NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Medical Technologies Evaluation Programme

Sponsor submission of evidence:

Evaluation title: HumiGard™ Surgical Humidification System for the prevention of inadvertent peri-operative hypothermia

Sponsor: Fisher & Paykel Healthcare

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Instructions for sponsors

This is the template for submission of evidence to the National Institute for Health and Care Excellence (NICE) as part of the Medical Technologies Evaluation Programme process for developing NICE medical technologies guidance. Use of the submission template is mandatory.

The purpose of the submission is for the sponsor to collate, analyse and present all relevant evidence that supports the case for adoption of the technology into the NHS in England, within the scope defined by NICE. Failure to comply with the submission template and instructions could mean that the NICE cannot issue recommendations on use of the technology.

The submission should be completed after reading the 'Medical Technologies Evaluation Programme Methods guide' and the 'Medical Technologies Evaluation Programme Process guide' available at www.nice.org.uk/mt. After submission to, and acceptance by, NICE, the submission will be critically appraised by an External Assessment Centre appointed by NICE.

Under exceptional circumstances, unpublished evidence is accepted under agreement of confidentiality. Such evidence includes 'commercial in confidence' information and data that are awaiting publication ('academic in confidence'). When data are 'commercial in confidence' or 'academic in confidence', it is the sponsor's responsibility to highlight such data clearly. For further information on disclosure of information, submitting cost models and equality issues, users should see section 11 of this document 'Related procedures for evidence submission'.

The submission should be concise and informative. The main body of the submission should not exceed 100 pages (excluding the pages covered by the template and appendices). The submission should be sent to NICE electronically in Word or a compatible format, not as a PDF file.

The submission must be a stand-alone document. Additional appendices may only be used for supplementary explanatory information that exceeds the level of detail requested, but that is considered to be relevant to the case

for adoption. Appendices will not normally be presented to the Medical Technologies Advisory Committee when developing its recommendations. Any additional appendices should be clearly referenced in the body of the submission. Appendices should not be used for core information that has been requested in the specification. For example, it is not acceptable to attach a key study as an appendix and to complete the economic evidence section with 'see appendix 9.11'.

All studies and data included in the submission must be referenced. Identify studies by the first author or trial ID, rather than by relying on numerical referencing alone (for example, 'Trial 123/Jones et al.[126], rather than 'one trial[126]').Please use a recognised referencing style, such as Harvard or Vancouver.

The sponsor should provide a PDF copy of full journal articles or reports – in electronic or hard copy form – included in the submission, if the sponsor is either the copyright owner or has adequate copyright clearance to permit the intended use by NICE. This clearance must be wide enough to allow NICE to make further copies, store the article electronically for a limited period of time on a shared drive to be accessed by a limited number of staff. Additionally, any full article obtained and submitted in electronic format must be done so in a manner compliant with the relevant contractual terms of use permitting the sponsor electronic access to the article. If the sponsor does not have sufficient copyright clearance, they are asked to submit references or links only, or details of contacts for unpublished research. NICE will then itself obtain full copies of all relevant papers or reports, paying a copyright fee where necessary. For unpublished studies for which a manuscript is not available, provide a structured abstract about future journal publication. If a structured abstract is not available, the sponsor must provide a statement from the authors to verify the data provided.

If a submission is based on preliminary regulatory recommendations, the sponsor must advise NICE immediately of any variation between the preliminary and final approval.

Document key

Boxed text with a grey background provides specific and/or important guidance for that section. This should not be removed.

Information in highlighted black italic is to help the user complete the submission and may be deleted.

The user should enter text at the point marked ‘Response’ or in the tables as appropriate. ‘Response’ text may be deleted.

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Glossary of terms

Term	Definition
°C	Degrees Celsius
ASA	American Society of Anaesthesiologists physical classification system
BTP	Bladder Temperature Probe
CI	Confidence Interval
CO_2	Carbon Dioxide
ECRI	Emergency Care Research Institute
ICU	Intensive Care Unit
ISPOR	The International Society for Pharmacoeconomics and Outcomes Research
MAUDE	Manufacturer and User Facility Device Experience
MHRA	Medicines & Healthcare products Regulatory Agency
NHS	National Health Service
NICE	The National Institute for Health and Care Excellence
NPP	Naso-Pharyngeal temperature Probe
OR	Odds Ratio
PAC	Pulmonary Artery Catheter
PbR	Payment by results
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
QUORUM	Quality of Reporting of Meta-analyses
RCT	Randomised Control Trial
RR	Relative Risk
SEM	Standard Error of the Mean
SSI	Surgical Site Infection
VAS	Visual Analogue Scale

Section A – Decision problem

Section A describes the decision problem, the technology and its clinical context. There is also information about ongoing studies, regulatory information and equality issues.

Sponsors should submit section A before the full submission (for details on timelines, see the NICE document 'Guide to the Medical Technologies Evaluation Programme process', available from www.nice.org.uk/mt

1 Statement of the decision problem

The decision problem is specified in the final scope issued by NICE. The decision problem states the key parameters that should be addressed by the information in the evidence submission. All statements should be evidence based and directly relevant to the decision problem.

Table A1: Statement of the decision problem

	Scope issued by NICE	**Variation from scope**	**Rationale for variation**
Population	People undergoing abdominal surgery, as an open or laparoscopic procedure.	None	
Intervention	HumiGard Surgical Humidification System for: • Open abdominal surgery • Laparoscopic abdominal surgery	None	
Comparator(s)	Open abdominal surgery: • No insufflant Laparoscopic abdominal surgery: • Unheated, unhumidified insufflant CO_2 gas	None	
Outcomes	The outcome measures to consider include: • Incidence of hypothermia in the intra- and post-operative period (defined as a core body temperature <36°C) • Incidence of surgical site infections (SSI) • Length of stay in post-operative recovery • Total length of hospital stay • Device-related adverse events • Patient-reported pain	Yes	Incidence of hypothermia in the operative period for included laparoscopic investigations is not documented. Therefore change in core temperature as a marker of temperature maintenance is considered as this is the standard reported temperature measure. Analgesic use will also be reported as an objective measure of patient reported pain.
Cost analysis	Costs will be considered from an NHS and personal social	None	

	services perspective. The time horizon for the cost analysis will be sufficiently long to reflect any differences in costs and consequences between the technologies being compared. Sensitivity analysis will be undertaken to address uncertainties in the model parameters, which will include scenarios in which different numbers and combinations of devices are needed.		
Subgroups to be considered	• People receiving adjunctive warming, such as from forced air warming devices or warming mattresses • High-risk groups as described in NICE guideline 65 (any 2 of: ASA grades II-V, pre-operative temperature below 36°C, combined general and regional anaesthesia, major or intermediate surgery or at risk of cardiovascular complications).	None	
Special considerations, including issues related to equality	None	None	

2 Description of technology under assessment

2.1 Give the brand name, approved name and details of any different versions of the same device.

Manufacturer: Fisher & Paykel Healthcare.
Brand name: HumiGard™ Surgical Humidification System.
Model: MR860 and SH870. Both models are equivalent in terms of therapeutic output. The SH870 offers a more simplified set up and a smaller device profile. Instructions for use for both models accompany this submission. The SH870 is due to be launched into the UK within the submission period.

2.2 What is the principal mechanism of action of the technology?

The technology reduces tissue evaporation caused by exposure to cold dry carbon dioxide (CO_2) in laparoscopic surgery and ambient air in open surgery. Insufflation gas is passed over a software controlled humidification system which warms and humidifies the gas to near physiologic conditions (body temperature and saturated). Using standard care (no insufflation or unheated, unhumidified insufflation), evaporation from the tissues results in cellular damage and evaporative cooling leading to consequences for the patient including increased operative heat loss, post-operative pain, lengthened stay in post-operative recovery, total hospital stay and incidence of surgical site infection (SSI).

3 Clinical context

3.1 Provide a brief overview of the disease or condition for which the technology is being considered in the scope issued by NICE.

The HumiGard™ system is intended for use in heating and humidifying insufflant gas for laparoscopy and open surgery, specifically to minimise evaporative cooling and desiccation and prevent intra-operative hypothermia. Hypothermia is a common but preventable complication of peri-operative procedures, which is associated with poor outcomes for patients. There are

909,905 potentially relevant abdominal procedures in 2013/2014 (NHS reference costs).

3.2 Give details of any relevant NICE or other national guidance or expert guidelines for the condition for which the technology is being used. Specify whether the guidance identifies specific subgroups and make any recommendations for their treatment. If available, these should be UK based guidelines.

NICE clinical guideline 65 (Inadvertent peri-operative hypothermia: The management of inadvertent peri-operative hypothermia in adults. NICE clinical guideline CG65 (2008)). The guidance recommends that all patients should be assessed for their risk of peri-operative hypothermia. All patients should receive warmed intravenous fluids and blood products; patients identified as higher risk should be warmed intra-operatively using a forced air warming device, as should any patient receiving anaesthesia for more than 30 minutes. Patients at high risk of peri-operative hypothermia are defined as those who are assessed by the peri-operative team as having an ASA grade greater than 2, and those patients who are at increased risk of a morbid cardiac event. Typically these patients are around 50 years of age, with an ischaemic heart disease profile. Regular temperature measurement is recommended before, during and after surgery, and forced air warming is recommended for any patient whose core temperature drops below 36°C. NICE medical guidance recommends the Inditherm patient warming mattress as a cost efficient alternative to forced air warming (medical technologies guidance 7). Current NICE guidance relates to the prevention of peri-operative hypothermia in the general surgical population and does not make any specific recommendations about the condition of insufflation gas.

CG65 did assess the use of heated insufflation with or without humidifcation, versus no insufflation or unheated, unhumidified insufflation, but failed to separate heated humdified gas which acts to reduce evaporation in comaprision with heated dry gas which facilitates evaporation. In addition, since the 2008 guidance 9 more randomised controlled trials have been published on the topic.

3.3 Describe the clinical pathway of care that includes the proposed use of the technology.

The management of inadvertent peri-operative hypothermia is the clinical pathway of care. However, the current guideline does not currently make any recommendation on heated humidified insufflation gas. The comparator is standard care: unheated, unhumidified insufflant in laparoscopic surgery and no insufflant, i.e. exposure to the ambient air, in open surgery.

3.4 Describe any issues relating to current clinical practice, including any uncertainty about best practice.

The current clinical pathway makes no recommendation on the use of heated humidified insufflation gas. Audits reveal that even with current guidelines the incidence of peri-operative hypothermia is in the order of 20% (1). None of the current recommendations to prevent hypothermia in the peri-operative pathway act to reduce evaporative heat loss from the surgical cavity. Evaporative heat loss is derived from the heat of vaporization of water. To vaporise liquid water requires 0.58 kcal/g, resulting in heat loss from the patient (2). Literature indicates that heat loss during laparoscopic insufflation is primarily due to evaporation and the amount of heat loss is proportional to the liquid water evaporated from the peritoneal surface to saturate the insufflated CO_2 (3). Animal investigations isolating the effect of gas types on laparoscopic surgery highlights the amount of heat loss due to evaporation (3). Heat loss was significantly reduced when the gas was heated and humidified. Similarly, evaporation from within the surgical incision in open surgery is substantial. It is well documented that hypothermia is more pronounced in larger incisions compared to smaller ones with most of the difference related to differences in evaporative heat loss from the open wound (4). When evaporation was reduced in a randomised controlled trial investigating insufflation of heated, humidified CO_2 in to the open wound during colorectal surgery there was as significant benefit in wound edge, wound area and core temperature (5, 6).

3.5 Describe the new pathway of care incorporating the new technology that would exist if the technology was adopted by the NHS in England.

The addition of the HumiGard™ Surgical Humidification System to deliver heated humidified insufflation could be easily implemented in the inadvertent peri-operative hypothermia pathway, during the intra-operative care phase. For laparoscopic surgery standard insufflation tubing would be replaced by the HumiGard™ Surgical Humidification System. The system easily integrates between the existing insufflation equipment and the patient interface. For open surgical procedures the system easily connects to piped gas sources or alternatively if piped gas is unavailable a gas supply stand is available to deliver heated humidified CO_2 in any theatre environment.

3.6 Describe any changes to the way current services are organised or delivered as a result of introducing the technology.

None known.

3.7 Describe any additional tests or investigations needed for selecting or monitoring patients, or particular administration requirements, associated with using this technology that are over and above usual clinical practice.

None known. There are no contraindications for the HumiGard™ Surgical Humidification System.

3.8 Describe any additional facilities, technologies or infrastructure that need to be used alongside the technology under evaluation for the claimed benefits to be realised.

None are anticipated.

3.9 Describe any tests, investigations, interventions, facilities or technologies that would no longer be needed with using this technology.

For laparoscopic surgery the standard insufflation tubing would not be needed.

3.10 Describe how the NHS in England can disinvest from tests, investigations, interventions, facilities or technologies described in section 3.9 that would no longer be needed with using this technology.

For laparoscopic surgery the standard insufflation tubing would not be needed.

4 Regulatory information

4.1 Provide PDF copies of the following documents:

- instructions for use
- CE mark certificate or equivalent UK regulatory approval such as EC declaration of conformity
- quality systems (ISO 13485) certificate (if required)

PDF copies of these documents accompanies this application.

4.2 Does the technology have CE mark for the indication(s) specified in the scope issued by NICE? If so, give the date that authorisation was received. If not, state current UK regulatory status, with relevant dates (for example, date of application and/or expected approval dates).

Yes, April 2013

4.3 Does the technology have regulatory approval outside the UK? If so, please provide details.

Yes, the technology is currently registered in New Zealand, Australia, and France. The technology is also sold in Germany, which does not require

further registration beyond carrying the CE mark. Approval documentation for New Zealand and Australia accompany this submission.

4.4 If the technology has not been launched in the UK provide the anticipated date of availability in the UK.

Not applicable.

4.5 If the technology has been launched in the UK provide information on the use in England.

The system was launched for laparoscopic surgery in 2007 and is currently used on ~450 patients per month. The open surgery system was more recently launched in the UK in November 2013, there are a number of evaluations currently underway with the system.

5 Ongoing studies

5.1 Provide details of all completed and ongoing studies on the technology from which additional evidence relevant to the decision problem is likely to be available in the next 12 months.

Three investigations that meet the scope (Frey *et al.(7)*, Weinberg *et al.(8)*, Mason *et al.(9)*) are in the final stages of manuscript generation. However abstract information is available in the public domain, as all have been presented at conferences. Details on the investigations are included in section B part 7 and copies of the draft manuscripts are provided as academic in confidence with author permission.

Fisher & Paykel Healthcare uses MEDDEV guidance to comply with the Medical Devices Directive (93/42/EEC) and ISO 13485 in the assessment of all complaints and reporting of all instances of adverse or near adverse events or incidents to the relevant authorities. Quality processes are audited annually by TŰV SŰD. Internal product complaint databases were searched from release (January 2007) to September 2015 for global complaints related to the HumiGard™ Surgical Humidification System and associated

accessories. Results showed that there are no complaints with injury, adverse events, near adverse events or reportable complaints with the Surgical Humidification System.

5.2 If the technology is, or is planned to be, subject to any other form of assessment in the UK, please give details of the assessment, organisation and expected timescale.

Not applicable.

6 Equality

NICE is committed to promoting equality of opportunity and eliminating unlawful discrimination on the grounds of age, disability, gender reassignment, race, religion or belief, sex, and sexual orientation, and to comply fully with legal obligations on equality and human rights.

Equality issues require special attention because of NICE's duties to have due regard to the need to eliminate unlawful discrimination, promote equality and foster good relations between people with a characteristic protected by the equalities legislation and others.

Any issues relating to equality that are relevant to the technology under assessment should be described. This section should identify issues described in the scope and also any equality issues not captured in the final scope.

Further details on equality may be found in section 11.3 of this document.

6.1.1 Describe any equality issues relating to the patient population and condition for which the technology is being used.

None known.

6.1.2 Describe any equality issues relating to the assessment of the technology that may require special attention.

None known.

6.1.3 How will the submission address these issues and any equality issues raised in the scope?

Not applicable.

Section B – Clinical evidence

7 Published and unpublished clinical evidence

Section B requires sponsors to present published and unpublished clinical evidence for their technology.

Sponsors should read section 6 of the Medical Technologies Evaluation Programme methods guide on published and unpublished evidence, available from www.nice.org.uk/mt

All statements should be evidence-based and directly relevant to the scope. Reasons for deviating from the scope should be clearly stated and explained in table A1.

Sponsors are required to submit section B in advance of the full submission (for details on timelines, see the NICE document 'Guide to the Medical Technologies Evaluation Programme process', available from www.nice.org.uk/mt

7.1 Identification of studies

Published studies

7.1.1 Describe the strategies used to retrieve relevant clinical data from the published literature. Exact details of the search strategy used should be provided in section 10, appendix 1.

A systematic review and meta-analysis was carried out in accordance with the preferred reporting items for systematic reviews and meta-analysis (PRISMA) statement. The aim of this analysis was to determine the benefits of heated, humidified CO_2 insufflation (the intervention) over unheated, unhumidified insufflant gas or no insufflant gas (standard care) in patients undergoing abdominal laparoscopy or laparotomy (open surgery). The outcomes considered in this analysis include intra-operative core body temperature change (with and without adjunctive warming), post-operative core temperature change, patient reported pain as measured by Visual Analogue Scale (VAS) and analgesic use, shoulder tip pain (via VAS), total

length of hospital stay, length of stay in post-operative recovery and adverse events. PubMed was utilised to search for published studies. For adverse events the databases used were the Emergency Care Research Institute (ECRI), the Manufacturer and User Facility Device Experience (MAUDE) institute and the Medicines & Healthcare products Regulatory Agency (MRA). No limits in terms of date, language or study design were applied to the searches. Search strategies and results are provided in Appendix 1 and 2.

Laparoscopic surgery

Randomised control trials were selected by searching published literature using the search parameters: “laparo*”, “humid*”, “randomised controlled trial” and “insufflation”. Documentation of this search can be found in Appendix 1.

Open surgery

Randomised control trials were selected by searching published literature using the search parameters: “open surgery”, “humid*” and “clinical”. Documentation of this search can be found in Appendix 1.

Adverse events

Adverse events reports were selected by searching 3 adverse event databases (ECRI, MAUDE and MHRA) using the search parameters: “laparo*”, “laparot*”, and “insuflow”. Insuflow was included as a brand name for an alternative heated humidification system which is available in the United States of America. The brand name was added to capture any adverse events relevant to the therapy. “Cardia” and “CarbonAid” were also searched for as this would encapsulate any advents associated with the diffuser used to insufflate wounds during open surgery. Search details are given in Appendix 2 and documentation of these searches can be found as accompanying documents.

7.1.2 Describe the strategies used to retrieve relevant clinical data from unpublished sources.

Unpublished literature searching included a review of relevant ongoing investigations on clinicaltrials.gov and via communication with lead investigators. No limits in terms of date, language or study design were applied to the searches. Three relevant studies were included in the analysis. Two manuscripts in preparation (acknowledged under unpublished studies (Frey *et al*., in progress(7) and Mason *et al*., in progress(9)) and one poster/abstract (Weinberg *et al*., in progress(8)) were all identified via communication with lead authors. Search strategies and results are provided in Appendix 1.

In addition, 2 studies were identified in the clinicaltrials.gov database but were deemed not suitable for evaluation. Neither study investigated outcomes relevant to the scope. Documentation of this database search can be found in Appendix 1.

7.2 Study selection

Published studies

7.2.1 Complete table B1 to describe the inclusion and exclusion criteria used to select studies from the published literature. Suggested headings are listed in the table below. Other headings should be used if necessary.

Table B 1: Selection criteria used for published studies

Inclusion criteria	
Population (#1)	People undergoing open or laparoscopic abdominal surgery.
Interventions (#2)	Heated, humidified insufflation vs. no insufflation or unheated, unhumidified insufflation
Outcomes (#3)	Intra-operative core body temperature change (with and without an adjunctive warming device), patient reported pain measured by VAS and analgesic use, shoulder tip pain by VAS, total length of hospital stay, length of stay in post-operative recovery and any device related adverse events.
Study design (#4)	Randomised Control Trials or prior meta-analyses
Language restrictions	None
Search dates	No start limit – 31 October 2015
Exclusion criteria	
Population	Any non-human data: i.e. murine, fish, *in vitro*. Any non-abdominal surgeries.
Interventions	Any that did not contain the interventions above.
Outcomes	Any that did not contain temperature as an outcome
Study design	No reviews or comments.
Language restrictions	N/A
Search dates	N/A

In addition to the HumiGard™ Surgical Humidification System, we report on publications with humidification systems that are deemed comparable in therapeutic output. A table to substantiate equivalence is detailed below.

Checklist used to assess comparable devices for laparoscopic procedures

Feature	**HumiGard** Manwaring et al. (10), Sammour et al.(11), Yu et al.(12), Herrmann et al.(13), Frey at al. (FPH) (5)	**Insuflow** Klugsberger et al.(14), Savel et al.(15), Ott et al.(16), Benavides et al.(17), Champion et al.(18), Davis et al.(19), Farley et al.(20), Hamza et al.(21), Nguyen et al.(22),	**Unnamed device** (made in house) Kissler et al. (23)	**Modified LINS-1000 insufflator with unnamed device** (made in house) Mouton et al. (24)	**Thermo Visap insufflator combined with unnamed humidifier** Agaev et al. (25)	**Optitherm** (modified, Karl Storz) Klugsberger et al. (14)	**Modified Hudson oxygen humidifier** (made in house) Frey et al. (6)
Intended Use							
Used for the same clinical condition or purpose		✓	✓	✓	✓	✓	✓
Similar indications for use		✓	✓	✓	✓	✓	✓
Technical							
Similar critical performance characteristics		✓	✓	✓	✓	✓	
Used under similar conditions of use		✓	✓	✓	✓	✓	✓
Use similar deployment methods (gas enters abdomen via cannula)		✓	✓	✓	✓	✓	✓
Have similar principles of operation (humidification of gas occurs via heating of water)		✓	✓	✓	✓	✓	✓

7.2.2 Report the numbers of published studies included and excluded at each stage in an appropriate format.

Laparoscopic surgery

Forty-eight publications were identified. Fifteen studies were excluded based on population evaluation: 13 were non-human, 2 were non-abdominal studies. Six studies were excluded due to a lack of relevant interventions and 3 to irrelevant outcomes (lacked temperature measurements and/or used warm, dry gas as a comparator instead of cold, dry insufflant). Four studies were not RCT's or pre-existing meta-analyses investigating RCT's for the relevant interventions and outcomes. Of the remaining human studies 1 was a follow-up study. The remaining 19 studies were deemed suitable for evaluation. Sixteen were RCT's (10-25) and 3 were meta-analyses (26-28) (Fig 1).

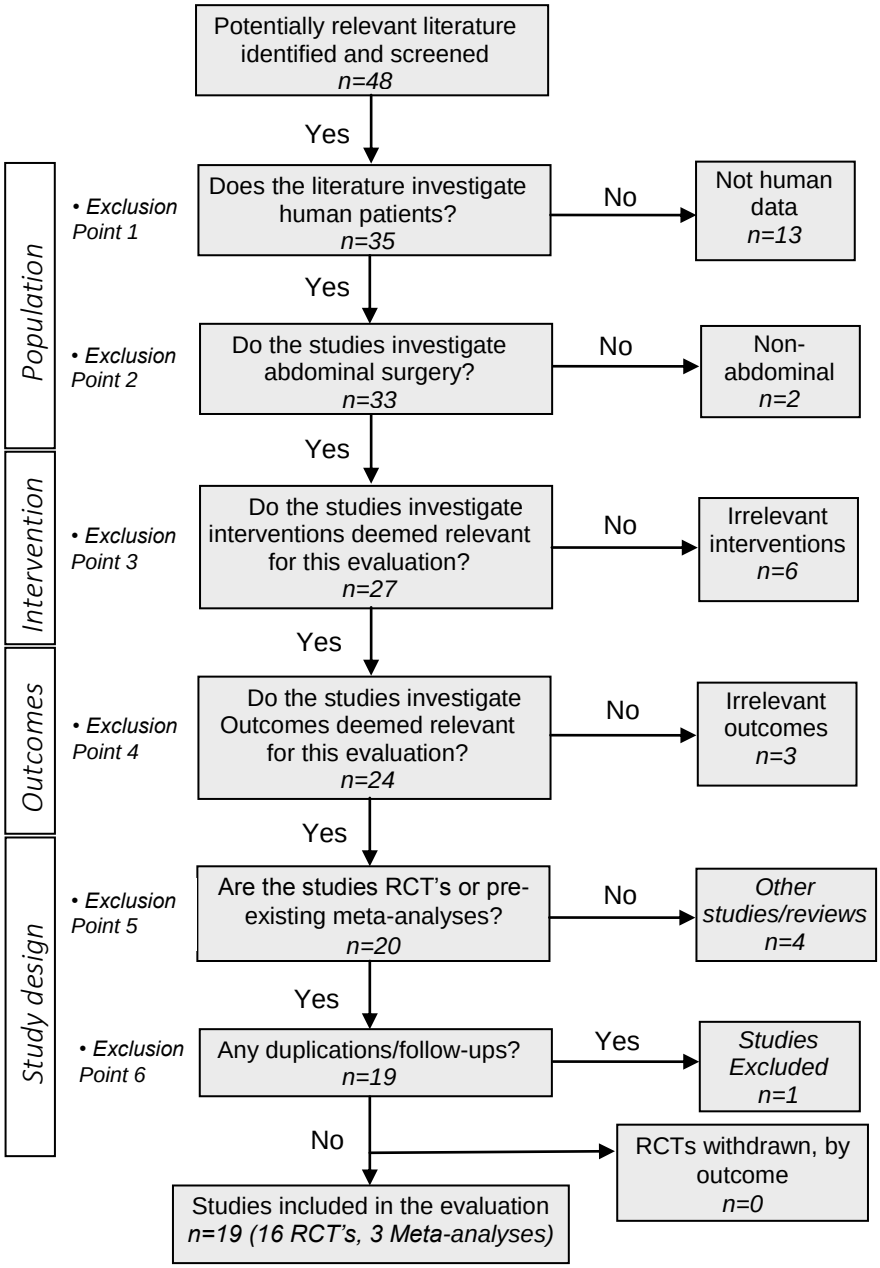


Figure 1: QUORUM diagram illustrating study selection used for laparoscopic surgery publications.

Open surgery

Twenty articles were identified in the open surgery search. Eleven studies were excluded based on population: 4 were non-human, 7 were non-abdominal studies. Four studies were excluded due to a lack of relevant

interventions and 1 to irrelevant outcomes. Two studies were not RCT's or pre-existing meta-analyses investigating RCT's for the relevant interventions and outcomes. There were no duplication/follow-up studies. The remaining 2 studies (RCT's; (5, 6)) were deemed suitable for evaluation.

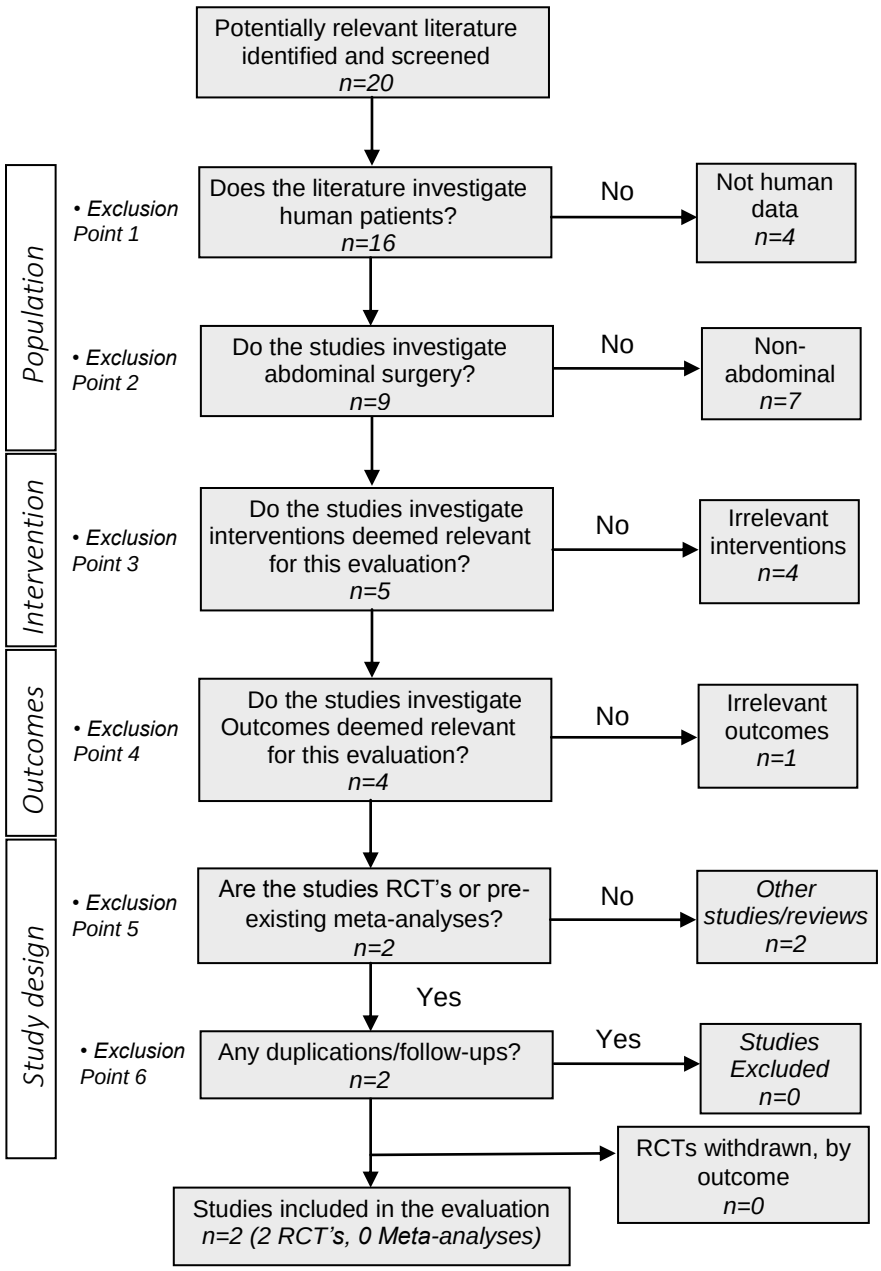


Figure 2: QUORUM diagram illustrating study selection used for open surgery publications.

Unpublished studies

7.2.3 Complete table B2 to describe the inclusion and exclusion criteria used to select studies from the unpublished literature. Suggested headings are listed in the table below. Other headings should be used if necessary.

Table B 2: Selection criteria used for unpublished studies

Inclusion criteria	
Population (#1)	People undergoing abdominal surgery, as an open or laparoscopic procedure.
Interventions (#2)	Heated, humidified insufflation vs no insufflation or unheated, unhumidified insufflation
Outcomes (#3)	Intra-operative core body temperature change (with and without an adjunctive warming device), patient reported pain measured by VAS and analgesic use, shoulder tip pain by VAS, total length of hospital stay, length of stay in post-operative recovery and incidence of SSI.
Study design (#4)	Any
Language restrictions	None
Search dates	No start limit – 31 October 2015
Exclusion criteria	
Population	Any non-human data
Interventions	Any that did not contain the interventions above
Outcomes	Any that did not contain temperature as an outcome
Study design	None
Language restrictions	None
Search dates	None

7.2.4 Report the numbers of unpublished studies included and excluded at each stage in an appropriate format.

Three studies were identified to be of interest to this evaluation. All unpublished studies that passed the selection criteria became common public knowledge through observation/communication of a poster/abstract at a conference or communication with lead authors about their manuscripts in preparation.

7.3 Complete list of relevant studies

The sponsor should provide a PDF copy of all studies included in the submission if the sponsor is either the copyright owner or has adequate copyright clearance to permit the intended use by NICE. If the sponsor does not have sufficient copyright clearance, they are asked to submit references or links only, or details of contacts for unpublished studies. For unpublished studies for which a manuscript is not available, provide a structured abstract about future journal publication. If a structured abstract is not available, the sponsor must provide a statement from the authors to verify the data provided.

7.3.1 Provide details of all published and unpublished studies identified using the selection criteria described in tables B1 and B2.

Studies used in this evaluation are listed in table B3 below. References found at the end of the document and an additional document with PubMed links can be found with supporting files.

Table B 3: List of relevant published studies

Primary study reference	Study name (acronym)	Population	Intervention	Comparator
Laparoscopic Surgery				
Agaev *et al*. 2013 (25) RCT	*The efficacy of the moisture and warmed CO_2 for laparoscopic surgery*	Human, adult	Heated, humidified insufflation	Unheated, unhumidified insufflation
Benavides *et al.* 2009 (17) RCT	*Improved outcomes for lap-banding using the Insuflow device compared with heated-only gas*	Human, adult	Heated, humidified insufflation	Unheated, unhumidified insufflation
Champion *et al.* 2006 (18) RCT	*Prospective randomised trial of heated humidified versus cold dry carbon dioxide insufflation during laparoscopic gastric bypass*	Human, adult	Heated, humidified insufflation	Unheated, unhumidified insufflation
Davis *et al.* 2006 (19) RCT	*Heating and humidifying of carbon dioxide during pneumoperitoneum is not indicated*	Human, adult	Heated, humidified insufflation	Unheated, unhumidified insufflation
Farley *et al.* 2004 (20) RCT	*Double-blind, prospective, randomised study of warmed, humidified carbon dioxide insufflation*	Human, adult	Heated, humidified insufflation	Unheated, unhumidified insufflation

	vs. standard carbon dioxide for patients undergoing laparoscopic cholecystectomy			
Hamza *et al*. 2005 (21) RCT	*Heated and humidified insufflation during laparoscopic gastric bypass surgery: effect on temperature, postoperative-pain, and recovery outcomes*	Human, adult	Heated, humidified insufflation	Unheated, unhumidified insufflation
Herrmann *et al.* 2015 (13) RCT	*Insufflation with humidified and heated carbon dioxide in short-term laparoscopy: a double-blinded randomised controlled trial*	Human, adult	Heated, humidified insufflation	Unheated, unhumidified insufflation
Kissler *et al.* 2004 (23) RCT	*Effect of humidified and heated CO_2 during gynecologic laparoscopic surgery on analgesic requirements and postoperative pain*	Human, adult	Heated, humidified insufflation	Unheated, unhumidified insufflation
Klugsberger *et al.* 2014 (14) RCT	*Warmed, humidified carbon dioxide insufflation versus standard carbon dioxide in laparoscopic cholecystectomy: a double-blinded randomised controlled trial*	Human, adult	Heated, humidified insufflation	Unheated, unhumidified insufflation
Manwaring *et al.* 2008 (10) RCT	*The effect of heated humidified carbon dioxide on postoperative pain, core temperature, and recovery times in patients having laparoscopic surgery: a randomised controlled trial*	Human, adult	Heated, humidified insufflation	Unheated, unhumidified insufflation
Mouton *et al.* 1999 (24) RCT	*A randomised controlled trial assessing the benefit of humidified insufflation gas during laparoscopic surgery*	Human, adult	Heated, humidified insufflation	Unheated, unhumidified insufflation
Nguyen *et al.* 2002 (22) RCT	*Effect of heated and humidified carbon dioxide gas on core temperature and postoperative pain*	Human, adult	Heated, humidified insufflation	Unheated, unhumidified insufflation
Ott *et al.* 1998 (16) RCT	*Reduction of laparoscopic-induced hypothermia, postoperative pain and recovery room length of stay by pre-conditioning gas with the Insuflow device: a prospective randomised controlled multi-centre study*	Human, adult	Heated, humidified insufflation	Unheated, unhumidified insufflation
Sammour *et al.* 2010 (11) RCT	*Warming and humidification of insufflation carbon dioxide in laparoscopic colonic surgery*	Human, adult	Heated, humidified insufflation	Unheated, unhumidified insufflation
Savel *et al.* 2005 (15) RCT	*Beneficial effects of humidified, warmed carbon dioxide insufflation during laparoscopic bariatric surgery: a randomised clinical trial*	Human, adult	Heated, humidified insufflation	Unheated, unhumidified insufflation
Yu *et al.* 2013 (12) RCT	*Warm, humidified carbon dioxide gas insufflation for laparoscopic appendectomy in children*	Human, paediatric	Heated, humidified insufflation	Unheated, unhumidified insufflation
Birch *et al.* 2011 (26) (Meta-analysis)	*Heated CO_2 with or without humidification for minimally invasive abdominal surgery (Review)*	Human, adult	Heated, humidified insufflation	Unheated, unhumidified insufflation
Sajid *et al.* 2008 (27) (Meta-analysis)	*Effect of heated and humidified carbon dioxide on patients after laparoscopic procedures*	Human, adult	Heated, humidified insufflation	Unheated, unhumidified insufflation
Sammour *et al.* 2008	*Meta-analysis of the effect of warm humidified insufflation in pain after*	Human, adult	Heated, humidified	Unheated, unhumidified

(28)(Meta-analysis)	*laparoscopy*		insufflation	insufflation
Open Surgery				
Frey, JM *et al.* 2012 (FPH) (5) RCT	*Local insufflation of warm humidified CO_2 increases open wound and core temperature during open colon surgery: A randomised clinical trial (Frey FPH)*	Human, adult	Heated, humidified insufflation	No insufflation
Frey, JM *et al.* 2012 (6) RCT	*Intra-operative local insufflation of warmed humidified CO_2 increases open wound and core temperatures: a randomised clinical trial (Frey)*	Human, adult	Heated, humidified insufflation	No insufflation

Table B 4: List of relevant unpublished studies

Data source	Study name (acronym)	Population	Intervention	Comparator
Frey *et al. (7)* (manuscript in preparation). Retrospective study of two RCTs (Open). Collaborator	*Relation of intra-operative temperature to postoperative mortality in open colon surgery - an analysis of two randomised controlled trials.*	Human, adult. Open surgery	Heated, humidified insufflation	No insufflation
Mason *et al. (9)* (manuscript in preparation). Cohort study Collaborator	*Peri-Operative Hypothermia and Surgical Site Infection following Peritoneal Insufflation with Warm, Humidified Carbon Dioxide during Laparoscopic Colorectal Surgery: a Cohort Study with Cost Effectiveness Analysis.*	Human, adult. Laparoscopic surgery	Heated, humidified insufflation	Unheated, unhumidified insufflation
Weinberg et al. (8) (Poster/abstract)	*Prevention of hypothermia in patients undergoing orthotopic liver transplantation using the Fisher and Paykel HumiGard open surgery humidification system: a prospective randomised pilot clinical trial*	Human, adult. Open surgery	Heated, humidified insufflation	No insufflation

7.3.2 State the rationale behind excluding any of the published studies listed in tables B3 and B4.

Papers were excluded from the search string based on the non-eligibility of criteria set in table B1. A table of excluded papers, including reasons for exclusion, are found in Appendix 1. For documentation of the search string and a list of all papers (included and excluded) please see Appendix 1.

7.4 Summary of methodology of relevant studies

7.4.1 Describe the study design and methodology for each of the published and unpublished studies using tables B5 and B6 as appropriate. A separate table should be completed for each study.

Table B 5: Summary of methodology for randomised controlled trials

Laparoscopic surgery:

Laparoscopic Surgery RCTs	Location	Heated, humidified (intervention)	Unheated, unhumidified (comparator)	Adjunctive warming device	Indication for surgery	Mean age (years)	Operating time (mean in minutes)	Randomisation	Double blinding	Statistical tests	Withdrawals/loss to follow-up/exclusions	Reported outcomes (**primary in bold**)
Agaev *et al*. 2013 (25)	Russia	66	84	Anaesthetic's discretion	Cholecystectomy/fundoplication	52	49	Yes: not stated	Not stated	*t* test, Wilcoxon test, X^2 test, Mantel-Haenszel test	Not stated	**- Intra-operative and post-operative core temperature (°C)** - Postoperative pain (analgesic use: recovery)
Benavides *et al.* 2009 (17)	USA	38	35	No	Gastric bypass	Range 21-61 years	28 (intervention), 31 (control)	Yes: Computerized	Yes	Lilliefors test, Wilcoxon test,	Not stated	**- Post-operative pain (VAS 12-24hrs)** **- Post-operative pain (analgesic use: recovery, day 1, day 2, day 3)** - Recovery room time (hours)
Champion *et al.* 2006 (18)	USA	25	25	No	Gastric bypass	43	61.7	Yes (inadequate): Blind Drawing	Yes (inadequate)	Chi-square (X^2) test with Greenhouse Geisser correction	Not stated	**- Intra-operative core temperature (°C)** - Post-operative pain (VAS scores and analgesic use: 4-6, 3-12, 24 and 48 hours post-surgery) - Recovery room time (hours) - Length of hospital stay (days)
Davis *et al.* 2006 (19)	USA	11	11	No	Gastric bypass	42	84	Yes: Block Fashion	Yes	t-test/ANOVA, Kruskal-Wallis test	Not stated	**- Intra-operative core temperature (°C)** - Post-operative pain (VAS scores and analgesic use: day 1, 2) - Recovery room time (hours) - Length of hospital stay (days)
Farley *et al.* 2004 (20)	USA	49	52	Anaesthetic's discretion	Laparoscopic cholecystectomy	52	91	Yes: Computerized	Yes	Two-sample t-test, X^2 test, Wilcoxon rank sum test	16	**- Intra-operative and post-operative core temperature (°C)** - Post-operative pain (VAS scores and analgesic use: recovery, 4-6hrs, 3-12hrs post-surgery) - Recovery room time (hours) - Length of hospital stay (days)
Hamza *et al*. 2005 (21)	USA	23	21	Warm cotton blankets	Gastric bypass	44	114	Yes: Computerized	Yes	ANOVA + Bonferroni's Correction, Chi-square test, Fisher exact test	6	**- Intra-operative and post-operative core temperature (°C)** - Post-operative pain (VAS scores and analgesic use at 15 minute intervals while in post-anaesthesia care unit) - Recovery time (hours) -Length of hospital stay (days)

Herrmann *et al.* 2015 (13)	Germany	48	49	Warming blanket	Gynaecological	47	84.1	Yes: Block Fashion	Yes	ANOVA with Greenhouse-Geiser's epsilon correction, Mann–Whitney U test	7	**- Intra-operative core temperature (°C)** - Post-operative pain (VAS total) - Post-operative pain (analgesic use: recovery, day 1, day 2) - Length of hospital stay (days)
Kissler *et al.* 2004 (23)	Germany	17	19	No	Gynaecological	36.5	84.5	Yes: Computerized	Yes (inadequate)	Mann-Whitney U-test, X^2 test	Not stated	**- Intra-operative core temperature (°C)**
Klugsberger *et al.* 2014 (14)	Austria	81	67	Anaesthetic's discretion	Laparoscopic cholecystectomy	56	63.5	Yes: Envelopes	Yes	t test, Mann–Whitney U test,	Not stated	**- Intra-operative core temperature (°C)** - Postoperative pain (VAS 4-6hrs, 24hrs)
Manwaring *et al.* 2008 (10)	Australia	30	30	Yes	Gynaecological	30	48.2	Yes: Random number generator	Yes	X^2 test, paired/unpaired t-test	Not stated	- **Intra-operative core temperature (°C)** - Pain: analgesic use recovery - Pain (VAS) recovery and 24hrs - Recovery room time (hours)
Mouton *et al.* 1999 (24)	Australia	20	20	No	cholecystectomy	Range 23-89 years	Not stated	Yes: not stated	No	X^2 test, paired/unpaired t-test	8	- **Intra-operative core temperature (°C)** - Post-operative pain (VAS scores 3-12hrs, 24hrs and 48hrs) -Length of hospital stay
Nguyen *et al.* 2002 (22)	USA	10	10	Upper body warming blanket	Nissen fundoplication	44	108	Yes (inadequate): Envelopes	No	Fisher's exact test, ANOVA, paired/unpaired t-test	Not stated	- **Intra-operative core temperature (°C)** - Post-operative pain (VAS score 24hrs) - Post-operative pain (analgesic use day 1) - Length of hospital stay
Ott *et al.* 1998 (16)	USA	31	30	No	Gynaecological	Range 18-48 years	Not stated	Yes: computerized	Yes (inadequate)	paired t-test	Not stated	- **Intra-operative core temperature (°C)** - Post-operative pain (VAS scores 4-6hrs, 24hrs) - Recovery room time (hours)
Sammour *et al.* 2010 (11)	New Zealand	41	41	Forced air blanket	Colonic resection	Median 70	180.5	Yes: Computerized	Yes	Shapiro-Wilk test, Fisher's exact test or X^2 test, Mann-Whitney U test	8	- **Intra-operative core temperature (°C)** - Post-operative pain (VAS 24hrs) - Post-operative pain (analgesic use recovery, day 1, day 2) - Length of hospital stay (days)
Savel *et al.* 2005 (15)	USA	15	15	Anaesthetic's discretion	Gastric bypass	40	89	Yes: Computerized	Yes (inadequate)	Fisher's exact test, Mann-Whitney U test, Welch Student's t-test	Not stated	- **Intra-operative core temperature (°C)** **- Postoperative pain** (VAS scores and analgesic use: 4-6hrs, 3-12hrs, 24hrs and 48 hours). -Post-operative pain (analgesic use: day 1, day 2) - Hospital length of stay (days)
Yu *et al.* 2013 (12)	New Zealand	95	95	Anaesthetic's discretion	Appendectomy	Range 5-14 years	65	Yes: Computerized envelopes	Yes	Mann-Whitney U tests, t-tests, X^2 test	5	**- Intra-operative core temperature (°C)** - Postoperative pain (analgesic use: recovery, day 1, day 2). - Length of hospital stay (days)

Open surgery:

Open Surgery RCTs	Location	Heated, humidified (intervention)	No insufflation (comparator)	Adjunctive warming device	Indication for surgery	Mean age (years)	Operating time (mean in minutes)	Randomisation	Double blinding	Statistical tests	Withdrawals/loss to follow-up/exclusions	Reported outcomes (primary in **bold**)
Frey, JM *et al.* 2012 (FPH device) (5)	Sweden	40	39	Warming blanket (upper and lower body)	Open colon surgery (various)	63.5	181.5 (intervention), 217 (control)	Yes: envelopes	Yes (inadequate)	Student t test, X^2 test or Fisher's exact test, Mann–Whitney U test or Wilcoxon test	4	**- Intra-operative temperature: core and wound (°C)** - Length of hospital stay (days)
Frey, JM *et al.* 2012 (6)	Sweden	38	36	Warming blanket (upper and lower body)	Open colon surgery (various)	63.5	219 (intervention), 205(control)	Yes: envelopes	Yes (inadequate)	Student's t-test, X^2 test, Fisher's exact test, Mann–Whitney U-test or Wilcoxon test	6	**- Intra-operative temperature: core and wound (°C)** - Length of hospital stay (days)

Unpublished literature:

Unpublished studies	Location	Heated, humidified (intervention)	Unheated, unhumidified OR no Insufl. (comparator)	Adjunctive warming device	Indication for surgery	Mean age (years)	Operating time (mean in minutes)	Randomisation	Double blinding	Statistical tests	Withdrawals/loss to follow-up/exclusions	Reported outcomes (primary in **bold**)
Frey, JM *et al. (7)* Retro. analysis (manuscript in progress)	Sweden	80	78	Not stated	Open colon surgery (various)	63 (median)	218	Yes (details not given)	Not stated	Univariate cox regression (survival), Chi-square tests/ t-tests (temp).	0	**- Intra-operative temperature: core and wound (°C)** **- Mortality: correlated with temperature**
Mason *et al.* (9) (manuscript in progress)	United Kingdom	123	123	Forced-air warming blanket	Laparoscopic colorectal resection	68	213	N/A (retrospective cohort)	No (retrospective cohort)	Pearson's X^2 test, Fishers exact test, Student t-test	N/A (retrospective cohort)	**- Temperature: Hypothermia (<36 °C) odds ratio** **- Incidence of SSI if hypothermic** - Length of hospital stay **-** Cost effectiveness analysis
Weinberg *et al. (8)*(Abstract/Poster)	Australia	11	11	Heating mattress and forced air blanket	Orthotopic liver transplant	Not stated	Not stated	Yes (details not given)	Not stated	Not stated	Not stated	**- Temperature: core (°C) - Varying measurement types**

7.4.2 Provide details on data from any single study that have been drawn from more than one source (for example a poster and unpublished report) and/or when trials are linked this should be made clear (for example, an open-label extension to randomised controlled trial).

