6 (0.5)	39	0.5 (0.7)		26.31%	0.16[-0.1,0.42]
Total ***	**96**		**98**			**100%**	**0.7[0.1,1.3]**
Heterogeneity: Tau^2=0.33; Chi^2=33.82, df=3(P<0.0001); I^2=91.13%							
Test for overall effect: Z=2.3(P=0.02)							



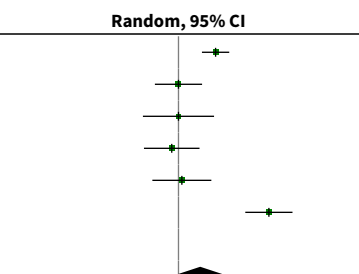
Analysis 1.4. Comparison 1 Core temperature (°C), Outcome 4 Change in core temperature with external warming.

Study or subgroup	Heated N	Heated Mean(SD)	Unheated N	Unheated Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Backlund 1998	13	0.2 (0.6)	13	-0.1 (0.7)		9.88%	0.3[-0.18,0.78]
Farley 2004	49	0.3 (0.6)	52	-0 (0.3)		15.22%	0.32[0.13,0.51]
Hamza 2005	23	-0.7 (0.6)	21	-1.7 (0.7)		11.86%	1[0.63,1.37]
Manwaring 2008	30	-0.2 (0.5)	30	-0.1 (0.6)		13.49%	-0.07[-0.36,0.22]
Nguyen 2002	10	0.4 (0.6)	10	0.3 (0.7)		8.79%	0.1[-0.45,0.65]
Sammour 2010	35	0.6 (0.5)	39	0.5 (0.7)		13.96%	0.16[-0.1,0.42]
Savel 2005	15	0.4 (0.6)	15	-0.3 (0.7)		10.45%	0.7[0.25,1.15]
Yu 2013	95	0.3 (0.3)	95	0.4 (0.3)		16.34%	-0.04[-0.14,0.06]
Total ***	**270**		**275**			**100%**	**0.29[0.05,0.52]**
Heterogeneity: Tau^2=0.09; Chi^2=44.63, df=7(P<0.0001); I^2=84.32%							
Test for overall effect: Z=2.35(P=0.02)							



Analysis 1.5. Comparison 1 Core temperature (°C), Outcome 5 Change in temperature without external warming.

Study or subgroup	Heated N	Heated Mean(SD)	Unheated N	Unheated Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Agaev 2013	66	0.5 (0.6)	84	-0.1 (0.7)		18.44%	0.55[0.35,0.75]
Champion 2006	25	-0.4 (0.6)	25	-0.4 (0.7)		17.08%	0[-0.35,0.35]
Davis 2006	11	0.4 (0.6)	11	0.4 (0.7)		14.96%	0[-0.53,0.53]
Kissler 2004	17	-0.5 (0.6)	19	-0.4 (0.7)		16.37%	-0.1[-0.51,0.31]
Mouton 1999	16	-0.2 (0.6)	16	-0.3 (0.7)		16.07%	0.05[-0.39,0.49]
Ott 1998	25	-0.3 (0.6)	25	-1.6 (0.7)		17.08%	1.34[0.99,1.69]
Total ***	**160**		**180**			**100%**	**0.32[-0.11,0.75]**
Heterogeneity: Tau^2=0.25; Chi^2=45.01, df=5(P<0.0001); I^2=88.89%							
Test for overall effect: Z=1.46(P=0.14)							

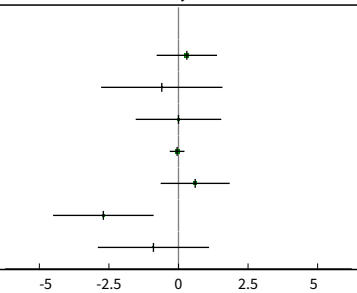


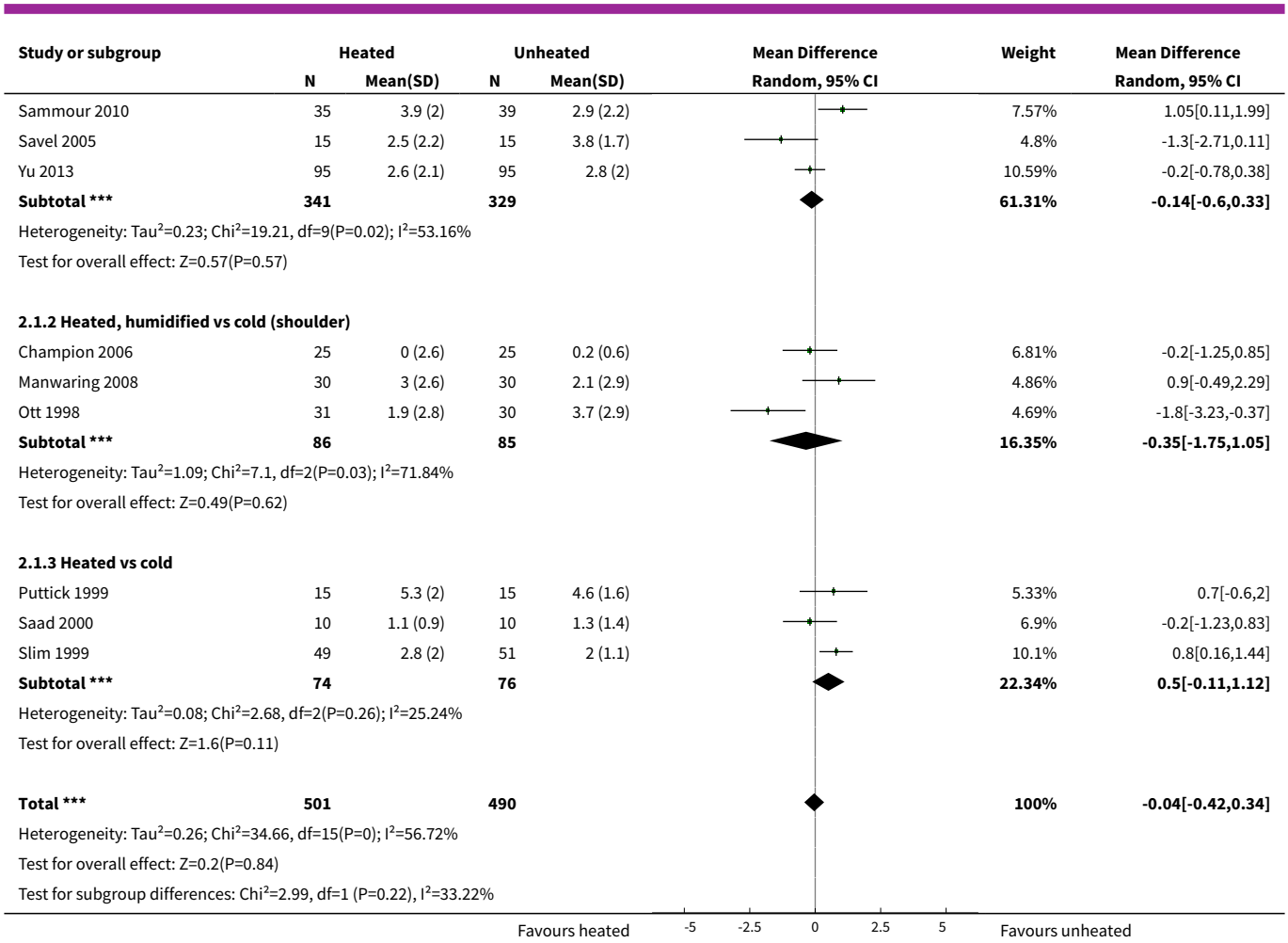
Comparison 2. Pain score (0 to 10-point VAS scale)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Day 1 pain score	14	991	Mean Difference (IV, Random, 95% CI)	-0.04 [-0.42, 0.34]
1.1 Heated, humidified vs cold (abdominal)	10	670	Mean Difference (IV, Random, 95% CI)	-0.14 [-0.60, 0.33]
1.2 Heated, humidified vs cold (shoulder)	3	171	Mean Difference (IV, Random, 95% CI)	-0.35 [-1.75, 1.05]
1.3 Heated vs cold	3	150	Mean Difference (IV, Random, 95% CI)	0.50 [-0.11, 1.12]
2 Day 1 pain score for low risk of bias studies	7	570	Mean Difference (IV, Random, 95% CI)	0.17 [-0.21, 0.55]
2.1 Heated, humidified vs cold (abdominal)	7	460	Mean Difference (IV, Random, 95% CI)	0.17 [-0.29, 0.63]
2.2 Heated, humidified vs cold (shoulder)	2	110	Mean Difference (IV, Random, 95% CI)	0.25 [-0.81, 1.31]
3 Day 2 pain score	10	695	Mean Difference (IV, Random, 95% CI)	-0.28 [-0.78, 0.21]
3.1 Heated, humidified vs cold (abdominal)	7	442	Mean Difference (IV, Random, 95% CI)	-0.40 [-1.07, 0.28]
3.2 Heated, humidified vs cold (shoulder)	2	111	Mean Difference (IV, Random, 95% CI)	-0.88 [-2.93, 1.17]
3.3 Heated vs cold	3	142	Mean Difference (IV, Random, 95% CI)	0.41 [-0.44, 1.27]
4 Day 2 pain score of low risk of bias studies	5	380	Mean Difference (IV, Random, 95% CI)	-0.29 [-0.65, 0.07]