One study Mason *et al*. (9) was reported from two sources. A published abstract and the unpublished manuscript in preparation (29). Data from both sources are discussed in section 7.8.2 and the draft manuscript is attached. There are two sources of data available for Frey *et al*. a published abstract and an unpublished manuscript in preparation (7). In this case, data is reported from the unpublished manuscript as it contains information from the final dataset. However the published abstract which is in the public domain accompanies this document.

7.4.3 Highlight any differences between patient populations and methodology in all included studies.

For laparoscopic studies a total of 16 RCTs were investigated. Of these 5 were gynaecological laparoscopies, 5 were gastric bypasses, 3 were cholecystectomies, 1 colonic resection, 1 Nissen fundoplication, and 1 appendectomy. A total of 1317 patients were included. As detailed in Table B5, all but 1 study was carried out on adults aged between 23 and 89. One study by Yu *et al.* (12) investigated the effects of heated, humidified insufflation on children (aged 5-14 years). In addition, 6 of the studies were female only (gynaecological) while the remaining 12 studies were both genders. For open studies both RCT's were done on open colorectal surgeries, including, but not limited to, colectomy, partial small bowel resection, new ileostomy, Urinary bladder resection, cholecystectomy, nephrectomy and appendectomy. Both studies were mixed gender.

7.4.4 Provide details of any subgroup analyses that were undertaken in the studies included in section 7.4.1. Specify the rationale and state whether these analyses were pre-planned or post-hoc.

A subgroup analysis was undertaken on laparoscopic studies reporting changes in temperature with adjunctive warming. The rationale for this subgroup analysis was to determine if the addition of adjunctive warming alongside heated, humidified insufflation had any effect on core body temperature during surgery. This subgroup analysis was pre-planned.

7.4.5 If applicable, provide details of the numbers of patients who were eligible to enter the study(s), randomised, and allocated to each treatment in an appropriate format.

For details please refer to table B5.

7.4.6 If applicable provide details of and the rationale for, patients that were lost to follow-up or withdrew from the studies.

A total of 8 publications reported exclusions, 6 laparoscopic RCT's and 2 open RCT's. The numbers are given in table B5 above and the rationale detailed in table B6 below:

Table B 6: Rationale for patient exclusion

Studies documented withdrawals/exclusions	Reasons
Laparoscopic surgery	
Farley *et al.* 2004 (20)	Eleven converted to open cholecystectomy, 3 underwent an additional operation that increased the duration of the procedure (2 patients umbilical hernia procedure; 1 patient had extensive lysis of adhesions), 2 patients had the insuflow device removed during surgery.
Hamza *et al*. 2005 (21)	Four converted to open procedures, 2 patients in the control group were "rescued" during the operation with a forced air warming blanket when their core body temperature decreased below 34 (°C).
Mouton *et al.* 1999 (24)	Eight patients (four patients from each group) were excluded from postoperative pain assessment and follow-up due to conversion to open cholecystectomy,

	postoperative pancreatitis, or postoperative hematoma.
Sammour *et al.* 2010 (11)	In the experimental group: two patients had a rectal lesion below 15 cm found intra-operatively, 2 patients did not have any colon resected despite initial plan, 1 patient had an unplanned diverting ileostomy performed due to a positive anastomotic air-leak test, and in 1 case the investigator was unblended when a nurse inadvertently lifted the plastic cover off the humidifier during surgery. In the control group: 1 patient did not have their colon resected and one patient had an allergic reaction to the anaesthetic.
Yu *et al.* 2013 (12)	Five excluded from data analysis because of major protocol violation, and the study's exclusion criteria. Specifics not given but due to one of either: 1) Diagnosis of mental retardation, developmental delay, neuromuscular impairment, attention-deficit disorder, chronic pain, or any psychiatric illness. (2) Previous abdominal surgery and/or the presence of any abdominal prosthesis (e.g., gastrostomy). (3) Immunosuppression including chronic use of, or dependency on, steroids. (4) Unable to speak and read English. (5) Partially sighted or blind. (6) Appendectomy not performed as planned. (7) Significant violation of study analgesia and anaesthetic protocol, including instalment of a regional nerve block or contraindication to morphine. (8) Written consent not obtained pre-operatively from participant and a parent or legal guardian.
Herrmann *et al.* 2015 (13)	Four patients in the control arm dropped out: 1 laparoscopy not possible due to obesity, 1 allergic reaction to morphine, 1 due to sever endometriosis and 1 due to severe adhesions. 3 patients in the experimental arm dropped out: 1 was un-blinded by study personnel, 2 had postoperative bleeding that required reoperation on the postoperative day.
Open surgery	
Frey, JM *et al*. 2012 (FPH device) (5)	One patient randomised to the control group and 2 patients randomised to the heated humidified CO_2 group were excluded due to a core temperature of ≥37.5°C measured after arrival to the operating room. One patient randomised to the control group was excluded from the study because the surgeon suddenly refused temperature measurements to be performed during surgery.
Frey, JM *et al.* 2012 (6)	Two patients (one from each group) were excluded due to the technical quality of the thermographic images which did not allow temperature measurement. One patient randomised to the control group was excluded because of pre-operative fever (38.0 °C). One patient originally randomised to the CO_2 group, who underwent liver resection and had most of the wound cavity covered with a plastic film during the procedure. Two patients were excluded, one from each group, because they were accidentally found to be lying on a warm air mattress intra-operatively (KANMED WarmCloud, KANMED AB, Bromma, Sweden), and one of them received first-degree

	burns on one of his heels. This heating device was thereafter not used in our department.

7.5 Critical appraisal of relevant studies

Quality assessment tables for each study are shown in tables B7 and B8 below.

Table B 7: Critical appraisal of relevant studies

	Questions and how they were addressed in the study						
Studies	**Appropriate randomisation?**	**Adequate concealment of treatment allocation?**	**Groups similar at outset of study?**	**Blinding adequate?**	**Unexpected imbalances in drop-outs between groups?**	**Evidence authors measured more outcomes than reported?**	**Did the analysis include an intention-to-treat analysis? Appropriate?**
Laparoscopic surgery							
Agaev *et al.* 2013 (25)	YES - Randomised by computer model after induction of anaesthesia.	YES - Only one un-blinded nurse knew the intervention allocation.	YES - No significant differences in baseline characteristics.	YES - Only one un-blinded nurse knew the allocation. All other staff were blinded.	NOT CLEAR - In the case of access conversion to laparotomy, the patients were excluded from the study. The number of drop outs and/or exclusions were not detailed	NO - Reported outcomes met the demand of the aims in question. They did not mention any non-formally analysed outcomes.	NO - Per protocol analysis.
Benavides *et al.* 2009 (17)	YES - Computerized randomisation, random number generator.	YES (NOT CLEAR) - Stated but details not given	YES (NOT CLEAR) - Data regarding past abdominal surgery, comorbidities, demographics, and anthropometry was obtained pre-operatively but not reported.	YES - Group assignment was unknown by any of the investigators throughout the entire study	YES - Drop outs and/or exclusions detailed in table 1.4.6. Imbalance was not corrected for.	NO - Reported outcomes met the demand of the aims in question. They did not mention any non-formally analysed outcomes.	NO - Per protocol analysis.
Champion *et al.* 2006 (18)	YES - Blind drawing by an impartial third party.	YES - The nurses who recorded the pain score was blinded	YES - No significant differences in baseline characteristics.	NO -The study was not double blinded however the patient and nurse reviewers which scored the analogue pain scale were unaware of the type of insufflation. The surgeons were aware of the intervention group, however all subjective measures taken in this investigation had appropriate blinding. Measures that may be effected by risk of bias are not included in this analysis but include lens cleaning. Nurses recording intra-operative measures were blinded as were the nurses recording post-operative pain scores and analgesic usage. The study was reported to be free of other problems that could put it at high risk of bias. The patients were assigned to the operating schedule in order of approval for surgery with no regard to any other factor. A drawing was held to determine	NO -Drop outs were not described. No exclusions occurred.	NO - Reported outcomes met the demand of the aims in question. They did not mention any non-formally analysed outcomes.	NO - Per protocol analysis

				which type of insufflation was to be used on the first case, after which the insufflation method was alternated for the next 99 cases consecutively, with no interruption of exclusions			
Davis *et al.* (19)	YES - Patients were randomised in a block fashion by assignment of a unique patient number for each, followed by random generation of the patients into four study groups of equal size.	YES - The patients then were randomised in block fashion by assignment of a unique patient number for each, followed by random generation of the patients into four study groups of equal size. The results of this randomisation were sealed into envelopes. A research nurse opened the envelopes on the morning of the procedure, then completed and randomisation and consent.	YES - No significant differences in baseline characteristics.	NO - Single blinded. The operating staff were not blinded to intervention allocation however outcome measures included in this analysis (Core temperature) are objective and unaffected by bias. Risk of bias relates to the objective measures included in the investigation such as lens fogging. A single blinded examiner assessed histology.	NOT CLEAR - Drop outs and/or exclusions were not detailed	NO - Reported outcomes met the demand of the aims in question. They did not mention any non-formally analysed outcomes.	NO - Per protocol analysis
Farley et al. (20)	YES - Computer model randomisation	YES - Results of the computer randomisation were revealed to the surgical scrub nurse at the time of anaesthetic induction.	YES - No significant differences in baseline characteristics.	YES - Double blind. Patients, surgeons, operating staff, floor staff and coordinators were all masked	NOT CLEAR - Double blind. Patients, surgeons, operating staff, floor staff and coordinators were all masked	NO - Reported outcomes met the demand of the aims in question. They did not mention any non-formally analysed outcomes.	NO - Per protocol analysis
Hamza *et al.* 2005 (21)	YES - Computer generated number sequence	YES - A non-study operating nurse connected to device. The intervention group was concealed from the operating surgeons by covering the indicator light on the heating unit and the plastic tubing connecting the unit to the patient.	YES - There were no significant differences in patient demographics.	YES - Patients, surgeons, operating staff, floor staff and coordinators were all blinded.	YES -4 Patients were converted to open procedures and excluded from statistical analysis. Two patients in the control group were “rescued” during the operation with a forced air warming blanket when their core body temperature decreased less than 34°C and were excluded from analysis. Subsequently the experimental arm had 2 fewer patients that the control arm that was not adjusted for.	NO - Reported outcomes met the demand of the aims in question. They did not mention any non-formally analysed outcomes.	NO - Per protocol analysis.

Studies	Appropriate randomisation?	Adequate concealment of treatment allocation?	Groups similar at outset of study?	Blinding adequate?	Unexpected imbalances in drop-outs between groups?	Evidence authors measured more outcomes than reported?	Did the analysis include an intention-to-treat analysis? Appropriate?
Herrmann *et al.* 2015 (13)	YES - Permuted block randomisation with block length of 4 and 6 was used.	YES - Opaque sealed envelopes opened before operation.	YES - No significant differences in baseline characteristics. All patients were undergoing laparoscopic gynaecological surgery. All women.	NO - No the surgeon was not blinded to the intervention allocation. Measures recorded in theatre were objective. The recording of pain was double blinded. All persons involved in the study were expressly advised that neither the patients nor the study nurse may obtain knowledge of the type of the intervention given.	YES - Drop outs and/or exclusions detailed in table 1.4.6. Groups were not balanced at analysis (n=1 difference).	NO - Reported outcomes met the demand of the aims in question. They did not mention any non-formally analysed outcomes.	NO - Per protocol analysis.
Kissler *et al.* 2004 (23)	YES - Computer generated randomisation	YES - Patients, data analyst, and interviewer were all blinded to randomisation.	YES - No significant differences in baseline characteristics.	NO - Double blind Patients, data analyst and interviewer were all blinded to randomisation. It is not clear if the surgeon was blinded to the allocation. The risk of bias if the surgeon was unblended is low as the operative measures in the investigation were objective.	NOT CLEAR-Cases that took less than 30 minutes were excluded from the study. The number excluded is not reported.	NO - Reported outcomes met the demand of the aims in question. They did not mention any non-formally analysed outcomes.	NO - Per protocol analysis.
Klugsberger *et al.* 2014 (14)	YES - Envelope randomisation	YES - Opaque sealed envelopes opened before operation	YES - No significant differences in baseline characteristics.	YES - The patient, study investigators, surgeon, anaesthetics, theatre personnel and the nursing staff for intra- and postoperative care of participants were all blinded. Only the secretary was privy to which method of gas was being used.	YES - Patients converted intra-operative to open cholecystectomy or those undergoing a concomitant procedure were excluded from the study. Other Criteria for exclusion were irregularities of the study protocol (absence of rectal probe, missing consent form, and conversion to open cholecystectomy) and patients with acute cholecystitis. Adjustment not stated.	NO - Reported outcomes met the demand of the aims in question. They did not mention any non-formally analysed outcomes.	NO - Per protocol analysis.
Manwaring *et al.* 2008 (10)	YES- Random number generator used for randomisation	YES- Randomly generated numbers were sealed in sequential opaque envelopes.	YES - No significant differences in baseline characteristics.	NO - Operating staff were not blind to allocation. All nursing staff recording subjective variables were blinded to the nature of insufflation gas used. Risk of bias in theatre is low as operative variables measured were objective measures.	NOT CLEAR- Drop outs and/or exclusions were not detailed. Operations that continued more than 90 minutes were excluded from the study the number that met this criteria was not detailed. Both arms had 30 women each at the end of the study.	NO - Reported outcomes met the demand of the aims in question. They did not mention any non-formally analysed outcomes.	NO - Per protocol analysis.
Mouton *et al.* 1999 (24)	YES (UNCLEAR)- No description	NOT CLEAR-No description	YES- The two patient groups were no different in terms of age (23–89 years), gender, previous abdominal surgery.	NOT CLEAR- No description	NO - Eight patients (four patients from each group) were excluded from postoperative pain assessment and follow-up due to conversion to open cholecystectomy, postoperative pancreatitis, or postoperative	NO - Reported outcomes met the demand of the aims in question. They did not mention any non-formally analysed outcomes.	NO - Per protocol analysis.

					hematoma. Equal exclusion.		
Nguyen *et al.* 2002 (22)	YES - Sealed envelopes, Intra-operative randomisation	YES - Sealed envelopes	YES - No statistical difference in baseline characteristics	NOT CLEAR - No details are given about the blinding procedure	NOT CLEAR - Drop outs and/or exclusions were not detailed	NO - Reported outcomes met the demand of the aims in question. They did not mention any non-formally analysed outcomes.	NO - Per protocol analysis.
Ott *et al*. 1998 (16)	YES (UNCLEAR) - No details given.	NOT CLEAR - No details given	YES - No significant differences in baseline characteristics.	NOT CLEAR - No details are given about the blinding procedure	NOT CLEAR - Drop outs and/or exclusions were not detailed	NO - Reported outcomes met the demand of the aims in question. They did not mention any non-formally analysed outcomes.	NO - Per protocol analysis. 88.9% of questionnaires were completed but there is no description on what was done with the missing data.
Sammour *et al.* 2010 (11)	YES - Random number generator. Randomisation was stratified by hospital to ensure equal distribution of intervention and control group patients between these, and minimize bias due to differences in pre-, intra-, and postoperative protocols between sites. The randomisation sequence was generated by a third party not involved in the study.	YES -Opaque numbered envelopes. The humidifier connected to the insufflation apparatus and power supply regardless of allocation, and covered with a specially designed plastic casing which concealed its LCD screen and water chamber	YES - No significant differences in baseline characteristics.	YES - Randomisation sequence was generated by a third party not involved in the study. The Patient, study investigators, surgeon and medical staff were all blinded to patient allocation. Very stringent measures taken by an unblended research assistant, who did not know the patient, was taken to ensure the humidifier was set up without noise or unblinding to the persons involved in the study. The blinding protocol was practiced prior to study implementation. Data analysis was blinded.	YES - Six patients in the experiment arm and two from the control arm as detailed in table 1.4.6. The imbalance to the groups was not corrected for.	YES - They report that the core body temperature was similar in both groups at all-time points when it was measured (data not shown). The instead reported the start, final, minimum, maximum and mean temperature which is more suitable. In addition they state “data not shown” for morphine equivalent usage per kilogram of patient weight. They state it was not different between groups (data not shown). Intra-operative core temperature was measures every 15 minutes but only the change in temperature between the start and end of the procedure, the minimum, maximum, and mean/median temperatures reported. No area under curve was reported.	YES - Intra-operative conversions were included as intention to treat. Conversion to open colectomy was at the discretion of the individual surgeon for concerns of patient safety, technical difficulties, or associated unexpected conditions requiring intervention by laparotomy. Conversions were recorded and analysed in the allocated group on an intention to treat basis. 2 were converted in the study group and 6 in the control group. No unplanned subgroup or adjusted analyses were performed.

Studies	Appropriate randomisation?	Adequate concealment of treatment allocation?	Groups similar at outset of study?	Blinding adequate?	Unexpected imbalances in drop-outs between groups?	Evidence authors measured more outcomes than reported?	Did the analysis include an intention-to-treat analysis? Appropriate?
Savel *et al*. 2005 (15)	YES - Patients randomised at the time of enrolment. Specifics not detailed.	NOT CLEAR - No details on how the clinicians were blinded is not given	YES - No significant differences in baseline characteristics.	YES - All study participants and clinicians were blinded other than one of the research physicians were blinded to the presence or absence of the Insuflow device.	NOT CLEAR - Drop outs and/or exclusions were not detailed	NO - Reported outcomes met the demand of the aims in question. They did not mention any non-formally analysed outcomes.	NO - Per protocol analysis.
Yu *et al*. 2013 (12)	YES - Patients randomised using computer randomisation	YES -Sealed envelopes opened intra-operatively. A commissioned opaque plastic cover was designed to conceal the surgical Humidifier from view during each study procedure. It covered the front LCD screen and the water chamber so that it was impossible for theatre occupants to tell whether the device was switched on and whether the chamber contained water	YES - No significant differences in baseline characteristics.	YES - The patient, study investigators, surgeon, anaesthetics, theatre personnel and the nursing staff for intra- and postoperative care of participants were all blinded.	NO - Drop outs and/or exclusions detailed in table 1.4.6. Groups were balanced at analysis.	YES - Authors report data not shown for data describing self-evaluated postoperative recovery which showed no differences between groups at day 10. Authors report recording temperature at 10 minute intervals but only report on Start of procedure, Absolute difference between start and end, Maximum during procedure, Minimum during procedure, Difference between maximum and minimum, Mean during procedure. No analysis of the area under the curve was completed.	NO - Per protocol analysis.

Open surgery							
Studies	**Appropriate randomisation?**	**Adequate concealment of treatment allocation?**	**Groups similar at outset of study?**	**Blinding adequate?**	**Unexpected imbalances in drop-outs between groups?**	**Evidence authors measured more outcomes than reported?**	**Did the analysis include an intention-to-treat analysis? Appropriate?**
Frey, JM *et al.* 2012 (FPH device) (5)	YES - Sealed envelopes with random allocation sequence	YES - Opaque sealed envelopes opened before operation	YES - No significant differences in baseline characteristics.	YES (INADEQUATE) - The patient, study investigators and the nursing staff for postoperative care of participants were all blinded but the surgeon, anaesthetics and theatre personnel were not blinded given the intervention was obvious in an open surgical setting. Risk of bias is low as operative measures are objective.	YES - Drop outs and/or exclusions detailed in table 1.4.6. Groups were imbalanced at analysis.	NO - Reported outcomes met the demand of the aims in question. They did not mention any non-formally analysed outcomes.	NO - Per protocol analysis.
Frey, JM *et al.* 2012 (6)	YES - Sealed envelopes with random allocation sequence	YES - Opaque sealed envelopes opened before operation	YES- No significant differences in baseline characteristics.	YES - The patient, study investigators and the nursing staff for postoperative care of participants were all blinded but the surgeon, anaesthetics and theatre personnel were not blinded given the intervention was obvious in an open surgical setting.	YES -Six patients were excluded before statistical analysis, three from the CO_2 group and three from the control group, leaving 74 to be analysed. Groups were imbalanced at analysis.	NO - Reported outcomes met the demand of the aims in question. They did not mention any non-formally analysed outcomes.	NO - Per protocol analysis.
Unpublished studies							
Frey *et al*. (7) (Manuscript in prep.), Retrospective analysis	YES - Both studies used sealed envelopes with random allocation sequence	YES - Both studies used opaque sealed envelopes opened before operation	YES - Both studies had no significant differences in baseline characteristics.	YES - In both studies the patient, study investigators and the nursing staff for postoperative care of participants were all blinded but the surgeon, anaesthetics and theatre personnel were not blinded given the intervention was obvious in an open surgical setting.	YES - In both studies there were unexpected drop outs which are detailed in the two tables directly above (both open RCT studies)	NO - Reported outcomes met the demand of the aims in question. They did not mention any non-formally analysed outcomes.	YES (retrospective) - Groups were analysed using Students t-test, Chi-squared test. Univariate and Multivariate analyses was done with Cox regression.
Weinberg *et al (8).* (abstract/poster).	Not clear	Not clear	Not clear	Not clear	Not clear	Not clear	Not clear

Table B 8: Critical appraisal of observational studies

	Questions and how they were addressed in the study						
Studies	**Acceptable recruitment of cohort?**	**Accurate measurement of exposure to minimise bias?**	**Accurate measurement of outcome to minimise bias?**	**Have the authors identified all important confounding factors?**	**Have the authors taken account of the confounding factors in the design and/or analysis?**	**Was the follow-up of patients complete?**	**How precise are the results?**
Mason *et al.* (9) (manuscript in preparation)	YES - Patient and operative data were collected from medical and computer records by a research scientist who was independent of the clinical care but was not formally blinded.	YES - Operative time was defined as the duration in minutes from initial surgical incision to the application of wound dressings. Core body temperatures were routinely measured tympanically on arrival to the post-anaesthetic recovery suite. Hypothermia was defined as a core body temperature of less than 36 degrees Celsius. SSI was defined using objective clinical and microbiological criteria, in accordance with guidance from Public Health England (2013). Surveillance for SSI was conducted by consultant surgeons, senior surgical nurses and infection control nurses, all trained in SSI identification.	YES -as per left	YES - Beyond the experimental intervention, both groups received identical pre-, peri - and post-operative care. Groups received no additional intervention that may influence the outcomes of interest and there was continuity in senior surgical personnel throughout the study period.	NOT CLEAR	YES - Post-operatively all patients were admitted to a dedicated elective surgical ward or a high dependency suite based on clinical need, with at least twice daily dedicated rounds from an enhanced recovery surgical team. For SSI's, all infections were identified within 30 days and included in the analysis, whether the SSI was diagnosed on a re-admission or at clinic follow-up.	PRECISE - Authors report odds ratios with 95% CI's along with p-values.

7.6 Results of the relevant studies

7.6.1 Complete a results table for each study with all relevant outcome measures pertinent to the decision problem. A suggested format is given in table B9.

The following tables detail specifics for each included study: Collective analyses follow in section 7.8. Values and 95% confidence intervals (CI) shown are for mean differences and not standardised mean differences (which are used in subsequent meta-analyses). Categorical data are shown as relative risk (RR) with a 95% CI while continuous data are shown as means with a 95% confidence interval. P-values and confidence intervals are given as per the values given in the literature. If no standard error of the mean (s.e.m) was provided then it is listed as “not given” unless a value was retrieved from the communication with the authors as indicated in the Birch *et al.* Cochrane meta-analysis (26).

Table B 9: Tables of results for relevant studies

Study name		Agaev *et al*. 2013 (25)
Size of study groups	**Treatment**	66
	Control	84
Study duration	**Time unit**	N/A; RCT
Type of analysis	**Intention-to - treat/per protocol**	Per protocol
Outcome 1: primary	**Name**	**Core temperature change (primary)**
	Unit	°C, mean differences
Effect size	**Value**	-0.55
	95% CI	Not given
Statistical test	**Type**	Two-sampled t-test
	p value	P<0.05
Outcome : secondary	**Name**	**Post-operative core temperature change**
	Unit	°C, mean differences
Effect size	**Value**	-0.99 (ICU admission), -0.80 (ICU 1hr), -0.20 (ICU 4hr)

	95% CI	Not given
Statistical test	**Type**	Two-sampled t-test
	p value	P<0.5 (ICU admission, 1hr and 4hr)
Outcome 3: secondary	**Name**	**Post-operative analgesic use**
	Unit	mean difference
Effect size	**Value**	-1.40 (recovery),
	95% CI	not given
Statistical test	**Type**	Mantel-Haenszel test
	p value	P<0.3, NS (recovery),
Comments		Agaev *et al.* carried out a RCT on 150 patients undergoing laparoscopic cholecystectomy/fundoplication were randomised into unheated, unhumidified insufflation or intervention insufflation groups. This study had a majority of women (109) compared with males (41) which were randomly allocated into either group. Patients receiving intervention showed significantly reduced core temperature loss and post-operative pain for either surgery compared to standard care insufflated patients.

Study name		Benavides *et al.* 2009 (17)
Size of study groups	**Treatment**	38
	Control	35
Study duration	**Time unit**	N/A; RCT
Type of analysis	**Intention-to - treat/per protocol**	Per protocol
Outcome 1: secondary	**Name**	**Post-operative shoulder tip VAS pain score**
	Unit	VAS, mean difference
Effect size	**Value**	-2.90
	95% CI	Not given
Statistical test	**Type**	variances pooled from Wilcoxon rank sum test
	p value	P<0.01
Outcome 2: secondary	**Name**	**Post-operative pain (analgesic use)**
	Unit	Morphine equivalent daily dose (MEDD) per kg; mean difference
Effect size	**Value**	-2.60, (recovery), -2.2 (1 day), -2.30 (2 days), -1.9 (3 days)
	95% CI	not given
Statistical	**Type**	t-test (variances pooled from Wilcoxon rank sum

test		test)
	p value	P<0.01 (recovery), P<0.05 (day 1), P<0.05 (day 2), P<0.05 (day 3)
Outcome 3: secondary	**Name**	**Recovery room time**
	Unit	Hours, mean difference
Effect size	**Value**	-15.00
	95% CI	Not given
Statistical test	**Type**	t-test (variances pooled from Lilliefors test)
	p value	P<0.05
Comments		Benavides *et al.* undertook a RCT on 75 patients receiving laparoscopic gastric bypass surgery. Patients were randomly allocated into intervention or unheated, unhumidified insufflation groups where the primary objective was post-operative pain. The authors report patients receiving heated, humidified insufflation had significantly reduced post-operative shoulder tip pain, post-operative analgesic use (all time points) and recovery room time.

Study name		Champion *et al.* 2006 (18)
Size of study groups	**Treatment**	25
	Control	25
Study duration	**Time unit**	N/A; RCT
Type of analysis	**Intention-to - treat/per protocol**	Per protocol
Outcome 1: primary	**Name**	**Core temperature change (primary)**
	Unit	°C, mean differences
Effect size	**Value**	0.01
	95% CI	-0.23, 0.25
Statistical test	**Type**	Chi-square test
	p value	Not significant (NS) (no value given)
Outcome 2: secondary	**Name**	**Post-operative pain (VAS)**
	Unit	VAS, mean difference
Effect size	**Value**	-0.20 (4-6hrs), -0.30 (3-12hrs), 0.30 (24hrs), 0.60 (48hrs)
	95% CI	-1.45, 1.05 (4-6hrs), -1.30, 0.70 (3-12hrs), -0.78, 1.38 (24hrs), -0.40, 1.60 (48hrs)
Statistical test	**Type**	One tailed t test with Greenhouse Geisser correction
	p value	NS (recovery), NS (4-6hrs), NS (3-12hrs), NS (24hrs), NS (48hrs). No values given
Outcome 3:	**Name**	**Post-operative pain (shoulder tip VAS)**

secondary		
	Unit	VAS, mean difference
Effect size	**Value**	-0.46
	95% CI	-1.00, 0.08
Statistical test	**Type**	One tailed t test with Greenhouse Geisser correction
	p value	NS (recovery), NS (4-6hrs), NS (3-12hrs), NS (24hrs), NS (48hrs). No values given
Outcome 4: secondary	**Name**	**Length of hospital stay**
	Unit	Days, mean difference
Effect size	**Value**	0.00
	95% CI	-2.77, 2.77
Statistical test	**Type**	One tailed t test with Greenhouse Geisser correction
	p value	NS, no value given
Comments		Champion *et al.* carried out an RCT on 50 laparoscopic gastric bypass patients receiving either unheated, unhumidified insufflation or heated, humidified insufflation (intervention). The patients had homogenous baseline characteristics between groups. They primarily investigated core temperature changes as well as post-operative pain (both overall and shoulder-tip specific) and length of hospital stay. There were no significant differences in core temperature difference, post-operative pain scores (all times between recovery and 48hrs, total or shoulder tip) and length of hospital stay or operation time. CI's estimated from standard deviations from meta-analytic statistics.

Study name		Davis *et al.* 2006 (19)
Size of study groups	**Treatment**	11
	Control	11
Study duration	**Time unit**	N/A; RCT
Type of analysis	**Intention-to - treat/per protocol**	Per protocol
Outcome 1: primary	**Name**	**Core temperature change (primary)**
	Unit	°C, mean differences
Effect size	**Value**	0.00
	95% CI	Not given
Statistical test	**Type**	t-test/ANOVA
	p value	NS, no value given
Outcome 2:	**Name**	**Post-operative pain (VAS) – these values**

secondary		**obtained from Cochran meta-analysis (26).**
	Unit	VAS, mean difference
Effect size	**Value**	-0.60 (24hrs), -0.50 (48hrs)
	95% CI	-2.78-1.58 (24h); -2.34-1.34 (48h)
Statistical test	**Type**	Kruskall-Wallis test
	p value	NS, no value given
Outcome 3: secondary	**Name**	**Post-operative pain (analgesic use)**
	Unit	Morphine equivalent daily dose (MEDD) per kg; mean difference
Effect size	**Value**	2.00 (1 day), 6.00 (2 days)
	95% CI	Not given
Statistical test	**Type**	Kruskall-Wallis test
	p value	NS, no value given
Outcome 4: secondary	**Name**	**Recovery room time**
	Unit	Hours (mean difference)
Effect size	**Value**	2.30
	95% CI	Not given
Statistical test	**Type**	t-test/ANOVA
	p value	NS
Outcome 5: secondary	**Name**	**Length of hospital stay**
	Unit	Days, mean difference
Effect size	**Value**	0.00
	95% CI	Not given
Statistical test	**Type**	t-test/ANOVA
	p value	NS, no value given
Comments		Davis *et al.* carried out an RCT on 44 patients undergoing laparoscopic Roux-en-Y gastric bypass surgery. The 44 patients were randomised equally into 4 groups to investigate 1) cold dry, 2) cold, humidified, 3) heated dry and 4) heated humidified. For the purpose of this evaluation we report only the results from groups 1 and 4. No differences reported in patient core temperature, post-operative analgesic usage, pain scale scores, recovery room time or length of hospital stay between any of the groups. Standard errors not reported, CI estimated according to the Cochran method of attributing the largest variance of any study to any single study where the variance is not reported.

Study name		Farley *et al.* 2004 (20)
Size of study groups	**Treatment**	49
	Control	52
Study duration	**Time unit**	N/A; RCT
Type of analysis	**Intention-to - treat/per protocol**	Per protocol
Outcome 1: primary	**Name**	**Core temperature change in OR (primary)**
	Unit	°C, mean differences
Effect size	**Value**	-0.32
	95% CI	-0.51, -0.13
Statistical test	**Type**	2-sample t-test
	p value	P=0.01
Outcome 2: secondary	**Name**	**Post-operative core temperature change**
	Unit	°C, mean differences
Effect size	**Value**	0.17 (ICU admission), -0.60 (ICU 1hr), 0.20 (ICU 4hr)
	95% CI	-0.23-0.56 (ICU admission), -0.99, -0.20 (ICH 1hr), -0.19, 0.59 (ICU 4hr)
Statistical test	**Type**	2-sample t-test
	p value	P=0.28 (ICU admission), P=0.52 (ICU 1hr), P=0.34 (ICU 4hr)
Outcome 3: secondary	**Name**	**Post-operative pain (VAS)**
	Unit	VAS, mean difference
Effect size	**Value**	-0.60 (recovery), 1.19 (3-12hrs); (authors contacted; pers. comm)
	95% CI	-1.19, -1.01 (recovery), 0.60, 1.78 (3-12hrs)(authors contacted; pers. comm)
Statistical test	**Type**	Mantel-Haenzel Chi-squared test
	p value	no values given
Outcome 4: secondary	**Name**	**Post-operative pain (shoulder tip VAS)**
	Unit	VAS, mean difference on entry to PACU
Effect size	**Value**	control group = 0.8; intervention group = 0.2;
	95% CI	Not given
Statistical test	**Type**	Mantel-Haenzel Chi-squared test
	p value	P=0.05
Outcome 5: secondary	**Name**	**Post-operative pain (analgesic use)**
	Unit	Morphine equivalent daily dose (MEDD) per kg; mean difference
Effect size	**Value**	0.20 (recovery), -6.00 (1 day)

	95% CI	-1.95, 2.35 (recovery), -18.25, 6.25(1 day)
Statistical test	**Type**	Chi-square test
	p value	P=0.8 (recovery). P=0.52 (1 day)
Outcome 6: secondary	**Name**	**Recovery room time**
	Unit	Hours, mean difference
Effect size	**Value**	-8.00
	95% CI	-19.32, 3.32
Statistical test	**Type**	Two tailed t-test
	p value	P=0.01
Outcome 7: secondary	**Name**	**Length of hospital stay**
	Unit	Days, mean difference
Effect size	**Value**	0.09
	95% CI	-0.28, 0.46
Statistical test	**Type**	Two tailed t-test
	p value	P=0.55
Comments		Farley *et al.* investigated 101 laparoscopic cholecystectomy patients randomised to unheated, unhumidified insufflation or intervention groups. Patients in the intervention group experienced significantly better intra-operative core temperatures (less heat loss), significantly quicker recovery room time, significantly reduced postoperative pain scores at recovery (shoulder tip pain) or at 14 days post operation (analgesic usage) . No difference was observed for length of hospital stay.

Study name		Hamza *et al*. 2005 (21)
Size of study groups	**Treatment**	23
	Control	21
Study duration	**Time unit**	N/A; RCT
Type of analysis	**Intention-to - treat/per protocol**	Per protocol
Outcome 1: primary	**Name**	**Core temperature change (primary)**
	Unit	°C, mean differences
Effect size	**Value**	-1.00
	95% CI	Not given
Statistical test	**Type**	Repeated measures ANOVA
	p value	P=0.01
Outcome 2: secondary	**Name**	**Post-operative core temperature change**

	Unit	°C, mean differences
Effect size	**Value**	-0.82 (ICU admission), -0.59 (ICU 1hr)
	95% CI	Not given
Statistical test	**Type**	Repeated measures ANOVA
	p value	P<0.05 (ICU admission), NS (no value given; ICU 1hr)
Outcome 3: secondary	**Name**	**Post-operative pain (VAS) in PACU**
	Unit	VAS, mean difference
Effect size	**Value**	maximum VRS pain scores and morphine consumption in the PACU were significantly lower in the Insuflow group
	95% CI	Not given
Statistical test	**Type**	Chi-square test with Fisher's exact test
	p value	P≤0.05
Outcome 4: secondary	**Name**	**Post-operative analgesic use**
	Unit	Morphine equivalent daily dose (MEDD) per kg; mean difference
Effect size	**Value**	-5.00 (recovery), -5 (1 day), -6.00 (2 days)
	95% CI	-7.51, -2.49 (recovery), -16.23, 6.23 (1 day), -15.13,3.13 (2 days)
Statistical test	**Type**	Repeated measures ANOVA
	p value	P<0.05 (recovery), NS (1 day), NS (2 days)
Outcome 5: secondary	**Name**	**Recovery room time**
	Unit	Hours, mean difference
Effect size	**Value**	-24.00
	95% CI	-55.96, 7.96
Statistical test	**Type**	ANOVA
	p value	P=0.08
Outcome 6: secondary	**Name**	**Length of hospital stay**
	Unit	Days, mean difference
Effect size	**Value**	0.00
	95% CI	Not given
Statistical test	**Type**	ANOVA
	p value	NS, no value
Comments		Hamza *et al.* underwent an RCT investigating 50 patients undergoing laparoscopic Roux-en-Y gastric bypass. Forty-four patients were split equally into 2 groups (intervention vs. unheated, unhumidified insufflation) using computerized randomisation but with no information of how they were specifically allocated. Patients who received intervention showed significantly

	higher intra-operative temperatures (less heat loss), a reduction in recovery room narcotic usage but no differences in recovery room time, length of hospital stay or morphine usage after recovery.

Study name		Herrmann *et al.* 2015 (13)
Size of study groups	**Treatment**	48
	Control	49
Study duration	**Time unit**	N/A; RCT
Type of analysis	**Intention-to - treat/per protocol**	Per protocol
Outcome 1: primary	**Name**	**Core temperature change (primary)**
	Unit	°C, mean differences
Effect size	**Value**	0.00
	95% CI	Not given
Statistical test	**Type**	ANOVA
	p value	P=0.768
Outcome 2: secondary	**Name**	**Post-operative pain (VAS); rest pain, total**
	Unit	VAS, median differences
Effect size	**Value**	0.05
	95% CI	-2.8, -3.1
Statistical test	**Type**	Mann-Whitney U-test
	p value	P0.977
Outcome 3: secondary	**Name**	**Post-operative pain (shoulder tip VAS)**
	Unit	VAS, median difference
Effect size	**Value**	1.25
	95% CI	0-2.1
Statistical test	**Type**	Mann-Whitney U-test
	p value	P=0.037
Outcome 4: secondary	**Name**	**Post-operative pain (analgesic use)**
	Unit	Morphine equivalent daily dose (MEDD) per kg; median difference
Effect size	**Value**	3.0 (recovery), 1.5 (1 day), 0 (2 days)
	95% CI	0-6 recovery; (recovery), 0-4.5 (1 day), -0(2 days)
Statistical test	**Type**	t-test
	p value	P=0.027 (recovery), P=0.030 (1 day), P=0.896 (2 days)
Outcome 6:	**Name**	**Length of hospital stay**

secondary	**Unit**	Days, mean difference
Effect size	**Value**	0.00
	95% CI	0
Statistical test	**Type**	Mann-Whitney U-test
	p value	P=0.392
Comments		Herrmann *et al.* carried out an RCT on 147 women undergoing laparoscopic gynaecological surgery that were randomly allocated using permuted-block randomisation to receive either intervention or unheated, unhumidified insufflation. The authors report significantly reduced shoulder tip pain 24hrs post-operation in patients receiving intervention but no significantly differences in other post-operative pain measures, core body temperature change or length of hospital stay.

Study name		Kissler *et al.* 2004 (23)
Size of study groups	**Treatment**	17
	Control	19
Study duration	**Time unit**	N/A; RCT
Type of analysis	**Intention-to - treat/per protocol**	Per protocol
Outcome 1: primary	**Name**	**Core temperature change (primary)**
	Unit	°C, mean differences
Effect size	**Value**	0.1
	95% CI	Not given
Statistical test	**Type**	Mann-Whitney U test
	p value	NS, no value given
Comments		Kissler *et al*. investigate 90 consecutive women scheduled for gynaecologic laparoscopic surgery that were randomised into two groups: unheated, unhumidified insufflation vs. heated, humidified insufflation. During the study on 30 patients were investigated before the trial was stopped due to less pain and better post-operative satisfaction in the cold, dry insufflated group. In the 30 patients investigated, no difference in operative core temperature was identified between groups.

Study name		Klugsberger *et al.* 2014 (14)
Size of study groups	**Treatment**	81
	Control	67
Study duration	**Time unit**	N/A; RCT
Type of analysis	**Intention-to - treat/per protocol**	Per protocol
Outcome 1: Primary	**Name**	**Mean intra-operative core temperature**
	Unit	°C
Effect size	**Value**	-0.54 AVERAGE MEAN DIFFERENCE
	95% CI	-0.87, -0.21
Statistical test	**Type**	Student's t-test
	p value	P=0.01
Outcome 2: Secondary	**Name**	**Postoperative VAS pain**
	Unit	Pain score scale, visual analogue score
Effect size	**Value**	4-6h -0.33; 24h -0.06Mean difference
	95% CI	-0.66, -0.01; -0.38, 0.26;
Statistical test	**Type**	Mann-Whitney test
	p value	P=0.025(4-6h); 0.437 (24h)
Comments		Klugsberger *et al*. investigated 154 patients undergoing laparoscopic cholecystectomy randomly distributed into heated, humid or unheated, unhumidified insufflation groups. They report significantly higher intra-operative core temperatures and reduced post-operative pain in recovery in heated, humidified insufflated patients compared to unheated, unhumidified insufflated patients. No difference was observed for post-operative pain at 24hrs.

Study name		Manwaring *et al.* 2008 (10)
Size of study groups	**Treatment**	30
	Control	30
Study duration	**Time unit**	N/A; RCT
Type of analysis	**Intention-to - treat/per protocol**	Per protocol
Outcome 1: primary	**Name**	**Core temperature change (primary)**
	Unit	°C, mean differences
Effect size	**Value**	0.07
	95% CI	-0.22, 0.36

Statistical test	**Type**	Paired t-test
	p value	P=0.027
Outcome 2: secondary	**Name**	**Post-operative pain (VAS)**
	Unit	VAS, mean difference
Effect size	**Value**	-0.70 (recovery), , 0.00 (24hrs)
	95% CI	-2.19, 0.79 (recovery), , -1.12, 1.12 (24hrs)
Statistical test	**Type**	Chi-squared test (unclear)
	p value	P=0.582 (recovery, 3-12hrs), P=0.948 (24hrs)
Outcome 3: secondary	**Name**	**Post-operative shoulder tip VAS pain score**
	Unit	VAS, mean difference
Effect size	**Value**	0.90
	95% CI	-0.49, 2.29
Statistical test	**Type**	Chi-squared test (unclear)
	p value	P=0.243
Outcome 4: secondary	**Name**	**Post-operative pain (analgesic use)**
	Unit	Morphine equivalent daily dose (MEDD) per kg; mean difference
Effect size	**Value**	-0.9 (recovery)
	95% CI	-4.12, 2.32 (recovery)
Statistical test	**Type**	Chi-squared test (unclear)
	p value	P=0.567 (recovery)
Outcome 5: secondary	**Name**	**Recovery room time**
	Unit	Hours, mean difference
Effect size	**Value**	-0.60
	95% CI	-10.11, 8.91
Statistical test	**Type**	Paired t-test (unclear)
	p value	P=0.892
Comments		Manwaring *et al.* carried out an RCT investigating 60 gynaecological patients split evenly into two groups: unheated, unhumidified insufflation or heated, humid insufflation. Intervention was not associated with any significant benefits in post-operative pain (total or shoulder specific), analgesic use or recovery room time and actually showed a significant higher core temperature loss (0.07 degrees) compared to unheated, unhumidified insufflation.

Study name		Mouton *et al.* 1999 (24)
Size of study groups	**Treatment**	20
	Control	20
Study duration	**Time unit**	N/A;RCT
Type of analysis	**Intention-to - treat/per protocol**	Per protocol
Outcome 1: primary	**Name**	**Core temperature change (primary)**
	Unit	°C, mean differences
Effect size	**Value**	-0.05
	95% CI	Not given
Statistical test	**Type**	t-test (unclear)
	p value	NS, not given
Outcome 2: secondary	**Name**	**Post-operative pain (VAS)**
	Unit	VAS, mean difference
Effect size	**Value**	-2.20 (3-12hrs), -2.70 (24hrs), -3.00 (48hrs)
	95% CI	Not given
Statistical test	**Type**	Chi-squared test (unclear)
	p value	P=0.02 (3-12 hours), P=0.03 (24hrs), P=0.04 (48hrs)
Outcome 3: secondary	**Name**	**Length of hospital stay**
	Unit	Days, mean difference
Effect size	**Value**	-0.60
	95% CI	Not given
Statistical test	**Type**	Chi-squared test (unclear)
	p value	NS, not given
Comments		Mouton *et al.* carried out an RCT on 40 cholecystectomy patients split into unheated, unhumidified insufflation or heated, humid insufflation groups (2x 16, 8 dropouts). No significant differences were found with core temperature change or length of hospital stay however patients receiving heated, humid insufflation experienced significantly lower post-operative pain (VAS) at 6hrs, 24hrs and 48hrs post operation.

Study name		Nguyen *et al.* 2002 (22)
Size of study groups	**Treatment**	10
	Control	10
Study duration	**Time unit**	N/A; RCT
Type of analysis	**Intention-to - treat/per protocol**	Protocol
Outcome 1: primary	**Name**	**Core temperature change (primary)**
	Unit	°C, mean differences
Effect size	**Value**	-0.10
	95% CI	Not given
Statistical test	**Type**	ANOVA with t-test
	p value	P=0.43
Outcome 2: secondary	**Name**	**Post-operative pain (VAS)**
	Unit	VAS, mean difference
Effect size	**Value**	0.9 (24hrs)
	95% CI	-1.10, 2.90 (24hrs)
Statistical test	**Type**	Two-sample t-test
	p value	P=0.38
Outcome 3: secondary	**Name**	**Post-operative pain (analgesic use)**
	Unit	Morphine equivalent daily dose (MEDD) per kg; mean difference
Effect size	**Value**	5.00 (1 day)
	95% CI	-7.19, 17.19 (1 day)
Statistical test	**Type**	Two-sample t-test
	p value	P=0.64 (1 day)
Outcome 4: secondary	**Name**	**Length of hospital stay**
	Unit	Days, mean difference
Effect size	**Value**	0.20
	95% CI	-0.33, 0.73
Statistical test	**Type**	Two-sample t-test
	p value	P=0.48
Comments		Nguyen *et al.* undertook an RCT on 20 laparoscopic Nissen fundoplication patients split evenly into two groups: unheated, unhumidified insufflation or heated, humid insufflation. No significant differences were identified for core temperature change, 24hr post-operative pain (VAS), 24hr analgesic use or length of hospital stay.

Study name		Ott *et al.* 1998 (16)
Size of study groups	**Treatment**	25
	Control	25
Study duration	**Time unit**	N/A; RCT
Type of analysis	**Intention-to - treat/per protocol**	Per protocol
Outcome 1: primary	**Name**	**Core temperature change (primary)**
	Unit	°C, mean differences
Effect size	**Value**	-1.34
	95% CI	Not given
Statistical test	**Type**	t-test (unclear)
	p value	P<0.05*, no specific value given
Outcome 2: secondary	**Name**	**Post-operative pain (VAS)**
	Unit	VAS, mean difference
Effect size	**Value**	2.30 (4-6hrs), , -1.80 (24hrs)
	95% CI	-4.55, -0.05 (4-6hrs), , -3.57, -0.03 (24hrs)
Statistical test	**Type**	Appropriate descriptive statistics
	p value	P<0.05*, no specific value given
Outcome 3: secondary	**Name**	**Post-operative pain (shoulder tip VAS)**
	Unit	VAS, mean difference
Effect size	**Value**	-1.80
	95% CI	-3.23,-0.37
Statistical test	**Type**	t-test (unclear)
	p value	P<0.05*, no specific value given
Outcome 4: secondary	**Name**	**Recovery room time**
	Unit	Hours, mean difference
Effect size	**Value**	-145.00
	95% CI	Not given
Statistical test	**Type**	t-test (unclear)
	p value	P<0.05*, no specific value given
Comments		Ott *et al.* carried out an RCT on 72 women undergoing laparoscopic gynaecological surgery. The allocation was unclear and number of drop outs (allegedly 22) was not detailed. They identified significant core temperature improvements, reduced post-operative pain and recovery room time in the Intervention group compared to the standard care group.

Study name		Sammour *et al.* 2010 (11)
Size of study groups	**Treatment**	41
	Control	41
Study duration	**Time unit**	N/A, RCT
Type of analysis	**Intention-to - treat/per protocol**	Intention-to-treat
Outcome 1: primary	**Name**	**Core temperature change (primary)**
	Unit	°C, mean differences
Effect size	**Value**	-0.20
	95% CI	-0.57, 0.17
Statistical test	**Type**	Mann-Whitney U-test
	p value	P=0.324
Outcome 2: secondary	**Name**	**Post-operative pain at rest (VAS) Day1**
	Unit	VAS, mean difference
Effect size	**Value**	2.0
	95% CI	not given
Statistical test	**Type**	Mann-Whitney U-test
	p value	0.01
Outcome 3: secondary	**Name**	**Post-operative (analgesic use; MEDD)**
	Unit	Morphine equivalent daily dose (MEDD) per kg; mean difference
Effect size	**Value**	-2(recovery), 14 (Day 1), 4 (Day 2),
	95% CI	Not given
Statistical test	**Type**	Mann-Whitney U-test
	p value	P=0.783 (recovery), P=0.344 (1 day), P=0.156 (2 days),
Outcome 4: secondary	**Name**	**Length of hospital stay**
	Unit	Days, mean difference
Effect size	**Value**	-2.0
	95% CI	Not given
Statistical test	**Type**	Mann-Whitney U-test
	p value	P=0.873
Comments		Sammour *et al*. carried out an RCT on 82 patients undergoing laparoscopic colon surgery randomised into heated, humidified or unheated, unhumidified insufflation groups (41 patients each). No significant differences were observed between groups for core temperature change, post-operative pain (all time points except 24hrs at rest), analgesic use (all time points) or length of hospital stay. Note that longitudinal analysis was not carried out for MEDD usage; had it been done it would most likely have shown that the study group had

	significantly less pain through time.

Study name		Savel *et al.* 2005 (15)
Size of study groups	**Treatment**	15
	Control	15
Study duration	**Time unit**	N/A; RCT
Type of analysis	**Intention-to - treat/per protocol**	Per protocol
Outcome 1: primary	**Name**	**Core temperature change (primary)**
	Unit	°C, mean differences
Effect size	**Value**	-0.70
	95% CI	-1.06, -0.34
Statistical test	**Type**	P=0.02
	p value	t-test
Outcome 2: secondary	**Name**	**Post-operative pain (VAS)**
	Unit	VAS, mean difference
Effect size	**Value**	0.50 (4-6hrs), 0.25 (3-12hrs), -1.30 (24hrs), 0.70 (48hrs)
	95% CI	-0.93, 1.93 (4-6hrs), -1.34, 1.84 (3-12hrs), -2.71, 0.11 (24hrs), -1.02, 2.42 (48hrs)
Statistical test	**Type**	Mann-Whitney U-test
	p value	NS (4-6hrs), NS (3-12hrs), NS (24hrs), NS (48hrs), no values given
Outcome 3: secondary	**Name**	**Post-operative analgesic use**
	Unit	Morphine equivalent daily dose (MEDD) per kg; mean difference
Effect size	**Value**	-5.00 (1 day), -1.00 (2 days)
	95% CI	-21.15, 11.15 (1 day), -19.62, 17.62 (2 days)
Statistical test	**Type**	Mann-Whitney U-test
	p value	NS (1 day), NS (2 days)
Outcome 4: secondary	**Name**	**Length of hospital stay**
	Unit	Days, mean difference
Effect size	**Value**	-0.80
	95% CI	-1.30, -0.30
Statistical test	**Type**	t-test
	p value	P=0.01
Comments		Savel *et al.* carried out an RCT on 30 patients undergoing laparoscopic Roux-en-Y gastric bypass surgery. Patients were randomised into heated, humidified insufflation or unheated, unhumidified insufflation groups. Patients receiving heated, humidified CO_2 showed

	significantly reduced length of hospital stay and reduced core body temperature changes while no differences were observed for post-operative pain at any time point.

Study name		Yu *et al.* 2013 (12)
Size of study groups	**Treatment**	95
	Control	95
Study duration	**Time unit**	N/A; RCT
Type of analysis	**Intention-to - treat/per protocol**	Per protocol
Outcome 1: primary	**Name**	**Core temperature change (primary)**
	Unit	°C, mean differences
Effect size	**Value**	0.04 (Absolute difference between start and end)
	95% CI	-0.06;0.14
Statistical test	**Type**	Student's t-test
	p value	P=0.201
Outcome 2: secondary	**Name**	**Post-operative pain (analgesic use)**
	Unit	Morphine equivalent daily dose (MEDD) per kg; mean difference
Effect size	**Value**	0.20 (recovery), -0.60 (1 day), -0.60 (2 days)
	95% CI	-0.33, 0.73 (recovery), -4.19, 2.99 (1 day), -2.74, 1.54 (2 days)
Statistical test	**Type**	Student's t-test
	p value	P=0.524 (recovery), P=0.737 (1 day), P=0.557 (2 days)
Outcome 3: secondary	**Name**	**Length of hospital stay**
	Unit	Days, median value
Effect size	**Value**	0.00
	95% CI	Not given
Statistical test	**Type**	Mann-Whitney U-test
	p value	P=0.683
Comments		Yu *et al.* carried out an RCT on 190 children undergoing appendectomies. Patients were randomly allocated to heated, humid or unheated, unhumidified insufflation groups. They identified no significant differences in core body temperature change, post-operative analgesic use or length of hospital stay.

Open studies:

Study name		Frey, JM et al. 2012 (FPH device) (5)
Size of study groups	**Treatment**	40
	Control	39
Study duration	**Time unit**	N/A; RCT
Type of analysis	**Intention-to - treat/per protocol**	Per protocol
Outcome 1: primary	**Name**	**Core temperature change (primary)**
	Unit	°C, mean differences
Effect size	**Value**	-0.40
	95% CI	-0.62, -0.18
Statistical test	**Type**	Student's t-test
	p value	P=0.001
Outcome 2: primary	**Name**	**Wound area temperature change (primary)**
	Unit	°C, mean differences at end of surgery
Effect size	**Value**	-1.70
	95% CI	-2.25, -1.15
Statistical test	**Type**	Student's t-test
	p value	P<0.001
Outcome 3: secondary	**Name**	**Length of hospital stay**
	Unit	Days, median difference
Effect size	**Value**	0.00
	95% CI	Not given
Statistical test	**Type**	Mann Whitney U-test
	p value	P=0.818
Comments		One of two RCTs carried out by Frey *et al.* This RCT used the Fisher and Paykel Healthcare HumiGard humidifier on patients undergoing open colorectal surgery (varying procedures). 79 patients were randomly allocated to either a heated, humidified or no insufflation group. The authors identified significant reduction in core and wound area temperature loss but not significant differences in length of hospital stay or time to extubation.

Study name		Frey, JM et al. 2012 (6)
Size of study groups	**Treatment**	38
	Control	36
Study duration	**Time unit**	N/A; RCT
Type of analysis	**Intention-to - treat/per protocol**	Per protocol
Outcome 1: primary	**Name**	**Core temperature change (primary)**
	Unit	°C, median differences
Effect size	**Value**	-0.50
	95% CI	Not given
Statistical test	**Type**	Mann-Whitney test
	p value	P=0.028
Outcome 2: primary	**Name**	**Wound area temperature change (primary)**
	Unit	°C, median differences at end of surgery
Effect size	**Value**	-1.20
	95% CI	Not given
Statistical test	**Type**	Mann Whitney U-test
	p value	P<0.001
Outcome 3: secondary	**Name**	**Length of hospital stay**
	Unit	Days, mean difference
Effect size	**Value**	0.50
	95% CI	Not given
Statistical test	**Type**	Mann Whitney U-test
	p value	P=0.895
Comments		The second of two RCTs carried out by Frey *et al.* 2012. This RCT used an unnamed self-assembled humidifier on patients undergoing open colorectal surgery (varying procedures). 74 patients were randomly allocated to either a heated, humidified insufflation or no insufflation group. The authors identified significant reduction in core and wound area temperature loss as well as time to extubation but no significant difference in length of hospital stay was identified.

Retrospective studies:

Study name		Frey, JM *et al.* Manuscript in progress (retrospective study)
Size of study groups	**Treatment**	80
	Control	78
Study duration	**Time unit**	Approximately 6 years
Type of analysis	**Intention-to - treat/per protocol**	Follow-up analysis
Outcome 1: primary	**Name**	[redacted]
	Unit	[redacted]
Effect size	**Value**	[redacted]
	95% CI	[redacted]
Statistical test	**Type**	[redacted]
	p value	[redacted]
Outcome 2: primary	**Name**	[redacted]
	Unit	[redacted]
Effect size	**Value**	[redacted]
	95% CI	[redacted]
Statistical test	**Type**	[redacted]
	p value	[redacted]
Outcome 3: secondary	**Name**	[redacted]
	Unit	[redacted]
Effect size	**Value**	[redacted]
	95% CI	[redacted]
Statistical test	**Type**	[redacted]
	p value	[redacted]
Comments		[redacted]

Study name		Weinberg *et al.* (Abstract/poster) – Randomised pilot clinical trial
Size of study groups	**Treatment**	11
	Control	11
Study duration	**Time unit**	N/A; RCT
Type of	**Intention-to -**	per protocol

analysis	**treat/per protocol**	
Outcome 1: primary	**Name**	**Core temperature difference (via naso-pharyngeal probe)**
	Unit	°C, mean differences
Effect size	**Value**	0.6
	95% CI	0.08- 1.15
Statistical test	**Type**	Not stated
	p value	P=0.02
Outcome 2: primary	**Name**	**Core temperature change (via pulmonary artery catheter)**
	Unit	°C, mean differences
Effect size	**Value**	0.4
	95% CI	-0.15, 1.03
Statistical test	**Type**	not stated
	p value	P=0.14
Outcome 3: secondary	**Name**	**Core temperature change (via bladder probe)**
	Unit	°C, mean differences
Effect size	**Value**	0.6
	95% CI	-0.12, 1.4
Statistical test	**Type**	Not stated
	p value	P=0.09
Comments		Weinberg *et al.* show that during open liver transplant surgery heated, humidified insufflation reduces the incidence of intra-operative hypothermia – confirmed via naso-pharyngeal temperature measurements

Observational studies:

Study name		Mason *et al.* (manuscript in progress)
Size of study groups	**Treatment**	123
	Control	123
Study duration	**Time unit**	Cohort study

Type of analysis	**Intention-to - treat/per protocol**	N/A
Outcome 1: primary	**Name**	[redacted]
	Unit	[redacted]
Effect size	**Value**	[redacted]
	95% CI	[redacted]
Statistical test	**Type**	[redacted]
	p value	[redacted]
Outcome 2: primary	**Name**	[redacted]
	Unit	[redacted]
Effect size	**Value**	[redacted]
	95% CI	[redacted]
Statistical test	**Type**	[redacted]
	p value	[redacted]
Outcome 3: secondary	**Name**	[redacted]
	Unit	[redacted]
Effect size	**Value**	[redacted]
	95% CI	[redacted]
Statistical test	**Type**	[redacted]
	p value	[redacted]
Comments		[redacted]

7.6.2 Justify the inclusion of outcomes in table B9 from any analyses other than intention-to-treat.

One study (Sammour *et al.* (11)) used intention to treat analysis and included patients who were converted to open surgery and did not receive the intervention for the duration of the surgery, introducing a risk of bias. The remaining included studies were analysed with per protocol analysis to avoid this bias. Patients who were excluded from analysis were due to conversion to open surgery, so were treated but not with a comparable method. A per-protocol method of analysis is the preferred analysis for studies investigating insufflation.

7.7 Adverse events

In section 7.7 the sponsor is required to provide information on the adverse events experienced with the technology being evaluated in relation to the scope.

For example, post-marketing surveillance data may demonstrate that the technology shows a relative lack of adverse events commonly associated with the comparator.

7.7.1 Using the previous instructions in sections 7.1 to 7.6, provide details of the identification of studies on adverse events, study selection, study methodologies, critical appraisal and results.

Studies retrieved using the search strategy described in section 7.1 were reviewed for description of adverse events. In addition the MAUDE database, ECRI database, MHRA database, and the Fisher & Paykel Healthcare Internal product complaint database was searched for any device related events.

ECRI database search strategy

For laparoscopic surgery search of the ECRI database was conducted using the search terms 'laparosco*'. The titles for each report were screened for subject relevance. When the subject of the report was not made clear in the title, the report summary was evaluate. Any reports on the safety concerns related to the device concept of warming and humidifying gases, were included for appraisal and evaluation.

For open surgery a search of the ECRI database was conducted using the search terms 'laparot*', or "open surgery". The titles for each report were screened. When the subject of the report was not made clear in the title, the report summary was read. Any reports on the safety concerns related to the device concept of warming and humidifying gases, were included for appraisal and evaluation.

MAUDE database search strategy

MAUDE is a US based database of adverse events. For laparoscopic surgery a search on MAUDE was conducted for 'Insuflow' in the 'Brand Name' search

category. The search was limited to reports from 2005 onwards. ‘Insuflow’ was the only device with a brand name that was identified during the literature search. Nevertheless a search for ‘lexion” and ‘HumiGard’ were also carried out. A MAUDE search for devices could not be conducted when the studies did not mention the brand name or manufacturer of the device. Any reports on the safety concerns related to the device concept of warming and humidifying gases were included for appraisal and evaluation.

For open surgery a search on the MAUDE database for “CarbonAid” in the “brand name” search category was also carried out. In addition a search was conducted using ‘Cardia Innovation” in the manufacturer search category. The search was limited to reports from 1990 onwards. Relevant reports found will be included for appraisal and evaluation.

MHRA database search strategy

The strategy employed for MHRA was the same as MAUDE for both laparoscopic and open surgery parameters. A search for “HumiGard”, “MR860”, “Insuflo” and “insufflat” was carried out with no time constraints.

7.7.2 Provide details of all important adverse events reported for each study. A suggested format is shown in table B10.

No published studies reported any adverse events associated directly with heated, humidified insufflation.

7.7.3 Describe all adverse events and outcomes associated with the technology in national regulatory databases such as those maintained by the MHRA and FDA (Maude).

ECRI database search results

A search on the ECRI database for the above criteria resulted in 227 reports. A copy of these results can be found in Appendix 2 and accompanying files.

Of these reports none found any safety concerns relating to the concept of applying heated, humidified gas during surgery.

MAUDE database search results

i) For laparoscopic surgery, no relevant reports of adverse events were found (Table B10). One entry was found documenting an issue with an Insuflow-Trocar where it had small black particles on it. No harm was caused to the patient and the event was not associated directly with the insufflation device. Details of the report are found in Appendix 2.

ii) For open surgery, no relevant reports were found (Table B10). A copy of the search results are included in the Appendix 2. One entry was found detailing a problem with the sponge on a diffuser but this was not related directly with the surgical humidifier. The sponge did not allow gas to pass through it and so it was not used and another diffuser was used instead. The patient was not affected.

Table B 10: MAUDE database search results

Brand Name*	Manufacturer	Number of Reports	Relevant Reports to be included in evaluation	Reason for Exclusion
Insuflow	Lexion Medical	5	0	Reports related to technical malfunctioning of the device, no clinical safety concerns.

HumiGard	Fisher and Paykel Healthcare	0	0	N/A
CarbonAid	Cardia	1	0	Not relevant to safety of the humidification device

* Includes number of reports found for each brand of laparoscopic humidifiers (commercially available).

MHRA database search results

No reports were found for any of the search parameters (Table B11).

Table B 11: MHRA database search results

Brand Name*	Manufacturer	Number of Reports	Relevant Reports to be included in evaluation	Reason for Exclusion
Insuflow	Lexion Medical	0	0	N/A
HumiGard	Fisher and Paykel Healthcare	0	0	N/A
Insuflat	N/A	0	0	N/A

* Includes number of reports found for each brand of laparoscopic humidifiers (commercially available).

7.7.4 Provide a brief overview of the safety of the technology in relation to the scope.

In summary, no adverse events directly associated with heated, humidified insufflation devices have been documented on the ECRI, MAUDE and MHRA databases. Furthermore, our internal product surveillance identified no reports or complaints relative to the safety or misuse of the HumiGard™ device.

7.8 Evidence synthesis and meta-analysis

When more than one study is available and the methodology is comparable, a meta-analysis should be considered.

Section 7.8 should be read in conjunction with the 'Medical Technologies Evaluation Programme Methods Guide', available from www.nice.org.uk/mt

7.8.1 Describe the technique used for evidence synthesis and/or meta-analysis. Include a rationale for the studies selected, details of the methodology used and the results of the analysis.

Introduction

A meta-analysis on heated CO_2 with or without humidification for minimally invasive abdominal surgery was published by the Cochrane collaboration in 2011(26). However there are significant data entry errors in the analysis which impacts the conclusion of the analysis. To overcome this and include publications published since 2011 an updated meta-analysis was completed to address the scope. The analysis was split into two groupings: i) laparoscopic surgery and ii) open surgery, beginning with a risk of bias analysis of included studies followed by a meta-analysis.

Methodology

Studies were selected as detailed in section 7.2. Values for investigated outcomes were taken directly from the publications or, if values could not be obtained directly from the study, values were taken from previous meta-analyses wherein they describe that the values were retrieved from communication with the authors (26-28). If no standard error of the mean (s.e.m) was provided then the largest s.e.m value in the meta-analysis group was taken and used. This method is the standard method of data extraction, as used by Cochrane, when no value is listed in the original publication or retrieved from contact with the corresponding author. Meta-analyses were conducted using an inverse variance statistical method with a random effects

analysis model. The effect measure was standardised mean difference with a 95% CI. Heterogeneity was calculated using Tau^2 and Chi^2 with differing degrees of freedom (shown in each analysis) to give an I^2 value shown as a percentage. A meta-analysis was deemed heterogeneous if an I^2 of greater than 20% was observed, determined as per reference (30).

Laparoscopic surgery meta-analysis

Results

A total of 16 RCTs were investigated. Of these 5 were gynaecological laparoscopies, 5 were gastric bypasses, 3 were cholecystectomies, 1 colonic resection, 1 Nissen fundoplication and 1 appendectomy. A total of 1317 patients were included, 190 of which were children. Risk of bias analyses for each outcome is included in Appendix 5.

Intra-operative temperature change

The majority of papers investigating temperature changes indicated the degrees of temperature gain or loss at the endpoint of surgery (in °C). Fourteen of the 16 RCTs recorded mean temperature change totalling 548 patients in the heated, humidified insufflation group and 564 in the unheated, unhumidified insufflated group. Ten of the 14 publications reporting temperature change used adjunctive warming devices. Due to the given heterogeneity (I^2=87% no warming, 82% warming) a random effects model was fitted.

A significant benefit in temperature maintenance was found in patients treated with heated, humidified insufflation with adjunctive warming (Fig 3). The benefit in temperature maintenance was greater in patients receiving adjunctive warming (P=0.004) than those with no/unknown adjunctive warming (P=0.33). Collectively, the data illustrates that patients receiving heated, humidified insufflation have significantly reduced temperature loss compared to those receiving unheated, unhumidified insufflation (P=0.003).

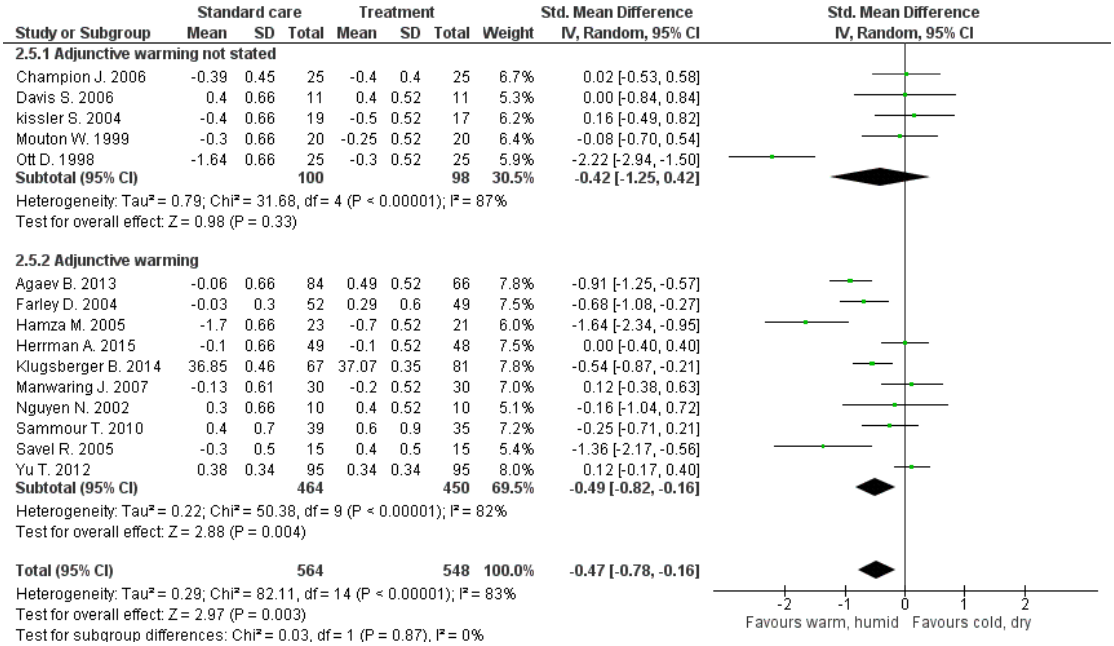


Figure 3: Core temperature changes during laparoscopic surgery, with adjunctive warming.

Post-operative temperature change

In addition to operative core temperature changes, three studies reported post-operative temperature differences. Post-operative time measurements varied and are reported in the table below. An overall meta-analysis identified a significant benefit in core body temperature as recorded in the Intensive Care Unit (ICU) in patients receiving the intervention (P=0.009; Fig 4).

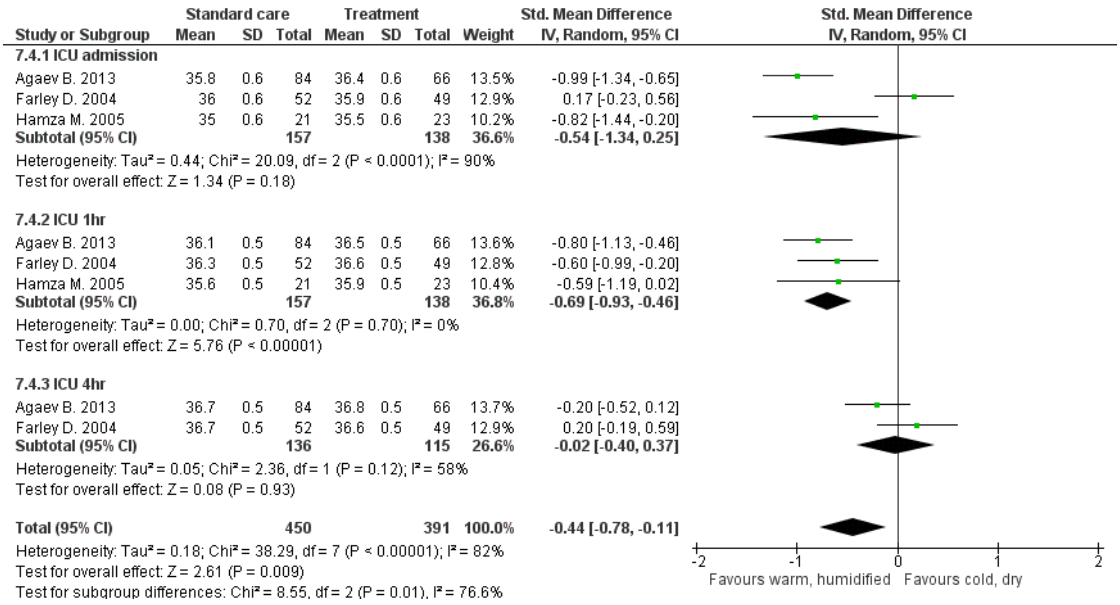


Figure 4: Post-operative core temperature analysis after laparoscopic surgery.

Patient reported pain

Two measurements of pain were investigated: pain by VAS and pain by analgesic usage.

Pain by Visual Analogue Scale (VAS)

The VAS system is a psychometric response scale ranked from 1 to 10 with 1 being little to no pain and 10 being significant pain. Meta-analysis of pain scores totalled 841 patients in the intervention group and 831 in the unheated, unhumidified insufflated group. Pain VAS scores were sub grouped into their recorded time points

A statistically significant reduction in VAS pain scores was observed in the intervention group at recovery (P=0.007) and between 4-6hrs post-surgery (P=0.02) while later time points showed no significant difference (P=0.99 3-12hrs; P=0.12, 24hrs; P=0.44, 48hrs) (Fig 5). Overall, a significant reduction in VAS pain scores was found in patients treated with heated, humidified insufflation compared with unheated, unhumidified insufflation (P=0.03).

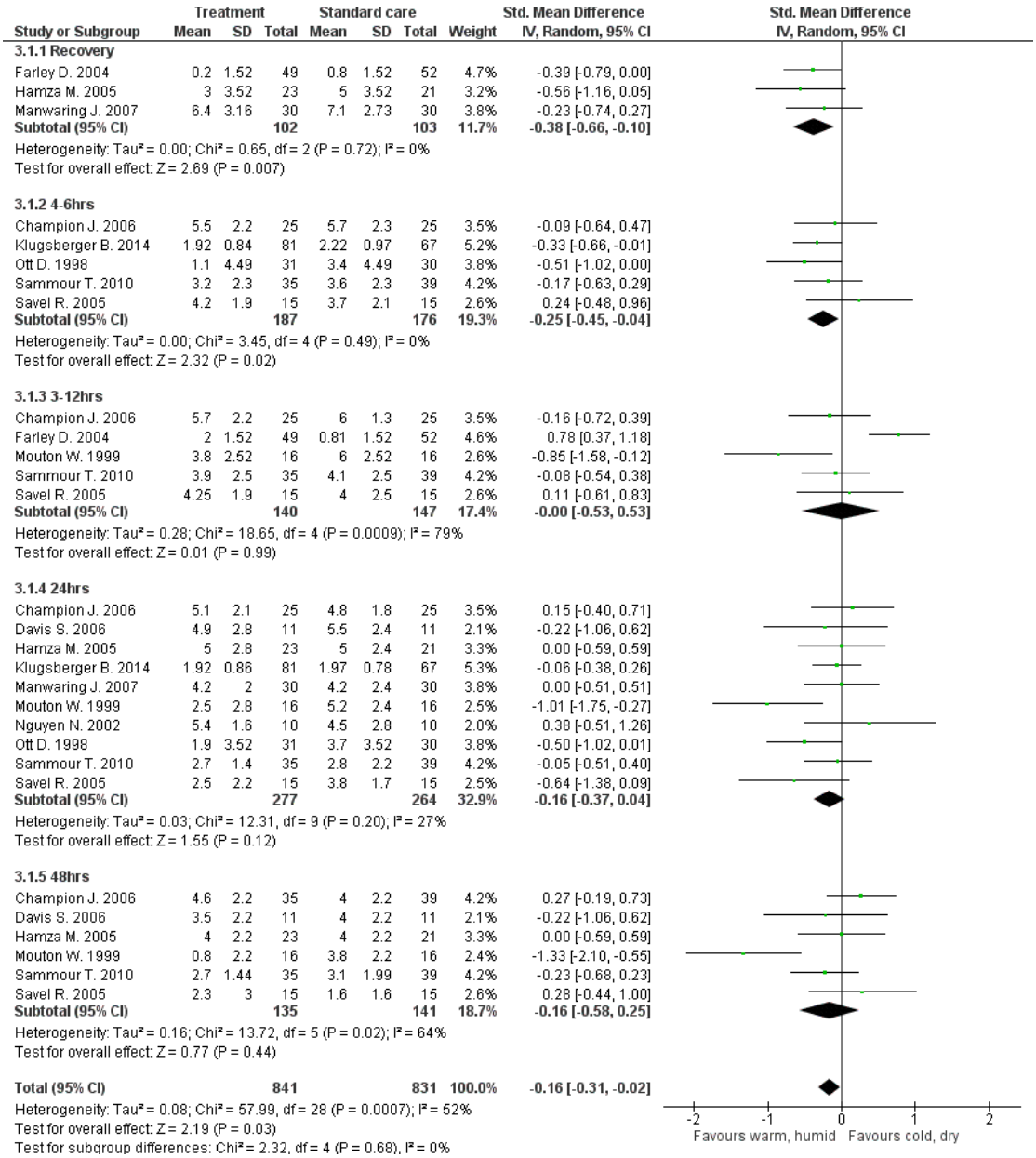


Figure 5: Pain VAS scores from recovery to 48hrs after laparoscopic surgery

Some studies also included shoulder tip pain via VAS. Six studies were found to record shoulder tip pain that collectively show that patients receiving heated, humidified insufflation have significantly reduced shoulder tip pain between 12-24 hours compared to patients receiving unheated, unhumidified insufflation (P=0.02; Fig 6).

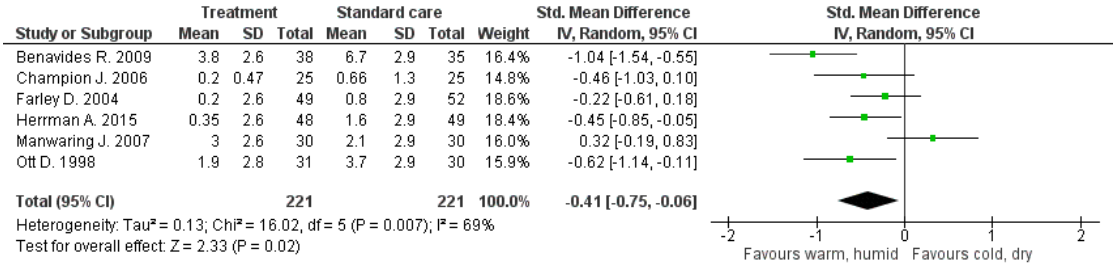


Figure 6: Shoulder tip pain from 12 to 24hrs after laparoscopic surgery

Pain by analgesic usage

In addition to VAS pain scores a number of studies measured total analgesic usage per unit time (mg). Values were entered as per the morphine equivalent scale of analgesic usage and analysed using a random effects model. In total, 1046 patients were recorded in the intervention group and 1183 patients in the unheated, unhumidified insufflated group. There was a significant reduction in analgesic usage in the intervention group at day 1 (P=0.05), day 2 (P=0.03) and day 3 (P=0.04) post-surgery while a non-significant reduction was observed in recovery (P=0.32). Overall, a significant reduction in analgesic usage was observed in heated, humidified insufflated patients between recovery and 72hrs (P=0.003; Fig 7).

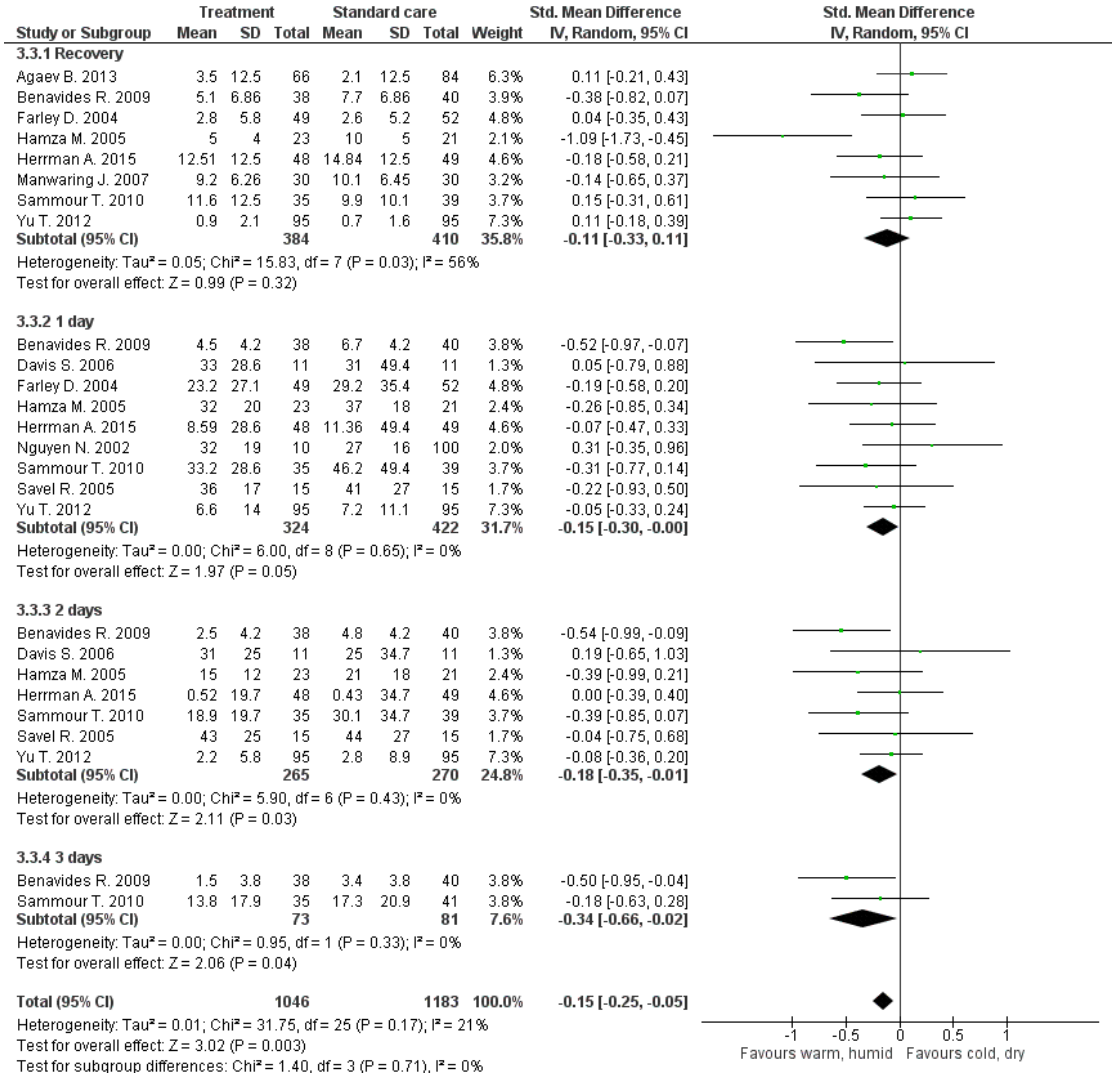


Figure 7: Analgesic usage from recovery to 72hrs after laparoscopic surgery

Total length of hospital stay (days)

Meta-analysis for the total length of hospital stay included 10 studies totalling 327 patients in the intervention group and 333 patients in the unheated, unhumidified insufflated group. No significant reduction in length of hospital stay was seen in patients who received intervention compared to those treated with standard care (P=0.42; Fig 8).

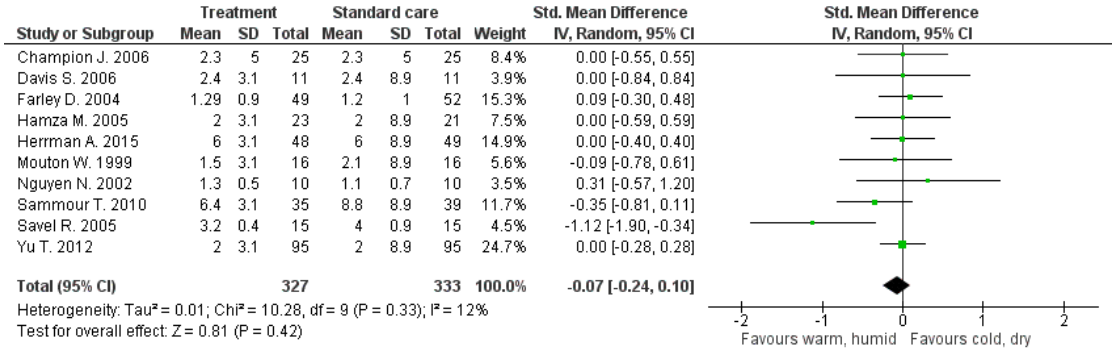


Figure 8: Total length of hospital stay after laparoscopic surgery

Length of stay in postoperative recovery (hours)

Six studies investigated the length of time it took patients to leave the recovery room following surgery totalling 176 patients in the intervention group and 174 patients in the unheated, unhumidified insufflated group. Overall, a near-significant reduction in the length of time spent in the recovery room was observed with patients treated with heated, humidified insufflation compared to patients treated with unheated, unhumidified insufflation (P=0.07; Fig 9).

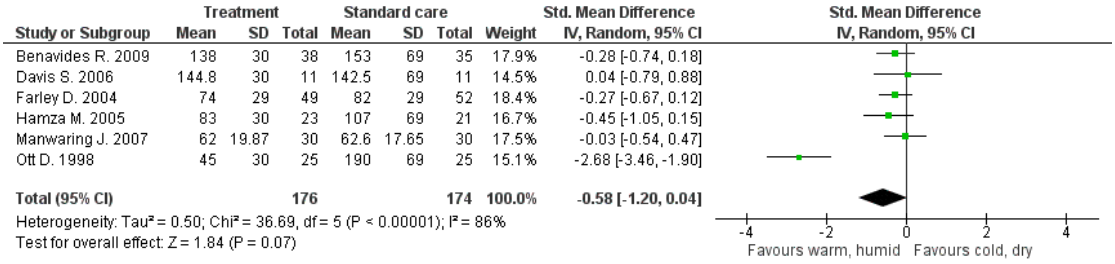


Figure 9: Total length of stay in postoperative recovery after laparoscopic surgery

<u>Sub group analysis of “high risk” patients:</u>

A subsequent evaluation was done on patients identified as “high risk” as detailed in the scope. Not all studies detailed ASA scores and so a subgroup of “high risk” patients was done on patients undergoing surgery and had pre-operative temperature below 36 degrees Celsius. Five studies were identified to have investigated “high risk” patients (11, 15, 16, 21, 22). Re-evaluation of outcomes identified significant benefits in patients receiving intervention for core temperature change (P=0.008), pain by VAS (P=0.03), and pain by

analgesic use (P=0.03), however total length of hospital stay (P=0.12) and time in recovery room (P=0.16) showed no differences (Figs. 10-14).

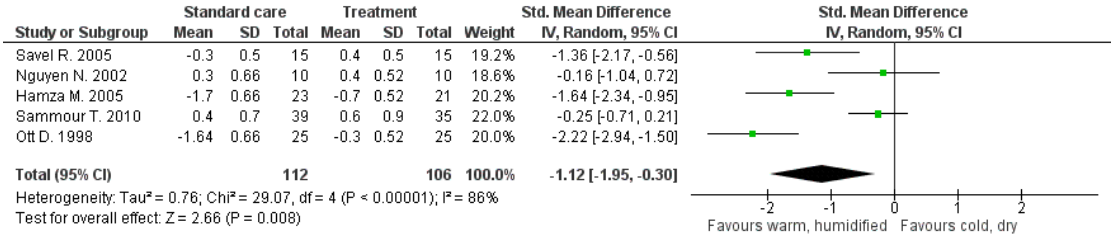


Figure 10: Core temperature change for "high risk" laparoscopic patients

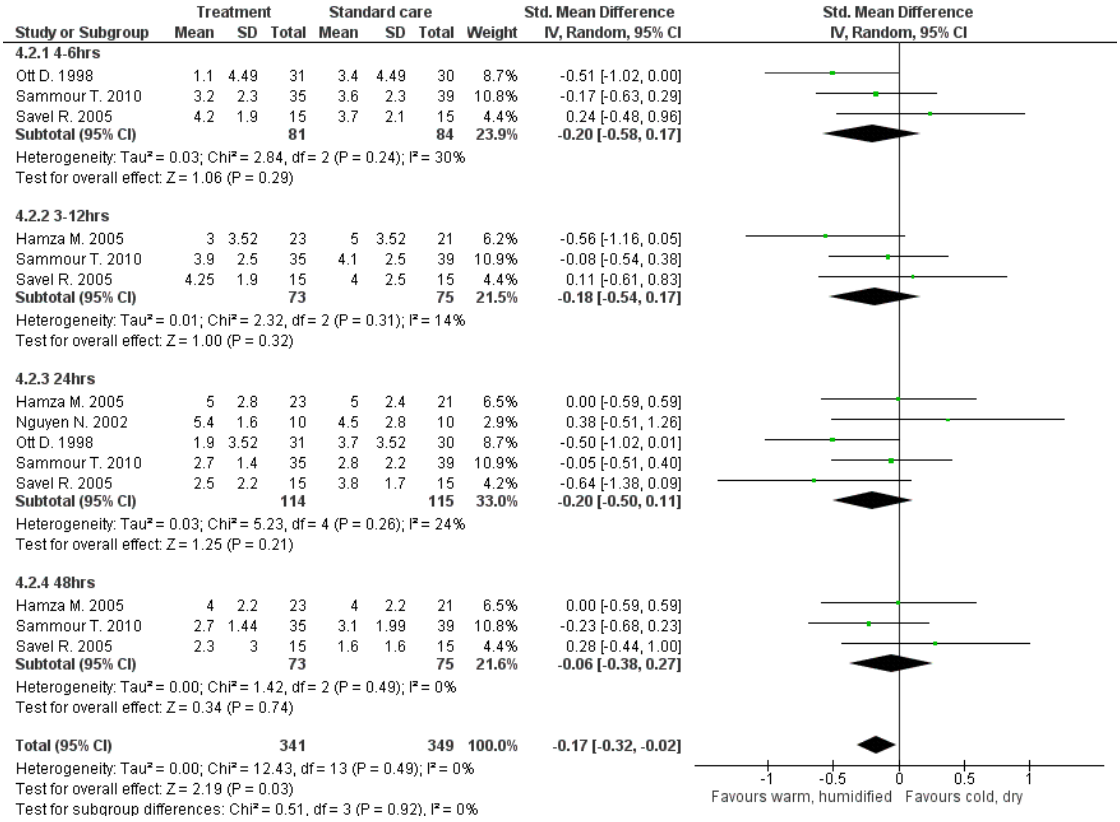


Figure 11: Patient reported pain (VAS) for "high risk" laparoscopic patients

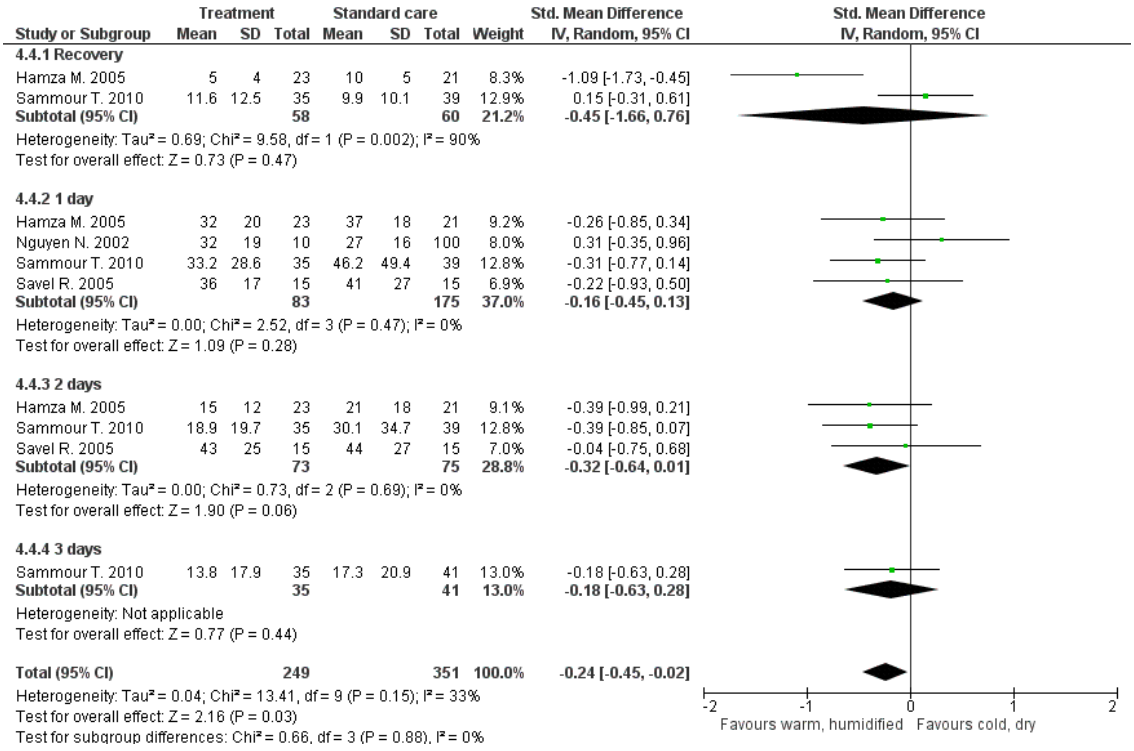


Figure 12: Patient reported pain (Analgesic use) for "high risk" laparoscopic patients

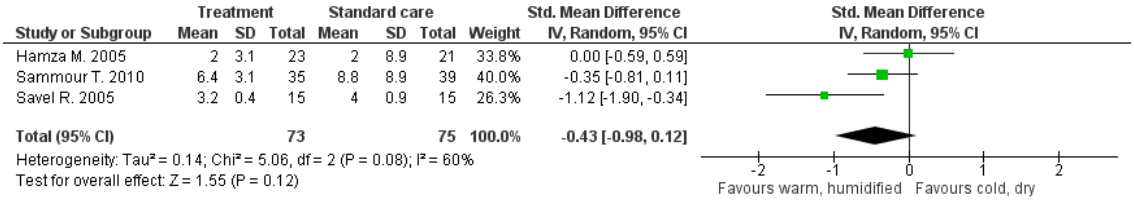


Figure 13: Length of hospital stay for "high risk" laparoscopic patients

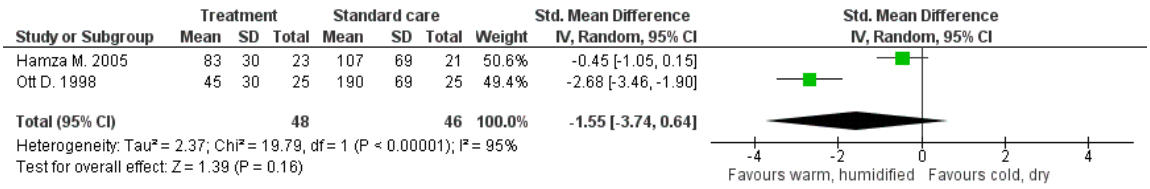


Figure 14: Time spent in recovery for "high risk" laparoscopic patients

Open surgery meta-analysis

Results

Two randomised control trials were identified to investigate heated, humidified insufflation in open surgery. Both studies investigated colorectal patients and were published in 2012 (5, 6). The specific surgeries carried out varied (1-8 patients per surgery type) and were pooled for analysis. Heterogeneity was low for all investigated objectives (I^2=0-4%) but a random effects model was employed to remain consistent with the data analysis used for laparoscopic studies (Funnel plots shown in Appendix 5). No sub-group analysis on high risk patients or adjunctive analysis was performed due to the low study number. Both included studies received adjunctive warming in addition to the intervention

Temperature change

Both core temperature and wound area temperature changes were investigated. For comparative reasons the mean temperatures recorded for core and wound area during surgery were analysed. Patients receiving heated, humidified insufflation in the open wound had significantly reduced core temperature changes during the procedure compared to patients receiving ambient air (no insufflation) (P<0.00001; Fig 15).