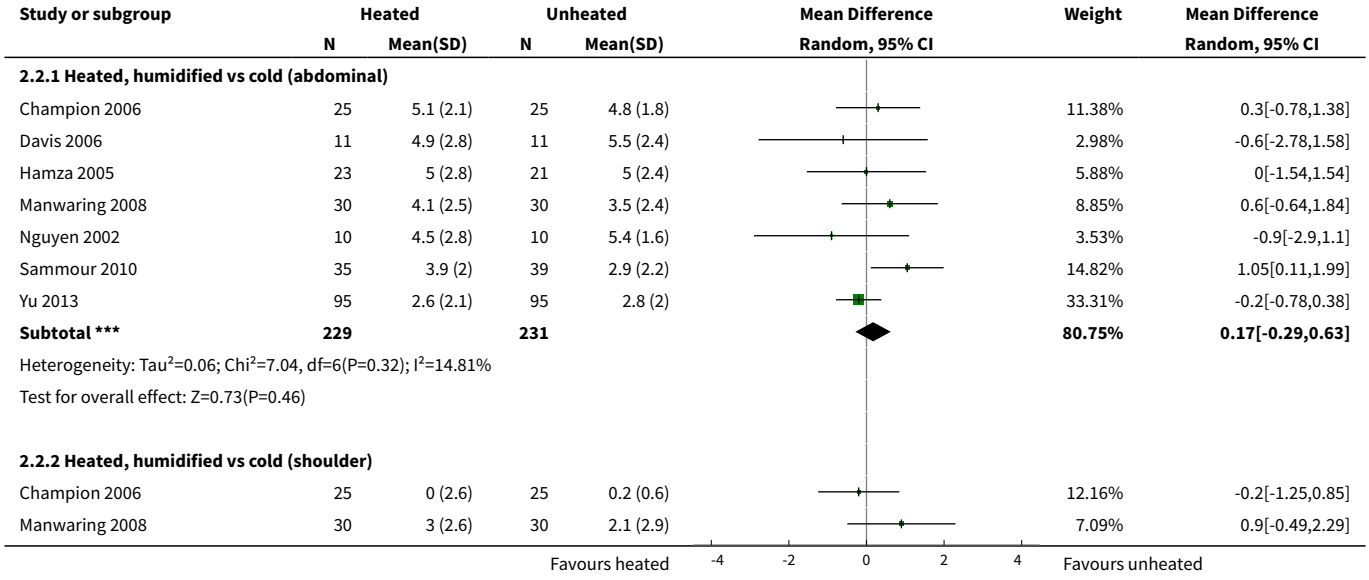
Analysis 2.1. Comparison 2 Pain score (0 to 10-point VAS scale), Outcome 1 Day 1 pain score.

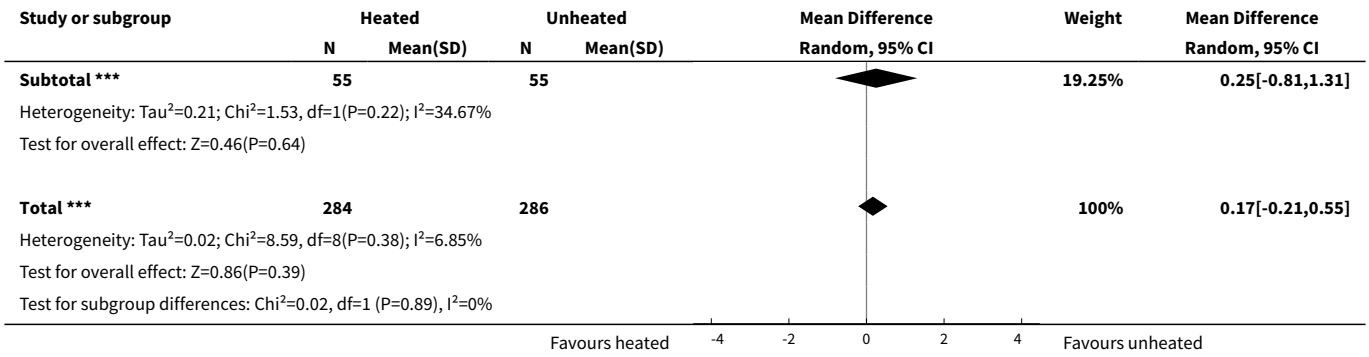
Study or subgroup	Heated N	Heated Mean(SD)	Unheated N	Unheated Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
2.1.1 Heated, humidified vs cold (abdominal)							
Champion 2006	25	5.1 (2.1)	25	4.8 (1.8)		6.55%	0.3[-0.78,1.38]
Davis 2006	11	4.9 (2.8)	11	5.5 (2.4)		2.49%	-0.6[-2.78,1.58]
Hamza 2005	23	5 (2.8)	21	5 (2.4)		4.25%	0[-1.54,1.54]
Klugsberger 2014	81	1.9 (0.9)	67	2 (0.8)		13.21%	-0.05[-0.31,0.21]
Manwaring 2008	30	4.1 (2.5)	30	3.5 (2.4)		5.62%	0.6[-0.64,1.84]
Mouton 1999	16	2.5 (2.8)	16	5.2 (2.4)		3.36%	-2.7[-4.51,-0.89]
Nguyen 2002	10	4.5 (2.8)	10	5.4 (1.6)		2.87%	-0.9[-2.9,1.1]



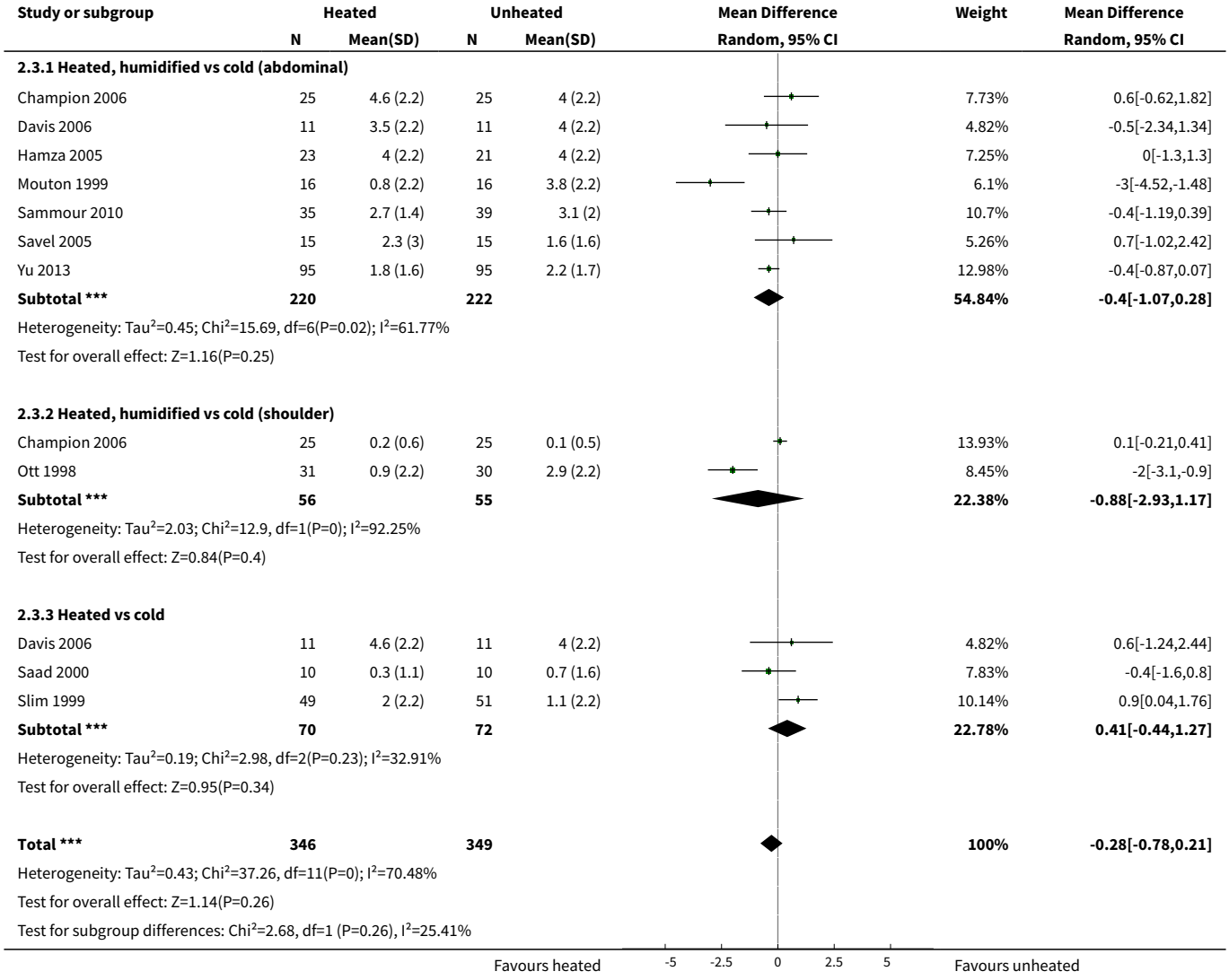


Analysis 2.2. Comparison 2 Pain score (0 to 10-point VAS scale), Outcome 2 Day 1 pain score for low risk of bias studies.





Analysis 2.3. Comparison 2 Pain score (0 to 10-point VAS scale), Outcome 3 Day 2 pain score.

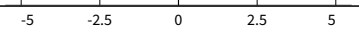


Analysis 2.4. Comparison 2 Pain score (0 to 10-point VAS scale), Outcome 4 Day 2 pain score of low risk of bias studies.

Study or subgroup	Heated N	Heated Mean(SD)	Unheated N	Unheated Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Champion 2006	25	4.6 (2.2)	25	4 (2.2)		8.71%	0.6[-0.62,1.82]
Davis 2006	11	3.5 (2.2)	11	4 (2.2)		3.83%	-0.5[-2.34,1.34]
Hamza 2005	23	4 (2.2)	21	4 (2.2)		7.65%	0[-1.3,1.3]
Sammour 2010	35	2.7 (1.4)	39	3.1 (2)		20.98%	-0.4[-1.19,0.39]
Yu 2013	95	1.8 (1.6)	95	2.2 (1.7)		58.81%	-0.4[-0.87,0.07]
Total ***	**189**		**191**			**100%**	**-0.29[-0.65,0.07]**

Heterogeneity: $Tau^2=0$; $Chi^2=2.57$, df=4(P=0.63); $I^2=0\%$

Test for overall effect: Z=1.56(P=0.12)



Comparison 3. Morphine consumption (morphine equivalent daily doses)

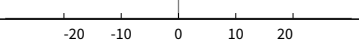
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Up to 6 hours	4	231	Mean Difference (IV, Random, 95% CI)	0.45 [-1.19, 2.08]
2 Day 1 morphine	9	573	Mean Difference (IV, Random, 95% CI)	-0.64 [-4.48, 3.20]
2.1 Heated, humidified vs cold	7	481	Mean Difference (IV, Random, 95% CI)	-1.66 [-4.79, 1.46]
2.2 Heated vs cold	3	92	Mean Difference (IV, Random, 95% CI)	11.93 [0.92, 22.94]
3 Day 2 morphine	7	532	Mean Difference (IV, Random, 95% CI)	-0.61 [-2.79, 1.57]
3.1 Heated, humidified vs cold	6	410	Mean Difference (IV, Random, 95% CI)	-0.94 [-1.90, 0.01]
3.2 Heated vs cold	2	122	Mean Difference (IV, Random, 95% CI)	9.79 [1.58, 18.00]

Analysis 3.1. Comparison 3 Morphine consumption (morphine equivalent daily doses), Outcome 1 Up to 6 hours.

Study or subgroup	Heated N	Heated Mean(SD)	Unheated N	Unheated Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Backlund 1998	13	11.4 (4.5)	13	11.7 (5.6)		17.54%	-0.3[-4.21,3.61]
Farley 2004	49	3.5 (5.5)	52	2.7 (4.3)		71.58%	0.8[-1.13,2.73]
Sammour 2010	35	15.7 (13.6)	39	15.8 (20.9)		4.22%	-0.1[-8.06,7.86]
Savel 2005	15	19 (6)	15	20 (11)		6.65%	-1[-7.34,5.34]
Total ***	**112**		**119**			**100%**	**0.45[-1.19,2.08]**

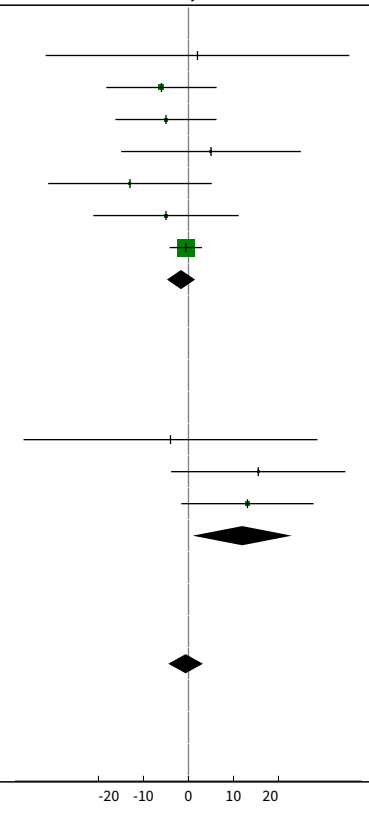
Heterogeneity: $Tau^2=0$; $Chi^2=0.49$, df=3(P=0.92); $I^2=0\%$

Test for overall effect: Z=0.54(P=0.59)



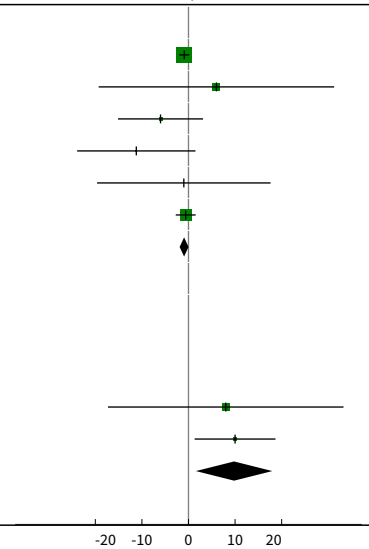
Analysis 3.2. Comparison 3 Morphine consumption (morphine equivalent daily doses), Outcome 2 Day 1 morphine.