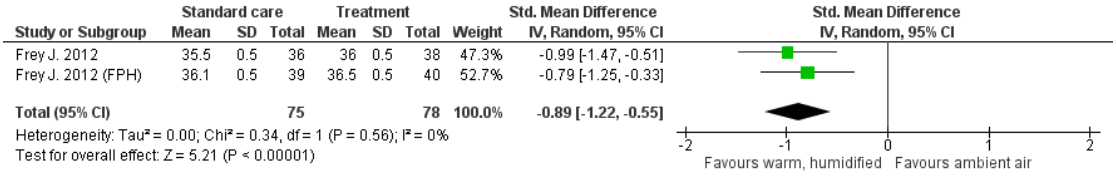


Figure 15: Core temperature change in open surgery

Patients receiving heated, humidified insufflation into the open wound had significantly better maintenance of wound area temperature compared to patients receiving no insufflation (P=0.0006; Fig 16).

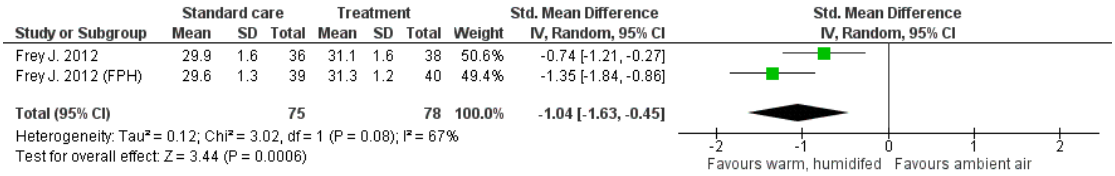


Figure 16: Wound area temperature change in open surgery

One study reported the percentage of hypothermic patients at the end of surgery. Frey *et al*.(5), using the HumiGard™ surgical humidifier, showed that 20% of patients receiving heated, humidified insufflation were <36.5°C compared to 62% receiving no insufflation and 0% patients receiving intervention had temperatures <36.0°C compared 18% receiving no insufflation (5).

Total length of hospital stay

Both RCT's investigated the total length of hospital stay (days) following open colorectal surgery. Both studies individually reported no significant difference between the intervention and no insufflant groups for length of hospital stay (p=0.818 (5); p=0.895 (6)).

Other outcomes:

Incidence of SSI, length to stay in recovery, and patient reported pain were not reported in the included open surgery investigations.

7.8.2 If evidence synthesis is not considered appropriate, give a rationale and provide a qualitative review. The review should summarise the overall results of the individual studies with reference to their critical appraisal.

For the three unpublished studies included in this evaluation the data was not included in the above meta-analysis and their summaries are given below:

Study 1. Relation of intra-operative temperature to postoperative mortality in open colon surgery - an analysis of two randomised controlled trials (Frey *et al.* in prep.(7)).

The aim was to evaluate if heated humidified CO_2 insufflated into an open surgical wound could affect long term overall mortality. This is a retrospective study of two clinical trials, where patients were randomised to heated humidified insufflation (n=80) or standard care (n=78). All patients underwent elective major open colon surgery. Patients in the intervention group received insufflation of heated humidified insufflation into the open wound cavity via a gas diffuser to create a local atmosphere of 100% CO_2. Temperature in the wound cavity was measured with a heat-sensitive infrared camera. Core temperature was measured at the tympanic membrane. Median follow-up was 73.7 months.

[redacted]

The authors concluded that a small end-of-operation temperature difference between final core and wound edge temperature was positively associated with patient survival in open colon surgery.

Study 2. Peri-Operative Hypothermia and Surgical Site Infection following Peritoneal Insufflation with Warm, Humidified Carbon Dioxide during Laparoscopic Colorectal Surgery: a Cohort Study with Cost Effectiveness Analysis (Mason *et al.* in prep.(9)).

This was a retrospective cohort study of patients undergoing elective laparoscopic colorectal resection for both benign and malignant disease, performed at a single UK specialist centre from September 2012 to July 2014. The standard care group (n=126) received peritoneal insufflation with cold, dry CO_2 whereas the intervention group (n=126) received insufflation with the HumiGard™ Surgical Humidification System. All patients received standard antimicrobial prophylaxis on induction.

The results of this study have been reported from two different sources – in abstract from (29) and as a completed manuscript (in prep.(9)). In the abstract, the incidence of SSI was significantly reduced from 12% to 4.7% following intervention with HumiGard™ (P=0.047) (29).

[redacted]

[redacted]The authors concluded that use of the intervention during laparoscopic colorectal surgery is a safe, feasible and a cost-effective intervention. It improved the quality of surgical care relating to SSIs, peri-operative hypothermia and length of stay.

Study 3. Prevention of Hypothermia in Patients Undergoing Orthotopic Liver Transplantation using the Fisher and Paykel HumiGard™ Open Surgery Humidification System: A Prospective Randomised Pilot Clinical Trial (Weinberg *et al.* in prep.(8)).

This was a randomised study of adult patients undergoing primary orthotopic liver transplant. Twenty-two Patients were randomised to receive either open wound humidification with the HumiGard™ Surgical Humidification System in addition to standard care (FPH group) or to standard care alone (standard care group). Temperature measurements were taken at multiple time-points using three different measurement sites on the body, for each patient: pulmonary artery catheter (PAC), naso-pharyngeal temperature probe (NPP) and a bladder temperature probe (BTP). Immediately prior to reperfusion the mean NPP temperature was 36.0°C (SD:0.41) in the FPH group and 35.4°C (SD: 0.74) in the standard care group (estimated difference: 0.6°C; 95%CI: 0.08 to 1.15, p=0.02); the mean PAC temperature was 35.9°C (SD:0.51) in the FPH group and 35.5°C (SD: 0.79) in the standard care group (estimated difference: 0.4°C; 95%CI: 0.15 to 1.03, p=0.14); the mean bladder temperature was 36.2°C (SD: 0.63) in the FPH group and 35.5°C (SD: 1.03) in the standard care group (estimated difference: 0.6°C; 95%CI: 0.12 to 1.4, p=0.09). On wound closure the FPH group had a higher mean NPP temperature compared to the standard care group: 36.7°C vs. 36.1°C (estimated difference 0.52°C; 95%CI: 0.02 to 1.03, p=0.041). At completion of surgery there was a trend towards higher PAC (36.8°C vs. 36.3°C, p= 0.09) and BTP (36.8°C vs. 36.5°C, p=0.27) temperatures in the FPH group. The authors concluded that the HumiGard™ open surgery humidification system reduces the incidence of intra-operative hypothermia during open liver transplants.

7.9 Interpretation of clinical evidence

7.9.1 Provide a statement of principal findings from the clinical evidence highlighting the clinical benefit and any risks relating to adverse events from the technology.

Incidence of hypothermia in the intra- and post-operative period:
The meta-analysis demonstrates that heated, humidified insufflation in both laparoscopic and open surgery significantly increased operative core temperature (P=0.003, P<0.0001, respectively) in patients undergoing abdominal surgery. Of the included papers in open surgery, Frey *et al*. (5) reported on the incidence of hypothermia in the operative period and showed that with a cut off of <36 °C none of the patients in the intervention group were hypothermic, compared to 18% of patients in the standard care group (P<0.005).

The meta-analysis demonstrates that heated, humidified insufflation in laparoscopic surgery significantly improves core temperature reported at post-operative recovery (P=0.009). [redacted] Post-operative temperature was not reported in the included open investigations.

A sub group analysis was performed on the laparoscopic group to assess adjunctive warming devices and high risk groups as described in NICE guideline 65. Results show that heated humidified insufflation significantly improves core temperature in studies with adjunctive warming (P=0.004). Analysis of patients deemed to be high risk also demonstrated significantly improved core temperature (P=0.008). A mild degree of hypothermia has been associated with significant morbidity and mortality (31).

[redacted]

Incidence of Surgical Site Infection:

Mild peri-operative hypothermia is associated with a threefold increase in SSI in colorectal surgery patients (32). Incidence of SSI was not reported in the included investigations so was not analysed via the meta-analysis. However Mason *et al*.(9)/Noor *et al.(29)* demonstrated in a retrospective audit that the introduction of heated humidified insufflation in laparoscopic colorectal surgery reduced the incidence of SSI from 12% to 4.7% (29). [redacted]

Length of stay in post-operative recovery and total length of hospital stay:

The meta-analysis for laparoscopic surgery demonstrated a near-significant reduction in the length of time spent in post-operative recovery with patients treated with heated, humidified insufflation compared to patients treated with standard care (P=0.07). The included open investigations did not report on length of stay in post-operative recovery.

The meta-analysis found no significant difference in total length of hospital stay for laparoscopic surgery (P=0.42). [redacted]

[redacted]

Two included open studies (5, 6) reported on length of stay in post-operative recovery and neither showed a significant difference in hospital stay (P = 0.818, P = 0.895 respectively).

Patient reported pain:

The meta-analysis demonstrates that heated, humidified insufflation in laparoscopic surgery significantly reduces total patient reported pain as measured by both the subjective VAS and objective values of analgesic consumption (P=0.03, P=0.003, respectively). In “high risk” patients, significant reductions in total patient reported pain was similarly observed for VAS (P=0.03) and analgesic use (P=0.03).

Shoulder tip pain is a common complaint after laparoscopic surgery even after minor laparoscopy (33). The meta-analysis demonstrates that shoulder tip pain was significantly reduced with intervention compared to unheated, unhumidified insufflation (P=0.02). Patient reported pain was not reported in the included open surgery investigations.

Device related adverse events:

The use of heated humidified insufflation in laparoscopic and open abdominal surgery is safe and effective with no adverse events reported to date.

7.9.2 Provide a summary of the strengths and limitations of the clinical-evidence base of the technology.

As with any meta-analysis there are some limitations. Although all the studies included in the analysis were randomised controlled trials that met the

designated inclusion criteria some lacked study design details, which could introduce uncertainty to the evaluation of study quality. The included studies are multi-specialty and subsequently increased the heterogeneity of the data.

Another potential limitation is that reported recovery time and total length of hospital stay may not be adequately reflected by the study design. Several studies (Hermann *et al*., Davis *et al*. (13, 19)) reported that total length of hospital stay and length of stay in recovery were determined by administration and not reflective of the actual condition of the patient. It would be more relevant to report on time fit for discharge as a measure of patient condition.

Another potential limitation is that the meta-analysis included a range of humidification devices in addition to the HumiGard™ Surgical Humidification System to deliver heated humidified insufflation for laparoscopic surgery. However, therapeutic equivalence was confirmed (Section 7.2.1) and the included devices deemed comparable.

The strength of this analysis is that it includes all published data up to 31st October 2015 and corrects for data entry errors and incorrect conclusions included in the 2011 Cochrane analysis of heated CO_2 with or without humidification for minimally invasive abdominal surgery (26).

7.9.2 Provide a brief statement on the relevance of the evidence base to the scope. This should focus on the claimed patient- and system-benefits described in the scope.

Evidence is in line with the scope as detailed in Table B12. Collectively, studies have shown that HumiGard™ intervention benefits the patient through decreased incidence of intra-operative hypothermia and improves post-operative recovery through prevention of evaporative heat loss and reductions in post-operative complications including SSI's and pain.

Table B 12: Relevance of the evidence base to the scope

Criteria	Scope	Evaluation
Population	People undergoing abdominal surgery, as an open or laparoscopic procedure	Eighteen published randomised control trials totalling 1357 patients plus an additional 3 unpublished trials.
Intervention	HumiGard Surgical Humidification System for: • Laparoscopic abdominal surgery • Open abdominal surgery	Laparoscopic: 16 published RCT's totalling 1204 patients (596 intervention, 599 comparator). One unpublished retrospective cohort study of 252 patients (126 in each group). Open: 2 open published RCT's totalling 153 patients (78 intervention, 75 comparator). One unpublished long term follow up of 158 patients 158 (80 intervention, 78 comparator).
Comparators	Laparoscopic abdominal surgery: • Unheated, unhumidified insufflant gas Open abdominal surgery: • No insufflant (ambient air)	As above.
Outcomes	The outcome measures to consider include: • Incidence of hypothermia in the intra- and post-operative period (defined as a core body temperature <36°C).	Relevance of the outcomes examined in this evaluation are listed below: • Meta-analysis showed that the intervention significantly increased intra-operative core temperature in laparoscopy. • Meta-analysis showed that the intervention significantly increased post-operative core temperature after laparoscopy. • Meta-analysis showed that the intervention significantly increased intra-operative core and wound area temperature in open surgery. • Frey *et al*. 2012 (5) demonstrated that the intervention significantly reduced the incidence of intra-operative hypothermia in open surgery.
	• Incidence of SSI's	• Mason *et al*. showed that the intervention reduced the incidence of

Criteria	Scope	Evaluation
		SSI. Hypothermic patients in the study had a significantly increased risk of developing an SSI. The reduction in SSI leads to a reduced cost-to-treat in patients receiving the intervention.
	• Length of stay in post-operative recovery	• Meta-analysis showed that the intervention trended towards a reduced length of stay in recovery in laparoscopy. • No significant difference was shown in open surgery.
	• Total length of hospital stay	• Meta-analysis showed no significant difference in total length of hospital stay in laparoscopy or open surgery.
	• Device-related adverse events	• No device-related adverse events were found for the intervention.
	• Patient-reported pain	• Meta-analysis showed a significant reduction in patient reported pain as measured by VAS after laparoscopy. • Meta-analysis showed a significant reduction in patient reported pain as measured by analgesic consumption after laparoscopy. • Meta-analysis showed a significant reduction in patient reported shoulder tip pain as measured by VAS after laparoscopy. • Patient reported pain was not recorded in included open surgery studies.
Subgroups to be considered	• People receiving adjunctive warming, such as from forced air warming devices or warming mattresses • High-risk groups as described in NICE guideline 65 (any 2 of: ASA grades II-V, pre-operative temperature below 36°C, combined general and regional anaesthesia, major or	• Meta-analysis showed that the intervention significantly increased intra-operative core temperature in laparoscopy for patients with adjunctive warming. • Meta-analysis showed that the intervention significantly increased intra-operative core temperature in laparoscopy for patients deemed as high risk. • Meta-analysis showed that the intervention significantly deceased

Criteria	Scope	Evaluation
	intermediate surgery or at risk of cardiovascular complications)	patient reported pain as measured by VAS in laparoscopy for patients deemed as high risk. • Meta-analysis showed that the intervention significantly deceased patient reported pain as measured by analgesic consumption in laparoscopy for patients deemed as high risk.

7.9.3 Identify any factors that may influence the external validity of study results to patients in routine clinical practice.

We are not aware of any factors that would adversely influence the use of and outcomes associated with the use of the HumiGard™ Surgical Humidification System for abdominal surgery. Inadvertent peri-operative hypothermia is an avoidable complication that affects all surgical patients. This analysis demonstrates that irrespective of demographics, sex or surgery type the application of heated, humidified insufflation significantly improves patient care and outcomes.

7.9.4 Based on external validity factors identified in 7.9.4 describe any criteria that would be used in clinical practice to select patients for whom the technology would be suitable.

Even with adjunctive warming technologies inadvertent hypothermia is still a common consequence of surgery. HumiGard™ Surgical Humidification System acts to ameliorate heat loss in surgery so is appropriate for all abdominal surgical patients. The consequences of mild peri-operative hypothermia are significant for the patient and the healthcare system so reducing the risk of hypothermia in surgery is valid. In addition, heated humidified insufflation reduces post-operative pain and risk of SSI which can be experienced by all surgical patients.

Section C – Economic Evidence

Section C requires sponsors to present economic evidence for their technology.

All statements should be evidence-based and directly relevant to the decision problem.

The approach to the de novo cost analysis expected to be appropriate for most technologies is cost-consequence analysis. Sponsors should read section 7 of the Medical Technologies Evaluation Programme Methods guide on cost-consequences analysis, available from www.nice.org.uk/mt

Sponsors are requested to submit section C with the full submission. For details on timelines, see the NICE document 'Guide to the Medical Technologies Evaluation Programme process', available from www.nice.org.uk/mt

8 Existing Economic Evaluations

8.1 Identification of studies

8.1.1 Describe the strategies used to retrieve relevant health economics studies from the published literature and to identify all unpublished data. The search strategy used should be provided as in section 10, appendix 3.

The literature search was designed to identify economic evaluations and cost studies on the use of the HumiGard™ Surgical Humidification System in people undergoing open or laparoscopic abdominal surgery. The strategy was developed for MEDLINE (Ovid interface). The main structure of the MEDLINE search strategy comprised four concepts:

- Economic evaluations / costs
- Carbon dioxide (CO_2)
- Humidification
- Heating

The search concepts were combined as follows:

(economic evaluations / costs) AND CO2 AND (humidification OR heating).

The terms for the CO_2 concept included terms relating to insufflation and pneumoperitoneum. The inclusion of these was designed to identify studies where the CO_2 concept was not explicit in the database record. For the same reason, the strategy included a focused set of stand-alone search lines which aimed to identify studies referring to the humidification, warming or heating of non-specific gases. The strategy also included a set of stand-alone search lines on terms related specifically to the HumiGard system and device manufacturer names.

The search strategy was devised using a combination of subject indexing terms and free text search terms in the title, abstract and keyword heading word fields. The search terms were identified through discussion within the research team, scanning background literature, browsing database thesauri and use of the PubMed PubReminer tool [2]. The terms for the economic evaluation / costs concept included those in the search filter developed and used by the University of York Centre for Reviews and Dissemination to identify studies for inclusion in the NHS Economic Evaluation Database [3], plus the floating economics subheading available in Ovid MEDLINE.

The strategy excluded animal studies using a standard algorithm. It also excluded studies which included the phrase 'case report' in the title, or which were indexed as the following publication types: news, comment, editorial, letter or case reports. The search was restricted to studies published in English language from 2007 to date. This date was identified by the research team as the earliest possible date from which studies on the HumiGard System could have been published.

Before running the searches, the sensitivity of the intervention section of the draft strategy was tested by checking retrieval of a sample of known, relevant clinical studies on the topic. These were sourced from two reviews of the clinical evidence - the clinical evidence MTEP submission (20 primary studies) and a Cochrane review (16 primary studies) [4]. The draft strategy successfully retrieved all studies. No sample set of relevant economic studies was available to check the sensitivity of the strategy as a whole, though the one economic study known to be relevant at project start was successfully retrieved by the draft strategy.

The MEDLINE strategy was translated appropriately for the other databases searched. The search was conducted in a range of relevant databases of published research and research presented as conference abstracts. The resources included those databases specified as a minimum for the economic evidence search in Section 10.3 of the NICE MTEP Sponsor Submission Template, plus the Health Technology Assessment Database and the Conference Proceedings Citation Index (CPCI). Two sources (Embase and CPCI) specifically include conference abstracts. The International Society for Pharmacoeconomics and Outcomes Research (ISPOR) conference was identified by the research team as the key conference of interest. Abstracts from ISPOR are included in Embase; at the date of search, however, abstracts from the 18th Annual European Congress were not yet included. This

conference was, therefore, searched using the ISPOR Scientific Presentations Database. Supplementary search approaches were undertaken to try and identify any further studies not retrieved through database searching. These included checking the reference lists of clinical studies relating to the HumiGard System and contact with the research team to identify any known studies.

Searching a number of databases produces a degree of duplication in the results. To manage this issue, the titles and abstracts of bibliographic records were downloaded and imported into EndNote bibliographic management software and duplicate records were removed using several algorithms.

The searches identified 1,007 records. Following deduplication 732 records were assessed for relevance.

The full search strategies for all search sources (including search dates and result numbers) are included in Appendix 3, Section 10.3.

8.1.2 Describe the inclusion and exclusion criteria used to select studies from the published and unpublished literature. Suggested headings are listed in the table below. Other headings should be used if necessary.

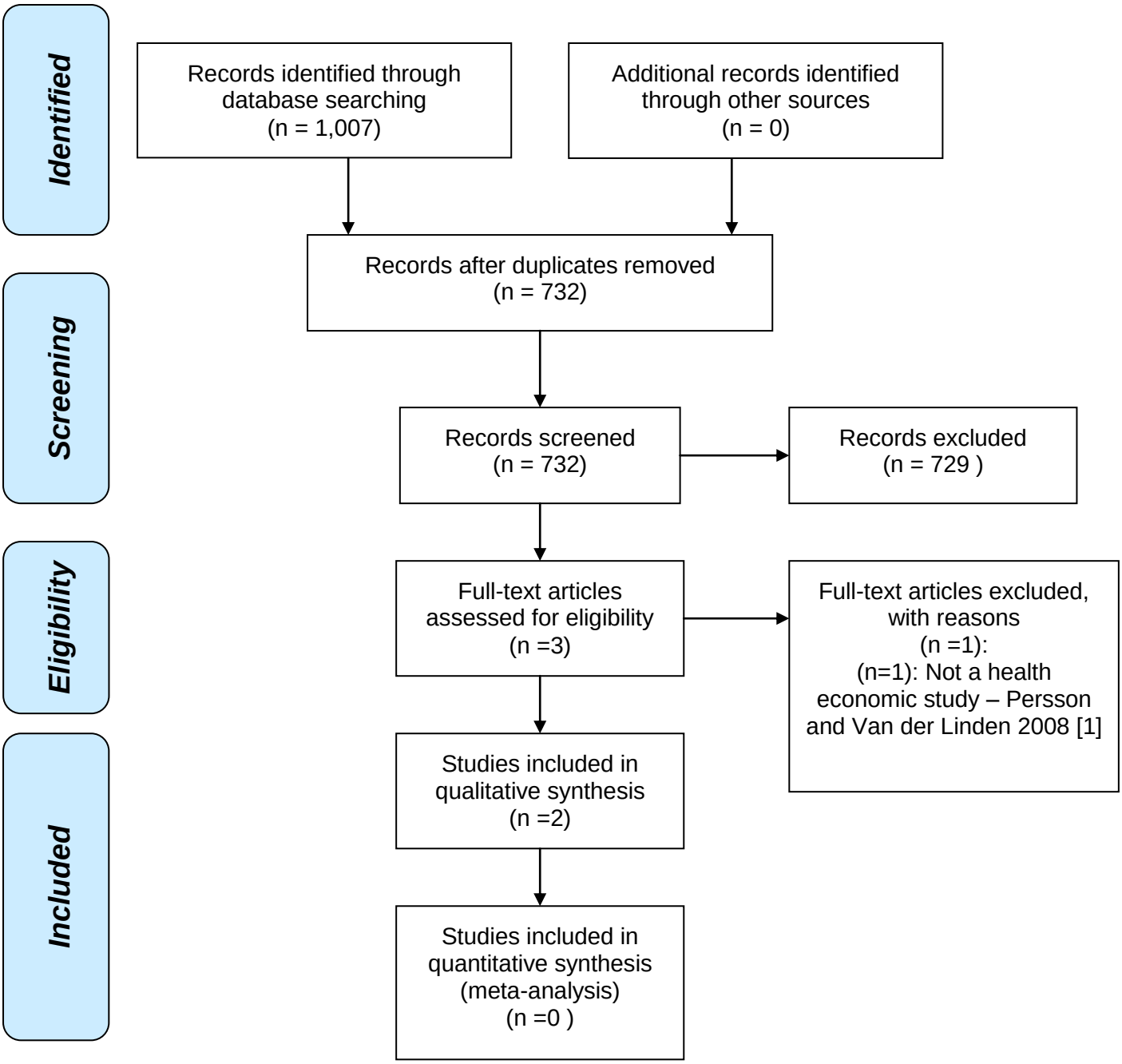
Table C1: Selection criteria used for health economic studies

Inclusion criteria	
Population	People undergoing open or laparoscopic abdominal surgery
Interventions	HumiGard surgical humidification system
Comparator	None specified (either no comparator or standard care)
Outcomes	Any
Study design	All types of economic evaluations and cost studies including cost analyses and cost-effectiveness and budget-impact analyses
Language restrictions	English
Search dates	2007 onwards
Exclusion criteria	
Population	People undergoing surgery that is not abdominal
Interventions	Any non-HumiGard System
Outcomes	None
Study design	Animal studies
Language restrictions	Non-English
Search dates	2007 onwards

8.1.3 Report the numbers of published studies included and excluded at each stage in an appropriate format.

The numbers of studies included and excluded at each stage of the health economic study review are shown in Figure C 1.

Figure C 1: PRISMA flow diagram of health economic studies



8.2 Description of identified studies

8.2.1 Provide a brief review of each study, stating the methods, results and relevance to the scope. A suggested format is provided in table C2.

Two health economic studies (both conference abstracts) were identified which are summarised in Table C2. Both studies found the HumiGard system to dominate over standard care, with both cost savings and greater health benefits estimated to be generated [5, 6].

Table C2: Summary list of all evaluations involving costs

Study name (year)	Location of study	Summary of model and comparators	Patient population (key characteristics, average age)	Costs (intervention and comparator)	Patient outcomes (clinical outcomes, utilities, life expectancy, time to recurrence)	Results (annual cost savings, annual savings per patient, incremental cost per QALY)
Jenks *et al.* (2015) [5]	UK	Cost-utility analysis using decision analytic model of the HumiGard system compared with standard care	Patients undergoing open or laparoscopic colorectal surgery	Not reported in abstract, but included: Device costs; Complication costs	QALYs	The HumiGard system dominated over standard care in both open and laparoscopic surgery patients.
Mason *et al.* (2015) [6]	UK	Trial based cost-benefit analysis of the HumiGard system compared with standard care	Patients undergoing laparoscopic colorectal surgery	Treatment costs of surgical site infection (SSI)	SSI	The HumiGard system dominated over standard care: Cost savings = £1,226 per SSI avoided. This cost saving already includes the offset costs of the avoided SSI.

8.2.2 Provide a complete quality assessment for each health economic study identified. A suggested format is shown in table C3.

As both included studies were published as conference abstracts, quality assessment of the studies is not appropriate and has, therefore, not been conducted.

9 De Novo Cost Analysis

Section 9 requires the sponsor to provide information on the de novo cost analysis.

The de novo cost analysis developed should be relevant to the scope.

All costs resulting from or associated with the use of the technology should be estimated using processes relevant to the NHS and personal social services.

Note that NICE cites the price of the product used in the model in the Medical Technology guidance.

9.1 Description of the de novo cost analysis

9.1.1 Provide the rationale for undertaking further cost analysis in relation to the scope.

Two studies were identified within Section 8 that assess the costs and benefits of the use of the HumiGard system in abdominal surgery. Mason *et al.* conducted an economic analysis alongside their clinical trial in patients undergoing laparoscopic colorectal surgery [6]. Therefore, this study is not fully applicable to the population within the scope (patients undergoing open or laparoscopic abdominal surgery). Jenks *et al.* reported on a model assessing the cost-utility of the use of the HumiGard system in patients undergoing open or laparoscopic colorectal surgery [5]. The model reported within this conference abstract has been adapted for submission to MTEP in order to meet the decision problem specified by NICE and forms the basis of this submission.

The objective of the current analysis is to determine the cost-effectiveness of the use of the HumiGard system to provide local insufflation of warmed humidified CO_2 during abdominal surgery compared with standard care from a UK NHS perspective.

Patients

9.1.2 What patient group(s) is (are) included in the cost analysis?

The cost analysis includes people undergoing open or laparoscopic abdominal surgery. The proportion of open and laparoscopic patients included in the model was derived from the literature, expert advice and insight from Fisher and Paykel Healthcare Ltd. The National Training Programme for Laparoscopic Colorectal surgery reported that, in 2012, 40% of elective colorectal resections were undertaken laparoscopically. The data show an upward trend in the proportion of resections undertaken laparoscopically between 2005 and 2012. It is, therefore, plausible that this trend has continued and currently, and in the future, greater than 40% of resections will be carried out laparoscopically.

Two experts advised that all cases of abdominal surgery in which the HumiGard system is used in their hospitals are conducted laparoscopically (Table C5.5). Fisher and Paykel Healthcare Ltd advised that the use of the HumiGard system in laparoscopic and open surgery within the UK NHS has a ratio of around 70:30. This proportion has been used in the base case, but varied in sensitivity and subgroup analyses, whereby results are reported for open and laparoscopic surgery patients separately.

The scope specified that the following subgroups be considered within the analysis:

- People receiving adjunctive warming, such as from forced air warming devices or warming mattresses.
- High-risk groups as described in NICE guideline 65 (any 2 of: ASA grades II-V, preoperative temperature below 36°C, combined general and regional anaesthesia, major or intermediate surgery or at risk of cardiovascular complications).

A description of how these subgroups fitted into the analysis is provided in Section 9.4.1.

Technology and comparator

9.1.3 Provide a justification if the comparator used in the cost analysis is different from the scope.

The comparators used in the analysis are in line with those in defined the scope, which are:

- Laparoscopic surgery: unheated, unhumidified insufflant gas;
- Open surgery: no insufflant.

Model structure

9.1.4 Provide a diagram of the model structure you have chosen.

The model structure for laparoscopic surgery patients is shown in Figure C2 and for open surgery patients in Figure C3.

Figure C2: Model structure for open surgery patients

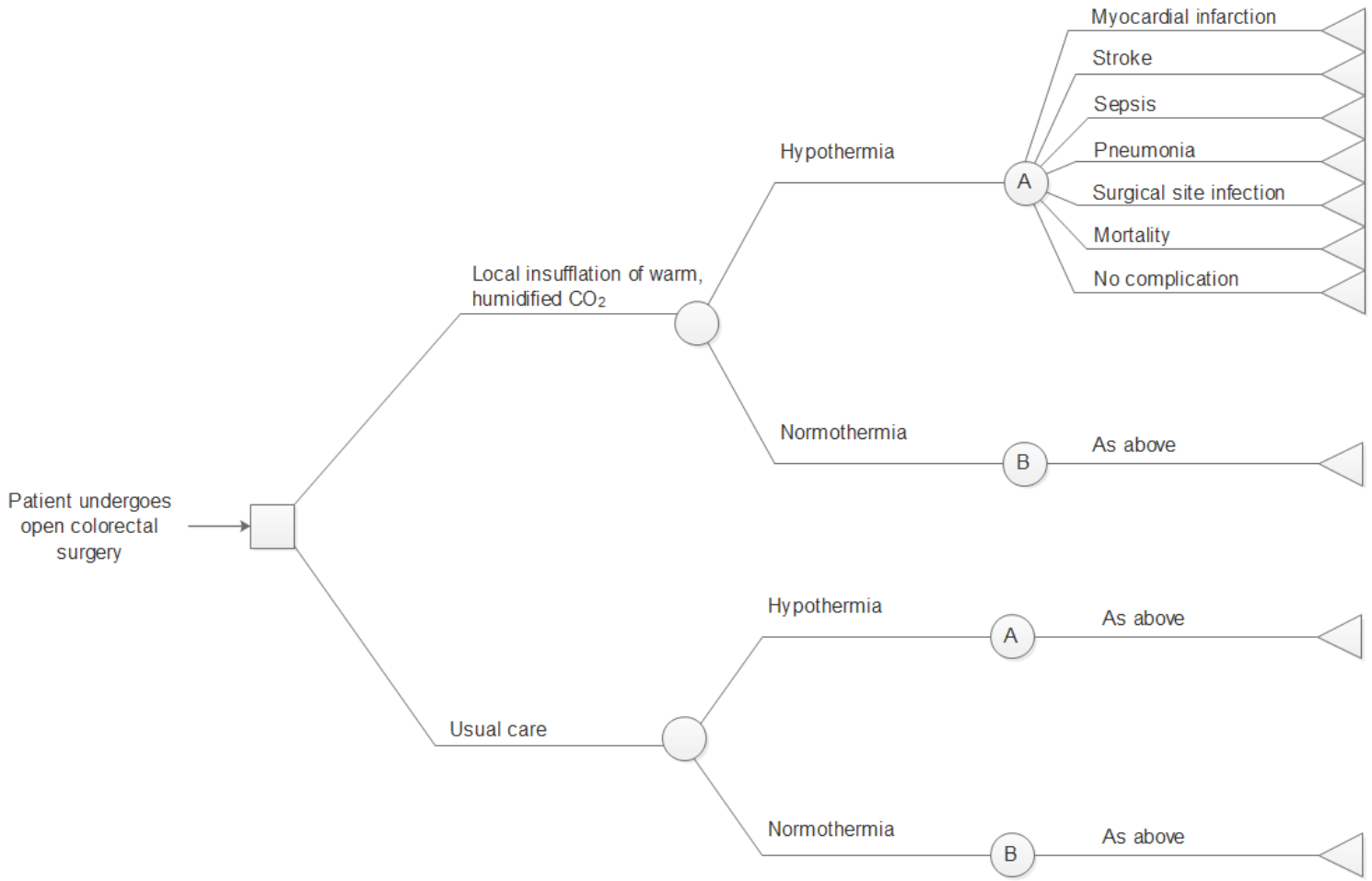
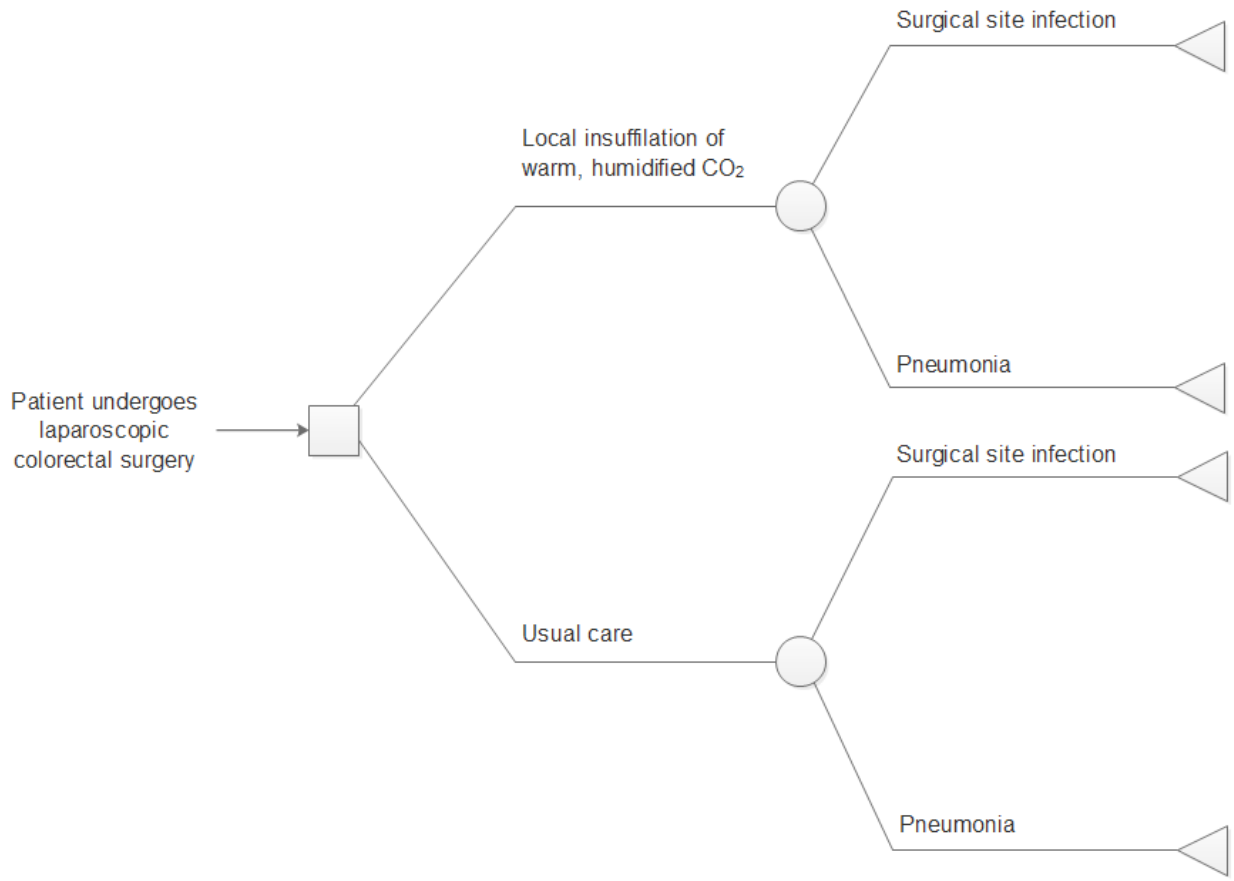

Patient undergoes open colorectal surgery
Local insufflation of warm, humidified CO_2
Hypothermia
A
Myocardial infarction
Stroke
Sepsis
Pneumonia
Surgical site infection
Mortality
No complication
Normothermia
B
As above
Usual care
Hypothermia
A
As above
Normothermia
B
As above

Figure C3: Model structure for laparoscopic surgery patients



9.1.5 Justify the chosen structure in line with the clinical pathway of care identified in response to question 3.3.

A *de novo* economic model was built in Microsoft Excel to estimate the potential cost savings associated with the use of the HumiGard system compared with usual care in people undergoing open or laparoscopic abdominal surgery. The HumiGard system can be used to provide local insufflation of warmed humidified CO2 during surgery. As described in Section 3.1, this aims to minimise evaporative cooling and desiccation and thus prevent intra-operative hypothermia. For open surgery patients, data were available on the incidence of post-operative hypothermia. Therefore, in this patient cohort, the model structure followed that used within NICE clinical guideline 65, whereby patients were at risk of clinical events, dependent upon their temperature status (defined as hypothermia or normothermia). Those clinical events included within the model were identified through a pragmatic literature review described in Section 9.2.3.

For laparoscopic surgery patients, data were available from Noor *et al.* (2015) describing clinical outcomes directly based on whether the HumiGard system was used on a patient, or not [7]. Therefore, these data were utilised directly to inform the model structure. The open surgery model structure has been adapted to laparoscopic surgery patients as a scenario analysis based on the limited data available.

As described in Section 3.5 the HumiGard system can be readily adopted within the current clinical pathway of care. There are some training needs associated with the use of the system and, therefore, the costs of these have been included within the model (see Section 9.3.7). Other costs accrued within the model are the costs of the technology and the comparator themselves, as well as the cost of any clinical events experienced. Although length of hospital stay was consistently reported within the clinical studies, this cost has not been included within the model due to the potential double counting of hospital costs already included within clinical event costs. The exclusion of any reduction in length of stay that may not be captured within the clinical events included within the model would mean that the results of the model would be conservative. The meta-analysis conducted in Section B of this submission found there to be a non-significantly shorter length of stay with the HumiGard system. Hence, any bias is likely to be minimal.

9.1.6 Provide a list of all assumptions in the cost model and a justification for each assumption.

The cost model has the following assumptions in open surgery patients:

- The data used in the base case analysis describing the clinical events for patients with and without hypothermia are not fully applicable to the model. Firstly, hypothermia is defined in this study as being lower than 35°C , rather than 36°C and second the patients included within the study did not all undergo abdominal surgery [8]. This study was utilised in the base case given that it reported upon the most complete set of clinical outcomes. However, scenario analyses were conducted using alternate studies to assess the impact of any bias on the model's results.

- The costs of complications were applied independently (as though clinical events were mutually exclusive), such that if any patients experienced multiple complications the cost may not be accurate. Multi-complication

patient costs may be higher due to greater severity or lower due to double counting of resource usage. This assumption has been tested by varying complication costs and also mitigated against through the use of one-year time horizon in the base case. As mortality and other complications within the model are not mutually exclusive, using a one-year time horizon aims to reduce the consequences of long term stroke or myocardial infarction costs being accrued for people who have died.

- Due to a paucity of data, the cost of each clinical event was based on patients experiencing each event generally, rather than those having undergone open abdominal surgery. Further, the costs were assumed to be incurred either as part of the initial stay or as an additional hospital visit. These costs were varied during sensitivity analysis to assess their impact on the model's results.

- The duration of surgery has been assumed to be the same in patients undergoing abdominal surgery with or without the HumiGard system. Clinical evidence reports that surgery times with the HumiGard system are non-significantly shorter (182 minutes versus 217 minutes) [9]. Exclusion of the difference in length of surgery time may mean that the results of the model are conservative in open surgery patients.

The cost model has the following assumptions in laparoscopic surgery patients:

- Due to a paucity of data, the cost of each clinical event was based on patients experiencing each event generally, rather than those having undergone laparoscopic abdominal surgery. Further, the costs were assumed to be incurred either as part of the initial stay or as an additional hospital visit. These costs were varied during sensitivity analysis to assess their impact on the model's results.

- Again, the costs of complications have been applied independently, as though each clinical event was mutually exclusive. In the laparoscopic surgery model only one patient experienced both SSI and pneumonia. This assumption has been tested by varying complication costs.

- The duration of surgery has been assumed to be the same in patients undergoing abdominal surgery with or without the HumiGard system. One expert advised that, in his experience, surgery is shorter with the HumiGard

system due to reduced lens fogging. Clinical evidence reported surgery time to be very similar with and without the HumiGard system [10-13].

9.1.7 Define what the model's health states are intended to capture.

There are no health states in the decision tree analytic model, rather clinical events are utilised to capture differences between the treatment and comparator.

9.1.8 Describe any key features of the cost model not previously reported. A suggested format is presented below.

Table C4: Key features of model not previously reported

Factor	Chosen values	Justification	Reference
Time horizon of model	1 year in base case, with 5 year time horizon considered in scenario analysis	Clinical studies reported on complications that generally occurred within the first month following surgery. Longer term costs have been captured within the 5 year time horizon presented in the scenario analysis.	Anannomcharoen *et al.* 2012, Kurz *et al.* 1996 and Flores-Malonado *et al.* 2011 [14-16]
Discount of 3.5% for costs	3.5% for costs	In scenario analysis with longer time horizons, costs are discounted at 3.5% per year	NICE, 2011 [17]
Perspective (NHS/PSS)	NHS and PSS perspective	Specified in NICE Methods guide	NICE, 2011 [17]
Cycle length	N/A	Model takes the form of a decision tree	
NHS, National Health Service; PSS, Personal Social Services			

9.2 Clinical parameters and variables

9.2.1 Describe how the data from the clinical evidence were used in the cost analysis.

The studies identified during the clinical evidence review were considered for suitability for inclusion within the economic model. Only those studies reporting on the HumiGard system were deemed relevant to the model.

Open surgery

Two studies using the HumiGard system were identified relating to open surgery patients. Frey *et al.* (2012) reported on the proportion of patients with post-surgery hypothermia [9]. This study was used to populate the economic model.

The second study by Weinburg *et al.* (2014) [19] has been reported as an abstract only and, therefore, contained limited information. As this study did not contain information relating to either the proportion of patients with post-surgical hypothermia or the rate of clinical events within the study population it was not utilised within the model.

Laparoscopic surgery

Five studies using the HumiGard system were included within the clinical evidence review submission for laparoscopic surgery patients. The study, by Noor *et al.* reported on clinical outcomes of patients undergoing laparoscopic surgery with or without the HumiGard system [7]. Given that this was a UK study reporting directly on clinical outcomes, it was utilised in the base case of the model. Due to the observational nature of the study and, therefore, potential for bias, extensive sensitivity analysis and scenario analysis testing the model's structure were conducted.

All five studies reported on temperature status: Sammour *et al.* (2010) [12], Yu *et al.* (2013) [13], Manwaring *et al.* (2008) [11], Hermann *et al.* (2015) [10] Mason (unpublished) [18]. All authors were contacted to see if data could be provided relating to the number of patients in each treatment group with hypothermia post-surgery. Where data were provided, studies were used within the sensitivity analyses, described in Section 9.4. Table C4.1 displays the studies from which data were provided. For the remaining studies no response had been received at the time of submission.

Table C4.1: Data on hypothermic/normothermic patients undergoing laparoscopic surgery

Study	Patients	Intervention	Comparator	Data on hypothermia and normothermia
Sammour *et al.* (2010) [12]	Adult patients undergoing colonic-resection	Warm, humidified CO_2 with the HumiGard system	Cold, Dry CO_2	Temperature below 36°c at end of surgery: HumiGard group = 5/35 (14%) Control = 9/39 (23%)
Mason (unpublished) [18]	[redacted]	[redacted]	[redacted]	[redacted]

9.2.2 Are costs and clinical outcomes extrapolated beyond the study follow-up period(s)? If so, what are the assumptions that underpin this extrapolation and how are they justified?

Clinical outcomes in the open surgery model were extrapolated beyond the study follow up period by linking post-surgery hypothermia (intermediate outcome) reported by Frey *et al.* (2012) to clinical events [9]. This is described in detail in Section 9.2.3. Costs have been attributed to clinical events. In the laparoscopic surgery model base case, clinical outcomes were not extrapolated beyond the length of the study follow-up period given that the data available reported on relevant clinical outcomes. Scenario analyses were conducted whereby the same modelling approach as that used in open surgery patients was followed.

9.2.3 Were intermediate outcome measures linked to final outcomes (for example, was a change in a surrogate outcome linked to a final clinical outcome)? If so, how was this relationship estimated, what sources of evidence were used and what other evidence is there to support it?

In the open surgery model (and scenario analysis for laparoscopic surgery) patients were at risk of a number of clinical events. The risk of clinical events depended on patient's temperature status post-surgery, with those patients who had post-surgical

hypothermia being at higher risk of clinical events than those with normothermia post-surgery. This modelling approach is consistent with the NICE clinical guideline on hypothermia prevention and management in patients undergoing general surgery [20].

A pragmatic review was conducted to identify studies reporting on the clinical outcomes of patients with hypothermia and normothermia post-surgery. In order for studies to be included they had to report on SSIs either alone or in combination with other outcomes. Studies suitable for use in the model met the following criteria:

- Patients: patients undergoing surgery (either general or open/laparoscopic abdominal surgery);
- Intervention: post-operative hypothermia (not for treatment purposes and not localised);
- Comparator: post-operative normothermia;
- Outcomes: SSI plus any other outcomes relevant to temperature status.

The review utilised studies identified during the NICE clinical guideline on hypothermia prevention, specifically the section on the consequences of hypothermia [20]. The 26 studies included by NICE were reviewed for suitability. Further, a search was undertaken to identify suitable studies published since the searches within the NICE guidance (conducted August 2007).

The targeted search was conducted in MEDLINE and identified studies added to the database since 2007 or with a publication date of 2007 to 2016. The main structure of the search strategy combined three concepts: (surgery AND infections AND hypothermia). The strategy also included an additional highly focused set of terms which aimed to identify a sample of those studies which report on infections, but which do not explicitly refer to infections in the database record. The search strategy was devised using a combination of subject indexing terms and free text search terms in the title, abstract and keyword heading word fields. The search terms for each of the concepts were identified through discussion within the research team, scanning background literature, browsing database thesauri and use of the PubMed PubReminer tool [2]. A total of 421 search records were identified.

Results

From the NICE review, 2 studies reported on the likelihood of SSI following either post-operative hypothermia or normothermia: Kurz *et al.* (1996) and Flores Maldonado *et al.* (2001) [15, 16]. A third study (Walz *et al.*, 2006) reported on both temperature status and SSIs, but did not report temperature status as a binary outcome (hypothermia/normothermia) so was not suitable for the model [21].

Two further studies were identified through the pragmatic literature review [8 , 14]. Anannamcharoen [14] reported on SSIs in patients with post-operative hypothermia or normothermia, whilst, the study by Billeter [8] reported on a range of outcomes depended on temperature status. Information on all included studies is shown in Table C4.2.

Table C4.2: Studies reporting on the impact of hypothermia/normothermia on clinical outcomes

Author and year	Setting and study type	Patients	Outcomes
Anannamcharoen *et al.* (2012) [14]	Thailand, prospective review of patients	Patients undergoing open colorectal surgery	SSI
Billeter *et al.* (2014) [8]	USA, retrospective review of hospital records	Patient undergoing elective surgery (non-cardiac) 25% gastrointestinal. Only a few patients underwent laparoscopic surgery (personal communication with author).	Mortality; myocardial infarction; stroke; sepsis; SSI; pneumonia.
Flores-Maldonado *et al.* (2001) [15]	Mexico, prospective review of patients	Patients undergoing cholecystectomy. 64.8% open surgery and 35.2% laparoscopic surgery	SSI
Kurz *et al.* (1996) [16]	USA, randomised control trial (RCT)	Patients undergoing colorectal surgery. Around 30% underwent laparoscopic surgery (personal communication)	SSI

The study by Billeter *et al.* (2014) was used in the model's base case given that this study reported on the broadest range of complications [8]. The applicability of this study is somewhat limited in that not all of the patients underwent abdominal surgery, and the definition of hypothermia in this study differs to the standard definition (35°C versus 36°C). Expert advice sought during the model's development suggested that although this discrepancy is a limitation of the analysis, the use of the study is still likely to be worthwhile. Sensitivity analyses have been conducted around the values taken from this study to assess the impact on the results of the likely overestimation of complications for patients with hypothermia. Scenario analyses have been conducted using data from the remaining three studies [14-16].

9.2.4 Were adverse events such as those described in Section 7.7 included in the cost analysis? If appropriate, provide a rationale for the calculation of the risk of each adverse event.

No adverse events were described in Section 7.7 and, therefore, none were included within the cost analysis. Clinical experts advised that they had not experienced any adverse events during their use of the HumiGard system (Table C5.5).

9.2.5 Provide details of the process used when the sponsor's clinical advisers assessed the applicability of available or estimated clinical model parameter and inputs used in the analysis.

A clinical advisor to the sponsor, Jonathan Sackier, was involved in teleconference meetings during the model development phase. He works on a consultancy basis to provide advice to Fisher and Paykel Healthcare Ltd. Dr Sackier provided advice on the model structure and also the clinical data used within the model.

9.2.6 Summarise all the variables included in the cost analysis. Provide cross-references to other parts of the submission. A suggested format is provided in Table C5 below.

All model input parameters and their values are displayed in Table C5. These are the inputs used in the base case only; those used throughout scenario analysis are detailed in Section 9.4.

Table C5: Summary of variables applied in the cost model

Variable	Value	Range or 95% CI	Source
Laparoscopic surgery			
HumiGard: SSI	4.7%	NR	Noor *et al.* (2015) [7]
HumiGard: pneumonia	0.79%	NR	Noor *et al.* (2015) [7]
Standard care: SSI	12%	NR	Noor *et al.* (2015) [7]
Standard care: pneumonia	3.17%	NR	Noor *et al.* (2015) [7]
Open surgery			
HumiGard: Proportion of patients with hypothermia post-surgery	0%	NR	Frey *et al.* (2012) [9]
Standard care: Proportion of patients with hypothermia post-surgery	18%	95% CI: 5-31%	Frey *et al.* (2012) [9]
Probability of myocardial infarction: normothermia	1.1%	NR	Billeter *et al.* (2014) [8]
Probability of myocardial infarction: hypothermia	3.3%	NR	Billeter *et al.* (2014) [8]
Probability of stoke: normothermia	1.0%	NR	Billeter *et al.* (2014) [8]
Probability of stroke: hypothermia	6.5%	NR	Billeter *et al.* (2014) [8]
Probability of sepsis: normothermia	2.6%	NR	Billeter *et al.* (2014) [8]
Probability of sepsis: hypothermia	7.5%	NR	Billeter *et al.* (2014) [8]
Probability of SSI: normothermia	3.3%	NR	Billeter *et al.* (2014) [8]
Probability of SSI: hypothermia	5.0%	NR	Billeter *et al.* (2014) [8]
Probability of pneumonia: normothermia	1.3%	NR	Billeter *et al.* (2014) [8]
Probability of pneumonia: hypothermia	5.1%	NR	Billeter *et al.* (2014) [8]
Probability of mortality: normothermia	4.0%	NR	Billeter *et al.* (2014) [8]
Probability of mortality: hypothermia	17.0%	NR	Billeter *et al.* (2014) [8]
CI, confidence interval; NR, Not reported			

9.3 Resource identification, measurement and valuation

NHS costs

9.3.1 Describe how the clinical management of the condition is currently costed in the NHS in terms of reference costs and the payment by results (PbR) tariff.

The patients included within the scope are those undergoing either open or laparoscopic abdominal surgery. Therefore, a wide range of reference costs and PbR tariffs might apply to these patients. These are listed in Appendix 5.

9.3.2 State the Office of Population, Censuses and Surveys Classification of Surgical Operations and Procedures (OPCS) codes for the operations, procedures and interventions relevant to the use of the technology for the clinical management of the condition.

A range of OPCS 47 codes may be applicable to patients undergoing either open or laparoscopic abdominal surgery. A list of relevant codes is presented in Appendix 5.

Resource identification, measurement and valuation studies

9.3.3 Provide a systematic search of relevant resource data for the NHS in England. Include a search strategy and inclusion criteria, and consider published and unpublished studies.

A separate literature search for resource use information was not required as information was taken from the clinical studies identified in Section B of this submission and expert advice. The HumiGard system can be readily adopted within clinical practice, replacing in the case of laparoscopic patients local insufflation of room temperature CO2. Therefore, no additional costs other than training costs and device/consumable costs have been included within the model. Clinical experts have validated this assumption (Table C5.5). One clinical expert found, that in his experience, surgery may be shorter when using the HumiGard system due to less lens fogging. A second expert stated that the tubing used in laparoscopic surgery is too short. However, no implications resulting from this were described. Frey *et al.* reported on operating time for open surgery, finding that surgery was shorter for

patients in the HumiGard system group (182 versus 217 minutes) [9]. This finding was not significant (p=0.312). Sammour *et al.* (2010) (176 versus 185 minutes, p=0.504) and Yu *et al.* (2013) (69 versus 72 minutes, p=0.685) found that operating time was also non-significantly shorter in laparoscopic surgery patients [12, 13], whilst Manwaring *et al.* (2008) (50 versus 47 minutes, p=0.543) and Hermann *et al.* (2015) (86 versus 83 minutes, p=NR) reported that operating time was non-significantly longer in laparoscopic surgery patients [10, 11]. Based on this non-significant and mixed evidence, it was assumed that surgery length was consistent for the HumiGard system and usual care in both open and laparoscopic surgery.

The costs of clinical events included within the model were derived from targeted searching of national cost databases (specifically NHS reference costs 2013/14 [22]) and previous NICE guidance rather than through a systematic search of the literature. These cost sources were used as they are directly applicable to the UK NHS and generally provide reliable and reputable cost estimates. Because no information regarding resource use from the general published literature was needed, a full systematic review was not required.

All costs within the model are for 2013-14. Where NHS reference costs were used to derive cost estimates, the total HRG costs were used. Clinical evidence reporting on complications in patients in the model included complications both during the initial hospital stay for abdominal surgery and readmissions [7, 8, 16]. Therefore, the total HRG cost combining both clinical events coded as elective (i.e. including those occurring during the abdominal surgery visit) and those coded as non-elective (i.e. including admissions requiring re-hospitalisation) were judged most applicable. Given these costs refer to all patients, not those specifically undergoing abdominal surgery, sensitivity analyses have been conducted on their values.

SSI

The cost of a SSI is reported by NICE to be difficult to estimate [23]. The NICE SSI quality standard reports that the cost is estimated to range from £2,100 to £10,500 depending on the nature of surgery [23]. Frampton reported on a study undertaken within the NHS in Leicester based on a small number of patients (n=29) and found the cost per SSI in colorectal patients to be £10,366 (2007 prices) [24]. This suggests that the cost of SSIs in patients within the scope may be toward the upper end of the range estimated by NICE. It is unclear whether this cost was based on open or laparoscopic surgery patients.

Within the model, a cost of £6,300 for SSIs was used. This is the mid-point of the range specified by NICE [23]. The full range was considered within a sensitivity analysis.

Pneumonia

The cost of pneumonia comprised a weighted average of relevant costs from NHS reference costs 2013/14 [22]. This resulted in an estimated cost of £1,825. The derivation of this cost is displayed in Table C5.1.

Table C5.1: Cost of an inpatient stay for pneumonia

Code	Description	Activity	Unit cost
DZ11D	Lobar, Atypical or Viral Pneumonia, with CC Score 15+	5,428	£4,817
DZ11E	Lobar, Atypical or Viral Pneumonia, with CC Score 12-14	26,905	£3,753
DZ11F	Lobar, Atypical or Viral Pneumonia, with CC Score 9-11	60,092	£2,666
DZ11G	Lobar, Atypical or Viral Pneumonia, with CC Score 6-8	97,494	£1,927
DZ11H	Lobar, Atypical or Viral Pneumonia, with CC Score 3-5	103,460	£1,433
DZ11J	Lobar, Atypical or Viral Pneumonia, with CC Score 0-2	49,864	£1,000
DZ23D	Bronchopneumonia with CC Score 13+	1,180	£4,066
DZ23E	Bronchopneumonia with CC Score 9-12	4,057	£2,718
DZ23F	Bronchopneumonia with CC Score 5-8	6,304	£1,737
DZ23G	Bronchopneumonia with CC Score 0-4	3,956	£1,279
DZ22D	Unspecified Acute Lower Respiratory Infection with CC Score 14+	1,115	£4,010
DZ22E	Unspecified Acute Lower Respiratory Infection with CC Score 11-13	5,660	£2,885
DZ22F	Unspecified Acute Lower Respiratory Infection with CC Score 8-10	14,871	£2,002
DZ22G	Unspecified Acute Lower Respiratory Infection with CC Score 5-7	31,839	£1,475
DZ22H	Unspecified Acute Lower Respiratory Infection with CC Score 2-4	38,234	£1,059
DZ22J	Unspecified Acute Lower Respiratory Infection with CC Score 0-1	17,873	£639
Weighted average cost			**£1,825**

Myocardial infarction

The cost of myocardial infarction was broken down into two phases: costs in the acute phase and longer term annual costs. Costs in the acute phase were derived from NHS reference costs [22] using a weighted average of the HRG codes shown in Table C5.2.

Table C5.2: Cost of an inpatient stay for myocardial infarction

Code	Description	Activity	Unit cost
EB10A	Actual or Suspected Myocardial Infarction, with CC Score 13+	5,010	£3,353
EB10B	Actual or Suspected Myocardial Infarction, with CC Score 10-12	12,834	£2,448
EB10C	Actual or Suspected Myocardial Infarction, with CC Score 7-9	21,600	£1,739
EB10D	Actual or Suspected Myocardial Infarction, with CC Score 4-6	30,780	£1,357
EB10E	Actual or Suspected Myocardial Infarction, with CC Score 0-3	25,604	£1,036
Weighted average cost			**£1,608**

The annual cost of myocardial infarction was taken from the NICE clinical guideline on managing hypertension [25]. Although a more recent edition of this guidance has been published, the annual cost of myocardial infarction is not reported within this update. The 2004 clinical guideline reports myocardial infarction to cost around £500 per year. This has been inflated to £646 (2013/14) prices using the Hospital & Community Health Services Pay & Prices Index [26]. Given that the original source of this figure is over 10 years old, it has been tested widely during sensitivity analysis.

The total cost of myocardial infarction was estimated to be £2,254 in the first year (combination of the acute and annual longer terms costs).

Stroke

Similarly to myocardial infarction, the cost of stroke was also broken down into two phases. Acute phase costs were again derived from NHS reference costs as shown in Table C5.3.

Table C5.3: Cost of an inpatient stay for stoke

Code	Description	Activity	Unit cost
AA35A	Stroke with CC Score 16+	2,829	£8,858
AA35B	Stroke with CC Score 13-15	7,511	£7,145
AA35C	Stroke with CC Score 10-12	15,671	£5,169
AA35D	Stroke with CC Score 7-9	28,755	£3,566
AA35E	Stroke with CC Score 4-6	46,153	£2,489
AA35F	Stroke with CC Score 0-3	41,484	£1,833
AA29C	Transient Ischaemic Attack with CC Score 11+	1,332	£2,605
AA29D	Transient Ischaemic Attack with CC Score 8-10	3,214	£1,386
AA29E	Transient Ischaemic Attack with CC Score 5-7	9,035	£971
AA29F	Transient Ischaemic Attack with CC Score 0-4	16,899	£715
Weighted average cost			**£2,788**

Longer term stroke costs were taken from the NICE costing template for dabigatran etexilate [27]. Within this document, the cost of stroke over 5 years was reported to be £15,306 (cost year 2002/2003). Inflating this cost to 2013/14 prices using the Hospital & Community Health Services Pay & Prices Index [26] gives a total cost of £21,532. Subtracting the cost of stroke in the acute phase results in a total cost of £18,744 or a cost of £3,749 per year (in years 1 to 5). This methodology was used by NICE within the costing template for dabigatran etexilate [27]. Therefore, the cost of stroke in the first year is estimate to be £6,537 (acute costs plus annual longer term cost). It is plausible that a greater proportion of these costs will be incurred in the first year following stroke, hence this cost may represent a conservative estimate in the one-year base case results. This cost has been varied during sensitivity analysis.

Sepsis

The cost of sepsis comprised an acute cost only, taken from NHS reference costs. This is detailed in Table C5.4.

Table C5.4: Cost of an inpatient stay for sepsis

Code	Description	Activity	Unit cost
WA03A	Septicaemia with CC Score 4+	3,186	£4,211
WA03B	Septicaemia with CC Score 2-3	16,485	£2,806
WA03C	Septicaemia with CC Score 0-1	50,799	£1,852
Weighted average cost			**£2,181**

Mortality

Mortality was conservatively assumed in the base case to have no cost given that it is likely that patients who died were already in hospital for either their abdominal surgery or a subsequent complication. This assumption has been varied within the deterministic sensitivity analysis.

9.3.4 Provide details of the process used when clinical advisers assessed the applicability of the resources used in the model[1].

A questionnaire was developed and emailed to four clinical advisors using the HumiGard system within the NHS to seek input on more specific model inputs.

[1] Adapted from Pharmaceutical Benefits Advisory Committee (2008) Guidelines for preparing submissions to the Pharmaceutical Benefits Advisory Committee (Version 4.3). Canberra: Pharmaceutical Benefits Advisory Committee.

Responses were received from two of the advisors. The questions asked and the answers provided are detailed in Table C5.5 below. The clinical advisors were selected by the UK sales manager at Fisher and Paykel Healthcare Ltd as frequent users (either past or continuing) of the HumiGard system. They were therefore judged to be familiar with the device and the therapy it delivers. None of the clinical experts have any known conflicts of interest.

Table C5.5: Clinical advice

Question	Mr Awad Sherif, Bariatric Surgeon, Derby Hospital	Rhona Eslabra Theatre Coordinator Surgical Innovation Centre Imperial College Trust
Approximately how many patients undergoing abdominal surgery use the HumiGard system per year within your hospital?	100	800 to 1,000
How many HumiGard systems do you have?	2	2
Do any patients not undergoing abdominal surgery use the HumiGard system? If so, please provide an estimate of this number.	No	No. The HumiGard we have in place is mainly for abdominal surgery.
Of those patients undergoing abdominal surgery and using HumiGard, what proportion have open surgery and what proportion have laparoscopic surgery?	All have lap surgery	The HumiGard is used mainly for laparoscopic cases. We haven't used the HumiGard for open cases.
Have you experienced any adverse events or complications during your use of HumiGard caused by the device?	No	My unit haven't experienced any complications brought about by the use of the equipment.
Please provide the brand name of any dry line tubing kits used for local insufflation of cold CO_2 that you are aware are used within the UK NHS.	None	LaproSurge Purple Medical
Open surgery		
Aside from the cost of the technology itself, are there any resource implications of using the HumiGard device compared with using standard care during surgery: a. During surgery itself (e.g. longer/shorter operating time)? b. Post-surgery?	N/A	N/A
Within our economic model we have assumed, based on clinical studies, that clinical events occurring post-surgery (such as SSIs) might occur both during the patient's hospital stay for abdominal surgery or after they have been discharged from hospital. a. Do you think that this is a reasonable assumption? b. If not, please provide detail on what would be a more accurate assumption.	N/A	N/A
Laparoscopic surgery		
Aside from the cost of the technology itself, are there any resource	a. Shorter op time due to	a. Laparoscopic: the tubing is

implications of using the HumiGard device compared with using standard care during surgery: a. During surgery itself (e.g. longer/shorter operating time)? b. Post-surgery?	reduced lens fogging b. Warmer patient and less pain	too short* b. NR
Within our economic model we have assumed, based on clinical studies, that clinical events occurring post-surgery (such as SSIs) might occur both during the patient's hospital stay for abdominal surgery or after they have been discharged from hospital. a. Do you think that this is a reasonable assumption? b. If not, please provide detail on what would be a more accurate assumption.	a. Yes b. N/A	a. Yes b. N/A
N/A = Not applicable; NR = Not reported		

* Fisher and Paykel Healthcare Ltd have been informed previously that the tubing length is both too long and too short, with equal frequency. The tubing length is an engineering related issue that has to do with the optimum length of tube required to maintain the gas condition over the distance to the patient. There are no known resource implications resulting from the tubing length.

Technology and comparators' costs

9.3.5 Provide the list price for the technology.

- MR860AEU Humidifier: £1,600 (This is a once-off purchase with a 5-year lifespan)
- For laparoscopic surgery: ST310 Humidified and Heated Tubing Kit: £75 per patient
- For open surgery: ST310 Humidified and Heated Tubing Kit plus VITA diffuser (ST300 DF): £99 per patient

9.3.6 If the list price is not used in the de novo cost model, provide the alternative price and a justification.

Not applicable

9.3.7 Summarise the annual costs associated with the technology and the comparator technology (if applicable) applied in the cost model. A suggested format is provided in Tables C6 and C7. Table C7 should only be completed when the most relevant UK comparator for the cost analysis refers to another technology.

The costs associated with the HumiGard system are displayed in Table C6. The number of patients using each device each year is estimated to be 75 in the base case. This number has been derived from a sample of Fisher and Paykel Healthcare Ltd sales data. The sample of hospitals has 65 bases which are in use within the UK and over the last 3 years, an average of 4,860 sets of consumables per year have been purchased. Therefore, 75 sets of consumables have been purchased per base device per year. This number is a crude estimation based on data from a sample of hospitals, so has therefore been varied during deterministic sensitivity analysis to consider those hospitals with lower and higher usage. The sample of data suggested that around 45 to 190 patients use each HumiGard device each year. No costs of surgery have been included as these will be incurred for both the treatment and comparator arms of the model and will thus cancel each other out. Further, no experts reported on any additional resources required setting up the HumiGard system compared with standard care. The available clinical evidence suggests that surgery time with the HumiGard system may be shorter than with usual care [9].

There is a cost of training nurses on the use of the device. Typically, 1 senior nurse per hospital is trained on the use of the device. These include team leaders, deputy team leaders, matrons, clinical nurse educators and senior nursing staff. Fisher and Paykel Healthcare Ltd are accredited by the AFPP to deliver 7.5 hours of training. Senior nurses are encouraged to share the training with others in their department and are given some materials to assist them with this. This would typically consist of a 10-20 minute group session. Within the model, it has been assumed that 10 hours of nurse time is required for training on the device. This covers the 7.5 hour training session and further time for sharing learning with others. Although this is unlikely to take 2.5 hours, this has been rounded up to include the time of the trainees. More recently, training has been provided at hospital audit days, taking 1 to 2 hours. This would likely involve a greater number of staff. Therefore within the sensitivity analysis, the hours of nurse time for training has been varied widely to capture the different ways in which training might be delivered.

The use of the HumiGard system does not have any further resource implications in addition to the cost of the device itself and any training.

Table C6: Costs per treatment associated with the technology in the cost model the HumiGard system

Items	Value	Source
Price of the technology per treatment	£1,600 (per humidifier with 5 year life span)	Fisher and Paykel Healthcare Ltd
Consumables Laparoscopic surgery: ST310 Humidified and Heated Tubing Kit Open surgery: ST310 Humidified and Heated Tubing Kit and VITA-diffuser (ST300 DF)	£75 per patient £99 per patient	Fisher and Paykel Healthcare Ltd
Maintenance cost Provided annually	£0	Fisher and Paykel Healthcare Ltd
Training cost 10 hours of nurse team manager time	£510	Training resource = Fisher and Paykel Healthcare Ltd Nurse team manager time = £51 per hour of non-patient contact
Other costs (staff) None	£0	Fisher and Paykel Healthcare Ltd
Total cost per treatment	Laparoscopic: £75+£5.63 = £80.63 Open: £99+£5.63 = £104.63	£1,600 cost of device and £510 of training spread among 75 patients per year for 5 years plus the cost of consumables.

In Table C7, the cost of the comparator technology is shown. Note that this applies to laparoscopic surgery patients only.

Table C7: Costs per treatment associated with the comparator technology in the cost model

Items	Value	Source
Price of the technology per treatment	£5	NHS Supply chain (Dry line tubing kit – reported in briefing note to cost between £5 and £10)
Consumables	N/A	
Maintenance cost	N/A	
Training cost	N/A	
Other costs (staff)	N/A	
Total cost per laparoscopic treatment	£5-10	A cost of £5 has been used within the model.

Health-state costs

9.3.8 If the cost model presents health states, the costs related to each health state should be presented in Table C8. The health states should refer to the states in Section 9.1.7. Provide a rationale for the choice of values used in the cost model.

The model does not present health states, but rather uses clinical events to capture differences between the HumiGard system and usual care (described in Section 9.3.3).

Adverse-event costs

9.3.9 Complete Table C9 with details of the costs associated with each adverse event referred to in 9.2.4 included in the cost model. Include all adverse events and complication costs, both during and after longer-term use of the technology.

No adverse events are included within the model as none have been reported in Section 7.7.

Miscellaneous costs

9.3.10 Describe any additional costs and cost savings that have not been covered anywhere else (for example, PSS costs, and patient and carer costs). If none, please state.

None

9.3.11 Are there any other opportunities for resource savings or redirection of resources that it has not been possible to quantify?

Within the clinical evidence submission a reduction in pain post-surgery was reported for patients receiving warmed humidified CO_2. This has not been included within the economic model due to the difficulties in quantifying any resource savings resulting from reduced pain as well as the potential for double counting if the reduction in pain resulted from any of the clinical events already included within the model.

9.4 Approach to sensitivity analysis

Section 9.4 requires the sponsor to carry out sensitivity analyses to explore uncertainty around the structural assumptions and parameters used in the analysis. All inputs used in the analysis will be estimated with a degree of imprecision. For technologies whose final price/acquisition cost has not been confirmed, sensitivity analysis should be conducted over a plausible range of prices.

Analysis of a representative range of plausible scenarios should be presented and each alternative analysis should present separate results.

9.4.1 Has the uncertainty around structural assumptions been investigated? State the types of sensitivity analysis that have been carried out in the cost analysis.

Open surgery model

Structural uncertainty in the open surgery model has been investigated through the use of alternative complication data. In the base case, data from Billeter *et al.* were used to model various clinical events [8]. The model structure was adapted such that only data relating to SSIs were included. Data from three studies were considered: Kurz *et al.* [16], Flores-Maldonado *et al.* [15] and Anannamcharoen *et al.* [14]. The parameters adopted during scenario analysis are shown in Table C10.2a.

Laparoscopic surgery model

The uncertainty associated with the structure of the laparoscopic surgery model was also assessed in an exploratory scenario analysis. Within this analysis, the model structure used for open surgery patients was adopted (i.e. clinical outcomes were dependent upon post-surgery temperature status). The evidence identified in the targeted literature review primarily included open surgery patients; hence this data is likely not fully applicable to laparoscopic patients. The studies considered within the scenario analysis were as follows: Billeter *et al.* (2014) [8], Kurz *et al.* (1996) [16] and

Flores-Maldonado *et al.* (2001) [15]. The study by Anannamcharoen *et al.* (2012) was omitted given that it was conducted in open surgery patients only [14].

Data on temperature status were derived through contacting the authors of the HumiGard system studies included within the clinical evidence submission as described in Section 9.2.1. The parameters adopted during scenario analysis are shown in Table C10.2b.

9.4.2 Was a deterministic and/or probabilistic sensitivity analysis undertaken? If not, why not? How were variables varied and what was the rationale for this? If relevant, the distributions and their sources should be clearly stated.

Deterministic sensitivity analysis

Univariate deterministic sensitivity analyses were undertaken around model input parameters to assess the impact on the model of changing input value and to identify the key drivers of the model. Where the direction of results changed during sensitivity analysis, threshold values have been reported.

The ranges considered were obtained, where possible, from the published literature. Where this was not possible ranges were based on conservative assumptions with a wide range of plausible input values considered. The rationale behind the range for each input parameter is provided in Table C10.1.

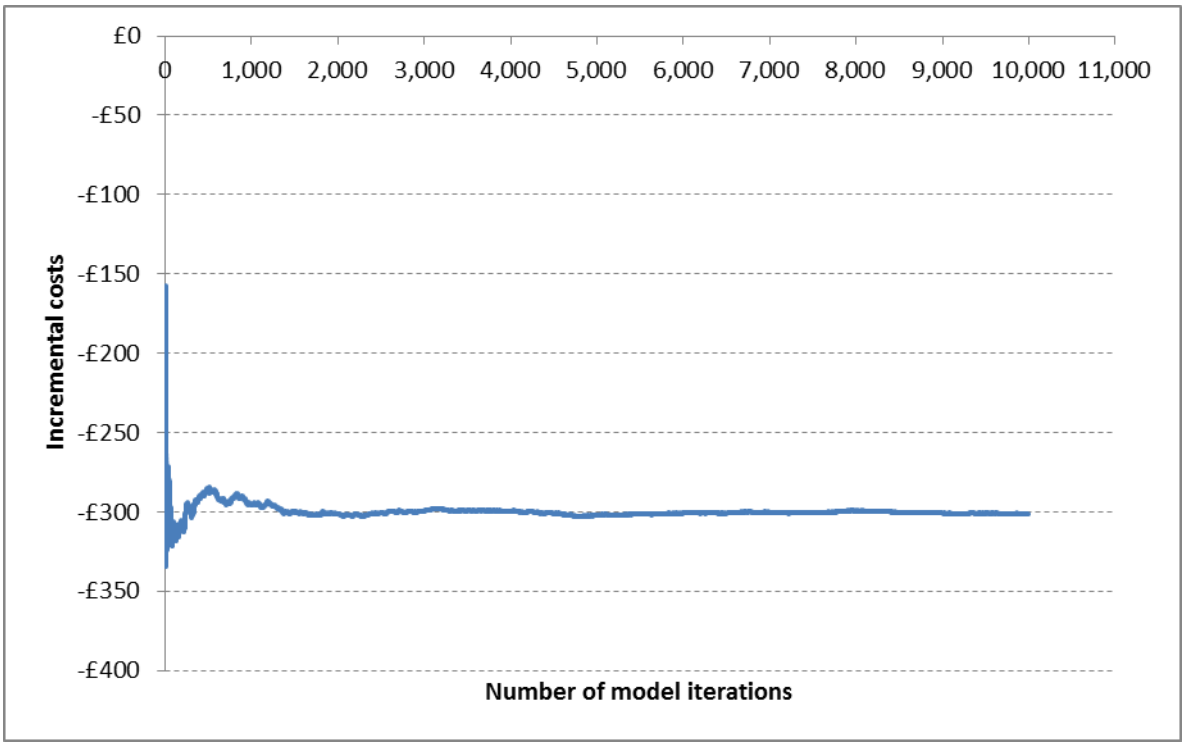
Multivariate analyses were conducted in the open surgery model using alternative complication data derived through the targeted evidence review (see Section 9.2.3). Further, a multiplier was applied to the complication data from Billeter *et al.* for patients with hypothermia to explore the impact of the discrepancy in definition of hypothermia in this study (35°C) compared with the standard definition of 36°C [8].

Finally, a scenario analysis was conducted in which the time horizon of the model was varied from 1 year in the base case to 5 years. In this scenario, complications including stroke and myocardial infarction had longer terms follow-up costs applied. These costs were discounted at a rate of 3.5% per year. Over 5 years, the cost of stroke applied was £20,307 and the cost of myocardial infarction was £4,627.

Probabilistic sensitivity analysis

Probabilistic sensitivity analysis has been conducted to show the joint effect parameter uncertainty on the models results. Probabilistic results have been presented for the base case and all scenarios considered. The results were based on 2,000 model iterations as this was above the number required to achieve stability in the models results (Figure C4).

Figure C4: *Probabilistic sensitivity analysis results by number of model iterations*



Subgroup analysis

Two subgroups were specified within the NICE scope and each are addressed below.

1. People receiving adjunctive warming, such as from forced air warming devices or warming mattresses

Open surgery: within the study by Frey *et al.* (2012) all patients received warming blankets [9]; hence the data included in the model pertaining to temperature status already represents this subgroup. It is possible that, had adjunctive warming not been utilised, the incidence of hypothermia in the control group would have been higher.

Laparoscopic surgery: the clinical data used within the model from Noor *et al.* (2015) included patients who used forced-air warming blankets [7]. Therefore, this subgroup is represented within the base case of the model.

2. High-risk groups as described in NICE guideline 65 (any 2 of: ASA grades II-V, preoperative temperature below 36°C, combined general and regional anaesthesia, major or intermediate surgery or at risk of cardiovascular complications)

Within Table C9.1, each of the clinical studies included within the model's base case or sensitivity analysis has been assessed for relevance to the second subgroup. None of the included studies report enough information to determine model inputs for this subgroup. Therefore, this subgroup cannot be modelled within a separate analysis. It is plausible that high risk groups will be at greater risk of hypothermia and subsequent complications and, therefore, patients within this subgroup may be reflected within the deterministic sensitivity analysis where greater risks are considered.

Table C9.1: Assessment of population in clinical studies

Study	Population in relation to subgroup
Frey *et al.* (2012)	Results not reported by any combination of the risk groups specified above.
Billeter *et al.* (2014)	Results not reported by any combination of the risk groups specified above.
Kurz *et al.* (1996)	Results not reported by any combination of the risk groups specified above.
Flores-Malonado *et al.* (2001)	Results not reported by any of the risk groups specified above. Included patients: ASA 1 = 77% and ASA 2 = 23%. All patients underwent major surgery.
Anannamcharoen *et al.* (2012)	Results not reported by any combination of the risk groups specified above.
Noor *et al.* (2015)	Results not reported by any combination of the risk groups specified above.
Sammour *et al.* (2010)	Results not reported by any of the risk groups specified above. Included patients (intervention/control): ASA 1 = 17.1%/7.7%, ASA 2 = 60%/59%, ASA 3 22.9%/33.3%

9.4.3 Complete table C10.1, C10.2 and/or C10.3 as appropriate to summarise the variables used in the sensitivity analysis.

Table C10.1: Variables used in univariate scenario-based deterministic sensitivity analysis

Variable	Base-case value	Range of values	Explanation of range used
Number of patients using each device per year	75	20 - 200	The sample of sales data showed that hospitals ranged between around 45 and 190 patients using each HumiGard device per year. This has been extended slightly to include those hospitals not included within the sample sales data.
Proportion of surgeries: laparoscopic	70%	0-100%	Model is run with all open surgery and all laparoscopic patients as well as each value in-between.
Proportion of surgeries: open	30%	0-100%	Model is run with all open surgery and all laparoscopic patients as well as each value in-between.
Laparoscopic surgery - effectiveness			
HumiGard: SSI	4.76%	0-10%	Range is assumed to assess the impact of this parameter on the results of the model.
HumiGard: pneumonia	0.79%	0-10%	Range is assumed to assess the impact of this parameter on the results of the model.
Standard care: SSI	11.90 %	0-20%	Range is assumed to assess the impact of this parameter on the results of the model.
Standard care: pneumonia	3.17%	0-10%	Range is assumed to assess the impact of this parameter on the results of the model.
Open surgery - effectiveness			
HumiGard: Proportion of patients with hypothermia post-surgery	0%	0-20%	Range is assumed to assess the impact of this parameter on the results of the model.
Standard care: Proportion of patients with hypothermia post-surgery	18%	0-30%	Range is assumed to assess the impact of this parameter on the results of the model.
Probability of myocardial infarction: normothermia	1.1%	0-5%	Range is assumed to assess the impact of this parameter on the results of the model.
Probability of myocardial infarction: hypothermia	3.3%	0-10%	Range is assumed to assess the impact of this parameter on the results of the model.
Probability of stoke: normothermia	1.0%	0-5%	Range is assumed to assess the impact of this parameter on the results of the model.
Probability of stroke: hypothermia	6.5%	0-15%	Range is assumed to assess the impact of this parameter on the results of the model.
Probability of	2.6%	0-5%	Range is assumed to assess the impact of this

Variable	Base-case value	Range of values	Explanation of range used
sepsis: normothermia			parameter on the results of the model.
Probability of sepsis: hypothermia	7.5%	0-15%	Range is assumed to assess the impact of this parameter on the results of the model.
Probability of SSI: normothermia	3.3%	0-10%	Range is assumed to assess the impact of this parameter on the results of the model.
Probability of SSI: hypothermia	5.0%	0-10%	Range is assumed to assess the impact of this parameter on the results of the model.
Probability of pneumonia: normothermia	1.3%	0-5%	Range is assumed to assess the impact of this parameter on the results of the model.
Probability of pneumonia: hypothermia	5.1%	0-10%	Range is assumed to assess the impact of this parameter on the results of the model.
Probability of mortality: normothermia	4.0%	0-10%	Range is assumed to assess the impact of this parameter on the results of the model.
Probability of mortality: hypothermia	17.0%	0-30%	Range is assumed to assess the impact of this parameter on the results of the model.
Training costs			
Hours of nurse time for training	10	2-100 hours	Range is assumed to assess the impact of this parameter on the results of the model.
Complication costs			
Cost of SSI	£6,300	£2,100 - £10,500	Range is reported within the NICE quality standard for SSIs (NICE, 2013).
Cost of pneumonia	£1825	£638 - £4917	Range represents the lowest and highest cost of NHS reference costs included within weighted average (Table C5.1).
Cost of myocardial infarction	£2,254	£1,036 - £4,353	Range represents the lowest and highest cost of NHS reference costs included within weighted average (Table C5.2) plus a range for the estimated annual cost of myocardial infarction of £0 to £1,000.
Cost of stroke	£6,537	£2,715 - £13,858	Range represents the lowest and highest cost of NHS reference costs included within weighted average (Table C5.3) plus a range for the estimated annual cost of stroke of £1,000 to £5,000.
Cost of sepsis	£2182	£1,852 - £4,211	Range represents the lowest and highest cost of NHS reference costs included within weighted average (Table C5.4).
Cost of mortality	£0	£0 - £1000	The range of costs considered is an assumption to assess the impact on the results of the model.

Table C10.2a: Variables used in multi-way scenario-based sensitivity analysis – Open surgery

Variable	*Base case (normothermia/hypothermia)*	*Open surgery: Kurz et al. (1996) data [16]*	*Open surgery: Anannamcharoen et al. (2012) data [14]*	*Open surgery: Flores-Maldonado et al. (2001) data [15]*	*Use of multiplier (m) on Billeter hypothermia data (m = 0.1, 0.5 and 0.8) [8]*
Myocardial infarction	1.1%/3.3%	N/A	N/A	N/A	3.3% * m
Stroke	1.0%/6.5%	N/A	N/A	N/A	6.5% * m
Sepsis	2.6%/7.5%	N/A	N/A	N/A	7.5% * m
SSI	3.3%/5.0%	6.0%/19.0%	17.6%/30.8%	1.9%/11.5%	5.0% * m
Pneumonia	1.3%/5.1%	N/A	N/A	N/A	5.1% * m
Mortality	4.0%/17.0%	N/A	N/A	N/A	17.0% * m

Table C10.2b: Variables used in multi-way scenario-based sensitivity analysis – Laparoscopic surgery

Variable	*Base case*	*Temperature data: Sammour [12] Clinical event data: Billeter [8]*	*Temperature data: Sammour [12] Clinical event data: Kurz [16]*	*Temperature data: Sammour [12] Clinical event data: Flores-Maldonado [15]*	*Temperature data: Mason [18] Clinical event data: Billeter [8]*	*Temperature data: Mason [18] Clinical event data: Kurz [16]*	*Temperature data: Mason [18] Clinical event data: Flores-Maldonado [15]*
Proportion of HumiGard patients with hypothermia post-surgery	N/A	14.3%	14.3%	14.3%	[redacted]	[redacted]	[redacted]
Proportion of non HumiGard patients with hypothermia post-surgery	N/A	23.1%	23.1%	23.1%	[redacted]	[redacted]	[redacted]
Myocardial infarction (by temperature status)	N/A	1.1%/3.3%	N/A	N/A	1.1%/3.3%	N/A	N/A
Stroke (by temperature status)	N/A	1.0%/6.5%	N/A	N/A	1.0%/6.5%	N/A	N/A
Sepsis (by temperature status)	N/A	2.6%/7.5%	N/A	N/A	2.6%/7.5%	N/A	N/A
SSI (by temperature status)	N/A	3.3%/5.0%	6.0%/19.0%	1.9%/11.5%	3.3%/5.0%	6.0%/19.0%	1.9%/11.5%
Pneumonia (by temperature status)	N/A	1.3%/5.1%	N/A	N/A	1.3%/5.1%	N/A	N/A
Mortality (by temperature status)	N/A	4.0%/17.0%	N/A	N/A	4.0%/17.0%	N/A	N/A

Table C10.3:Variable values used in probabilistic sensitivity analysis

Parameter	Mean	Distribution	Reference
Complication costs			
Cost of SSI	£6,300	Uniform Range = £2,100 to £10,500	NICE (2013) [23]
Cost of pneumonia	£1,825	Gamma Standard error = £365 (mean divided by 5)	Assumption
Cost of myocardial infarction	£2,254	Gamma Standard error = £451 (mean divided by 5)	Assumption
Cost of stroke	£6,537	Gamma Standard error = £1,307 (mean divided by 5)	Assumption
Cost of sepsis	£2,182	Gamma Standard error = £436 (mean divided by 5)	Assumption
Laparoscopic surgery effectiveness data			
HumiGard: SSI	4.7%	Beta (6,120)	Noor *et al.* (2015) [7]
HumiGard: pneumonia	0.79%	Beta (1,125)	Noor *et al.* (2015) [7]
Standard care: SSI	12%	Beta (15,111)	Noor *et al.* (2015) [7]
Standard care: pneumonia	3.17%	Beta (4, 121)	Noor *et al.* (2015) [7]
Open surgery – effectiveness data			
HumiGard: Proportion of patients with hypothermia post-surgery	0%	Beta (0.051,39.949)*	Frey *et al.* (2012) [9]
Standard care: Proportion of patients with hypothermia post-surgery	18%	Beta (7,25)	Frey *et al.* (2012) [9]
Probability of myocardial infarction: normothermia	1.1%	Beta (8, 690)	Billeter *et al.* (2014) [8]
Probability of myocardial infarction: hypothermia	3.3%	Beta (23,684)	Billeter *et al.* (2014) [8]
Probability of stoke: normothermia	1.0%	Beta (7, 691)	Billeter *et al.* (2014) [8]
Probability of stroke: hypothermia	6.5%	Beta (46, 661)	Billeter *et al.* (2014) [8]
Probability of sepsis: normothermia	2.6%	Beta (18, 680)	Billeter *et al.* (2014) [8]
Probability of sepsis: hypothermia	7.5%	Beta (53, 654)	Billeter *et al.* (2014) [8]

Parameter	Mean	Distribution	Reference
Probability of SSI: normothermia	3.3%	Beta (23,675)	Billeter *et al.* (2014) [8]
Probability of SSI: hypothermia	5.0%	Beta (35,672)	Billeter *et al.* (2014) [8]
Probability of pneumonia: normothermia	1.3%	Beta (9, 689)	Billeter *et al.* (2014) [8]
Probability of pneumonia: hypothermia	5.1%	Beta (36, 671)	Billeter *et al.* (2014) [8]
Probability of mortality: normothermia	4.0%	Beta (28, 670)	Billeter *et al.* (2014) [8]
Probability of mortality: hypothermia	17.0%	Beta (120, 587)	Billeter *et al.* (2014) [8]

* Alpha has not been set to 0, since there is likely some uncertainty in this result. In order to capture this uncertainty an estimation has been made. Based on a sample size of 40 and an underlying probability of hypothermia in the HumiGard system patients of 0.00128, there is a 95% chance of the trial showing no patients had hypothermia (alpha = 0). With an underlying probability of 0.00128, alpha is equal to 0.051 and beta is equal to 39.949.

9.4.4 If any parameters or variables listed in section 9.2.6 were omitted from the sensitivity analysis, provide the rationale.

The purchase cost and consumable costs relating to the HumiGard system and its comparator were omitted due to certainty in these costs.

Further, those parameters that were variable, as opposed to uncertain, were not included within the probabilistic sensitivity analysis. This included the proportion of open and laparoscopic surgery patients within the model; the number of abdominal surgery patients using the HumiGard system each year and variability around staff training on the device.

9.5 Results of de novo cost analysis

Section 9.5 requires the sponsor to report the de novo cost analysis results. These should include the following:

- costs
- disaggregated results such as costs associated with treatment, costs associated with adverse events, and costs associated with follow-up/subsequent treatment
- a tabulation of the mean cost results
- results of the sensitivity analysis.

Base-case analysis

9.5.1 Report the total costs associated with use of the technology and the comparator(s) in the base-case analysis. A suggested format is presented in table C11.

Table C11: Base-case results

	Total per patient cost (£)
The HumiGard system	£419
Usual care	£724

9.5.2 Report the total difference in costs between the technology and comparator(s).

In the base case, the HumiGard system has estimated cost savings of £305 per patient.

9.5.3 Provide details of the costs for the technology and its comparator by category of cost. A suggested format is presented in table C12.

Table C12: Summary of costs by category of cost per patient =

Item	Cost *the HumiGard system*	Cost *usual care*	Increment	Absolute increment	% of absolute increment
Equipment costs	£88	£4	£84	£84	17.7%
Clinical event costs:					
Myocardial infarction	£7	£10	-£3	£3	0.6%
Stroke	£20	£39	-£19	£19	4.0%
Sepsis	£17	£23	-£6	£6	1.3%
Surgical site infection	£270	£597	-£328	£328	69.2%
Pneumonia	£17	£51	-£34	£34	7.2%
Mortality	£0	£0	£0	£0	0.0%
Total	£419	£724	-£305	£474	100%
Adapted from Pharmaceutical Benefits Advisory Committee (2008) Guidelines for preparing submissions to the Pharmaceutical Benefits Advisory Committee (Version 4.3). Canberra: Pharmaceutical Benefits Advisory Committee					

9.5.4 If appropriate, provide details of the costs for the technology and its comparator by health state. A suggested format is presented in table C13.

No health states were included within the model.

9.5.5 If appropriate, provide details of the costs for the technology and its comparator by adverse event. A suggested format is provided in table C14.

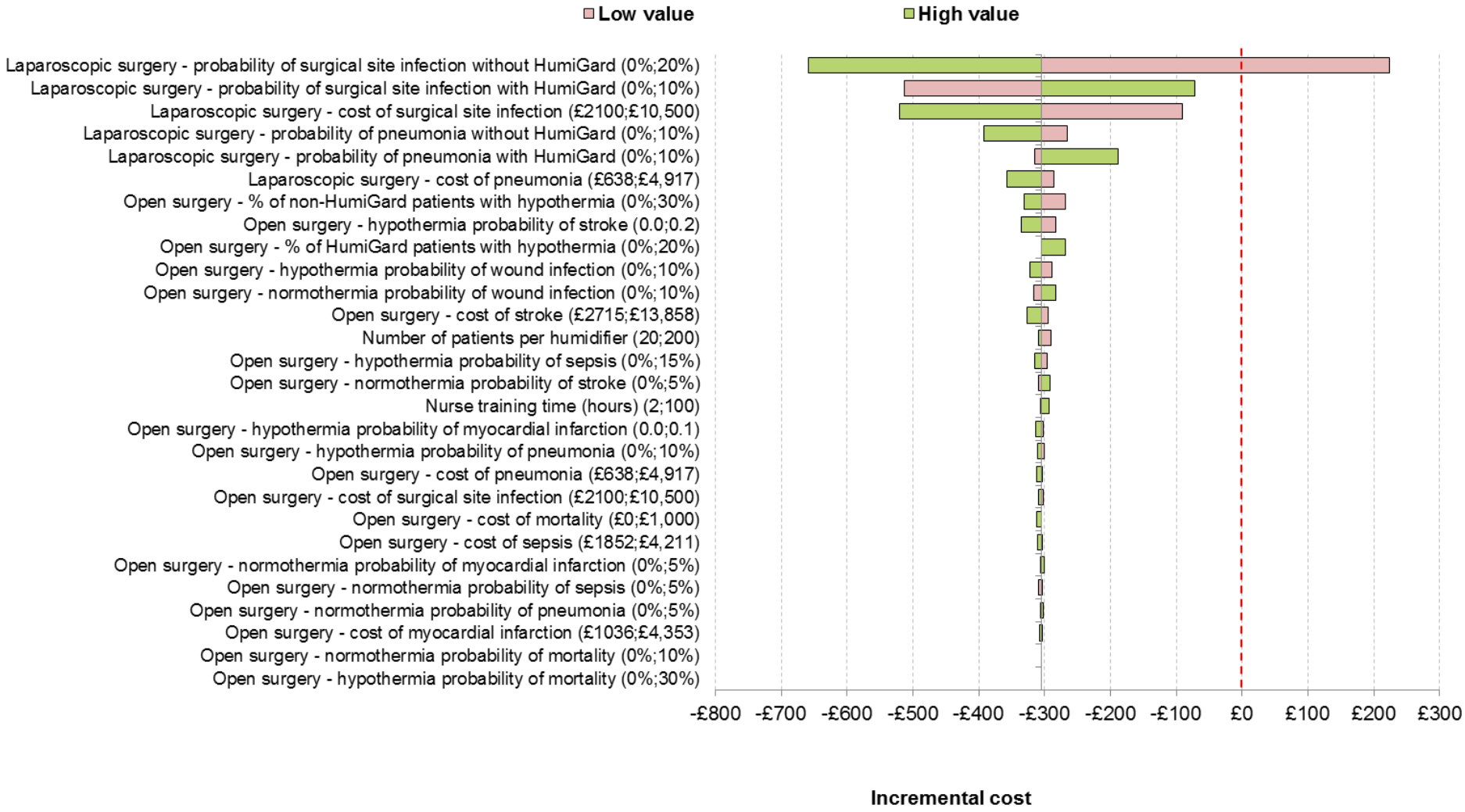
No adverse events were included within the cost model.