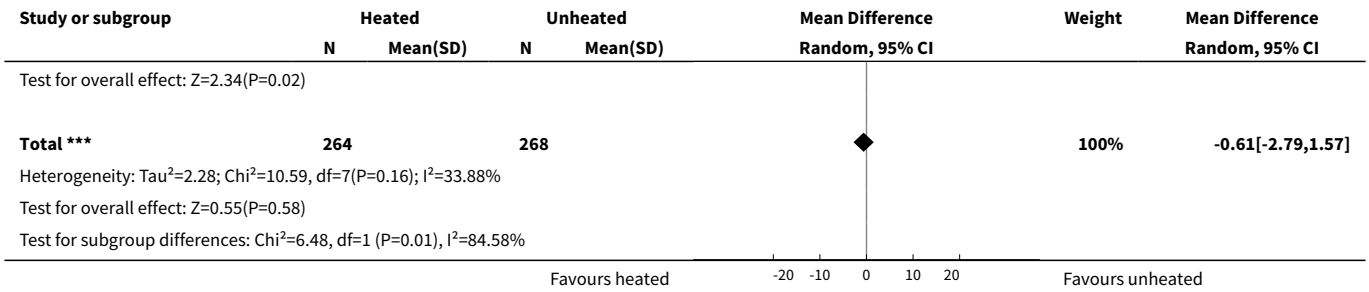
Study or subgroup	Heated N	Heated Mean(SD)	Unheated N	Unheated Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
3.2.1 Heated, humidified vs cold							
Davis 2006	11	33 (28.6)	11	31 (49.4)		1.28%	2[-31.73,35.73]
Farley 2004	49	23.2 (27.1)	52	29.2 (35.4)		8.98%	-6[-18.25,6.25]
Hamza 2005	23	32 (20)	21	37 (18)		10.52%	-5[-16.23,6.23]
Nguyen 2002	10	32 (19)	10	27 (26)		3.58%	5[-14.96,24.96]
Sammour 2010	35	33.2 (28.6)	39	46.2 (49.4)		4.29%	-13[-31.17,5.17]
Savel 2005	15	36 (17)	15	41 (27)		5.37%	-5[-21.15,11.15]
Yu 2013	95	6.6 (14)	95	7.2 (11.1)		54.4%	-0.6[-4.19,2.99]
Subtotal ***	**238**		**243**			**88.41%**	**-1.66[-4.79,1.46]**
Heterogeneity: Tau^2=0; Chi^2=3.29, df=6(P=0.77); I^2=0%							
Test for overall effect: Z=1.04(P=0.3)							
3.2.2 Heated vs cold							
Davis 2006	11	27 (24.7)	11	31 (49.4)		1.37%	-4[-36.64,28.64]
Puttick 1999	15	52.3 (24.7)	15	36.8 (29.2)		3.8%	15.5[-3.85,34.85]
Wills 2001	19	46 (23.8)	21	32.9 (23.5)		6.42%	13.1[-1.58,27.78]
Subtotal ***	**45**		**47**			**11.59%**	**11.93[0.92,22.94]**
Heterogeneity: Tau^2=0; Chi^2=1.07, df=2(P=0.59); I^2=0%							
Test for overall effect: Z=2.12(P=0.03)							
Total ***	**283**		**290**			**100%**	**-0.64[-4.48,3.2]**
Heterogeneity: Tau^2=3.7; Chi^2=9.78, df=9(P=0.37); I^2=7.97%							
Test for overall effect: Z=0.32(P=0.75)							
Test for subgroup differences: Chi^2=5.42, df=1 (P=0.02), I^2=81.55%							



Analysis 3.3. Comparison 3 Morphine consumption (morphine equivalent daily doses), Outcome 3 Day 2 morphine.

Study or subgroup	Heated N	Heated Mean(SD)	Unheated N	Unheated Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
3.3.1 Heated, humidified vs cold							
Champion 2006	25	3.7 (2.1)	25	4.6 (1.8)		47.89%	-0.9[-1.98,0.18]
Davis 2006	11	31 (25)	11	25 (34.7)		0.73%	6[-19.27,31.27]
Hamza 2005	23	15 (12)	21	21 (18)		5.16%	-6[-15.13,3.13]
Sammour 2010	35	18.9 (19.7)	39	30.1 (34.7)		2.8%	-11.2[-23.9,1.5]
Savel 2005	15	43 (25)	15	44 (27)		1.34%	-1[-19.62,17.62]
Yu 2013	95	2.2 (5.8)	95	2.8 (8.9)		35.7%	-0.6[-2.74,1.54]
Subtotal ***	**204**		**206**			**93.61%**	**-0.94[-1.9,0.01]**
Heterogeneity: Tau^2=0; Chi^2=4.08, df=5(P=0.54); I^2=0%							
Test for overall effect: Z=1.94(P=0.05)							
3.3.2 Heated vs cold							
Davis 2006	11	33 (25)	11	25 (34.7)		0.73%	8[-17.27,33.27]
Slim 1999	49	31 (24)	51	21 (20)		5.65%	10[1.32,18.68]
Subtotal ***	**60**		**62**			**6.39%**	**9.79[1.58,18]**
Heterogeneity: Tau^2=0; Chi^2=0.02, df=1(P=0.88); I^2=0%							

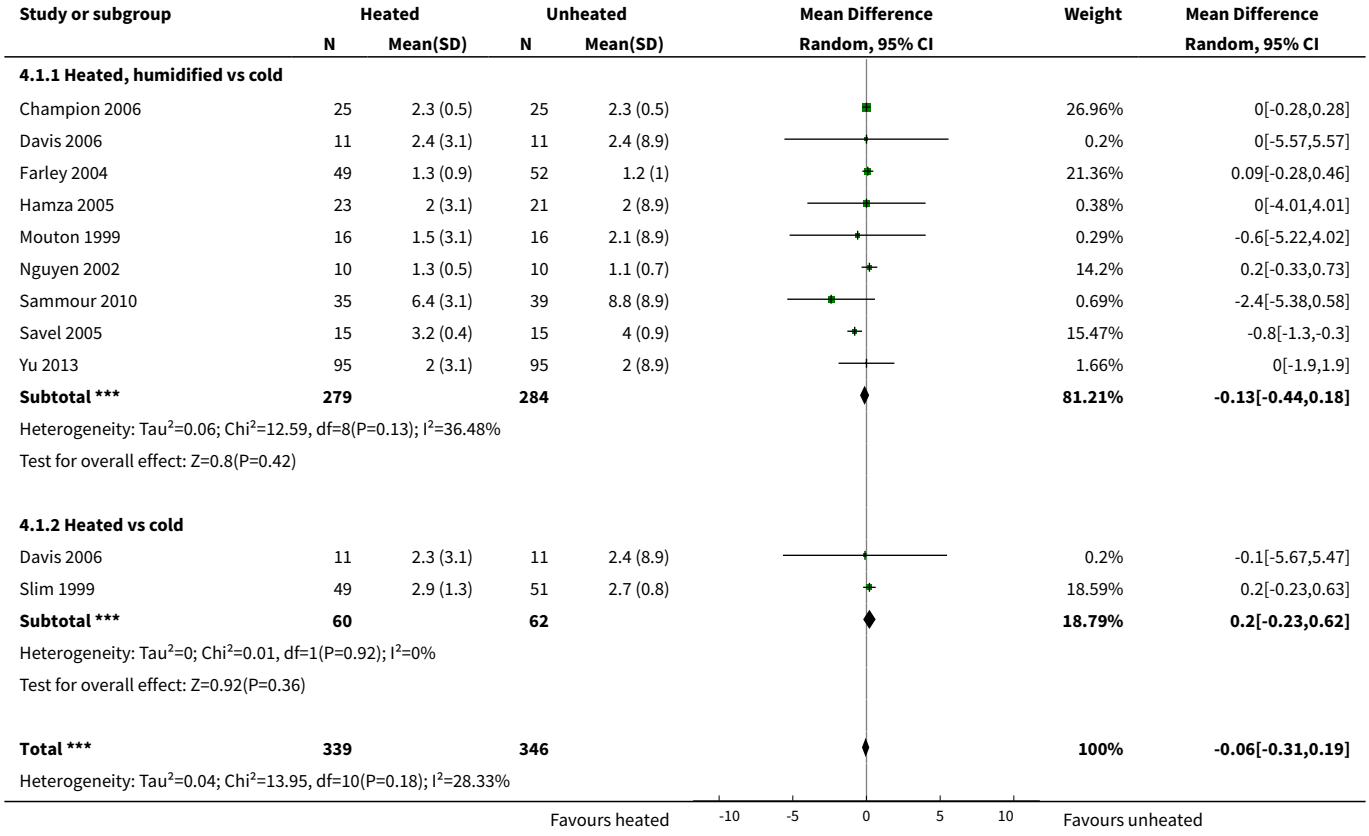




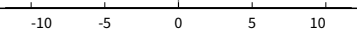
Comparison 4. Hospital stay (days)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Hospital stay	10	685	Mean Difference (IV, Random, 95% CI)	-0.06 [-0.31, 0.19]
1.1 Heated, humidified vs cold	9	563	Mean Difference (IV, Random, 95% CI)	-0.13 [-0.44, 0.18]
1.2 Heated vs cold	2	122	Mean Difference (IV, Random, 95% CI)	0.20 [-0.23, 0.62]

Analysis 4.1. Comparison 4 Hospital stay (days), Outcome 1 Hospital stay.



Study or subgroup	Heated N	Heated Mean(SD)	Unheated N	Unheated Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Test for overall effect: Z=0.45(P=0.65)							
Test for subgroup differences: Chi²=1.47, df=1 (P=0.22), I²=32.1%							

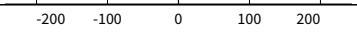


Comparison 5. Recovery room stay (minutes)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Recovery time	6	327	Mean Difference (IV, Random, 95% CI)	-26.79 [-51.34, -2.25]
2 Recovery time for low risk of bias studies	5	277	Mean Difference (IV, Random, 95% CI)	-1.22 [-6.62, 4.17]

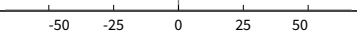
Analysis 5.1. Comparison 5 Recovery room stay (minutes), Outcome 1 Recovery time.