Sensitivity analysis results

9.5.6 Present results of deterministic one-way sensitivity analysis of the variables described in table C10.1.

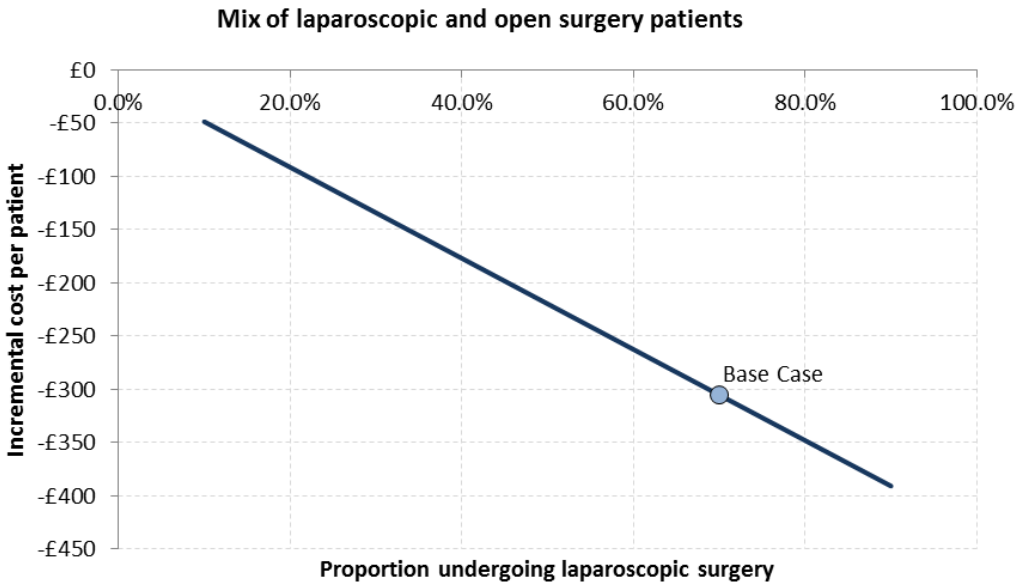
The results of the univariate sensitivity analysis are shown in Figure C5 and Figure C6.

Figure C5: Tornado diagram showing univariate sensitivity analysis on base case


Low value
High value
Laparoscopic surgery - probability of surgical site infection without HumiGard (0%;20%)
Laparoscopic surgery - probability of surgical site infection with HumiGard (0%;10%)
Laparoscopic surgery - cost of surgical site infection (£2100;£10,500)
Laparoscopic surgery - probability of pneumonia without HumiGard (0%;10%)
Laparoscopic surgery - probability of pneumonia with HumiGard (0%;10%)
Laparoscopic surgery - cost of pneumonia (£638;£4,917)
Open surgery - % of non-HumiGard patients with hypothermia (0%;30%)
Open surgery - hypothermia probability of stroke (0.0;0.2)
Open surgery - % of HumiGard patients with hypothermia (0%;20%)
Open surgery - hypothermia probability of wound infection (0%;10%)
Open surgery - normothermia probability of wound infection (0%;10%)
Open surgery - cost of stroke (£2715;£13,858)
Number of patients per humidifier (20;200)
Open surgery - hypothermia probability of sepsis (0%;15%)
Open surgery - normothermia probability of stroke (0%;5%)
Nurse training time (hours) (2;100)
Open surgery - hypothermia probability of myocardial infarction (0.0;0.1)
Open surgery - hypothermia probability of pneumonia (0%;10%)
Open surgery - cost of pneumonia (£638;£4,917)
Open surgery - cost of surgical site infection (£2100;£10,500)
Open surgery - cost of mortality (£0;£1,000)
Open surgery - cost of sepsis (£1852;£4,211)
Open surgery - normothermia probability of myocardial infarction (0%;5%)
Open surgery - normothermia probability of sepsis (0%;5%)
Open surgery - normothermia probability of pneumonia (0%;5%)
Open surgery - cost of myocardial infarction (£1036;£4,353)
Open surgery - normothermia probability of mortality (0%;10%)
Open surgery - hypothermia probability of mortality (0%;30%)
-£800 -£700 -£600 -£500 -£400 -£300 -£200 -£100 £0 £100 £200 £300
Incremental cost

The graph presented in Figure C6 shows the impact of varying the patient mix on the model's results. Where a higher proportion of patients undergo laparoscopic surgery, greater cost savings are potentially generated. This is because the savings per patient are greater for laparoscopic patients compared with open surgery patients.

Figure C6: Mix of open and laparoscopic surgery patients



9.5.7 Present results of deterministic multi-way scenario sensitivity analysis described in table C10.2.

The results from the scenarios shown in Table 10.2a and Table 10.2b and described in Section 9.4.2 are presented in Table C13. Within each of these scenarios the proportion of laparoscopic and open surgery patients are set to their base case value (70:30).

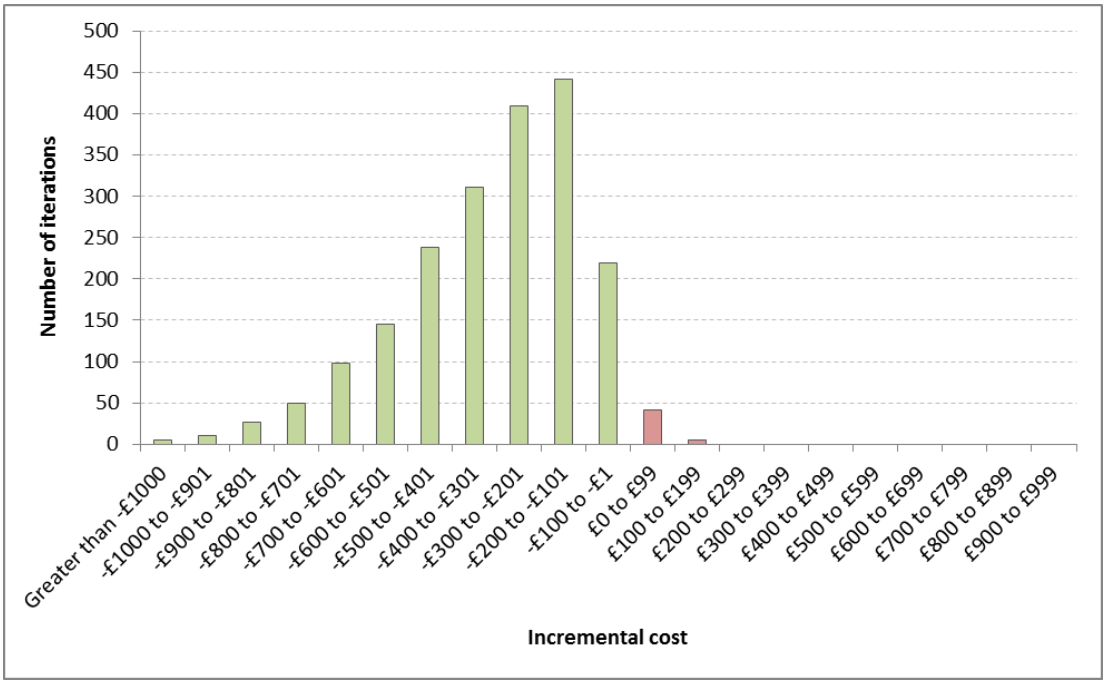
Table C13: Scenario analyses results

	The HumiGard system costs	Usual care costs	Incremental costs
Base case results (per patient)	*£419*	*£724*	*-£305*
Open surgery scenario			
Open surgery: Kurz et al. (1996) data [16]	£419	£731	-£312
Open surgery: Anannamcharoen et al. (2012) data [14]	£638	£951	-£313
Open surgery: Flores-Maldonado et al. (2001) data [15]	£341	£642	-£301
Use of multiplier (m) on Billeter hypothermia data:(m = 0.1 [8]	£419	£672	-£253
Use of multiplier (m) on Billeter hypothermia data: m = 0.5 [8]	£419	£695	-£276
Use of multiplier (m) on Billeter hypothermia data: m = 0.8 [8]	£419	£713	-£294
Time horizon of 5 years	£468	£817	-£349
Laparoscopic surgery scenario			
Temperature data: Sammour [12] Clinical event data: Billeter [8]	£536	£531	£5
Temperature data: Sammour [12] Clinical event data: Kurz [16]	£548	£558	-£10
Temperature data: Sammour [12] Clinical event data: Flores-Maldonado [15]	£269	£254	£14
Temperature data: Mason [18] Clinical event data: Billeter [8]	£530	£696	-£166
Temperature data: Mason [18] Clinical event data: Kurz [16]	£540	£753	-£212
Temperature data: Mason [18] Clinical event data: Flores-Maldonado [15]	£263	£398	-£135

9.5.8 Present results of the probabilistic sensitivity analysis described in table C10.3.

Probabilistic sensitivity analysis was conducted based on 2,000 model iterations. The HumiGard system was cost saving in 97.4% of iterations and the average probabilistic cost savings were £302 per patient. Figure C7 Figure C7displays the distribution of these results. These results use the base case inputs with the distribution and ranges shown in Table 10.3 applied. The probabilistic sensitivity analysis outputs displayed in Figure C7 are skewed because the costs of complications within the model are the driver of this analysis. These costs have a gamma distribution fitted which is bound by 0, but have no upper limit. Given that in most instances the HumiGard system is at least as effective as usual care, it is very unlikely that the incremental costs will be greater than £84 (the cost per patient of the HumiGard system). This is reflected in the graph shown in Figure C7.

Figure C7: Probabilistic sensitivity analysis distribution



Probabilistic sensitivity analyses have also been conducted using the alternate clinical data for open surgery patients with/without hypothermia. The results are displayed in Table C14.

Table C14: Probabilistic sensitivity analysis results for alternative clinical data (open surgery)

Scenario	Iterations in which the HumiGard system is cost-saving	Probabilistic incremental costs
Base case	97.4%	-£302
Open surgery: Kurz *et al.* (1996) data Normothermia: alpha = 6, beta = 98 Hypothermia: alpha = 18, beta = 78	97.4%	-£297
Open surgery: Anannamcharoen *et al.* (2012) data Normothermia: alpha = 22, beta = 103 Hypothermia: alpha = 32, beta = 72	97.5%	-£307
Open surgery: Flores-Maldonado *et al.* (2001) data Normothermia: alpha = 2, beta = 103 Hypothermia: alpha = 18, beta = 138	97.5%	-£295

9.5.9 What were the main findings of each of the sensitivity analyses?

The main findings of each of the sensitivity analyses are reported under the following headings:

Univariate sensitivity analysis

The HumiGard system remains cost-saving in all instances, except where the probability of SSI is lowered in patients undergoing usual care. Provided the probability of SSI is 5% or higher in the usual care patients (compared with that of the HumiGard system of 4.7%) then the HumiGard system is cost saving. Thus, the absolute difference in SSIs between patients undergoing surgery with the HumiGard system and usual care must be 0.3% or greater for the HumiGard system to be cost saving.

The inputs relating to open surgery patients have a limited impact on the results of the model, due to these patients only comprising 30% of the patient population within the model. Varying the inputs relating to the cost of the HumiGard system, i.e. the training costs and the number of patients using each humidifier per year also have a very limited impact on the model's results.

Two-way sensitivity analysis

The two-way sensitivity analysis regarding the mix of patients included within the model showed that the greater proportion of laparoscopic surgery patients, the greater the potential cost savings generated. This is explored further in the subgroup analysis presented in Section 9.6.

Scenario analysis

Scenario analyses were conducted around the clinical data used within the model. This included exploration of structural uncertainty within the model. The four studies reporting on clinical outcomes including infections in open surgery patients with unintentional hypothermia were used to populate the model. The use of these studies and indeed the use of the multiplier on the outcomes from the study by Billeter *et al.* (2014) had a limited impact on the model's results [8]. This is because these changes only impacted upon 30% of the patients within the model.

The scenario analyses conducted around the laparoscopic model structure and inputs had a greater impact on the model's results. Where the structure of the model was adapted to match that of the open surgery model and temperature data from Sammour *et al.* (2010) used, the HumiGard system hovers around being cost-neutral dependent on the clinical event data used [12]. Where the temperature data from Mason *et al.* (unpublished) are used, the HumiGard remains cost saving. However, these cost savings are lower than in the base case [18]. The clinical event data used in both of these analyses may be of limited applicability, given that the studies were largely conducted in laparoscopic surgery patients. Further the model structure used in these analyses has greater uncertainty than that used in the base case which is derived directly from a UK NHS study on the HumiGard system.

Probabilistic sensitivity analysis

Probabilistic sensitivity analysis was carried out, finding that the base case results were robust to joint input parameter uncertainty. Where probabilistic sensitivity analysis were conducted using the alternate open surgery clinical event data, the results were similar to those in the base case. Again, this was largely due to the results being driven by the majority of laparoscopic surgery patients. However, this analysis was judged important to conduct given the discrepancies with the definition of hypothermia between the study by Frey *et al.* (2012) [9] and the study by Billeter *et al.* (2014) [8]. Due to a paucity of data around the confidence in individual parameter inputs, assumptions had to be made which somewhat limits the reliability of the probabilistic analyses results. Where possible these assumptions were conservative and attempted to understate confidence in the parameter values.

9.5.10 What are the key drivers of the cost results?

The key drivers of the model relate to SSIs in laparoscopic surgery patients. This is understandable given that these patients comprise 70% of those in the model and SSIs are a costly complication. Consideration of the tornado diagram provided in Figure C5 shows that the probability of getting a SSI both with and without the HumiGard system as well as the cost of a SSI are the three key drivers of the model's results.

In the base case, cost savings are generated as a result of the lower risk of SSI with the HumiGard system (4.7% versus 12%) [7]. As described in Section 9.5.9 where this absolute difference reduces to around 0.3% (e.g. 4.7% versus 5%) the HumiGard system becomes cost increasing. This difference remains fairly consistent regardless of which of the four open surgery clinical event data studies are used [8, 14-16]. The evidence identified as part of the clinical submission identified only the study used in model's base case by Noor *et al.* (2015) and Mason *et al.* (unpublished) as reporting on SSIs [7, 18]. Based on the values reported in the abstract by Noor *et al.* (2015), this threshold difference seems extremely low [7]. However, the unpublished manuscript by Mason *et al.*

[redacted]

[redacted]

The cost of SSIs is also a key driver of the model. This was varied over a wide range (£2,100 to £10,500) given the uncertainty in this cost report by NICE [23]. Whilst this cost is a key driver of the model, the direction of the model's result does not change with variation in the cost across the range specified. Further, the cost of SSI may actually be higher still, as NICE has received expert opinion stating that the cost can be as high as £20,000 for complex surgery and £14,000 for general surgery [23]. Where a cost of £14,000 for SSIs is inputted into the model, the HumiGard system is cost saving provided that the absolute difference in probability of SSI between the HumiGard system and usual care for laparoscopic patients is around 0.1% (e.g. 4.8% versus 4.7%).

Miscellaneous results

9.5.11 Describe any additional results that have not been specifically requested in this template. If none, please state.

There are no additional results.

9.6 Subgroup analysis

For many technologies, the capacity to benefit from treatment will differ for patients with differing characteristics. Sponsors are required to complete section 9.6 in accordance with the subgroups identified in the scope and for any additional subgroups considered relevant.

Types of subgroups that are not considered relevant are those based solely on the following factors.

- Subgroups based solely on differential treatment costs for individuals according to their social characteristics.
- Subgroups specified in relation to the costs of providing treatment in different geographical locations within the UK (for example, if the costs of facilities available for providing the technology vary according to location).

As discussed in Section 9.4.1, two subgroups were specified in the scope: patients with adjunct warming and high risk patients. Patients included in the clinical evidence utilised within the model received adjunct warming, hence the base case results already apply to this subgroup. Further, as discussed in Section 9.4.1, data were not available to model high risk patients specifically.

Subgroup results are presented for open surgery patients and laparoscopic surgery patients.

Open surgery

The summary of costs by category for open surgery patients using the clinical event data from Billeter *et al.* (2014) are presented in Table C15 [8].

Table C15: Summary of costs by category of cost per open surgery patient

Item	Cost with *the HumiGard system*	Cost *usual care*	Increment	Absolute increment	% of absolute increment
Equipment costs	£105	0	£105	£105	45.9%
Clinical event costs:					
Myocardial infarction	£25	£34	-£9	£9	3.9%
Stroke	£65	£130	-£65	£65	28.4%
Sepsis	£57	£76	-£19	£19	8.3%
Surgical site infection	£208	£227	-£19	£19	8.3%
Pneumonia	£24	£36	-£12	£12	5.2%
Mortality	£0	£0	£0	£0	0%
Total	£483	£503	-£20	£229	100%
Adapted from Pharmaceutical Benefits Advisory Committee (2008) Guidelines for preparing submissions to the Pharmaceutical Benefits Advisory Committee (Version 4.3). Canberra: Pharmaceutical Benefits Advisory Committee					

The deterministic and probabilistic results of the model for open surgery patients, only, are presented in Table C16. These show that the HumiGard system appears to be cost-saving in open surgery patients. However, these results are not as certain as those for the combined group.

Table C16: Results for open surgery patients

	The HumiGard system	Usual care	Incremental	Probabilistic results (percentage cost saving and incremental cost)
Cost per open surgery patient: Billeter data [8]	£483	£503	-£20	60.8% -£18
Cost per open surgery patient: Kurz data [16]	£483	£525	-£43	59.4% -£42
Cost per open surgery patient: Flores-Malonado data [15]	£225	£229	-£5	43.6% -£5
Cost per open surgery patient: Anannamcharoen data [14]	£1,213	£1,258	-£45	58.3% -£44

Laparoscopic surgery

The summary of costs by category for laparoscopic surgery patients are presented in Table C17.

Table C17: Summary of costs by category of cost per laparoscopic surgery patient

Item	Cost with *the HumiGard system*	Cost *usual care*	Increment	Absolute increment	% of absolute increment
Equipment costs	£81	£5	£76	£76	13.1%
Clinical event costs:					
Surgical site infection	£296	£756	-£460	£460	79.4%
Pneumonia	£14	£58	-£43	£43	7.4%
Total	£391	£819	-£428	£579	100%
Adapted from Pharmaceutical Benefits Advisory Committee (2008) Guidelines for preparing submissions to the Pharmaceutical Benefits Advisory Committee (Version 4.3). Canberra: Pharmaceutical Benefits Advisory Committee					

The deterministic and probabilistic results of the model for laparoscopic surgery patients, only, are presented in Table C18. This is based on the base case data described in Sections 9.2 and 9.3 and the model structure shown in Figure C3. These show that the HumiGard system is estimated to be robustly cost saving in laparoscopic surgery patients. These results are applicable to those hospitals using the device in laparoscopic surgery patients, only. For example, the two centres from which expert advice was elicited.

Table C18: Results for laparoscopic surgery patients

	The HumiGard system	Usual care	Incremental	Probabilistic results (percentage cost saving and incremental cost)
Cost per laparoscopic surgery patient	£391	£819	-£428	96.6% -£420

9.7 Validation

9.7.1 Describe the methods used to validate and cross-validate (for example with external evidence sources) and quality-assure the model. Provide references to the results produced and cross-reference to evidence identified in the clinical and resources sections.

The economic model was created in Microsoft Excel by one health economist and checked for errors through rebuilding of the base case by a second health economist who had not been involved in the development of the model. A third health economist who sits on a NICE Public Health Appraisal Committee was involved in the development of the model and quality assessed both the model and economic submission.

The model's results were cross-validated against the published cost-effectiveness analyses relating to the HumiGard system. The current model found the HumiGard system to be cost-saving, in line with the published evidence (see Section 9.8.1).

9.8 Interpretation of economic evidence

9.8.1 Are the results from this cost analysis consistent with the published economic literature? If not, why do the results from this evaluation differ, and why should the results in the submission be given more credence than those in the published literature?

The results of this cost analysis are in line with those reported in the published literature. In the two abstracts identified from the economic evidence review, the HumiGard system was reported to generate cost savings compared to usual care whilst generating greater benefits in the form of QALYs (Jenks *et al.,* 2015) or from a reduction in SSIs (Mason *et al.,* 2015) [5, 6].

9.8.2 Is the cost analysis relevant to all groups of patients and NHS settings in England that could potentially use the technology as identified in the scope?

The cost-analysis builds upon clinical data relevant to the patients identified within the scope. The clinical studies used within the model, namely Frey *et al.* (2012) and Noor *et al.* (2015) reported on patients undergoing colorectal surgery [7, 9]. Therefore, these people constitute a large subgroup of the population identified in the scope – people undergoing abdominal surgery. However, it is likely that the results of this analysis are generalisable to all patients specified within the scope.

In addition, the cost-analysis does not include subgroup analysis directly addressing those specified in the scope. All patients included within the clinical studies utilised received adjunct warming, thus addressing the first specified subgroup. However, data were not available to consider high-risk patients independently. High risk patients are, by definition, at greater risk of hypothermia and other clinical events. Therefore, it is possible that in these patients the HumiGard system may have a greater capacity to benefit. If this is the case, then the cost-savings in this population may be greater than the general population undergoing abdominal surgery.

9.8.3 What are the main strengths and weaknesses of the analysis? How might these affect the interpretation of the results?

This analysis attempts to estimate the potential cost savings associated with the use of the HumiGard system compared with usual care in patients undergoing open or laparoscopic abdominal surgery. Modelling exercises may not accurately represent local clinical practice as simplifications and assumptions have to be made. There are a number of limitations associated with the analysis.

First, costs of complications were applied independently within the model. However, it is plausible that some patients may have experienced multiple complications and as such bias has been introduced into the analysis. The direction of this bias is unknown. Resource usage, such as hospital stay, may have been double counted, or multi-complication patients may experience greater length of stay than two patients experiencing single complications. The sensitivity analysis conducted around the costs of complications showed that varying these costs did not impact heavily on the results of the model. This is with the exception of the cost of SSIs in laparoscopic surgery patients. However, given that the number of laparoscopic surgery patients experiencing pneumonia was low, the potential for double counting in this population is minimal in any case.

Second, the clinical event data from Billeter *et al.* (2014) was based upon patients experiencing hypothermia (defined as temperature below 35°C) [8]. As described in Section 9.2.3 this definition is inconsistent with that used in the HumiGard system RCT by Frey *et al.* (2012) [9]. Therefore, the number of clinical events in hypothermic patients may be overstated and that in normothermia patients understated. These data were used in the base case as it reported on the most complete set of clinical events associated with hypothermia. Scenario analyses were conducted using alternative data and a multiplier on clinical event rates to assess the impact of this discrepancy on the model's results. During these analyses, the HumiGard system remained cost saving.

Third, the study by Noor *et al.* used to populate the clinical event inputs for laparoscopic surgery patients was an observational study and therefore may be potentially biased [7]. Univariate sensitivity analyses were conducted around the values used to mitigate against this and further scenario analyses using an alternative model structure were conducted. The results of these analyses varied depending on the data used, but in the majority of cases the HumiGard system remained cost saving.

Finally, it was not possible to utilise data from all of the HumiGard system clinical studies identified in Section B of this submission. Although all authors were contacted, data from Manwaring *et al.* (2008), Hermann *et al.* (2015) and Yu *et al.* (2013) pertaining to temperature status (i.e. hypothermia or normothermia) post-surgery was not received [10, 11, 13]. Regarding core temperature, Manwaring *et al.* (2008) and Yu *et al.* (2013) both reported non-significantly slightly higher mean temperature at the end of surgery at the end of surgery in the HumiGard system group compared with the control group [11, 13]. Hermann *et al.* (2015) reported no difference in the change in temperature between the two groups [10]. However, the proportion of hypothermic patients in each group remains unknown in all three studies. The exclusion of running scenario analyses using potentially useful data relating to the HumiGard system from these studies is a limitation of the analysis.

9.8.4 What further analyses could be undertaken to enhance the robustness/completeness of the results?

In order to enhance the robustness of the results further studies could be conducted to address the limitations described in the previous section. Namely, this would involve conducting a RCT in open and laparoscopic surgery patients which reported on both clinical events and the resource implications of these clinical events. However, prior to conducting such a study the value of gaining further information should be assessed given that the uncertainty in the current base case results is relatively low.

10 References

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11 Appendices

11.1 Appendix 1: Search strategy for clinical evidence (section 7.1.1)

The following information should be provided:

10.1.1 The specific databases searched and the service provider used (for example, Dialog, DataStar, OVID, Silver Platter), including at least:

- Medline
- Embase
- Medline (R) In-Process
- The Cochrane Library.

Published studies

The purpose of the literature search was to identify data relating to the performance claims of the device concept of warming and humidifying gases for laparoscopic procedures and open procedures. Published scientific literature were identified using PubMed and incident report databases (ECRI, MAUDE and MHRA) were searched. Performance claim topics, device output claims and safety concerns were researched separately.

The following sources were used to retrieve information:

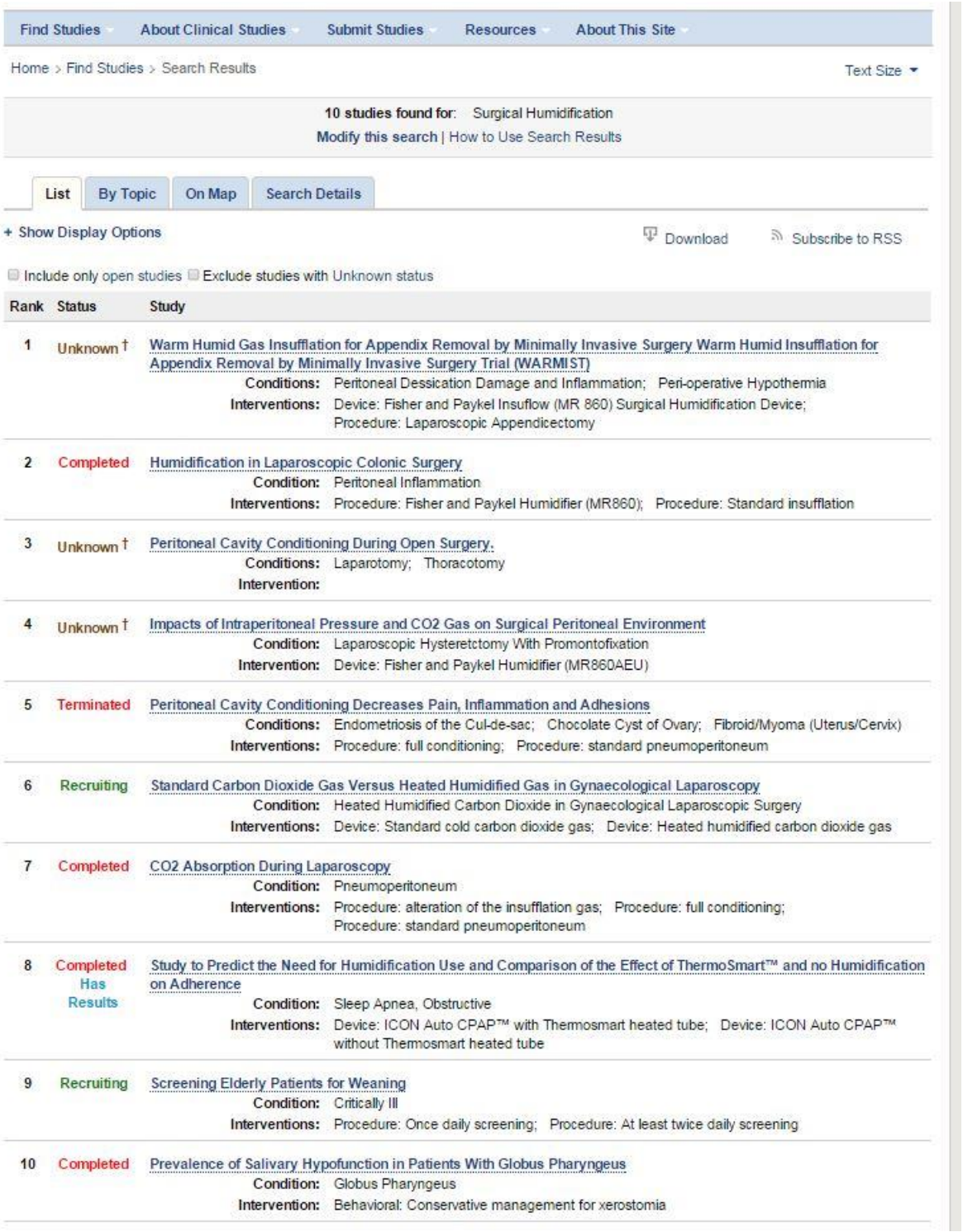
- PubMed database (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=PubMed)
- ECRI database of adverse events (https://members.ecri.org/Alerts/CPIssues/Issue.aspx?CH=1&ChName=Medical%20Devices&rid=0)
- MAUDE database of adverse events (http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfMAUDE/search.cfm).

- MHRA database of adverse events
  https://www.gov.uk/government/organisations/medicines-and-healthcare-products-regulatory-agency

Unpublished studies

Unpublished studies used in this evaluation were identified through information attained from collaborators. Search string evidence of Clinicaltrials.govt database found below:

Clinicaltrials.govt database
Search: “Surgical Humidification”. 10x entries



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10 studies found for: Surgical Humidification

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Include only open studies | Exclude studies with Unknown status

Rank	Status	Study
1	Unknown †	Warm Humid Gas Insufflation for Appendix Removal by Minimally Invasive Surgery Warm Humid Insufflation for Appendix Removal by Minimally Invasive Surgery Trial (WARMIST) **Conditions:** Peritoneal Dessication Damage and Inflammation; Peri-operative Hypothermia **Interventions:** Device: Fisher and Paykel Insuflow (MR 860) Surgical Humidification Device; Procedure: Laparoscopic Appendicectomy
2	Completed	Humidification in Laparoscopic Colonic Surgery **Condition:** Peritoneal Inflammation **Interventions:** Procedure: Fisher and Paykel Humidifier (MR860); Procedure: Standard insufflation
3	Unknown †	Peritoneal Cavity Conditioning During Open Surgery. **Conditions:** Laparotomy; Thoracotomy **Intervention:**
4	Unknown †	Impacts of Intraperitoneal Pressure and CO2 Gas on Surgical Peritoneal Environment **Condition:** Laparoscopic Hysteretctomy With Promontofixation **Intervention:** Device: Fisher and Paykel Humidifier (MR860AEU)
5	Terminated	Peritoneal Cavity Conditioning Decreases Pain, Inflammation and Adhesions **Conditions:** Endometriosis of the Cul-de-sac; Chocolate Cyst of Ovary; Fibroid/Myoma (Uterus/Cervix) **Interventions:** Procedure: full conditioning; Procedure: standard pneumoperitoneum
6	Recruiting	Standard Carbon Dioxide Gas Versus Heated Humidified Gas in Gynaecological Laparoscopy **Condition:** Heated Humidified Carbon Dioxide in Gynaecological Laparoscopic Surgery **Interventions:** Device: Standard cold carbon dioxide gas; Device: Heated humidified carbon dioxide gas
7	Completed	CO2 Absorption During Laparoscopy **Condition:** Pneumoperitoneum **Interventions:** Procedure: alteration of the insufflation gas; Procedure: full conditioning; Procedure: standard pneumoperitoneum
8	Completed Has Results	Study to Predict the Need for Humidification Use and Comparison of the Effect of ThermoSmart™ and no Humidification on Adherence **Condition:** Sleep Apnea, Obstructive **Interventions:** Device: ICON Auto CPAP™ with Thermosmart heated tube; Device: ICON Auto CPAP™ without Thermosmart heated tube
9	Recruiting	Screening Elderly Patients for Weaning **Condition:** Critically Ill **Interventions:** Procedure: Once daily screening; Procedure: At least twice daily screening
10	Completed	Prevalence of Salivary Hypofunction in Patients With Globus Pharyngeus **Condition:** Globus Pharyngeus **Intervention:** Behavioral: Conservative management for xerostomia

Of the 10 entries, the 2 have been published and are included in our evaluation (Yu et al. 2013,#1; and Sammour et al. 2010, #2). Six studies were not included because they were not investigating the correct population (#8, 9, 10), or the correct outcome of temperature (#3, 7), or the study was cancelled

(#5). Two studies were found to be of interest to the evaluation (#4, 6). One abstract was found for #4 (below) but no data or abstract was found for #6. Regardless, while they state that temperature is an outcome measure there is no evidence to date to show this and so both studies were not followed-up for this evaluation.

[P-389] IMPACT OF A WARM, HUMIDIFIED CO_2 PNEUMOPERITONEUM ON THE SURGICAL PERITONEAL ENVIRONMENT.

S. Matsuzaki, R. Botchorishvili. CHU Clermont-Ferrand, Clermont-Ferrand, France; Clermont Université, Université d'Auvergne, ISIT UMR6284, Clermont-Ferrand, France; CNRS, ISIT UMR6284, Clermont-Ferrand, France.

OBJECTIVE: The objective of the present study was to investigate the impact of a warm, humidified CO_2 pneumoperitoneum on the surgical peritoneal environment.
DESIGN: Prospective study.
MATERIALS AND METHODS: A total of 30 patients undergoing laparoscopic hysterectomy with promontofixation for genital prolapse were recruited. Cool and dry CO_2 gas was applied to the first 15 patients (CD group), whereas warm (37 C), humidified CO_2 gas was applied to the remaining 15 patients (WH group). 12 mmHg of intreperitoneal pressure was applied to all the patients. Normal peritoneum was collected from the parietal wall at the beginning of surgery and every 60 minutes thereafter. All surgeries were performed by the same surgeon in the present study. Expression levels of hyaluronan synthase 1 (HAS 1), HAS 2, HAS 3, hyaluronidase 1 (Hyal 1), Hyal 2, tissue plasminogen activator (tPA), plasminogen activator inhibitor-1 (PAI-1), connective tissue growth factor (CTGF), matrix metalloproteinase 9 (MMP9), E-selectin, and thrombospondin 2 (TSP-2) were measured in peritoneal tissues using real-time PCR. Statistical significance was defined as a *P*-value of <0.05.
RESULTS: CTGF and PAI-1 expression was significantly lower in the WH group compared with the CD group at 1 hour or 2 hours. MMP-9, E-selectin and HAS 1 expression were significantly lower in the WH group compared with the CD group at 2 hours. TSP-2 expression was significantly higher in the WH group compared with the CD group at 2 hours. HAS2 and HAS3 mRNA expression levels were significantly higher in the WH group compared with the CD group at 1 hour and 2 hours. Hyal-1 and Hyal-2 mRNA expression was significantly lower in the WH group compared with the CD group at 1 hour.
CONCLUSION: The present findings suggest that warm, humidified CO_2 gas may be better than cool and dry CO_2 gas to minimize the adverse impact on the surgical peritoneal environment during a CO_2 pneumoperitoneum.
Supported by: Karl Storz Endoscopy & GmbH (Tuttlingen, Germany).

Wednesday, October 24, 2012 7:00 AM

Poster Session: Female Reproductive Surgery

11.1.2 The date on which the search was conducted.

Published literature

- *Laparoscopic surgery*

  The search was conducted on August 16th 2015. A follow-up search was conducted on October 13th 2015.

- *Open surgery*

  The search was conducted on October 13th 2015.

10.1.3 The date span of the search.

Published literature

- *Laparoscopic surgery*

  No date limits were imposed on the search

- *Open surgery*

  No date limits were imposed on the search

10.1.4 The complete search strategies used, including all the search terms: textwords (free text), subject index headings (for example, MeSH) and the relationship between the search terms (for example, Boolean).

PubMed database search strategy

a) Laparoscopic surgery

Search evidence:

Articles were searched for the following parameter with no time restraint "laparo* AND (humid* OR insuflo*) AND randomised". A total of 48 were found.

The table following the search evidence details publications excluded in this evaluation and the reasons for their exclusion.

Search evidence:

PubMed ▼ laparo* AND (humid* OR insuflo*) AND randomized Search

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Summary 50 per page Sort by Most Recent Send to:

Results: 48

1. Re: Warmed, **humidified** carbon dioxide insufflation versus standard carbon dioxide in **laparoscopic** cholecystectomy: a double-blinded **randomized** controlled trial.
   Cadeddu JA.
   J Urol. 2015 Apr;193(4):1276-7. doi: 10.1016/j.juro.2015.01.005. Epub 2015 Jan 10. No abstract available.
   PMID: 25890519
   Similar articles

2. Five year follow-up of a **randomized** controlled trial on warming and **humidification** of insufflation gas in **laparoscopic** colonic surgery-impact on small bowel obstruction and oncologic outcomes.
   Sammour T, Hill AG.
   Int Surg. 2015 Apr;100(4):608-16. doi: 10.9738/INTSURG-D-14-00210.1.
   PMID: 25875541
   Similar articles

3. Intra-operative tissue oxygen tension is increased by local insufflation of **humidified**-warm CO2 during open abdominal surgery in a rat model.
   Marshall JK, Lindner P, Tait N, Maddocks T, Riepsamen A, van der Linden J.
   PLoS One. 2015 Apr 2;10(4):e0122838. doi: 10.1371/journal.pone.0122838. eCollection 2015.
   PMID: 25835954 Free PMC Article
   Similar articles

4. Insufflation with **humidified** and heated carbon dioxide in short-term **laparoscopy**: a double-blinded **randomized** controlled trial.
   Herrmann A, De Wilde RL.
   Biomed Res Int. 2015;2015:412618. doi: 10.1155/2015/412618. Epub 2015 Jan 28.
   PMID: 25722977 Free PMC Article
   Similar articles

5. Peritoneal adhesions after **laparoscopic** gastrointestinal surgery.
   Mais V.
   World J Gastroenterol. 2014 May 7;20(17):4917-25. doi: 10.3748/wjg.v20.i17.4917. Review.
   PMID: 24803803 Free PMC Article
   Similar articles

6. Warmed, **humidified** carbon dioxide insufflation versus standard carbon dioxide in **laparoscopic** cholecystectomy: a double-blinded **randomized** controlled trial.
   Klugsberger B, Schreiner M, Rothe A, Haas D, Oppelt P, Shamiyeh A.
   Surg Endosc. 2014 Sep;28(9):2656-60. doi: 10.1007/s00464-014-3522-x. Epub 2014 Apr 23.
   PMID: 24756487
   Similar articles

7. Peritoneal full-conditioning reduces postoperative adhesions and pain: a randomised controlled trial in deep endometriosis surgery.
   Koninckx PR, Corona R, Timmerman D, Verguts J, Adamyan L.
   J Ovarian Res. 2013 Dec 11;6(1):90. doi: 10.1186/1757-2215-6-90.
   PMID: 24326155 Free PMC Article
   Similar articles

8. [The efficacy of the moisture and warmed CO(2) for **laparoscopic** surgery].
   Agaev BA, Muslimov GF, Ibragimov TR, Alieva GR.
   Khirurgiia (Mosk). 2013;(11):35-9. Russian.
   PMID: 24300609
   Similar articles

9. To perform operative procedures in an optimized local atmosphere: can it reduce post-operative adhesion formation?
de Vries A, Mårvik R, Kuhry E.
Int J Surg. 2013;11(10):1118-22. doi: 10.1016/j.ijsu.2013.09.005. Epub 2013 Sep 29.
PMID: 24080114
Similar articles

10. Warm, **humidified** carbon dioxide gas insufflation for **laparoscopic** appendicectomy in children: a double-blinded **randomized** controlled trial.
Yu TC, Hamill JK, Liley A, Hill AG.
Ann Surg. 2013 Jan;257(1):44-53. doi: 10.1097/SLA.0b013e31825f0721.
PMID: 22824858
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11. Heat loss during carbon dioxide insufflation: comparison of a nebulization based **humidification** device with a **humidification** and heating system.
Noll E, Schaeffer R, Joshi G, Diemunsch S, Koessler S, Diemunsch P.
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12. Limitations regarding double-blinding, adherence to the intention to treat principle, and postoperative dosage of paracetamol.
Frey J, van der Linden J.
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PMID: 21694579
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13. Heated CO(2) with or without **humidification** for minimally invasive abdominal surgery.
Birch DW, Manouchehri N, Shi X, Hadi G, Karmali S.
Cochrane Database Syst Rev. 2011 Jan 19;(1):CD007821. doi: 10.1002/14651858.CD007821.pub2. Review.
PMID: 21249696
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Schlotterbeck H, Greib N, Dow WA, Schaeffer R, Geny B, Diemunsch PA.
J Surg Res. 2011 Dec;171(2):427-32. doi: 10.1016/j.jss.2010.04.003. Epub 2010 Nov 10.
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15. Warming and **humidification** of insufflation carbon dioxide in **laparoscopic** colonic surgery: a double-blinded **randomized** controlled trial.
Sammour T, Kahokehr A, Hayes J, Hulme-Moir M, Hill AG.
Ann Surg. 2010 Jun;251(6):1024-33. doi: 10.1097/SLA.0b013e3181d77a25.
PMID: 20485147
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16. Bupivacaine use in the **Insuflow** device during **laparoscopic** cholecystectomy: results of a prospective **randomized** double-blind controlled trial.
Zimmer PW, McCann MJ, O'Brien MM.
Surg Endosc. 2010 Jul;24(7):1524-7. doi: 10.1007/s00464-009-0804-9. Epub 2010 Jan 28.
PMID: 20108156
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17. Improved outcomes for lap-banding using the **Insuflow** device compared with heated-only gas.
Benavides R, Wong A, Nguyen H.
JSLS. 2009 Jul-Sep;13(3):302-5.
PMID: 19793466 Free PMC Article
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18. Beneficial effects of **humidified**, warmed carbon dioxide insufflation during **laparoscopic** bariatric surgery: a **randomized** clinical trial. What if sample size calculation made difference?
La Colla L, Mangano A, Albertin A.
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19. The hemodynamic effects of CO2-induced pressure on the kidney in an isolated perfused rat kidney model.
Khoury W, Szold A, Klausner JM, Weinbroum AA.
Surg **Laparosc** Endosc Percutan Tech. 2008 Dec;18(6):573-8. doi: 10.1097/SLE.0b013e3181875ba4.
PMID: 19098663
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20. Effect of heated and **humidified** carbon dioxide on patients after **laparoscopic** procedures: a meta-analysis.
Sajid MS, Mallick AS, Rimpel J, Bokari SA, Cheek E, Baig MK.
Surg **Laparosc** Endosc Percutan Tech. 2008 Dec;18(6):539-46. doi: 10.1097/SLE.0b013e3181886ff4. Review.
PMID: 19098656
Similar articles

21. Heated and **humidified** CO2 prevents hypothermia, peritoneal injury, and intra-abdominal adhesions during prolonged **laparoscopic** insufflations.
Peng Y, Zheng M, Ye Q, Chen X, Yu B, Liu B.
J Surg Res. 2009 Jan;151(1):40-7. doi: 10.1016/j.jss.2008.03.039. Epub 2008 Apr 23.
PMID: 18639246
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Sammour T, Kahokehr A, Hill AG.
Br J Surg. 2008 Aug;95(8):950-6. doi: 10.1002/bjs.6304. Review.
PMID: 18618870
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PMID: 18347861
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24. The effect of heated **humidified** carbon dioxide on postoperative pain, core temperature, and recovery times in patients having **laparoscopic** surgery: a **randomized** controlled trial.
Manwaring JM, Readman E, Maher PJ.
J Minim Invasive Gynecol. 2008 Mar-Apr;15(2):161-5. doi: 10.1016/j.jmig.2007.09.007.
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Beste TM, Daucher JA, Holbert D.
Obstet Gynecol. 2006 Feb;107(2 Pt 1):263-8.
PMID: 16449110
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Davis SS, Mikami DJ, Newlin M, Needleman BJ, Barrett MS, Fries R, Larson T, Dundon J, Goldblatt MI, Melvin WS.
Surg Endosc. 2006 Jan;20(1):153-8. Epub 2005 Dec 7.
PMID: 16333546
Similar articles

30. Effect of warmed, **humidified** insufflation gas and anti-inflammatory agents on cytokine response to **laparoscopic** nephrectomy: porcine model.
Margulis V, Matsumoto ED, Tunc L, Taylor G, Duchenne D, Cadeddu JA.
J Urol. 2005 Oct;174(4 Pt 1):1452-6.
PMID: 16145469
Similar articles

31. Heated and **humidified** insufflation during **laparoscopic** gastric bypass surgery: effect on temperature, postoperative pain, and recovery outcomes.
Hamza MA, Schneider BE, White PF, Recart A, Villegas L, Ogunnaike B, Provost D, Jones D.
J **Laparoendosc** Adv Surg Tech A. 2005 Feb;15(1):6-12.
PMID: 15772469
Similar articles

32. Beneficial effects of **humidified**, warmed carbon dioxide insufflation during **laparoscopic** bariatric surgery: a **randomized** clinical trial.
Savel RH, Balasubramanya S, Lasheen S, Gaprindashvili T, Arabov E, Fazylov RM, Lazzaro RS, Macura JM.
Obes Surg. 2005 Jan;15(1):64-9.
PMID: 15760500
Similar articles

33. Effect of **humidified** and heated CO2 during gynecologic **laparoscopic** surgery on analgesic requirements and postoperative pain.
Kissler S, Haas M, Strohmeier R, Schmitt H, Rody A, Kaufmann M, Siebzehnruebl E.
J Am Assoc Gynecol **Laparosc**. 2004 Nov;11(4):473-7.
PMID: 15701188
Similar articles

34. Double-blind, prospective, **randomized** study of warmed, **humidified** carbon dioxide insufflation vs standard carbon dioxide for patients undergoing **laparoscopic** cholecystectomy.
Farley DR, Greenlee SM, Larson DR, Harrington JR.
Arch Surg. 2004 Jul;139(7):739-43; discussion 743-4.
PMID: 15249406
Similar articles