Study or subgroup	Heated N	Heated Mean(SD)	unheated N	unheated Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Champion 2006	25	58.8 (11.3)	25	56.5 (11.1)		19.55%	2.3[-3.91,8.51]
Davis 2006	11	144.8 (30)	11	142.5 (69)		12%	2.3[-42.16,46.76]
Farley 2004	49	74 (29)	52	82 (29)		19%	-8[-19.32,3.32]
Hamza 2005	23	83 (30)	21	107 (69)		14.82%	-24[-55.96,7.96]
Manwaring 2008	30	62 (19.9)	30	62.6 (17.6)		19.23%	-0.6[-10.11,8.91]
Ott 1998	25	45 (30)	25	190 (69)		15.4%	-145[-174.49,-115.51]
Total * **	**163**		**164**			**100%**	**-26.79[-51.34,-2.25]**
Heterogeneity: Tau²=792.09; Chi²=94.3, df=5(P<0.0001); I²=94.7%							
Test for overall effect: Z=2.14(P=0.03)							



Analysis 5.2. Comparison 5 Recovery room stay (minutes), Outcome 2 Recovery time for low risk of bias studies.

Study or subgroup	Heated N	Heated Mean(SD)	unheated N	unheated Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Champion 2006	25	58.8 (11.3)	25	56.5 (11.1)		49.72%	2.3[-3.91,8.51]
Davis 2006	11	144.8 (30)	11	142.5 (69)		1.46%	2.3[-42.16,46.76]
Farley 2004	49	74 (29)	52	82 (29)		19.66%	-8[-19.32,3.32]
Hamza 2005	23	83 (30)	21	107 (69)		2.8%	-24[-55.96,7.96]
Manwaring 2008	30	62 (19.9)	30	62.6 (17.6)		26.37%	-0.6[-10.11,8.91]
Total * **	**138**		**139**			**100%**	**-1.22[-6.62,4.17]**
Heterogeneity: Tau²=5.2; Chi²=4.56, df=4(P=0.34); I²=12.19%							
Test for overall effect: Z=0.44(P=0.66)							



Comparison 6. Lens fogging

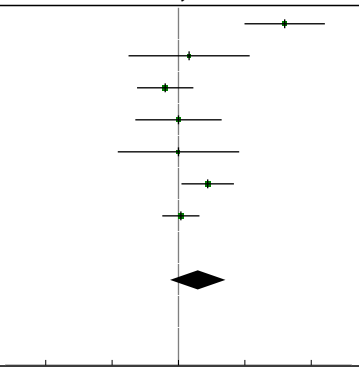
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Times cleaned	7	341	Mean Difference (IV, Random, 95% CI)	0.73 [-0.32, 1.77]

Analysis 6.1. Comparison 6 Lens fogging, Outcome 1 Times cleaned.

Study or subgroup	Heated N	Heated Mean(SD)	Unheated N	Unheated Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Champion 2006	25	6 (2.3)	25	2 (3.1)		14.1%	4[2.49,5.51]
Davis 2006	11	1.7 (2.3)	11	1.3 (3.1)		10.24%	0.4[-1.88,2.68]
Farley 2004	49	1.1 (2.3)	52	1.6 (3.1)		16.6%	-0.5[-1.56,0.56]
Hamza 2005	23	2 (2.3)	21	2 (3.1)		13.48%	0[-1.63,1.63]
Nguyen 2002	10	1.6 (2)	10	1.6 (3.1)		10.21%	0[-2.29,2.29]
Sammour 2010	35	4.2 (2.3)	39	3.1 (2)		16.99%	1.1[0.11,2.09]
Savel 2005	15	1.3 (0.9)	15	1.2 (1)		18.38%	0.09[-0.61,0.79]
Total * **	**168**		**173**			**100%**	**0.73[-0.32,1.77]**

Heterogeneity: Tau²=1.41; Chi²=27.25, df=6(P=0); I²=77.98%

Test for overall effect: Z=1.36(P=0.17)

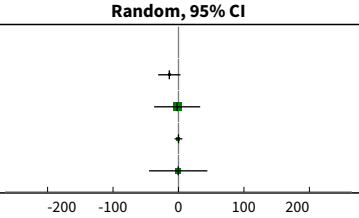


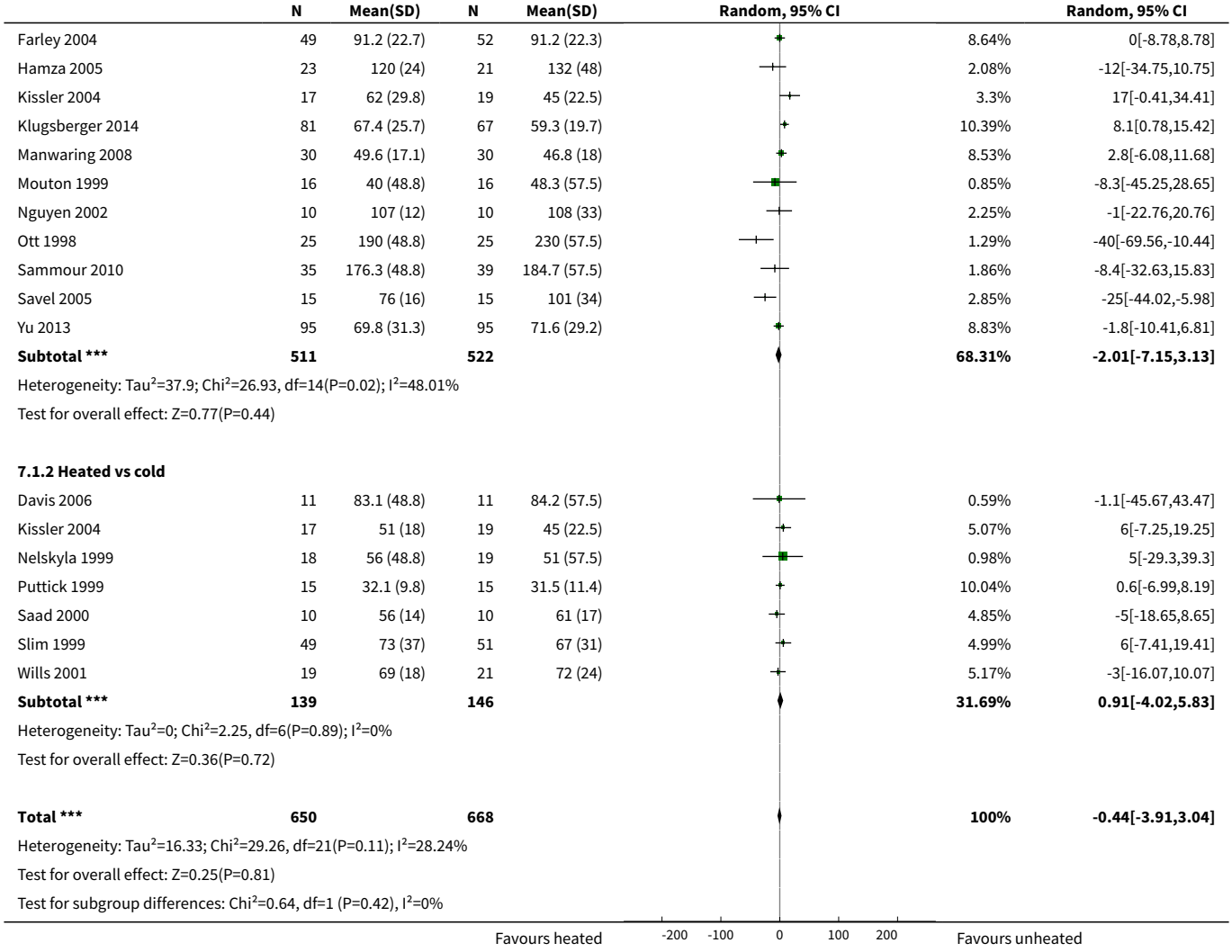
Comparison 7. Operative time (minutes)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Operative time	20	1318	Mean Difference (IV, Random, 95% CI)	-0.44 [-3.91, 3.04]
1.1 Heated, humidified vs cold	15	1033	Mean Difference (IV, Random, 95% CI)	-2.01 [-7.15, 3.13]
1.2 Heated vs cold	7	285	Mean Difference (IV, Random, 95% CI)	0.91 [-4.02, 5.83]

Analysis 7.1. Comparison 7 Operative time (minutes), Outcome 1 Operative time.