35. The effect of warm **humidified** CO2 on the dissipation of residual gas following **laparoscopy** in piglets.
Glew PA, Campher MJ, Pearson K, Schofield JC, Davey AK.
J Am Assoc Gynecol **Laparosc**. 2004 May;11(2):204-10.
PMID: 15200776
Similar articles

36. Effects of L-arginine-enriched total enteral nutrition on body weight gain, tumor growth, and in vivo concentrations of blood and tissue metabolites in rats inoculated with Walker tumor in the kidney.
Gonzaga Silva LF, Odorico de Moraes M, Santos Dias Soares F, Mota Moura Fé D, Cavalcante JL, Anselmo JN, Leitao Vasconcelos PR.
Nutrition. 2004 Feb;20(2):225-9.
PMID: 14962691
Similar articles

37. Impact of temperature and **humidity** of carbon dioxide pneumoperitoneum on body temperature and peritoneal morphology.
Hazebroek EJ, Schreve MA, Visser P, De Bruin RW, Marquet RL, Bonjer HJ.
J **Laparoendosc** Adv Surg Tech A. 2002 Oct;12(5):355-64.
PMID: 12470410
Similar articles

38. Effect of heated and **humidified** carbon dioxide gas on core temperature and postoperative pain: a **randomized** trial.
Nguyen NT, Furdui G, Fleming NW, Lee SJ, Goldman CD, Singh A, Wolfe BM.
Surg Endosc. 2002 Jul;16(7):1050-4. Epub 2002 Mar 26.
PMID: 12165821
Similar articles

39. Evaluation of core temperature during **laparoscopic** and open gastric bypass.
Nguyen NT, Fleming NW, Singh A, Lee SJ, Goldman CD, Wolfe BM.
Obes Surg. 2001 Oct;11(5):570-5.
PMID: 11594097
Similar articles

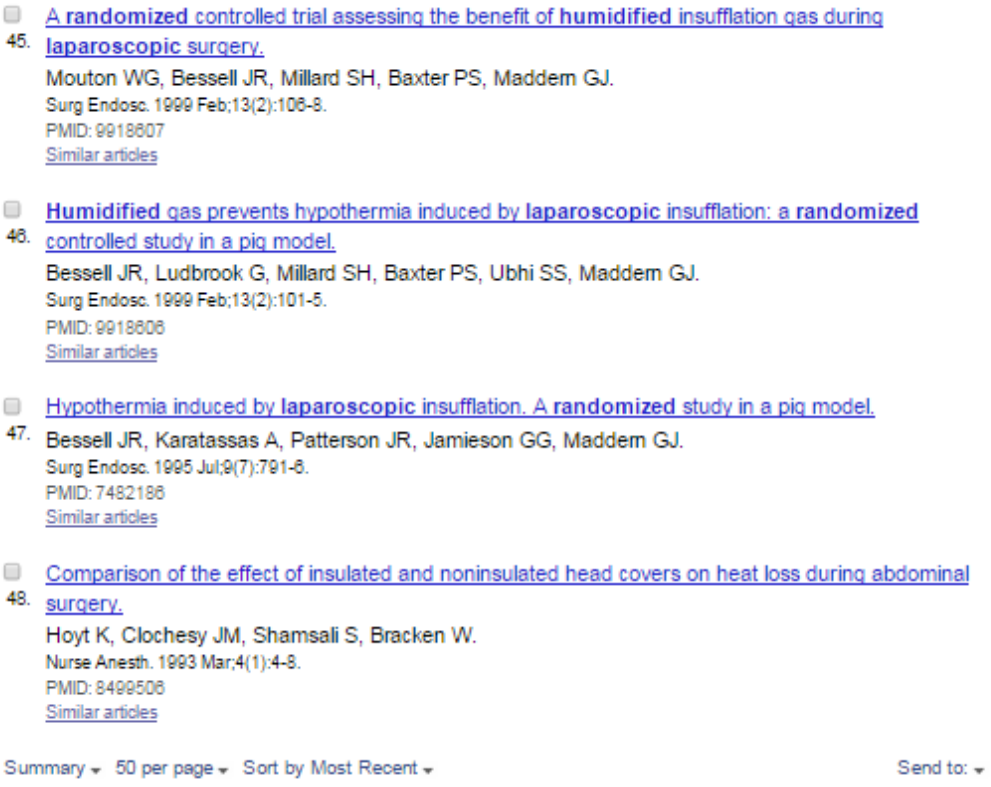
40. A **randomized** controlled trial to determine the effect of **humidified** carbon dioxide (CO2) insufflation on postoperative pain following thoracoscopic procedures.
Mouton WG, Naef M, Bessell JR, Otten KT, Wagner HE, Maddern GJ.
Surg Endosc. 2001 Jun;15(6):579-81. Epub 2001 Apr 3.
PMID: 11591944
Similar articles

41. Effect of heating and **humidifying** gas on patients undergoing awake **laparoscopy**.
Demco L.
J Am Assoc Gynecol **Laparosc**. 2001 May;8(2):247-51.
PMID: 11342732
Similar articles

42. The mouse as a model to study adhesion formation following endoscopic surgery: a preliminary report.
Yesildaglar N, Ordoñez JL, Laermans I, Koninckx PR.
Hum Reprod. 1999 Jan;14(1):55-9.
PMID: 10374094 Free Article
Similar articles

43. A **randomized** controlled trial to determine the effects of **humidified** carbon dioxide insufflation during thoracoscopy.
Mouton WG, Bessell JR, Pfitzner J, Dymock RB, Brealey J, Maddern GJ.
Surg Endosc. 1999 Apr;13(4):382-5.
PMID: 10094752
Similar articles

44. 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.
Ott DE, Reich H, Love B, McCorvey R, Toledo A, Liu CY, Syed R, Kumar K.
JSLS. 1998 Oct-Dec;2(4):321-9.
PMID: 10036122 Free PMC Article
Similar articles



45. A **randomized** controlled trial assessing the benefit of **humidified** insufflation gas during **laparoscopic** surgery.
Mouton WG, Bessell JR, Millard SH, Baxter PS, Maddern GJ.
Surg Endosc. 1999 Feb;13(2):106-8.
PMID: 9918607
Similar articles

46. **Humidified** gas prevents hypothermia induced by **laparoscopic** insufflation: a **randomized** controlled study in a pig model.
Bessell JR, Ludbrook G, Millard SH, Baxter PS, Ubhi SS, Maddern GJ.
Surg Endosc. 1999 Feb;13(2):101-5.
PMID: 9918606
Similar articles

47. Hypothermia induced by **laparoscopic** insufflation. A **randomized** study in a pig model.
Bessell JR, Karatassas A, Patterson JR, Jamieson GG, Maddern GJ.
Surg Endosc. 1995 Jul;9(7):791-6.
PMID: 7482186
Similar articles

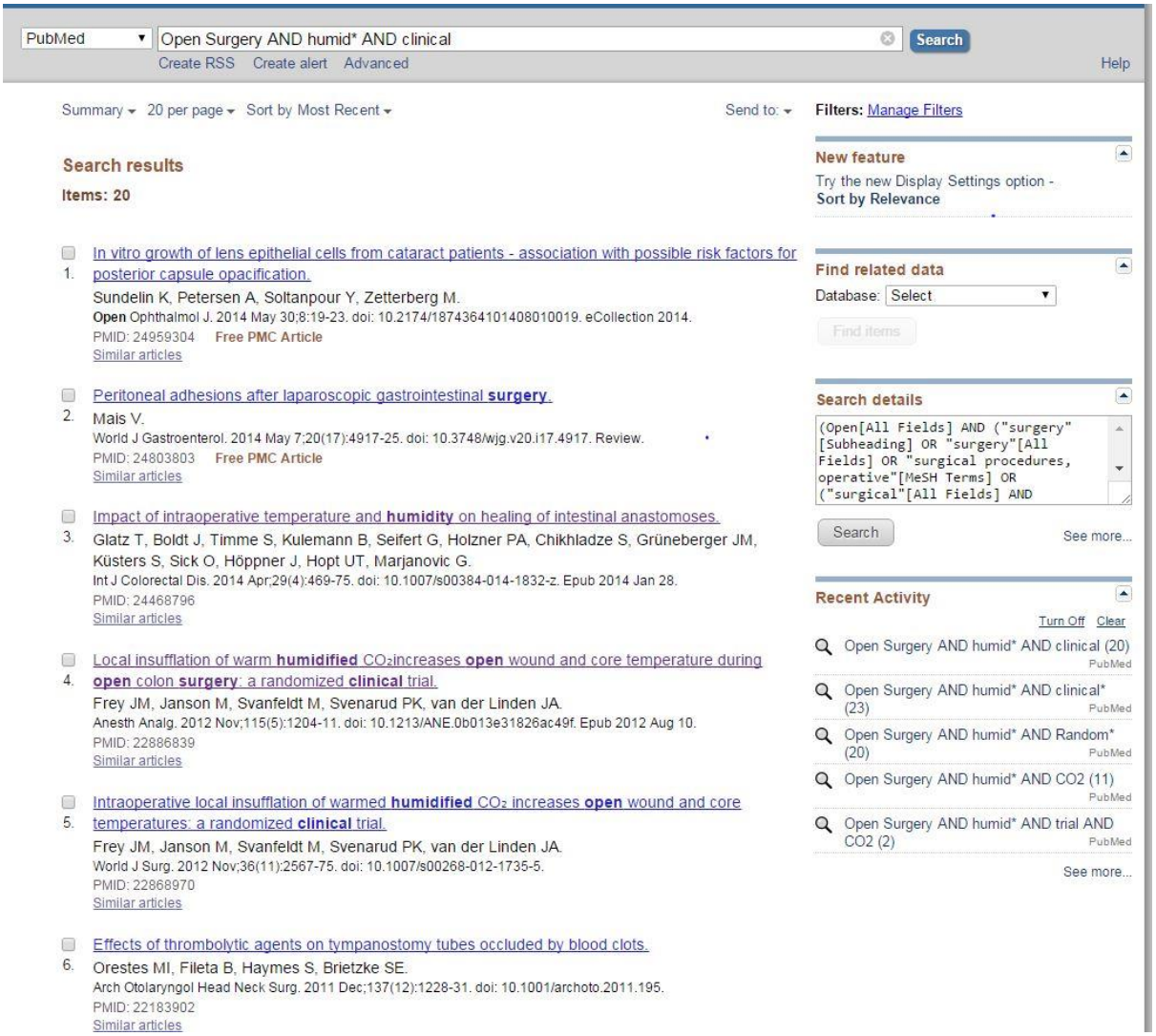
48. Comparison of the effect of insulated and noninsulated head covers on heat loss during abdominal surgery.
Hoyt K, Clochesy JM, Shamsali S, Bracken W.
Nurse Anesth. 1993 Mar;4(1):4-8.
PMID: 8499506
Similar articles

Summary 50 per page Sort by Most Recent Send to:

b) Open surgery

Search evidence:

Articles were searched for the following parameter with no time restraint “Open Surgery AND humid* AND clinical”. A total of 20 were found.


PubMed
Open Surgery AND humid* AND clinical
Search
Create RSS
Create alert
Advanced
Help
Summary
20 per page
Sort by Most Recent
Send to:
Filters: Manage Filters
Search results
Items: 20
1. In vitro growth of lens epithelial cells from cataract patients - association with possible risk factors for posterior capsule opacification.
Sundelin K, Petersen A, Soltanpour Y, Zetterberg M.
Open Ophthalmol J. 2014 May 30;8:19-23. doi: 10.2174/1874364101408010019. eCollection 2014.
PMID: 24959304 Free PMC Article
Similar articles
2. Peritoneal adhesions after laparoscopic gastrointestinal surgery.
Mais V.
World J Gastroenterol. 2014 May 7;20(17):4917-25. doi: 10.3748/wjg.v20.i17.4917. Review.
PMID: 24803803 Free PMC Article
Similar articles
3. Impact of intraoperative temperature and humidity on healing of intestinal anastomoses.
Glatz T, Boldt J, Timme S, Kulemann B, Seifert G, Holzner PA, Chikhladze S, Grüneberger JM, Küsters S, Sick O, Höppner J, Hopt UT, Marjanovic G.
Int J Colorectal Dis. 2014 Apr;29(4):469-75. doi: 10.1007/s00384-014-1832-z. Epub 2014 Jan 28.
PMID: 24468796
Similar articles
4. Local insufflation of warm humidified CO2increases open wound and core temperature during open colon surgery: a randomized clinical trial.
Frey JM, Janson M, Svanfeldt M, Svenarud PK, van der Linden JA.
Anesth Analg. 2012 Nov;115(5):1204-11. doi: 10.1213/ANE.0b013e31826ac49f. Epub 2012 Aug 10.
PMID: 22886839
Similar articles
5. Intraoperative local insufflation of warmed humidified CO2 increases open wound and core temperatures: a randomized clinical trial.
Frey JM, Janson M, Svanfeldt M, Svenarud PK, van der Linden JA.
World J Surg. 2012 Nov;36(11):2567-75. doi: 10.1007/s00268-012-1735-5.
PMID: 22868970
Similar articles
6. Effects of thrombolytic agents on tympanostomy tubes occluded by blood clots.
Orestes MI, Fileta B, Haymes S, Brietzke SE.
Arch Otolaryngol Head Neck Surg. 2011 Dec;137(12):1228-31. doi: 10.1001/archoto.2011.195.
PMID: 22183902
Similar articles
New feature
Try the new Display Settings option - Sort by Relevance
Find related data
Database: Select
Find items
Search details
(Open[All Fields] AND ("surgery"[Subheading] OR "surgery"[All Fields] OR "surgical procedures, operative"[MeSH Terms] OR ("surgical"[All Fields] AND
Search
See more...
Recent Activity
Turn Off Clear
Open Surgery AND humid* AND clinical (20) PubMed
Open Surgery AND humid* AND clinical* (23) PubMed
Open Surgery AND humid* AND Random* (20) PubMed
Open Surgery AND humid* AND CO2 (11) PubMed
Open Surgery AND humid* AND trial AND CO2 (2) PubMed
See more...

7. PET-CT scan positive pulmonary nodule revealing histoplasmosis: a case report.
Matos Figueroa JR, Vázquez Torres OL, Hernández I, Vila A.
Bol Asoc Med P R. 2010 Oct-Dec;102(4):47-50.
PMID: 21766547
Similar articles

8. Short-term endotracheal climate changes and **clinical** effects of a heat and moisture exchanger with an integrated electrostatic virus and bacterial filter developed for laryngectomized individuals.
Scheenstra RJ, Muller SH, Vincent A, Ackerstaff AH, Jacobi I, Hilgers FJ.
Acta Otolaryngol. 2010 Jun;130(6):739-46. doi: 10.3109/00016480903382790.
PMID: 20001445
Similar articles

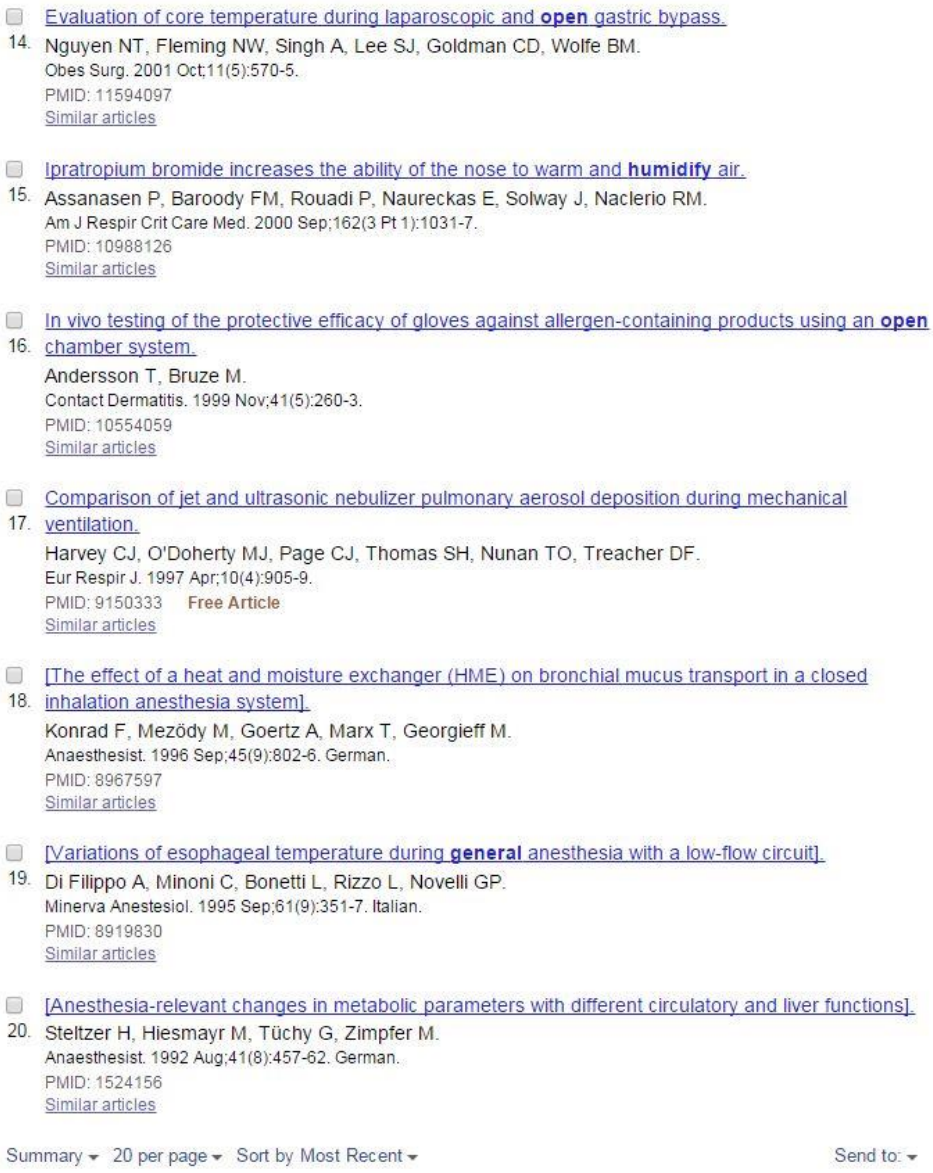
9. Intraoperative field flooding with warm **humidified** CO2 may help to prevent adhesion formation after **open surgery**.
Persson M, van der Linden J.
Med Hypotheses. 2009 Oct;73(4):521-3. doi: 10.1016/j.mehy.2009.06.009. Epub 2009 Jul 8.
PMID: 19589645
Similar articles

10. [Intensive care medicine -- update 2005].
Flohé S, Lendemans S, Schmitz D, Waydhas C.
Zentralbl Chir. 2006 Jun;131(3):175-87. Review. German.
PMID: 16739056
Similar articles

11. Topical **humidified** carbon dioxide to keep the **open surgical** wound warm: the greenhouse effect revisited.
Persson M, Elmqvist H, van der Linden J.
Anesthesiology. 2004 Oct;101(4):945-9.
PMID: 15448528
Similar articles

12. Green iguana nephrology: a review of diagnostic techniques.
Hernandez-Divers SJ.
Vet Clin North Am Exot Anim Pract. 2003 Jan;6(1):233-50. Review.
PMID: 12616842
Similar articles

13. The European Association for Endoscopic **Surgery clinical** practice guideline on the pneumoperitoneum for laparoscopic **surgery**.
Neudecker J, Sauerland S, Neugebauer E, Bergamaschi R, Bonjer HJ, Cuschieri A, Fuchs KH, Jacobi Ch, Jansen FW, Koivusalo AM, Lacy A, McMahon MJ, Millat B, Schwenk W.
Surg Endosc. 2002 Jul;16(7):1121-43. Epub 2001 May 20.
PMID: 12015619
Similar articles



14. Evaluation of core temperature during laparoscopic and **open** gastric bypass.
Nguyen NT, Fleming NW, Singh A, Lee SJ, Goldman CD, Wolfe BM.
Obes Surg. 2001 Oct;11(5):570-5.
PMID: 11594097
Similar articles

15. Ipratropium bromide increases the ability of the nose to warm and **humidify** air.
Assanasen P, Baroody FM, Rouadi P, Naureckas E, Solway J, Naclerio RM.
Am J Respir Crit Care Med. 2000 Sep;162(3 Pt 1):1031-7.
PMID: 10988126
Similar articles

16. In vivo testing of the protective efficacy of gloves against allergen-containing products using an **open** chamber system.
Andersson T, Bruze M.
Contact Dermatitis. 1999 Nov;41(5):260-3.
PMID: 10554059
Similar articles

17. Comparison of jet and ultrasonic nebulizer pulmonary aerosol deposition during mechanical ventilation.
Harvey CJ, O'Doherty MJ, Page CJ, Thomas SH, Nunan TO, Treacher DF.
Eur Respir J. 1997 Apr;10(4):905-9.
PMID: 9150333 Free Article
Similar articles

18. [The effect of a heat and moisture exchanger (HME) on bronchial mucus transport in a closed inhalation anesthesia system].
Konrad F, Mezödy M, Goertz A, Marx T, Georgieff M.
Anaesthesist. 1996 Sep;45(9):802-6. German.
PMID: 8967597
Similar articles

19. [Variations of esophageal temperature during **general** anesthesia with a low-flow circuit].
Di Filippo A, Minoni C, Bonetti L, Rizzo L, Novelli GP.
Minerva Anestesiol. 1995 Sep;61(9):351-7. Italian.
PMID: 8919830
Similar articles

20. [Anesthesia-relevant changes in metabolic parameters with different circulatory and liver functions].
Steltzer H, Hiesmayr M, Tüchy G, Zimpfer M.
Anaesthesist. 1992 Aug;41(8):457-62. German.
PMID: 1524156
Similar articles

Summary 20 per page Sort by Most Recent Send to:

Table: excluded papers (in order of search results; chronological)

Primary study reference	Study name	Exclusion criteria?	Reason for exclusion
Laparoscopic Surgery			
Cadeddu *et al.* 2015	*Re: Warmed, humidified carbon dioxide insufflation versus standard carbon dioxide in laparoscopic cholecystectomy: a double-blinded randomised controlled trial.*	#4 Study design	A response article

Sammour *et al.* 2015	*Five year follow-up of a randomised controlled trial on warming and humidification of insufflation gas in laparoscopic colonic surgery-impact on small bowel obstruction and oncologic outcomes.*	#4 Study design	Follow up to Sammour et al. 2010 (11). Recorded as a "duplicate" study
Marshal *et al.* 2015	*Intra-operative tissue oxygen tension is increased by local insufflation of humidified-warm CO_2 during open abdominal surgery in a rat model.*	#1 Population	Animal study
Mais V. 2014	*Peritoneal adhesions after laparoscopic gastrointestinal surgery.*	#4 Study design	Review
Koninckx *et al.* 2013 (34) RCT	*Peritoneal full-conditioning reduces postoperative adhesions and pain: a randomised controlled trial In deep endometriosis surgery*	#2 Intervention	No temperature intervention
de Vines *et al.* 2013	*To perform operative procedures in an optimized local atmosphere: can it reduce post-operative adhesion formation?*	#3/4 Outcomes /Study design	Did not primarily investigate an outcome of interest for this evaluation
Noll *et al*. 2013	*Heat loss during carbon dioxide insufflation: comparison of a nebulization based humidification device with a humidification and heating system.*	#3/4 Outcomes /Study design	Did not primarily investigate an outcome of interest for this evaluation
Frey *et al.* 2011	*Limitations regarding double-blinding, adherence to the intention to treat principle, and postoperative dosage of paracetamol.*	#4 Study design	Review
Schlotterbeck *et al.* 2011	*Changes in core temperature during peritoneal insufflation: comparison of two CO_2 humidification devices in pigs.*	#1 Population	Animals
Zimmer *et al.* 2010	*Bupivacaine use in the Insuflow device during laparoscopic cholecystectomy: results of a prospective randomised double-blind controlled trial.*	#2/3 Interventions/Outcomes	Did not primarily investigate an intervention of interest for this evaluation. Bupivacaine was the focus.
La Colla *et al.* 2010	*Beneficial effects of humidified, warmed carbon dioxide insufflation during laparoscopic bariatric surgery: a randomised clinical trial. What if sample size calculation made difference?*	#4 Study design	Review
Khoury *et al.* 2008	*The hemodynamic effects of CO_2-induced pressure on the kidney in an isolated perfused rat kidney*	#2 Intervention	Did not primarily investigate an intervention of

	model.	n	interest for this evaluation
Peng *et al.* 2009	*Heated and humidified CO_2 prevents hypothermia, peritoneal injury, and intra-abdominal adhesions during prolonged laparoscopic insufflations.*	#1 Population	Animals
Schlotterbeck *et al.* 2008	*Cold nebulization used to prevent heat loss during laparoscopic surgery: an experimental study in pigs.*	#1 Population	Animals
Binda *et al.* 2007	*Efficacy of barriers and hypoxia-inducible factor inhibitors to prevent CO(2) pneumoperitoneum-enhanced adhesions in a laparoscopic mouse model.*	#1 Population	Animals
Binda *et al.* 2006	*Effect of desiccation and temperature during laparoscopy on adhesion formation in mice.*	#1 Population	Animals
Beste *et al.*	*Humidified compared with dry, heated carbon dioxide at laparoscopy to reduce pain.*	#2 Intervention	Used Hot dry gas as the treatment, not hot, humidified gas
Margulis *et al.* 2005	*Effect of warmed, humidified insufflation gas and anti-inflammatory agents on cytokine response to laparoscopic nephrectomy: porcine model.*	#1 Population	Animals
Glew *et al.* 2004	*The effect of warm humidified CO_2 on the dissipation of residual gas following laparoscopy in piglets.*	#1 Population	Animals
Gonzaga *et al.* 2004	*Effects of L-arginine-enriched total enteral nutrition on body weight gain, tumor growth, and in vivo concentrations of blood and tissue metabolites in rats inoculated with Walker tumor in the kidney.*	#2 Intervention	Did not primarily investigate an intervention of interest for this evaluation
Hazebroek *et al.* 2002	*Impact of temperature and humidity of carbon dioxide pneumoperitoneum on body temperature and peritoneal morphology.*	#1 Population	Animals
Nguyen *et al.* 2001	*Evaluation of core temperature during laparoscopic and open gastric bypass.*	#2/4 Intervention/study design	No intervention group/evaluation
Mouton *et al.* 2001	*A randomised controlled trial to determine the effect of humidified carbon dioxide (CO_2) insufflation on postoperative pain following thoracoscopic procedures.*	#1 Population	Not abdominal surgery

Demco L. 2001	*Effect of heating and humidifying gas on patients undergoing awake laparoscopy.*	#3 Outcomes	Did not primarily investigate an intervention of interest for this evaluation (no temperature investigation).
Yesildaglar *et al.* 1999	*The mouse as a model to study adhesion formation following endoscopic surgery: a preliminary report.*	#1 Population	Animals
Mouton *et al.* 1999	*A randomised controlled trial to determine the effects of humidified carbon dioxide insufflation during thoracoscopy.*	#1 Population	Animals. Not abdominal surgery
Bessell *et al.* 1999	*Humidified gas prevents hypothermia induced by laparoscopic insufflation: a randomised controlled study in a pig model.*	#1 Population	Animals
Bessell *et al.* 1995	*Hypothermia induced by laparoscopic insufflation. A randomised study in a pig model.*	#1 Population	Animals
Hoyt *et al.* 1993	*Comparison of the effect of insulated and noninsulated head covers on heat loss during abdominal surgery.*	#1 Population	Not abdominal surgery
Open surgery			
Sundelin *et al.* 2014	*In vitro growth of lens epithelial cells from cataract patients - association with possible risk factors for posterior capsule opacification.*	#1 Population	Not abdominal surgery
Mais V. 2014	*Peritoneal adhesions after laparoscopic gastrointestinal surgery.*	#4 Study design	Review
Glatz *et al.* 2014	*Impact of intra-operative temperature and humidity on healing of intestinal anastomoses.*	#1 Population	Animals
Orestes *et al.* 2011	*Effects of thrombolytic agents on tympanostomy tubes occluded by blood clots.*	#1 Population	Not abdominal surgery
Matos Figueroa *et al.* 2010	*PET-CT scan positive pulmonary nodule revealing histoplasmosis: a case report.*	#1 Population	Not abdominal surgery
Scheenstra *et al.* 2010	*Short-term endotracheal climate changes and clinical effects of a heat and moisture exchanger with an integrated electrostatic virus and bacterial filter developed for laryngectomized individuals.*	#1 Population	Not abdominal surgery

Persson *et al.* 2009	*Intra-operative field flooding with warm humidified CO_2 may help to prevent adhesion formation after open surgery.*	#4 Study design	Hypothesis
Flohe *et al.* 2006	*[Intensive care medicine -- update 2005].*	#3 Outcomes	Did not primarily investigate any outcomes of interest for this evaluation
Persson *et al.* 2004	*Topical humidified carbon dioxide to keep the open surgical wound warm: the greenhouse effect revisited.*	#1 Population	*In vitro*
Hernandez-Divers SJ. 2003	*Green iguana nephrology: a review of diagnostic techniques.*	#1 Population	Animals
Neudecker *et al.* 2002	*The European Association for Endoscopic Surgery clinical practice guideline on the pneumoperitoneum for laparoscopic surgery.*	#2 Interventions	Did not primarily investigate any interventions of interest for this evaluation
Nguyen *et al.* 2001	*Evaluation of core temperature during laparoscopic and open gastric bypass.*	#2/4 Intervention/study design	No intervention group/evaluation
Assanasen *et al.* 2000	*Ipratropium bromide increases the ability of the nose to warm and humidify air.*	#1 Population	Not abdominal surgery
Anderson *et al.* 1999	*In vivo testing of the protective efficacy of gloves against allergen-containing products using an open chamber system.*	#1 Population	*In vitro*
Harvey *et al.* 1997	*Comparison of jet and ultrasonic nebulizer pulmonary aerosol deposition during mechanical ventilation.*	#1 Population	Not abdominal surgery
Konrad *et al.* 1996	*[The effect of a heat and moisture exchanger (HME) on bronchial mucus transport in a closed inhalation anesthesia system].*	#2 Intervention	Did not primarily investigate any interventions of interest for this evaluation
Di Filippo *et al.* 1995	*[Variations of esophageal temperature during general anesthesia with a low-flow circuit].*	#1 Population	Not abdominal surgery
Steltzer *et al.* 1992	*[Anesthesia-relevant changes in metabolic parameters with different circulatory and liver functions].*	#2 Intervention	Did not primarily investigate any interventions of interest for this evaluation

10.1.5 Details of any additional searches, such as searches of company or professional organisation databases (include a description of each database).

The Fisher and Paykel Healthcare internal database was searched for all terms associated with risk or reports of harm. This database details all complaints made about the safety of the HumiGard device. The Product surveillance search included the search of two databases, namely the 'closed' and 'all except closed' categories. The Products Complaints Database (old database) was searched using the search terms: 'Product Number' = RT350 OR MR860 OR MR820 OR HI200 OR HI100. The Products Surveillance Database (new database) was searched using the search terms: 'Ref' = RT350 or MR860AEA or MR860AEK or 900MR441 or 900ST100 each entered into the database separately. Complaints related to the safety concerns and any other safety concern related to the device concept of warming and humidifying gases as described in the intended use, were included for appraisal and evaluation.

10.1.6 The inclusion and exclusion criteria.

Selection criteria:

Articles had to satisfy the following inclusion criteria:

- Population (#1): People undergoing open or laparoscopic abdominal surgery more than 30 minutes in duration
- Interventions (#2): Heated, humidified insufflation vs no insufflation or unheated, unhumidified insufflation
- Outcomes (#3): Intra-operative core body temperature change (with and without an external heating device), pain measured by visual analogue scale (VAS), shoulder tip pain (via VAS), analgesic usage, total length of hospital stay and length of stay in post-operative recovery as well as any adverse events.

- Study design (#4): Randomised Control Trials or prior meta-analyses

Justification for selection criteria:

1. Only human data is acceptable for NICE evaluation of products.
2. The intended use of the Surgical Humidification System is for laparoscopic and open procedures. Hence research on laparoscopic or open procedures was included in the appraisal and evaluation.
3. The intended use of the Surgical Humidification System is to humidify the insufflation gas. Furthermore, some research has been conducted on the effect of heated (not humidified) gas, which is not relevant to the conclusions on the effect of humidification of insufflation gas. Hence only articles that specified humidification of the insufflation gas were included in the appraisal and evaluation.
4. The performance claims for the Surgical Humidification System are in comparison to laparoscopic procedures using dry gas. Hence, only literature comparing these two methods of insufflation was included in the appraisal and evaluation.
5. To ensure consistent evaluation and appraisal methodologies selected studies must have in some way investigated temperature changes with the interventions above. It did not have to be the primary outcome measure of the study. Additional outcomes listed above were sought but not critical for selection.
6. Only original research articles provide evidence for the use of a device. Publications such as author replies and comments that reflect an individual's opinion were not included. Systematic reviews may provide a useful summary of the available literature but were not of relevance to this evaluation. However, previous meta-analyses of articles of interest were evaluated if they were relevant to this evaluation.

10.1.7 Data abstraction strategy

Data was identified and abstracted by clinical research scientists within Fisher and Paykel Healthcare. Data were abstracted as per a data abstraction checklist independent to each scientist. This checklist included the search parameters, inclusion and exclusion criteria and statistics of interest. Any discrepancies between the investigators were discussed and all abstracted data used in this evaluation was entered following agreement from both scientists.

10.2 Appendix 2: Search strategy for adverse events (section 7.7.1)

The following information should be provided.

10.2.1 The specific databases searched and the service provider used (for example, Dialog, DataStar, OVID, Silver Platter), including at least:

- Medline
- Embase
- Medline (R) In-Process
- The Cochrane Library.

Published studies

The purpose of the literature search was to identify data relating to the performance claims of the device concept of warming and humidifying gases for laparoscopic procedures and open procedures. Published scientific literature was identified using PubMed and incident report databases (ECRI, MAUDE and MHRA) were searched. Performance claims, device output claims and safety concerns were addressed and researched separately.

The following sources were used to retrieve information:

- PubMed database
  (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=PubMed)
- ECRI database of adverse events
  (https://members.ecri.org/Alerts/CPIssues/Issue.aspx?CH=1&ChName=Medical%20Devices&rid=0)
- MAUDE database of adverse events
  (http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfMAUDE/search.cfm)
- MHRA database of adverse events
  https://www.gov.uk/government/organisations/medicines-and-healthcare-products-regulatory-agency

Unpublished studies

Unpublished studies were identified through information attained from collaborators.

10.2.2 The date on which the search was conducted.

ECRI database search results

A search of the ECRI database was conducted on 11 January 2008 and 215 reports were found. Of these reports only one report was found that discussed a safety concern related to the device concept of warming and humidifying gases as described in the intended use. Details of this report are outlined in section 7.7. The search mentioned above was repeated on 9 February 2009. The search resulted in 0 findings of 'laparosco*'. The search mentioned above was repeated on 17th of July 2009. The search resulted in 0 new findings for laparosco*. In 2015 a search for laparosco* between July 2012-August 2015 resulted in 12 entries but none that were new between these dates.

MAUDE database search results

a) Laparoscopic surgery

A search of the MAUDE adverse events database for 'Insuflow' was conducted on 10 January 2008. For results in which the brand name did not provide sufficient information, the full event description was reviewed. No reports were found discussing risks related to the safety concerns of the device concept of warming and humidifying gases for laparoscopic procedures as described in the intended use. A repeat of the above search was completed on 9 February 2009. A search of the Insuflow device returned 0 reports since the last search on 5th May 2008 until 9th February 2009. A repeat search was completed on the 17th of July 2012. A search for the Insuflow device returned 2 reports since the last search. The two reports were related to product malfunction where the Insuflow device was found to blow smoke into the patient cavity. No harm was caused to the patient. No reports were found discussing risks related to the safety concerns of the device concept of warming and humidifying gases for laparoscopic procedures as described in the intended use. A repeat search was carried out on the 12th of August 2015. A search for the "Insuflow" device found one entry documenting an issue with the Insuflow-Trocar where it had small black particles on it. No harm was caused to the patient. No hits were found for "Lexion medical" 2012-2015. "HumiGard" similarly gave back 0 entries between 2012 and 2015.

b) Open surgery

The original MAUDE database search was undertaken for the date period 01st January 1990 to the 31st October 2015. A search for "Carbonaid" found one entry associated with a problem around the sponge on the diffuser. The device was not used and another diffuser was used instead. The patient was not affected. A search for "Cardia innovation" found no entries between 2012 and 2015.

MHRA database search results

A search for “HumiGard”, “MR860”, “Insuflo” and “Insufflat” was done on 23 October 2015. No hits were found. This was confirmed with our internal regulatory team that records any known adverse or near-adverse events.

10.2.3 The date span of the search.

No date limits were imposed on the MAUDE or MHRA search. For ECRI search was done from 1990-2015.

10.2.4 The complete search strategies used, including all the search terms: textwords (free text), subject index headings (for example, MeSH) and the relationship between the search terms (for example, Boolean).

Search evidence

ECRI database search: see accompanying word document (search evidence folder)

MAUDE database search: see accompanying word document (search evidence folder)

MHRA database search: see accompanying word document (search evidence folder)

10.2.5 Details of any additional searches (for example, searches of company databases [include a description of each database]).

The Fisher and Paykel Healthcare internal database was searched for all terms associated with risk or reports of harm. The Product surveillance search included the search of two databases. Reports in the ‘closed’ and ‘all except closed’ categories were searched. The Products Complaints Database (old database) was searched using the search terms: ‘Product Number’ = RT350 OR MR860 OR MR820 OR HI200 OR HI100. The Products Surveillance Database (new database) was searched using the search terms: ‘Ref’ = RT350 or MR860AEA or MR860AEK or 900MR441 or 900ST100 each entered into the database separately. Complaints related to the safety

concerns and any other safety concern related to the device concept of warming and humidifying gases as described in the intended use, were included for appraisal and evaluation.

10.2.6 The inclusion and exclusion criteria.

ECRI, MAUDE and MHRA database

Selection criteria:

The brand name, event description and manufacturers narrative was screened on all databases. Applicable reports were identified based on the selection criteria below.

- The product causing the adverse report is due to insufflation of CO_2 into laparoscopic or open surgical field.
- The event description is relevant to the surgical humidification device.
- The event description is present and sufficient.

Justification:

1. Product Reports retrieved where humidification (used as intended) during open surgical procedures is the origin of the adverse event will be considered.
2. Event Description – Availability.
   Only reports where the event description is present and in sufficient detail will be utilised.
3. Event Description – Relevance
   Reports regarding use of humidification of gases in surgical procedures and producing the adverse event will be included. This criterion excludes malfunction or misuse of humidification during surgery, as these circumstances directly produce adverse events that would not have occurred under normal indicated use.

10.2.7 The data abstraction strategy

Adverse events were identified and abstracted by clinical research scientists within Fisher and Paykel Healthcare. Events were abstracted as per a data abstraction checklist independent to each scientist. This checklist included the search parameters, inclusion and exclusion criteria and events of interest. Any discrepancies between the investigators were discussed and all abstracted events used in this evaluation was entered following agreement from both scientists.

11.3 Appendix 3: Search strategy for economic evidence (Section 8.1.1)

The following information should be provided.

11.3.1 The specific databases searched and the service provider used (for example, Dialog, DataStar, OVID, Silver Platter), including at least:

- Medline
- Embase
- Medline (R) In-Process
- EconLIT
- NHS EED.

The following databases were searched:

- MEDLINE and MEDLINE In-Process (via OvidSP)
- EMBASE (via OvidSP)
- Econlit (via OvidSP)
- NHS Economic Evaluation Database (via Cochrane Library/Wiley Interscience)
- Health Technology Assessment Database (via Cochrane Library/Wiley Interscience)
- Conference Proceedings Citation Index- Science (CPCI-S) - 1990-present (via Web of Science)
- ISPOR Scientific Presentations Database (via https://www.ispor.org/RESEARCH_STUDY_DIGEST/research_index.asp)The date on which the search was conducted.

11.3.2 The date on which the search was conducted.

For search dates, see details of search strategies given in section 10.3.4 below.

11.3.3 The date span of the search.

The search was limited to studies published from 2007 to date.

11.3.4 The complete search strategies used, including all the search terms: textwords (free text), subject index headings (for example, MeSH) and the relationship between the search terms (for example, Boolean).

The database search strategies are detailed below (sources A.1 to A.7).