Study or subgroup	Heated N	Heated Mean(SD)	Unheated N	Unheated Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
7.1.1 Heated, humidified vs cold							
Agaev 2013	66	42 (48.8)	84	56 (57.5)		3.43%	-14[-31.02,3.02]
Backlund 1998	13	161 (50)	13	163 (41)		0.93%	-2[-37.15,33.15]
Champion 2006	25	61.7 (10.4)	25	61.7 (10.7)		12.47%	0[-5.85,5.85]
Davis 2006	11	84.2 (48.8)	11	84.6 (57.5)		0.59%	-0.4[-44.97,44.17]





ADDITIONAL TABLES

Table 1. Demographics of included studies

Study	Number of participants	Mean age (years)	% Female	Mean BMI (kg/m^2) or weight (kg)
Agaev 2013	150	52	72.7	
Backlund 1998	26	$49^{W}/53^{C}$	42.3	$25^{W}/25^{C}$ (BMI)
Champion 2006	50	$41.5^{WH}/44^{C}$	86	$50^{W}/52.9^{C}$ (BMI)
Davis 2006	44	$42.3^{WH}/40.6^{W}/44.8^{H}/42.5^{C}$		$47.2^{WH}/49.1^{W}/48.5^{H}/52.4^{C}$ (BMI)
Demco 2001	40		100	

Table 1. Demographics of included studies *(Continued)*

Farley 2004	117 (16 excluded)	52	68.3	$29.5^{W}/29.7^{C}$ (BMI)
Hamza 2005	50 (6 excluded)	$44^{WH}/45^{C}$	89.1	$125^{W}/128^{C}$ (weight)
Kissler 2004	90 (53 with data)	$37^{WH}/33^{W}/36^{C}$	100	$63^{WH}/63^{W}/65^{C}$ (weight)
Klugsberger 2014	148	55.7	69.6	28.56 (BMI)
Lee 2011	30	$60.1^{W}/55.1^{C}$	36.7	
Manwaring 2008	60	$30^{WH}/30^{C}$	100	$25^{W}/24^{C}$ (BMI)
Mouton 1999	32	23-89 (range)		
Nelskyla 1999	37	$46^{W}/47^{C}$	100	$63^{W}/66^{C}$ (weight)
Nguyen 2002	20	$43^{WH}/45^{C}$	45	
Ott 1998	72 (50 with data)		100	
Puttick 1999	30	$46.2^{W}/53.7^{C}$		
Saad 2000	20	$62^{W}/51^{C}$	60	$75^{W}/83^{C}$ (weight)
Sammour 2010	82 (8 excluded)	$71^{WH}/69^{C}$	57.1W/59C	$26.5^{W}/25.5^{C}$ (BMI)
Savel 2005	30	$41^{WH}/39^{C}$	80	$50.6^{W}/52.3^{C}$ (BMI)
Slim 1999	108 (8 excluded)	$52^{W}/53^{C}$	58	$26.9^{W}/25.7^{C}$ (BMI)
Wills 2001	41 (1 excluded)	$47.5^{W}/52.2^{C}$	45	$27^{W}/29.2^{C}$ (BMI)
Yu 2013	195 (5 excluded)	12	36.8	$49.6^{W}/50.3^{C}$ (weight)

W = warmed cohort, C = cold cohort, H = humidified cohort, WH = warmed and humidified cohort

Table 2. Methodology of included studies

Study	Procedures	Method of temperature measurement	Insufflation gas	Gas temperature (°C)	Heating device	Humidification (%)	Duration of surgery (minutes)	External warming
Agaev 2013	110 laparoscopic cholecystectomy, 40 laparoscopic fundoplication		Carbon dioxide		WISAP Flow Thermo	Not specified	42[WH]/56[C]	None
Backlund 1998	Laparoscopic fundoplication, hernioplasty, sigmoid colon resection, rectopexy	Pulmonary artery catheter	Carbon dioxide	37	WISAP Flow Thermo	None	161[W]/163[C]	Warm blanket/ warm waterbath mattress
Champion 2006	Laparoscopic Roux-en-Y gastric bypass	Rectal thermometer	Carbon dioxide	35	Lexion Insuflow	95	61.7[WH]/61.7[C]	None
Davis 2006	Laparoscopic Roux-en-Y gastric bypass	Foley catheter for bladder temperature	Carbon dioxide	37	Lexion Insuflow	95	78-84 (range)	None
Demco 2001	Awake laparoscopy		Carbon dioxide	35	Lexion Insuflow	95		None
Farley 2004	Laparoscopic cholecystectomy	Oesophageal probe	Carbon dioxide	35	Lexion Insuflow	95	91.2	Bair Hugger forced air warmer (32 °C[W]/34 °C [C])
Hamza 2005	Laparoscopic Roux-en-Y gastric bypass	Oesophageal/ tympanic membrane	Carbon dioxide	37	Lexion Insuflow	95	120[WH]/132[C]	Warm cotton blankets
Kissler 2004	Laparoscopic gynaecologic surgery	Intravesical temperature	Carbon dioxide	38	Laparo-CO2-Pneu2232	95-100	62[WH]/51[W]/45[C]	None
Klugsberger 2014	Laparoscopic cholecystectomy	Rectal probe	Carbon dioxide	35	Storz Optitherm	95	63.88	None
Lee 2011	Laparoscopic low anterior resection, colectomy, gastrectomy	Oesophageal temperature probe	Carbon dioxide	37	WISAP Flow Thermo	None	212[W]/230[C]	Bair Hugger forced air warmer/ warming mattress with circulating water at 38 °C

Table 2. Methodology of included studies *(Continued)*

Manwaring 2008	49 laparoscopy for endometriosis, 16 laparoscopy for adhesions		Carbon dioxide	37	Fisher & Paykel	100	49.6^{WH}/46.8^{C}	Upper body warming blanket
Mouton 1999	Laparoscopic cholecystectomy	Oesophageal thermoresistor	Carbon dioxide	34-37	LINS-1000	88-90	40^{WH}/48.3^{WH}	None
Nelskyla 1999	Laparoscopic hysterectomy	Tympanic and nasopharyngeal infrared technique	Carbon dioxide	37		None	56^{W}/51^{C}	None
Nguyen 2002	Laparoscopic Nissen fundoplication	Oesophageal probe	Carbon dioxide	37	Georgia Bio-Medical Insuflow	95	35.6^{WH}/35.6^{C}	Bair Hugger forced air warmer
Ott 1998	Laparoscopic gynaecologic surgery	Endotracheal temperature probe	Carbon dioxide	36.2	Insuflow	95	38-262 (range)	None
Puttick 1999	Laparoscopic cholecystectomy	Oesophageal probe	Carbon dioxide	37	WISAP Flow Thermo	None	31.5^{W}/32.1^{C}	None
Saad 2000	Laparoscopic cholecystectomy	Oesophageal probe	Carbon dioxide	37	WISAP Flow Thermo	None	56^{W}/61^{C}	None
Sammour 2010	Laparoscopic colon resection	Oesophageal probe	Carbon dioxide	37	Fisher & Paykel	98	176.3^{WH}/184.7^{C}	Bair Hugger forced air warmer
Savel 2005	Laparoscopic Roux-en-Y gastric bypass	Oesophageal probe	Carbon dioxide	35	Lexion Insuflow	95	76^{WH}/101^{C}	Bair Hugger forced air warmer at discretion of blinded anaesthesiologist
Slim 1999	Laparoscopic cholecystectomy, fundoplication, myotomy	Subdiaphragmatic thermometric probe	Carbon dioxide	37	ThermoFlator	None	73^{W}/67^{C}	None
Wills 2001	Laparoscopic fundoplication	Nasopharyngeal thermistor	Carbon dioxide	37	Cook LINS-2000	None	69^{W}/72^{C}	Bair Hugger forced air warmer
Yu 2013	Laparoscopic appendectomy	Naso-oesophageal probe	Carbon dioxide	37	Fisher & Paykel	98	69.8^{WH}/71.6^{C}	Forced-air warming blanket

W = warmed cohort, C = cold cohort, H = humidified cohort, WH = warmed and humidified cohort

Table 3. Outcomes of included studies

Study	Mean change in core temperature (°C)			Adverse events (Clavien-Dindo ≥ III)		
	Heated and humidified	Heated only	Cold	Heated and humidified	Heated only	Cold
Agaev 2013	0.49		-0.06	Not reported		Not reported
Backlund 1998	0.2		-0.1	Not reported		Not reported
Champion 2006	-0.4		-0.4	Not reported		Not reported
Davis 2006	0.4	0.2	0.4	Not reported	Not reported	Not reported
Demco 2001	Not reported		Not reported	Not reported		Not reported
Farley 2004	0.29		-0.03	Not reported		Not reported
Hamza 2005	-0.7		-1.7	Not reported		Not reported
Kissler 2004	-0.5	-0.6	-0.4	Not reported	Not reported	Not reported
Klugsberger 2014	Not reported		Not reported	0		0
Lee 2011		-0.4	-0.7		Not reported	Not reported
Manwaring 2008	-0.2		-0.13	Not reported		Not reported
Mouton 1999	-0.25		-0.3	0		0
Nelskyla 1999		-0.2	0		Not reported	Not reported
Nguyen 2002	0.4		0.3	0		0
Ott 1998	-0.3		-1.64	0		0
Puttick 1999		-0.24	-0.42		Not reported	Not reported
Saad 2000		0	-0.1		Not reported	Not reported
Sammour 2010	0.64		0.48	3 (8.6%)		5 (12.8%)
Savel 2005	0.4		-0.3	Not reported		Not reported
Slim 1999		Not reported	Not reported		0	0
Wills 2001		0.2	0		0	1 (4.8%)

Table 3. Outcomes of included studies *(Continued)*

Yu 2013	0.1	0.1	3 (10.3%)	0

APPENDICES

Appendix 1. CENTRAL search strategy

Cochrane Central Register of Controlled Trials (CENTRAL; *The Cochrane Library* 2016, Issue *8*))**(September 2016)**

#1 MeSH descriptor: [endoscopy] explode all trees

#2 MeSH descriptor: [minimal invasive surgical procedures] explode all trees

#3 MeSH descriptor: [pneumoperitoneum, artificial] explode all trees

#4 (endoscop* or laparoscop* or peritoneoscop* or laparotom*):ti,ab.kw

#5 (#1 or #2 or #3 or #4)

#6 MeSH descriptor: [carbon dioxide] explode all trees

#7 MeSH descriptor: [nitrous oxide] explode all trees

#8 MeSH descriptor: [argon] explode all trees

#9 MeSH descriptor: [helium] explode all trees

#10 (Gas* or carbon dioxide or CO2 or nitrous oxide or N2O or helium or argon or laughing gas):ti,ab,kw

#11 (#6 or #7 or #8 or #9 or #10)

#12 (Heat* or temperature* or warm* or isotherm*):ti,ab,kw

#13 (Humidification or humidif*):ti,ab,kw

#13 (#12 or #13)

#14 (#5 and #11 and #14)

Appendix 2. MEDLINE search strategy

MEDLINE (PubMed) (1950 to 23 September 2016)

1. Exp endoscopy/

2. Exp minimally invasive surgical procedures/

3. Exp pneumoperitoneum, artificial/

4. (endoscop* or laparoscop* or peritoneoscop* or laparotom*).mp.

5. 1 or 2 or 3 or 4

6. Exp carbon dioxide/

7. Exp Nitrous oxide/

8. Exp Argon/

9. Exp Helium/

10. (Gas* or carbon dioxide or CO2 or nitrous oxide or N2O or helium or argon or laughing gas).mp.

11. 6 or 7 or 8 or 9 or 10

12. (Heat* or temperature* or warm* or isotherm* or hypotherm* or thermoregulation).mp.

13. (Humidification or humidif*).mp.

14. 12 or 13

15. 5 and 11 and 14

16. Randomized controlled trial.pt.

17. Controlled clinical trial.pt.

18. Randomized.ab.

19. Placebo.ab.

20. Clinical trials as topic.sh.

21. Randomly.ab.

22. Trial.ti.

23. 16 or 17 or 18 or 19 or 20 or 21 or 22

24. Exp animals/ not humans.sh.

25. 23 not 24

26. 15 and 25

Appendix 3. Embase search strategy

Embase (1974 to 23 September 2016)

1. Exp abdominal-surgery/

2. Exp minimally-invasive-surgery/

3. Exp endoscopic-surgery/

4. Exp pneumoperitoneum/

5. (endoscop* or laparoscop* or laparotom* or peritoneoscop*).mp.

6. 1 or 2 or 3 or 4 or 5

7. (Gas* or carbon dioxide or CO2 or nitrous oxide or N2O or helium or argon or laughing gas).mp.

8. Exp carbon dioxide/

9. Exp nitrous oxide/

10. Exp Argon/

11. Exp Helium

12. 7 or 8 or 9 or 10 or 11

13. (heat* or temperature* or warm* or isotherm* or hypotherm* or thermoregulation).mp.

14. (Humidification or humidif*).mp.

15. 13 or 14

16. 6 and 12 and 15

17. crossover procedure.sh.

18. double-blind procedure.sh.

19. single-blind procedure.sh.

20. (crossover* or cross over*).ti,ab.

21. placebo*.ti,ab.

22. (doubl* adj blind*).ti,ab.

23. allocat*.ti,ab.

24. trial.ti.

25. randomized controlled trial.sh.

26. random*.ti,ab.

27. 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27

28. (exp animal/ or exp invertebrate/ or animal.hw. or nonhuman/) not (exp human/ or human cell/ or (human or humans or man or men or wom?n).ti.)

29. 27 not 28

30. 16 and 29

Appendix 4. Scopus, search strategy

1. TOPIC: (minimally invasive) *OR* TOPIC: (laparoscop*) *OR* TOPIC: (endoscop*) *OR* TOPIC: (artificial pneumoperitoneum) *OR* TOPIC: (peritoneoscop*)*OR* TOPIC: (laparotom*)

2. TOPIC: (carbon dioxide) *OR* TOPIC: (nitrous oxide) *OR* TOPIC: (argon) *OR* TOPIC: (helium) *OR* TOPIC: (Gas*) *OR* TOPIC: (CO2) *OR* TOPIC: (N2O)*OR* TOPIC: (laughing gas)

3. TOPIC: (Heat*) *OR* TOPIC: (temperature*) *OR* TOPIC: (warm*) *OR* TOPIC: (isotherm*) TOPIC: (thermoregulation) *OR*TOPIC: (hypotherm*)*OR* TOPIC: (humidif*)

4. #1 AND #2 AND #3

Appendix 5. Web of Science, search strategy

1. TITLE-ABS-KEY (minimally invasive) OR TITLE-ABS-KEY (laparoscop*) OR TITLE-ABS-KEY (endoscop*) OR TITLE-ABS-KEY (artificial pneumoperitoneum) OR TITLE-ABS-KEY (peritoneoscop*) OR TITLE-ABS-KEY (laparotom*)

2. TITLE-ABS-KEY (carbon dioxide) OR TITLE-ABS-KEY (co2) OR TITLE-ABS-KEY (nitrous oxide) OR TITLE-ABS-KEY (n2o) OR TITLE-ABS-KEY (gas*) OR TITLE-ABS-KEY (laughing gas) OR TITLE-ABS-KEY (argon) OR TITLE-ABS-KEY (helium)

3. TITLE-ABS-KEY (heat*) OR TITLE-ABS-KEY (temperature*) OR TITLE-ABS-KEY (warm*) OR TITLE-ABS-KEY (isotherm*) OR TITLE-ABS-KEY (humidif*) OR TITLE-ABS-KEY (hypotherm*) OR TITLE-ABS-KEY (thermoregulation)

4. #1 AND #2 AND #3

Appendix 6. Other searches

We performed keyword searches from the following websites:

- International Pharmaceutical Abstracts
- ClinicalTrials.gov
- National Research Register
- Google Scholar

Appendix 7. Criteria for judging risk of bias in the 'Risk of bias' assessment tool

Random Sequence Generation

Selection bias (biased allocation to interventions) due to inadequate generation of a randomised sequence.

(Continued)

Criteria for a judgement of 'Low risk' of bias	The investigators describe a random component in the sequence generation process such as: · referring to a random number table; · using a computer random number generator; · coin tossing; · shuffling cards or envelopes; · throwing dice; · drawing of lots; · minimisation*. *Minimisation may be implemented without a random element, and this is considered to be equivalent to being random.
Criteria for the judgement of 'High risk' of bias	The investigators describe a non-random component in the sequence generation process. Usually, the description would involve some systematic, non-random approach, for example: · sequence generated by odd or even date of birth; · sequence generated by some rule based on date (or day) of admission; · sequence generated by some rule based on hospital or clinic record number. Other non-random approaches happen much less frequently than the systematic approaches mentioned above and tend to be obvious. They usually involve judgement or some method of non-random categorisation of participants, for example: · allocation by judgement of the clinician; · allocation by preference of the participant; · allocation based on the results of a laboratory test or a series of tests; · allocation by availability of the intervention.
Criteria for the judgement of 'Unclear risk' of bias	Insufficient information about the sequence generation process to permit judgement of 'Low risk' or 'High risk'.

Allocation concealment

Selection bias (biased allocation to interventions) due to inadequate concealment of allocations prior to assignment.

Criteria for a judgement of 'Low risk' of bias	Participants and investigators enrolling participants could not foresee assignment because one of the following, or an equivalent method, was used to conceal allocation: · central allocation (including telephone, web-based and pharmacy-controlled randomisation); · sequentially numbered drug containers of identical appearance; · sequentially numbered, opaque, sealed envelopes.
Criteria for the judgement of 'High risk' of bias	Participants or investigators enrolling participants could possibly foresee assignments and thus introduce selection bias, such as allocation based on: · using an open random allocation schedule (e.g. a list of random numbers); · assignment envelopes were used without appropriate safeguards (e.g. if envelopes were unsealed or nonopaque or not sequentially numbered);

(Continued)

	· alternation or rotation; · date of birth; · case record number; · any other explicitly unconcealed procedure.
Criteria for the judgement of 'Unclear risk' of bias	Insufficient information to permit judgement of 'Low risk' or 'High risk'. This is usually the case if the method of concealment is not described or not described in sufficient detail to allow a definite judgement – for example if the use of assignment envelopes is described, but it remains unclear whether envelopes were sequentially numbered, opaque and sealed.

Blinding of participants and personnel

Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.

Criteria for a judgement of 'Low risk' of bias	Any one of the following: · no blinding or incomplete blinding, but the review authors judge that the outcome is not likely to be influenced by lack of blinding; · blinding of participants and key study personnel ensured, and unlikely that the blinding could have been broken.
Criteria for the judgement of 'High risk' of bias	Any one of the following: · no blinding or incomplete blinding, and the outcome is likely to be influenced by lack of blinding; · blinding of key study participants and personnel attempted, but likely that the blinding could have been broken, and the outcome is likely to be influenced by lack of blinding.
Criteria for the judgement of 'Unclear risk' of bias	Any one of the following: · insufficient information to permit judgement of 'Low risk' or 'High risk'; · the study did not address this outcome.

Blinding of outcome assessment

Detection bias due to knowledge of the allocated interventions by outcome assessors.

Criteria for a judgement of 'Low risk' of bias	Any one of the following: · no blinding of outcome assessment, but the review authors judge that the outcome measurement is not likely to be influenced by lack of blinding; · blinding of outcome assessment ensured, and unlikely that the blinding could have been broken.
Criteria for the judgement of 'High risk' of bias	Any one of the following: · no blinding of outcome assessment, and the outcome measurement is likely to be influenced by lack of blinding; · blinding of outcome assessment, but likely that the blinding could have been broken, and the outcome measurement is likely to be influenced by lack of blinding.
Criteria for the judgement of 'Unclear risk' of bias	Any one of the following: · insufficient information to permit judgement of 'Low risk' or 'High risk'; · the study did not address this outcome.

(Continued)

Incomplete outcome data

Attrition bias due to amount, nature or handling of incomplete outcome data.

Criteria for a judgement of 'Low risk' of bias	Any one of the following: · no missing outcome data; · reasons for missing outcome data unlikely to be related to true outcome (for survival data, censoring unlikely to be introducing bias); · missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups; · for dichotomous outcome data, the proportion of missing outcomes compared with observed event risk not enough to have a clinically relevant impact on the intervention effect estimate; · for continuous outcome data, plausible effect size (difference in means or standardised difference in means) among missing outcomes not enough to have a clinically relevant impact on observed effect size; · missing data have been imputed using appropriate methods.
Criteria for the judgement of 'High risk' of bias	Any one of the following: · reason for missing outcome data likely to be related to true outcome, with either imbalance in numbers or reasons for missing data across intervention groups; · for dichotomous outcome data, the proportion of missing outcomes compared with observed event risk enough to induce clinically relevant bias in intervention effect estimate; · for continuous outcome data, plausible effect size (difference in means or standardized difference in means) among missing outcomes enough to induce clinically relevant bias in observed effect size; · 'as-treated' analysis done with substantial departure of the intervention received from that assigned at randomization; · potentially inappropriate application of simple imputation.
Criteria for the judgement of 'Unclear risk' of bias	Any one of the following: · insufficient reporting of attrition/exclusions to permit judgement of 'Low risk' or 'High risk' (e.g. number randomised not stated, no reasons for missing data provided); · the study did not address this outcome.

Selective reporting

Reporting bias due to selective outcome reporting.

Criteria for a judgement of 'Low risk' of bias	Any of the following: · the study protocol is available and all of the study's pre-specified (primary and secondary) outcomes that are of interest in the review have been reported in the pre-specified way; · the study protocol is not available but it is clear that the published reports include all expected outcomes, including those that were pre-specified (convincing text of this nature may be uncommon).
Criteria for the judgement of 'High risk' of bias	Any one of the following: · not all of the study's pre-specified primary outcomes have been reported;

(Continued)

	· one or more primary outcomes is reported using measurements, analysis methods or subsets of the data (e.g. subscales) that were not pre-specified; · one or more reported primary outcomes were not pre-specified (unless clear justification for their reporting is provided, such as an unexpected adverse effect); · one or more outcomes of interest in the review are reported incompletely so that they cannot be entered in a meta-analysis; · the study report fails to include results for a key outcome that would be expected to have been reported for such a study.
Criteria for the judgement of 'Unclear risk' of bias	Insufficient information to permit judgement of 'Low risk' or 'High risk'. It is likely that the majority of studies will fall into this category.

Other bias

Bias due to problems not covered elsewhere in the table.

Criteria for a judgement of 'Low risk' of bias	The study appears to be free of other sources of bias.
Criteria for the judgement of 'High risk' of bias	There is at least one important risk of bias. For example, the study: · had a potential source of bias related to the specific study design used; or · has been claimed to have been fraudulent; or · had some other problem.
Criteria for the judgement of 'Unclear risk' of bias	There may be a risk of bias, but there is either: · insufficient information to assess whether an important risk of bias exists; or · insufficient rationale or evidence that an identified problem will introduce bias.

WHAT'S NEW

Date	Event	Description
17 October 2016	New citation required but conclusions have not changed	Updated to include six new trials

HISTORY

Protocol first published: Issue 2, 2009
Review first published: Issue 1, 2011

Date	Event	Description
30 September 2015	New search has been performed	Update and Amendment
26 July 2010	Amended	Final amendment

Date	Event	Description
12 July 2010	Amended	Final draft

CONTRIBUTIONS OF AUTHORS

- **DWB:** protocol development, screening retrieved papers for eligibility criteria, analysing and editing review, providing guidance on methodology and quality control
- **JD:** analysis and review editing
- **NS:** analysis and review editing
- **NM:** analysis and review editing
- **XS:** literature search, screening search results, retrieving and analysing data, draft preparation
- **GH:** protocol development, literature search, screening search results, draft preparation
- **SK:** analysis and review editing, quality control

DECLARATIONS OF INTEREST

- **DWB:** no conflict of interest
- **JD:** no conflict of interest
- **NS:** no conflict of interest
- **NM:** no conflict of interest
- **XS:** no conflict of interest
- **GH:** no conflict of interest
- **SK:** no conflict of interest

SOURCES OF SUPPORT

Internal sources

- University of Alberta Library, Canada.

External sources

- Cochrane Colorectal Cancer Group, Denmark.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

There were no deviations from protocol.

INDEX TERMS

Medical Subject Headings (MeSH)

*Carbon Dioxide; Analgesics, Opioid [administration & dosage]; Body Temperature; Hot Temperature [*therapeutic use]; Humidity; Hypothermia [*prevention & control]; Insufflation [*methods]; Intraoperative Complications [*prevention & control]; Laparoscopy [methods]; Morphine [administration & dosage]; Pain, Postoperative [prevention & control]; Pneumoperitoneum, Artificial [methods]; Randomized Controlled Trials as Topic

MeSH check words

Adult; Female; Humans; Male