A.1: Source: MEDLINE In-Process & Other Non-Indexed Citations and MEDLINE 1946 to Present

Interface / URL: OvidSP

Search date: 17/11/15

Retrieved records: 390

Search strategy:

1 Economics/ (27220)

2 exp "costs and cost analysis"/ (195528)

3 economics, dental/ (1888)

4 exp "economics, hospital"/ (20912)

5 economics, medical/ (9034)

6 economics, nursing/ (3956)

7 economics, pharmaceutical/ (2651)

8 (economic$ or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic$).ti,ab,kf. (550464)

9 (expenditure$ not energy).ti,ab,kf. (21087)

10 value for money.ti,ab,kf. (1125)

11 budget$.ti,ab,kf. (21365)

12 or/1-11 (673531)

13 ((energy or oxygen) adj cost).ti,ab. (3161)

14 (metabolic adj cost).ti,ab. (959)

15 ((energy or oxygen) adj expenditure).ti,ab. (19029)

16 or/13-15 (22352)

17 12 not 16 (668486)

18 ec.fs. (362148)

19 17 or 18 (828311)

20 Carbon Dioxide/ (77354)

21 (carbon dioxide or carbonic anhydride or carbonic acid gas$2 or carbonic dioxide or carbon$ oxide or carbonic gas$2).ti,ab,kf,rn. (97118)

22 (CO2 or CO-2).ti,ab,kf. (88381)

23 (142M471B3J or 124-38-9 or 58561-67-4).ti,ab,kf,rn. (77354)

24 or/20-23 (150923)

25 Insufflation/ (1694)

26 (insufflat$ or insufflan$).ti,ab,kf. (6008)

27 or/25-26 (6513)

28 Pneumoperitoneum, Artificial/ (3914)

29 pneumoperitoneum.ti,ab,kf. (6606)

30 or/28-29 (7890)

31 24 or 27 or 30 (160861)

32 Humidity/ (13669)

33 humid$.ti,ab,kf. (26744)

34 or/32-33 (32542)

35 Hot Temperature/ (100288)

36 (heat$ or warm$ or precondition$ or pre-condition$ or conditioning).ti,ab,kf. (311031)

37 or/35-36 (363567)

38 34 or 37 (389127)

39 31 and 38 (9283)

40 ((humid$ or heat$ or warm$ or precondition$ or pre-condition$ or conditioning) and (gas or gases)).ti,kf. (714)

41 ((humid$ or heat$ or warm$ or precondition$ or pre-condition$ or conditioning) adj5 (gas or gases)).ab. (2201)

42 (humidif$ and (gas or gases)).ab. (768)

43 or/40-42 (2976)

44 humigard$.ti,ab,kf. (0)

45 humidification system$1.ti,ab,kf. (62)

46 surgical humidifier$1.ti,ab,kf. (0)

47 laparoscopic humidification.ti,ab,kf. (1)

48 (MR860 or ST310).ti,ab,kf. (8)

49 (fisher adj2 paykel).ti,ab,kf,in. (82)

50 or/44-49 (147)

51 39 or 43 or 50 (11783)

52 19 and 51 (696)

53 exp animals/ not humans/ (4148744)

54 (news or comment or editorial or letter or case reports).pt. (3283848)

55 case report.ti. (176457)

56 52 not (53 or 54 or 55) (621)

57 limit 56 to (english language and yr="2007 -Current") (399)

58 remove duplicates from 57 (390)

A.2: Source: Embase <1974 to 2015 November 16>

Interface / URL: OvidSP

Search date: 17/11/15

Retrieved records: 522

Search strategy:

1 Health Economics/ (34939)

2 exp Economic Evaluation/ (235147)

3 exp Health Care Cost/ (226262)

4 pharmacoeconomics/ (6170)

5 (econom$ or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic$).ti,ab,kw. (713298)

6 (expenditure$ not energy).ti,ab,kw. (27788)

7 (value adj2 money).ti,ab,kw. (1612)

8 budget$.ti,ab,kw. (27855)

9 or/1-8 (933665)

10 (metabolic adj cost).ti,ab. (1046)

11 ((energy or oxygen) adj cost).ti,ab. (3462)

12 ((energy or oxygen) adj expenditure).ti,ab. (23163)

13 or/10-12 (26779)

14 9 not 13 (927952)

15 cost/ (54858)

16 "program cost effectiveness"/ (251)

17 pe.fs. (64830)

18 or/14-17 (960179)

19 carbon dioxide/ (82499)

20 (carbon dioxide or carbonic anhydride or carbonic acid gas$2 or carbonic dioxide or carbon$ oxide or carbonic gas$2).ti,ab,kw,rn. (101949)

21 (CO2 or CO-2).ti,ab,kw. (97309)

22 (142M471B3J or 124-38-9 or 58561-67-4).ti,ab,kw,rn. (80481)

23 or/19-22 (158863)

24 aeration/ (9550)

25 (insufflat$ or insufflan$).ti,ab,kw. (8088)

26 or/24-25 (14784)

27 gastrointestinal radiography/ (5427)

28 pneumoperitoneum.ti,ab,kw. (8071)

29 or/27-28 (12415)

30 23 or 26 or 29 (180181)

31 humidifier/ (2931)

32 humidity/ (24304)

33 humid$.ti,ab,kw. (33954)

34 or/31-33 (43391)

35 warming/ (7541)

36 heating/ (22207)

37 heat/ (59425)

38 (heat$ or warm$ or precondition$ or pre-condition$ or conditioning).ti,ab,kw. (372084)

39 or/35-38 (408159)

40 34 or 39 (443079)

41 30 and 40 (11500)

42 ((humid$ or heat$ or warm$ or precondition$ or pre-condition$ or conditioning) and (gas or gases)).ti,kw. (1315)

43 ((humid$ or heat$ or warm$ or precondition$ or pre-condition$ or conditioning) adj5 (gas or gases)).ab. (3080)

44 (humidif$ and (gas or gases)).ab. (1095)

45 or/42-44 (4454)

46 humigard$.ti,ab,kw,dv. (4)

47 humidification system$1.ti,ab,kw,dv. (97)

48 surgical humidifier$1.ti,ab,kw,dv. (0)

49 laparoscopic humidification.ti,ab,kw,dv. (1)

50 (MR860 or ST310).ti,ab,kw,dv. (8)

51 (fisher adj2 paykel).ti,ab,kw,dv,dm,in. (220)

52 laparoscopic humidification system/ (3)

53 or/46-52 (316)

54 41 or 45 or 53 (15285)

55 18 and 54 (1103)

56 (animal/ or animal experiment/ or animal model/ or animal tissue/ or nonhuman/) not exp human/ (5266360)

57 (editorial or letter).pt. (1414624)

58 case report.ti. (223678)

59 55 not (56 or 57 or 58) (943)

60 limit 59 to (english language and yr="2007 -Current") (550)

61 remove duplicates from 60 (522)

A.3: Source: NHS Economic Evaluation Database: Issue 2 of 4, April 2015

Interface / URL: Cochrane Library / Wiley Interscience

Search date: 17/11/15

Retrieved records: 1

Search strategy:

#1 [mh ^"Carbon Dioxide"] 2496

#2 ("carbon dioxide" or "carbonic anhydride" or carbonic next acid next gas* or "carbonic dioxide" or carbon* next oxide or carbonic next gas*) 5282

#3 (CO2 or CO-2) 2835

#4 (142M471B3J or 124-38-9 or 58561-67-4) 1

#5 [28-#4] 6636

#6 [mh ^Insufflation] 212

#7 (insufflat* or insufflan*) 890

#8 #6 or #7 890

#9 [mh ^"Pneumoperitoneum, Artificial"] 236

#10 pneumoperitoneum 656

#11 #9 or #10 656

#12 #5 or #8 or #11 7429

#13 [mh ^Humidity] 473

#14 humid* 1556

#15 #13 or #14 1556

#16 [mh ^"Hot Temperature"] 1422

#17 (heat* or warm* or precondition* or pre-condition* or conditioning) 15301

#18 #16 or #17 15677

#19 #15 or #18 16431

#20 #12 and #19 467

#21 ((humid* or heat* or warm* or precondition* or pre-condition* or conditioning) and (gas or gases)) 772

#22 humigard* 1

#23 humidification next system* 16

#24 surgical next humidifier* 0

#25 "laparoscopic humidification" 1

#26 (MR860 or ST310) 0

#27 (fisher next/2 paykel) 52

#28 {or #22-#27} 65

#29 #20 or #21 or #28 Publication Year from 2007 to 2015 624

#30 #29 in Economic Evaluations 1

A.4: Source: Health Technology Assessment Database: Issue 4 of 4, October 2015

Interface / URL: Cochrane Library / Wiley Interscience

Search date: 17/11/15

Retrieved records: 1

Search strategy:

#1 [mh ^"Carbon Dioxide"] 2496

#2 ("carbon dioxide" or "carbonic anhydride" or carbonic next acid next gas* or "carbonic dioxide" or carbon* next oxide or carbonic next gas*) 5282

#3 (CO2 or CO-2) 2835

#4 (142M471B3J or 124-38-9 or 58561-67-4) 1

#5 [28-#4] 6636

#6 [mh ^Insufflation] 212

#7 (insufflat* or insufflan*) 890

#8 #6 or #7 890

#9 [mh ^"Pneumoperitoneum, Artificial"] 236

#10 pneumoperitoneum 656

#11 #9 or #10 656

#12 #5 or #8 or #11 7429

#13 [mh ^Humidity] 473

#14 humid* 1556

#15 #13 or #14 1556

#16 [mh ^"Hot Temperature"] 1422

#17 (heat* or warm* or precondition* or pre-condition* or conditioning) 15301

#18 #16 or #17 15677

#19 #15 or #18 16431

#20 #12 and #19 467

#21 ((humid* or heat* or warm* or precondition* or pre-condition* or conditioning) and (gas or gases)) 772

#22 humigard* 1

#23 humidification next system* 16

#24 surgical next humidifier* 0

#25 "laparoscopic humidification" 1

#26 (MR860 or ST310) 0

#27 (fisher next/2 paykel) 52

#28 {or #22-#27} 65

#29 #20 or #21 or #28 Publication Year from 2007 to 2015 624

#30 #29 in Economic Evaluations 1

#31 #29 in Technology Assessments 1

A.5: Source: Econlit 1886 to October 2015

Interface / URL: OvidSP

Search date: 17/11/15

Retrieved records: 60

Search strategy:

1 (carbon dioxide or carbonic anhydride or carbonic acid gas$2 or carbonic dioxide or carbon$ oxide or carbonic gas$2).af. (1425)

2 (CO2 or CO-2).af. (3112)

3 (142M471B3J or 124-38-9 or 58561-67-4).af. (0)

4 or/1-3 (4004)

5 (insufflat$ or insufflan$).af. (0)

6 pneumoperitoneum.af. (0)

7 or/4-6 (4004)

8 humid$.af. (143)

9 (heat$ or warm$ or precondition$ or pre-condition$ or conditioning).af. (21034)

10 or/8-9 (21135)

11 7 and 10 (2369)

12 ((humid$ or heat$ or warm$ or precondition$ or pre-condition$ or conditioning) and (gas or gases)).ti,kw. (73)

13 ((humid$ or heat$ or warm$ or precondition$ or pre-condition$ or conditioning) adj5 (gas or gases)).af. (180)

14 (humidif$ and (gas or gases)).af. (0)

15 or/11-14 (2550)

16 (surgic$ or surger$ or surgeon$ or intra-operat$ or peri-operat$ or per-operat$ or post-operat$).af. (743)

17 operat$.ti,kw. (6887)

18 operat$.ab. /freq=2 (8738)

19 (incision$ or resect$).af. (6)

20 (celioscop$ or coelioscop$ or endoscop$ or laparoscop$ or laparotom$ or pleuroscop$ or thoracoscop$).af. (22)

21 (keyhole or key-hole or minimal access or minimally invasive or video-assist$).af. (12)

22 (abdom$ or adrenal gland$ or appende$ or appendi$ or bariatric$ or biliar$ or bladder$ or bowel$ or c-section$ or caesarean$ or cesarean$ or cecum$ or chole$ or colon$ or colorect$ or digest$ or duoden$ or fallop$ or gallbladder$ or gastr$ or gyne$ or gynae$ or hepar$ or hepat$ or hernia$ or hysterectom$ or hysterotom$ or ileum$ or intestin$ or intraabdom$ or kidney$ or liver$ or ovary or ovaries or pancrea$ or pariet$ or pelvis$ or pelvic or periton$ or rectum$ or rectal or retroperiton$ or spleen$ or splenect$ or stomach$ or ureter$ or urinary or uteri$ or uterus$).af. (9030)

23 or/16-22 (23437)

24 15 and 23 (66)

25 humigard$.af. (0)

26 humidification system$1.af. (0)

27 surgical humidifier$1.af. (0)

28 laparoscopic humidification.af. (0)

29 (MR860 or ST310).af. (0)

30 (fisher adj2 paykel).af. (0)

31 or/25-30 (0)

32 24 or 31 (66)

33 limit 32 to (yr="2007 -Current" and english) (60)

A.6: Source: Conference Proceedings Citation Index- Science (CPCI-S) - 1990-present

Interface / URL: Web of Science

Search date: 17/11/15

Retrieved records: 33

Search strategy:

45 33 (#44) AND LANGUAGE: (English) Indexes=CPCI-S Timespan=2007-2015

44 62 #42 not #43

43 208,041 TI=("rat" or "rats" or "rodent" or "rodents" or "mouse" or "mice" or "murine" or "hamster" or "hamsters" or "gerbil" or "gerbils" or "animal" or "animals" or "dogs" or "dog" or "canine" or "pig" or "pigs" or "piglet" or "piglets" or "cats" or "bovine" or "cow" or "cows" or "cattle" or "sheep" or "ewe" or "ewes" or "horse" or "horses" or "equine" or "ovine" or "porcine" or

"monkey" or "monkeys" or "primate" or "primates" or "rhesus macaque" or "rhesus macaques" or "rabbit" or "rabbits") NOT TS=human*

42 63 #11 and #41

41 407 #33 or #40

40 36 #39 OR #38 OR #37 OR #36 OR #35 OR #34

39 11 TS=("fisher" near/2 "paykel") or AD=("fisher" near/2 "paykel")

38 0 TS=("MR860" or "ST310")

37 0 TS=("laparoscopic humidification")

36 0 TS=("surgical humidifier*")

35 26 TS=("humidification system*")

34 1 TS=(humigard*)

33 373 #25 and #32

32 638,512 #31 OR #30 OR #29 OR #28 OR #27 OR #26

31 435,701 TS=(abdom* or "adrenal gland*" or appende* or appendi* or bariatric* or biliar* or bladder* or bowel* or "c-section*" or caesarean* or cesarean* or cecum* or chole* or colon* or colorect* or digest* or duoden* or fallop* or gallbladder* or gastr* or gyne* or gynae* or hepar* or hepat* or hernia* or hysterectom* or hysterotom* or ileum* or intestin* or intraabdom* or kidney* or liver* or "ovary" or "ovaries" or pancrea* or pariet* or pelvis* or "pelvic" or periton* or rectum* or "rectal" or retroperiton* or spleen* or splenect* or stomach* or ureter* or "urinary" or uteri* or uterus*)

30 7,958 TS=("keyhole" or "key-hole" or "minimal access" or "minimally invasive" or "video-assist*")

29 39,180 TS=(celioscop* or coelioscop* or endoscop* or laparoscop* or laparotom* or pleuroscop* or thoracoscop*)

28 29,286 TS=(incision* or resect*)

27 129,458 TS=(surgic* or surger* or surgeon* or "intra-operat*" or "peri-operat*" or "per-operat*" or "post-operat*")

26 208,209 WC=(surgery) OR SU=(surgery)

25 16,638 #24 OR #23 OR #22 OR #21

24 440 TS=(humidif* and ("gas" or "gases"))

23 8,110 TS=((humid* or heat* or warm* or precondition* or "pre-condition*" or "conditioning") near/5 ("gas" or "gases"))

22 1,773 TI=((humid* or heat* or warm* or precondition* or "pre-condition*" or "conditioning") and ("gas" or "gases"))

21 9,012 #17 and #20

20 255,579 #19 OR #18

19 238,447 TS=(heat* or warm* or precondition* or "pre-condition*" or "conditioning")

18 21,204 TS=(humid*)

17 54,832 #16 OR #15 OR #14 OR #13 OR #12

16 541 TS=("pneumoperitoneum")

15 544 TS=(insufflat* or insufflan*)

14 0 TS=(142M471B3J or "124-38-9" or "58561-67-4")

13 45,417 TS=(CO2 or "CO-2")

12 18,117 TS=("carbon dioxide" or "carbonic anhydride" or "carbonic acid gas*" or "carbonic dioxide" or "carbon* oxide" or "carbonic gas*")

11 404,449 #6 not #10

10 4,977 #9 OR #8 OR #7

9 2,714 TS=(("energy" or "oxygen") near/0 "expenditure")

8 123 TS=("metabolic" near/0 "cost")

7 2,225 TS=(("energy" or "oxygen") near/0 "cost")

6 406,987 #5 OR #4 OR #3 OR #2 OR #1

5 16,615 TS=(budget*)

4 172 TS=("value for money")

3 3,584 TS=(expenditure* not "energy")

2 378,687 TS=(economic* or "cost" or "costs" or "costly" or "costing" or "price" or "prices" or "pricing" or pharmacoeconomic*)

1 20,563 WC=(economic* not agricultural)

A.7: Source: ISPOR Scientific Presentations Database

Interface / URL:
https://www.ispor.org/RESEARCH_STUDY_DIGEST/research_index.asp

Search date: 17/11/15

Retrieved records: 0

Search strategy:

The following searches were carried out using the keyword field (titles / abstracts selected as indicated). The Meeting selected was the 18th Annual European Congress. Returned results were assessed online by the searcher. Choice of records retrieved for further consideration was based on the searcher's judgement. Only records which had not already been found through other sources were retrieved.

carbon [titles] = 0 (1 returned and excluded as irrelevant)

carbon [abstracts] = 0 (5 returned and excluded as irrelevant)

carbonic [titles] = 0 returned

carbonic [abstracts] = 0 returned

CO2 [titles] = 0 (1 returned, excluded as duplicate of record retrieved from a previously searched resource)

CO2 [abstracts] = 0 returned

CO-2 [titles] = 0 returned

CO-2 [abstracts] = 0 returned

gas [titles] = 0 (13 returned and excluded as irrelevant)

gas [abstracts] = 0 (84 returned and excluded as irrelevant)

gases [titles] = 0 returned

gases [abstracts] = 0 returned

11.3.5 Details of any additional searches (for example, searches of company databases [include a description of each database]).

The reference lists of those HumiGard studies included within the clinical evidence review were assessed to retrieve any further studies suitable studies. None were identified. Further, the research team discussed any knowledge of studies assessing the cost-effectiveness of the HumiGard system. No studies other than those identified through database searches were identified.

11.4 Appendix 4: Resource identification, measurement and valuation (Section 9.3.2)

The following information should be provided.

11.4.1 The specific databases searched and the service provider used (for example, Dialog, DataStar, OVID, Silver Platter), including at least:

- Medline
- Embase
- Medline (R) In-Process
- NHS EED
- EconLIT

No additional literature search was conducted for resource use.

11.4.2 The date on which the search was conducted.

N/A

11.4.3 The date span of the search.

N/A

11.4.4 The complete search strategies used, including all the search terms: textwords (free text), subject index headings (for example, MeSH) and the relationship between the search terms (for example, Boolean).

N/A

11.4.5 Details of any additional searches (for example, searches of company databases [include a description of each database]).

N/A

11.4.6 The inclusion and exclusion criteria.

N/A

11.4.7 The data abstraction strategy.

N/A

11.5 Appendix 5 Reference costs, PbR taffif and OPCS codes (Section 9.3)

Table 10A contains a list of relevant NHS reference costs and PbR tariff costs for patients undergoing open or laparoscopic abdominal surgery.

Table 10A: Relevant NHS reference costs and PbR tariff costs

HRG code	Description	NHS Reference Cost (2013-14) Total HRGs	PbR Tariff (2014-15)
FZ12D	General Abdominal - Very Major or Major Procedures 19 years and over with Major CC		£4,338
FZ12E	General Abdominal - Very Major or Major Procedures 19 years and over with Intermediate CC		£2,539

HRG code	Description	NHS Reference Cost (2013-14) Total HRGs	PbR Tariff (2014-15)
FZ12F	General Abdominal - Very Major or Major Procedures 19 years and over without CC		£1,884
FZ12G	General Abdominal - Very Major or Major Procedures 18 years and under		£2,384
FZ12L	Major General Abdominal Procedures, 19 years and over, with CC Score 10+	£8,350	
FZ12M	Major General Abdominal Procedures, 19 years and over, with CC Score 6-9	£7,578	
FZ12N	Major General Abdominal Procedures, 19 years and over, with CC Score 3-5	£5,027	
FZ12P	Major General Abdominal Procedures, 19 years and over, with CC Score 1-2	£3,710	
FZ12Q	Major General Abdominal Procedures, 19 years and over, with CC Score 0	£2,562	
FZ12R	Major General Abdominal Procedures, between 2 and 18 years, with CC Score 1+	£7,303	
FZ12S	Major General Abdominal Procedures, between 2 and 18 years, with CC Score 0	£3,608	
FZ12T	Major General Abdominal Procedures, 1 year and under, with CC Score 2+	£6,051	
FZ12U	Major General Abdominal Procedures, 1 year and under, with CC Score 0-1	£5,073	
FZ17D	Abdominal Hernia Procedures, 18 years and under	£1,581	£1,133
FZ17A/FZ17E	Abdominal Hernia Procedures, 19 years and over, with CC Score 4+	£5,252	£3,423
FZ17B/FZ17F	Abdominal Hernia Procedures, 19 years and over, with CC Score 1-3	£3,318	£2,308
FZ17C/FZ17G	Abdominal Hernia Procedures, 19 years and over, with CC Score 0	£2,281	£1,689
FZ27D	Intermediate Therapeutic General Abdominal Procedures, 18 years and under	£1,603	£1,274
FZ27A/FZ27E	Intermediate Therapeutic General Abdominal Procedures, 19 years and over, with CC Score 3+	£4,073	£1,747
FZ27B/FZ27F	Intermediate Therapeutic General Abdominal Procedures, 19 years and over, with CC Score 1-2	£2,749	£1,377
FZ27C/FZ27G	Intermediate Therapeutic General Abdominal Procedures, 19 years and over, with CC Score 0	£2,043	£1,047
FZ79C	Complex General Abdominal Procedures with CC Score 6+	£14,625	

HRG code	Description	NHS Reference Cost (2013-14) Total HRGs	PbR Tariff (2014-15)
FZ79D	Complex General Abdominal Procedures with CC Score 3-5	£8,702	
FZ79E	Complex General Abdominal Procedures with CC Score 0-2	£6,187	
FZ04A	Very Major Stomach or Duodenum Procedures with Major CC		£8,626
FZ80C	Very Complex, Oesophageal, Stomach or Duodenum Procedures, 19 years and over, with CC Score 6+	£17,690	
FZ80D	Very Complex, Oesophageal, Stomach or Duodenum Procedures, 19 years and over, with CC Score 3-5	£12,172	
FZ82C	Very Complex or Complex, Oesophageal, Stomach or Duodenum Procedures, 18 years and under, with CC Score 2+	£13,670	
FZ81C	Complex, Oesophageal, Stomach or Duodenum Procedures, 19 years and over, with CC Score 4+	£10,877	
FZ81D	Complex, Oesophageal, Stomach or Duodenum Procedures, 19 years and over, with CC Score 2-3	£8,262	
FZ04B	Very Major Stomach or Duodenum Procedures without Major CC		£5,364
FZ80E	Very Complex, Oesophageal, Stomach or Duodenum Procedures, 19 years and over, with CC Score 0-2	£8,785	
FZ82D	Very Complex or Complex, Oesophageal, Stomach or Duodenum Procedures, 18 years and under, with CC Score 0-1	£7,755	
FZ81E	Complex, Oesophageal, Stomach or Duodenum Procedures, 19 years and over, with CC Score 0-1	£5,391	
FZ05A	Major Stomach or Duodenum Procedures 2 years and over with CC		£3,482
FZ83C	Major, Oesophageal, Stomach or Duodenum Procedures, between 2 and 18 years, with CC Score 1+	£7,995	
FZ83G	Major, Oesophageal, Stomach or Duodenum Procedures, 19 years and over, with CC Score 7+	£7,332	
FZ83H	Major, Oesophageal, Stomach or Duodenum Procedures, 19 years and over, with CC Score 4-6	£5,240	
FZ83J	Major, Oesophageal, Stomach or Duodenum Procedures, 19 years and over, with CC Score 2-3	£3,922	

HRG code	Description	NHS Reference Cost (2013-14) Total HRGs	PbR Tariff (2014-15)
FZ05B	Major Stomach or Duodenum Procedures 2 years and over without CC		£2,076
FZ83D	Major, Oesophageal, Stomach or Duodenum Procedures, between 2 and 18 years, with CC Score 0	£3,847	
FZ83K	Major, Oesophageal, Stomach or Duodenum Procedures, 19 years and over, with CC Score 0-1	£1,606	
FZ05C	Major Stomach or Duodenum Procedures 1 year and under		£5,227
FZ83E	Major, Oesophageal, Stomach or Duodenum Procedures, 1 year and under, with CC Score 1+	£7,835	
FZ83F	Major, Oesophageal, Stomach or Duodenum Procedures, 1 year and under, with CC Score 0	£3,637	
FZ84Z	Stomach Bypass Procedures for Obesity	£5,008	
FZ85Z	Restrictive Stomach Procedures for Obesity	£3,821	
FZ87D	Complex Hernia Procedures with CC Score 5+	£6,397	
FZ87E	Complex Hernia Procedures with CC Score 3-4	£4,516	
FZ87F	Complex Hernia Procedures with CC Score 1-2	£3,453	
FZ87G	Complex Hernia Procedures with CC Score 0	£2,328	
FZ08A	Complex Large Intestine Procedures with Major CC		£8,890
FZ11A	Large Intestine - Major Procedures with Major CC		£5,320
FZ73C	Very Complex Large Intestine Procedures with CC Score 9+	£17,368	
FZ73D	Very Complex Large Intestine Procedures with CC Score 6-8	£14,220	
FZ73E	Very Complex Large Intestine Procedures with CC Score 3-5	£10,890	
FZ74C	Complex Large Intestine Procedures, 19 years and over, with CC Score 9+	£10,657	
FZ74D	Complex Large Intestine Procedures, 19 years and over, with CC Score 6-8	£9,224	
FZ74E	Complex Large Intestine Procedures, 19 years and over, with CC Score 3-5	£7,912	
FZ77C	Major Large Intestine Procedures, 19 years and over, with CC Score 3+	£5,515	
FZ77D	Major Large Intestine Procedures, 19 years and over, with CC Score 1-2	£4,002	

HRG code	Description	NHS Reference Cost (2013-14) Total HRGs	PbR Tariff (2014-15)
FZ78A	Complex or Major, Large Intestine Procedures, between 2 and 18 years, with CC Score 1+	£8,093	
FZ78C	Complex or Major, Large Intestine Procedures, 1 year and under, with CC Score 1+	£8,601	
FZ08B/FZ74F	Complex Large Intestine Procedures without Major CC/CC Score 0-2	£6,519	£5,709
FZ11B	Large Intestine - Major Procedures without Major CC		£2,586
FZ73F	Very Complex Large Intestine Procedures with CC Score 0-2	£8,792	
FZ77E	Major Large Intestine Procedures, 19 years and over, with CC Score 0	£2,953	
FZ78B	Complex or Major, Large Intestine Procedures, between 2 and 18 years, with CC Score 0	£5,941	
FZ78D	Complex or Major, Large Intestine Procedures, 1 year and under, with CC Score 0	£5,960	
FZ09A	Proximal Colon Procedures with Major CC		£6,837
FZ75C	Proximal Colon Procedures, 19 years and over, with CC Score 6+	£8,334	
FZ75D	Proximal Colon Procedures, 19 years and over, with CC Score 3-5	£6,396	
FZ09B/FZ75E	Proximal Colon Procedures without Major CC/ CC Score 0-2	£5,513	£4,666
FZ10A/FZ76C	Distal Colon Procedures with Major CC/CC score 3+	£7,387	£7,949
FZ10B/FZ76D	Distal Colon Procedures without Major CC/CC score 0-2	£5,088	£5,104
FZ13Z	General Abdominal - Diagnostic Procedures		£787
FZ13C	Minor Therapeutic or Diagnostic, General Abdominal Procedures, 19 years and over	£864	
FZ13D	Minor Therapeutic or Diagnostic, General Abdominal Procedures, 18 years and under	£1,133	
FZ14Z	Complex Procedures for Inflammatory Bowel Disease		£6,552
FZ15Z	Major Procedures for Inflammatory Bowel Disease		£4,919
FZ16Z	Very Major Procedures for Gastrointestinal Bleed		£6,496
FZ18A/FZ18G	Inguinal Umbilical or Femoral Hernia Repairs 19 years and over with Major CC/CC score 6+	£4,080	£1,744

HRG code	Description	NHS Reference Cost (2013-14) Total HRGs	PbR Tariff (2014-15)
FZ18B	Inguinal Umbilical or Femoral Hernia Repairs 19 years and over with Intermediate CC		Day case: £1,292 Ordinary elective spell: £996
FZ18H	Inguinal, Umbilical or Femoral Hernia Procedures, 19 years and over, with CC Score 3-5	£2,575	
FZ18J	Inguinal, Umbilical or Femoral Hernia Procedures, 19 years and over, with CC Score 1-2	£1,968	
FZ18C/FZ18K	Inguinal Umbilical or Femoral Hernia Repairs 19 years and over without CC	£1,748	Day case: £1,088 Ordinary elective spell: £792
FZ18D	Inguinal Umbilical or Femoral Hernia Repairs 18 years and under		£1,100
FZ18E	Inguinal, Umbilical or Femoral Hernia Procedures, between 2 and 18 years	£1,472	
FZ18F	Inguinal, Umbilical or Femoral Hernia Procedures, 1 year and under	£2,225	
FZ19Z	Herniotomy Procedures		£1,062
FZ19A	Herniotomy Procedures, 2 years and over	£1,328	
FZ19B	Herniotomy Procedures, 1 year and under	£1,852	
FZ20A	Appendicectomy Procedures 19 years and over with Major CC		£2,110
FZ20F	Appendicectomy Procedures, 19 years and over, with CC Score 5+	£5,617	
FZ20G	Appendicectomy Procedures, 19 years and over, with CC Score 3-4	£4,072	
FZ20B	Appendicectomy Procedures 19 years and over without Major CC		£1,579
FZ20H	Appendicectomy Procedures, 19 years and over, with CC Score 1-2	£3,210	
FZ20J	Appendicectomy Procedures, 19 years and over, with CC Score 0	£2,734	
FZ20C	Appendicectomy Procedures 18 years and under		£2,089
FZ20K	Appendicectomy Procedures, 18 years and under, with CC Score 3+	£5,265	
FZ20L	Appendicectomy Procedures, 18 years and under, with CC Score 1-2	£3,497	
FZ20M	Appendicectomy Procedures, 18 years and under, with CC Score 0	£2,757	
FZ21Z	Major Anal Procedures		£1,091

HRG code	Description	NHS Reference Cost (2013-14) Total HRGs	PbR Tariff (2014-15)
FZ21B	Major Anal Procedures, 18 years and under	£2,675	
FZ21C	Major Anal Procedures, 19 years and over, with CC Score 1+	£2,179	
FZ21D	Major Anal Procedures, 19 years and over, with CC Score 0	£1,380	
FZ22A	Intermediate Anal Procedures 19 years and over		£843
FZ22C	Intermediate Anal Procedures, 19 years and over, with CC Score 3+	£2,583	
FZ22D	Intermediate Anal Procedures, 19 years and over, with CC Score 1-2	£1,443	
FZ22E	Intermediate Anal Procedures, 19 years and over, with CC Score 0	£1,159	
FZ22B	Intermediate Anal Procedures 18 years and under	£1,404	£974
FZ23Z	Minor Anal Procedures		£603
FZ23A	Minor Anal Procedures, 19 years and over	£496	
FZ23B	Minor Anal Procedures, 18 years and under	£867	
FZ24A/G	Major Therapeutic Open or Endoscopic Procedures 19 years and over with Major CC/CC score 3+	£1,943	£812
FZ24B/H	Major Therapeutic Open or Endoscopic Procedures 19 years and over with Intermediate CC/ CC score 1-2	£917	£724
FZ24C/J	Major Therapeutic Open or Endoscopic Procedures 19 years and over without CC	£803	£648
FZ24D	Major Therapeutic Open or Endoscopic Procedures 18 years and under		£1,346
FZ24E	Major Therapeutic Endoscopic, Upper or Lower Gastrointestinal Tract Procedures, between 2 and 18 years	£1,437	
FZ24F	Major Therapeutic Endoscopic, Upper or Lower Gastrointestinal Tract Procedures, 1 year and under	£1,883	
FZ25A/FZ70Z	Therapeutic Endoscopic or Intermediate Stomach or Duodenum Procedures 19 years and over	£645	£490
FZ25B	Therapeutic Endoscopic or Intermediate Stomach or Duodenum Procedures 18 years and under		£1,038
FZ28A	Endoscopic or Intermediate Procedures for Inflammatory Bowel Disease 19 years and over with CC		£610

HRG code	Description	NHS Reference Cost (2013-14) Total HRGs	PbR Tariff (2014-15)
FZ28B	Endoscopic or Intermediate Procedures for Inflammatory Bowel Disease 19 years and over without CC		£563
FZ28C	Endoscopic or Intermediate Procedures for Inflammatory Bowel Disease 18 years and under		£1,009
FZ58A	Endoscopic or Intermediate, Lower Gastrointestinal Tract Procedures, between 2 and 18 years	£744	
FZ58B	Endoscopic or Intermediate, Lower Gastrointestinal Tract Procedures, 1 year and under	£1,515	
FZ29Z	Major or Therapeutic Endoscopic Procedures for Gastrointestinal Bleed		£611
FZ30Z	Diagnostic Endoscopic or Intermediate Procedures for Gastrointestinal Bleed		£563
FZ50Z	Intermediate Large Intestine Procedures 19 years and over	£441	£465
FZ58Z	Endoscopic or Intermediate Large Intestine Procedures 18 years and under		£805
FZ59Z	Intermediate Procedures on the Upper GI Tract 19 years and over	£346	£342
FZ62A	Endoscopic or Intermediate, Upper Gastrointestinal Tract Procedures, between 2 and 18 years	£896	
FZ62B	Endoscopic or Intermediate, Upper Gastrointestinal Tract Procedures, 1 year and under	£806	
FZ64Z	Combined Upper and Lower GI Tract Diagnostic Endoscopic Procedures with biopsy		£655
FZ66A	Very Major Small Intestine Procedures 19 years and over with CC		£7,574
FZ66C	Very Major Small Intestine Procedures, 19 years and over, with CC Score 8+	£10,315	
FZ66D	Very Major Small Intestine Procedures, 19 years and over, with CC Score 5-7	£8,364	
FZ66E	Very Major Small Intestine Procedures, 19 years and over, with CC Score 2-4	£6,741	
FZ66B/F	Very Major Small Intestine Procedures 19 years and over without CC/CC score 0-1	£5,307	£4,254
FZ67A	Major Small Intestine Procedures 19 years and over with CC		£4,122
FZ67C	Major Small Intestine Procedures, 19 years and over, with CC Score 7+	£9,587	

HRG code	Description	NHS Reference Cost (2013-14) Total HRGs	PbR Tariff (2014-15)
FZ67D	Major Small Intestine Procedures, 19 years and over, with CC Score 4-6	£6,791	
FZ67E	Major Small Intestine Procedures, 19 years and over, with CC Score 2-3	£4,952	
FZ67B/F	Major Small Intestine Procedures 19 years and over without CC/CC score 0-1	£3,550	£2,950
FZ68A	Very Major and Major Small Intestine Procedures 18 years and under with CC		£6,831
FZ68G	Very Major or Major, Small Intestine Procedures, between 2 and 18 years, with CC Score 2+	£11,108	
FZ68J	Very Major or Major, Small Intestine Procedures, 1 year and under, with CC Score 3+	£14,532	
FZ68K	Very Major or Major, Small Intestine Procedures, 1 year and under, with CC Score 1-2	£8,536	
FZ68B	Very Major and Major Small Intestine Procedures 18 years and under without CC		£3,543
FZ68H	Very Major or Major, Small Intestine Procedures, between 2 and 18 years, with CC Score 0-1	£5,277	
FZ68L	Very Major or Major, Small Intestine Procedures, 1 year and under, with CC Score 0	£5,413	
FZ69B	Complex Small Intestine Procedures, 18 years and under	£21,346	
FZ69C	Complex Small Intestine Procedures, 19 years and over, with CC Score 7+	£18,240	
FZ69D	Complex Small Intestine Procedures, 19 years and over, with CC Score 3-6	£12,056	
FZ69E	Complex Small Intestine Procedures, 19 years and over, with CC Score 0-2	£8,270	
GA01A	Hepatobiliary Transplant, 1 year and under	£23,630	
GA01B	Hepatobiliary Transplant, between 2 and 17 years	£18,311	
GA01C	Hepatobiliary Transplant, 18 years and over	£19,136	
GA03A	Hepatobiliary Procedures category 7 with CC		£11,095
GA03C	Very Complex Open, Hepatobiliary or Pancreatic Procedures, with CC Score 4+	£13,433	
GA03D	Very Complex Open, Hepatobiliary or Pancreatic Procedures, with CC Score 2-3	£10,258	
GA03B	Hepatobiliary Procedures category 7 without CC		£7,722

HRG code	Description	NHS Reference Cost (2013-14) Total HRGs	PbR Tariff (2014-15)
GA03E	Very Complex Open, Hepatobiliary or Pancreatic Procedures, with CC Score 0-1	£8,659	
GA04A	Hepatobiliary Procedures category 6 with CC		£8,236
GA04C	Complex Open, Hepatobiliary or Pancreatic Procedures, with CC Score 3+	£11,372	
GA04D	Complex Open, Hepatobiliary or Pancreatic Procedures, with CC Score 0-2	£7,796	
GA04B	Hepatobiliary Procedures category 6 without CC		£6,506
GA05A	Hepatobiliary Procedures category 5 with CC		£6,375
GA05C	Very Major Open, Hepatobiliary or Pancreatic Procedures, with CC Score 3+	£9,484	
GA05D	Very Major Open, Hepatobiliary or Pancreatic Procedures, with CC Score 0-2	£6,382	
GA05B	Hepatobiliary Procedures category 5 without CC		£5,120
GA06A	Hepatobiliary Procedures category 4 with CC		£4,729
GA06C	Major Open, Hepatobiliary or Pancreatic Procedures, with CC Score 2+	£7,093	
GA06B	Hepatobiliary Procedures category 4 without CC		£3,557
GA06D	Major Open, Hepatobiliary or Pancreatic Procedures, with CC Score 0-1	£4,251	
GA07A	Hepatobiliary Procedures category 3 with CC		£4,548
GA07C	Intermediate Open, Hepatobiliary or Pancreatic Procedures, with CC Score 3+	£5,863	
GA07D	Intermediate Open, Hepatobiliary or Pancreatic Procedures, with CC Score 1-2	£4,223	
GA07B	Hepatobiliary Procedures category 3 without CC		£3,252
GA07E	Intermediate Open, Hepatobiliary or Pancreatic Procedures, with CC Score 0	£3,477	
GA10C/N	Open Cholecystectomy without CC	£3,515	£2,207
GA10G	Open or Laparoscopic Cholecystectomy, 18 years and under	£3,152	
GA10D	Laparoscopic Cholecystectomy with length of stay 1 day or more without CC		£1,353
GA10E	Laparoscopic Cholecystectomy with length of stay 0 days without CC		£1,353
GA10K	Laparoscopic Cholecystectomy, 19 years and over, with CC Score 0	£2,258	
GA10H	Laparoscopic Cholecystectomy, 19 years and over, with CC Score 4+	£4,333	

HRG code	Description	NHS Reference Cost (2013-14) Total HRGs	PbR Tariff (2014-15)
GA10J	Laparoscopic Cholecystectomy, 19 years and over, with CC Score 1-3	£2,862	
GA10F	Open or Laparoscopic Cholecystectomy with CC		£2,207
GA10L	Open Cholecystectomy, 19 years and over, with CC Score 3+	£6,674	
GA10M	Open Cholecystectomy, 19 years and over, with CC Score 1-2	£4,390	
GA11Z	Pancreatic Necrosectomy	£14,944	£13,465
GA13A	Hepatobiliary Procedures category 1 or 2 with CC	£3,208	£2,033
GA13B	Hepatobiliary Procedures category 1 or 2 without CC	£1,979	£1,498
LB05D	Intermediate Percutaneous, Kidney or Ureter Procedures, 18 years and under	£3,434	
LB05E	Intermediate Percutaneous, Kidney or Ureter Procedures, 19 years and over, with CC Score 6+	£4,630	
LB05F	Intermediate Percutaneous, Kidney or Ureter Procedures, 19 years and over, with CC Score 3-5	£2,201	
LB05G	Intermediate Percutaneous, Kidney or Ureter Procedures, 19 years and over, with CC Score 0-2	£1,623	
LB10Z	Bladder Major Open Procedures / Reconstruction		£5,501
LB10B	Major Open Bladder Procedures or Reconstruction, 18 years and under	£5,526	
LB10C	Major Open Bladder Procedures or Reconstruction, 19 years and over, with CC Score 2+	£7,041	
LB10D	Major Open Bladder Procedures or Reconstruction, 19 years and over, with CC Score 0-1	£3,304	
LB11A	Urinary Diversion without Cystectomy with Malignancy		£8,427
LB11B	Urinary Diversion without Cystectomy without Malignancy		£5,391
LB12Z	Bladder Intermediate Open Procedure	£3,362	£1,595
LB15D	Bladder Minor Procedure 18 years and under	£683	£625
LB15E	Bladder Minor Procedure 19 years and over	£374	£292
LB21Z	Bladder Neck Open Procedures - Male		£3,725
LB21A	Major Open, Prostate or Bladder Neck Procedures (Male), with CC Score 2+	£5,423	

HRG code	Description	NHS Reference Cost (2013-14) Total HRGs	PbR Tariff (2014-15)
LB21B	Major Open, Prostate or Bladder Neck Procedures (Male), with CC Score 0-1	£4,569	
LB22Z	Laparoscopic Bladder Neck Procedures - Male	£5,204	£4,823
LB39A/C	Cystectomy with Urinary Diversion and Reconstruction with CC/CC score 3+	£11,627	£9,623
LB39B/D	Cystectomy with Urinary Diversion and Reconstruction without CC/ CC score 0-2	£8,291	£7,196
LB59Z	Bladder Neck Open and Laparoscopic Procedures - Female	£3,334	£2,657
LB60A	Complex Open or Laparoscopic, Kidney or Ureter Procedures, with Major CC		£7,563
LB60C	Complex, Open or Laparoscopic, Kidney or Ureter Procedures, with CC Score 7+	£9,840	
LB60D	Complex, Open or Laparoscopic, Kidney or Ureter Procedures, with CC Score 4-6	£6,706	
LB60E	Complex, Open or Laparoscopic, Kidney or Ureter Procedures, with CC Score 2-3	£6,074	
LB60B	Complex Open or Laparoscopic, Kidney or Ureter Procedures, without Major CC		£4,365
LB60F	Complex, Open or Laparoscopic, Kidney or Ureter Procedures, with CC Score 0-1	£5,033	
LB61A	Major Open Kidney or Ureter Procedures, 19 years and over with Major CC		£5,672
LB61C	Major, Open or Percutaneous, Kidney or Ureter Procedures, 19 years and over, with CC Score 10+	£8,176	
LB61D	Major, Open or Percutaneous, Kidney or Ureter Procedures, 19 years and over, with CC Score 7-9	£5,593	
LB61E	Major, Open or Percutaneous, Kidney or Ureter Procedures, 19 years and over, with CC Score 4-6	£4,985	
LB61F	Major, Open or Percutaneous, Kidney or Ureter Procedures, 19 years and over, with CC Score 2-3	£4,123	
LB61B	Major Open Kidney or Ureter Procedures, 19 years and over without Major CC		£3,691
LB61G	Major, Open or Percutaneous, Kidney or Ureter Procedures, 19 years and over, with CC Score 0-1	£3,694	
LB62A/C	Major Laparoscopic Kidney or Ureter Procedures, 19 years and over with CC/CC score 3+	£6,445	£4,360

HRG code	Description	NHS Reference Cost (2013-14) Total HRGs	PbR Tariff (2014-15)
LB62B/D	Major Laparoscopic Kidney or Ureter Procedures, 19 years and over without CC/CC score 0-2	£5,405	£3,976
LB63A/C	Major Open or Laparoscopic, Kidney or Ureter Procedures, 18 years and under with CC/CC Score 2+	£6,256	£5,056
LB63B/D	Major Open or Laparoscopic, Kidney or Ureter Procedures, 18 years and under without CC/CC score 0-1	£4,340	£3,843
LB67C	Complex Open Bladder Procedures with CC Score 3+	£12,893	
LB67D	Complex Open Bladder Procedures with CC Score 0-2	£8,512	
LB69Z	Major Robotic, Prostate or Bladder Neck Procedures (Male)	£7,013	
LB71Z	Total Pelvic Exenteration	£15,946	
MA07C	Upper Genital Tract Major Procedures with Major CC		£3,892
MA07E	Major Open Upper Genital Tract Procedures with CC Score 5+	£5,477	
MA07F	Major Open Upper Genital Tract Procedures with CC Score 3-4	£3,978	
MA07D/G	Upper Genital Tract Major Procedures without Major CC	£3,299	£2,829
MA08Z	Upper Genital Tract Laparoscopic / Endoscopic Major Procedures		£2,165
MA08A	Major, Laparoscopic or Endoscopic, Upper Genital Tract Procedures, with CC Score 2+	£3,240	
MA08B	Major, Laparoscopic or Endoscopic, Upper Genital Tract Procedures, with CC Score 0-1	£2,718	
MA09Z	Upper Genital Tract Laparoscopic / Endoscopic Intermediate Procedures	£2,141	£1,618
MA01Z	Complex Open, Upper or Lower Genital Tract Procedures	£5,161	
MA02A	Very Major Open, Upper or Lower Genital Tract Procedures, with CC Score 4+	£5,951	
MA02B	Very Major Open, Upper or Lower Genital Tract Procedures, with CC Score 2-3	£4,435	
MA02C	Very Major Open, Upper or Lower Genital Tract Procedures, with CC Score 0-1	£3,706	
MA03C	Major Open Lower Genital Tract Procedures with CC Score 3+	£3,044	
MA03D	Major Open Lower Genital Tract Procedures with CC Score 0-2	£2,430	

HRG code	Description	NHS Reference Cost (2013-14) Total HRGs	PbR Tariff (2014-15)
MA04C	Intermediate Open Lower Genital Tract Procedures with CC Score 3+	£2,448	
MA04D	Intermediate Open Lower Genital Tract Procedures with CC Score 0-2	£2,022	
MA06A	Major, Open or Laparoscopic, Upper or Lower Genital Tract Procedures for Malignancy, with CC Score 4+	£4,977	
MA06B	Major, Open or Laparoscopic, Upper or Lower Genital Tract Procedures for Malignancy, with CC Score 2-3	£3,873	
MA06C	Major, Open or Laparoscopic, Upper or Lower Genital Tract Procedures for Malignancy, with CC Score 0-1	£3,356	
MA10Z	Minor, Laparoscopic or Endoscopic, Upper Genital Tract Procedures	£1,314	
MA11Z	Intermediate Open Upper Genital Tract Procedures	£2,629	
MA12Z	Resection or Ablation Procedures for Intra-Uterine Lesions	£1,026	
MA26A	Complex, Open or Laparoscopic, Upper or Lower Genital Tract Procedures for Malignancy, with CC Score 5+	£7,623	
MA26B	Complex, Open or Laparoscopic, Upper or Lower Genital Tract Procedures for Malignancy, with CC Score 2-4	£5,350	
MA26C	Complex, Open or Laparoscopic, Upper or Lower Genital Tract Procedures for Malignancy, with CC Score 0-1	£4,852	
MA28Z	Complex, Laparoscopic or Endoscopic, Upper Genital Tract Procedures	£3,553	
MA29Z	Major Female Pelvic Peritoneum Adhesion Procedures	£2,315	
MA30Z	Intermediate Female Pelvic Peritoneum Adhesion Procedures	£1,546	
QZ01A	Aortic or Abdominal Surgery with CC		£7,492
QZ01B	Aortic or Abdominal Surgery without CC		£5,798
YQ01A	Multiple or Revisional, Open Repair of Abdominal or Thoracoabdominal Aortic Aneurysm, with CC Score 6+	£11,269	
YQ01B	Multiple or Revisional, Open Repair of Abdominal or Thoracoabdominal Aortic Aneurysm, with CC Score 0-5	£7,240	
YQ02Z	Open Repair of Thoracoabdominal Aortic Aneurysm	£10,531	

HRG code	Description	NHS Reference Cost (2013-14) Total HRGs	PbR Tariff (2014-15)
YQ03A	Open Repair of Abdominal Aortic Aneurysm with CC Score 6+	£8,366	
YQ03B	Open Repair of Abdominal Aortic Aneurysm with CC Score 0-5	£5,561	
YQ04A	Multiple Open Procedures on Aorta or Abdominal Blood Vessels, with CC Score 4+	£9,678	
YQ04B	Multiple Open Procedures on Aorta or Abdominal Blood Vessels, with CC Score 0-3	£6,790	
YQ05A	Single Open Procedure on Aorta or Abdominal Blood Vessel, with CC Score 4+	£8,253	
YQ05B	Single Open Procedure on Aorta or Abdominal Blood Vessel, with CC Score 0-3	£5,537	

In Table 10B, a list of relevant OPCS 4.7 codes are presented. The list of potentially relevant OPCS 4.7 codes is very large, so this list may not be exhaustive.

Table 10B: Relevant OPCS 4.7 codes

OPCS 4.7 Code	Description
G01.1	Oesophagogastrectomy and anastomosis of oesophagus to stomach
G01.8	Other specified excision of oesophagus and stomach
G01.9	Unspecified excision of oesophagus and stomach
G02.1	Total oesophagectomy and anastomosis of pharynx to stomach
G02.4	Total oesophagectomy and interposition of microvascularly attached colon
G02.5	Total oesophagectomy and interposition of colon NEC
G03.5	Partial oesophagectomy and interposition of microvascularly attached colon
G03.6	Partial oesophagectomy and interposition of colon NEC
G05.2	Bypass of oesophagus by anastomosis of oesophagus to stomach
G05.5	Bypass of oesophagus by interposition of microvascularly attached colon
G05.6	Bypass of oesophagus by interposition of colon NEC
G07.1	Closure of tracheo-oesophageal fistula
G11.1	Insertion of tubal prosthesis into oesophagus through stomach
G23.1	Repair of oesophageal hiatus using thoracic approach
G23.2	Repair of diaphragmatic hernia using thoracic approach NEC
G23.3	Repair of oesophageal hiatus using abdominal approach
G23.4	Repair of diaphragmatic hernia using abdominal approach NEC

OPCS 4.7 Code	Description
G23.8	Other specified repair of diaphragmatic hernia
G23.9	Unspecified repair of diaphragmatic hernia
G24.4	Antireflux gastropexy
G24.5	Gastroplasty and antireflux procedure HFQ
G25.1	Revision of fundoplication of stomach
G26.1	Allotransplantation of stomach
G26.8	Other specified transplantation of stomach
G26.9	Unspecified transplantation of stomach
G27.2	Total gastrectomy and anastomosis of oesophagus to duodenum
G27.8	Other specified total excision of stomach
G27.9	Unspecified total excision of stomach
G28.1	Partial gastrectomy and anastomosis of stomach to duodenum
G28.2	Partial gastrectomy and anastomosis of stomach to transposed jejunum
G28.3	Partial gastrectomy and anastomosis of stomach to jejunum NEC
G28.8	Other specified partial excision of stomach
G28.9	Unspecified partial excision of stomach
G29.1	Open excision of polyp of stomach
G29.2	Open excision of lesion of stomach NEC
G29.3	Open laser destruction of lesion of stomach
G29.8	Other specified open extirpation of lesion of stomach
G29.9	Unspecified open extirpation of lesion of stomach
G30.1	Gastroplasty NEC
G30.2	Partitioning of stomach NEC
G30.3	Partitioning of stomach using band
G30.4	Partitioning of stomach using staples
G30.8	Other specified plastic operations on stomach
G30.9	Unspecified plastic operations on stomach
G31.0	Conversion from previous anastomosis of stomach to duodenum
G31.1	Bypass of stomach by anastomosis of oesophagus to duodenum
G31.2	Bypass of stomach by anastomosis of stomach to duodenum
G31.3	Revision of anastomosis of stomach to duodenum
G31.4	Conversion to anastomosis of stomach to duodenum
G31.5	Closure of connection of stomach to duodenum
G31.6	Attention to connection of stomach to duodenum
G31.8	Other specified connection of stomach to duodenum
G31.9	Unspecified connection of stomach to duodenum
G32.0	Conversion from previous anastomosis of stomach to transposed jejunum
G32.1	Bypass of stomach by anastomosis of stomach to transposed jejunum

OPCS 4.7 Code	Description
G32.2	Revision of anastomosis of stomach to transposed jejunum
G32.3	Conversion to anastomosis of stomach to transposed jejunum
G32.4	Closure of connection of stomach to transposed jejunum
G32.5	Attention to connection of stomach to transposed jejunum
G32.8	Other specified connection of stomach to transposed jejunum
G32.9	Unspecified connection of stomach to transposed jejunum
G33.0	Conversion from previous anastomosis of stomach to jejunum NEC
G33.1	Bypass of stomach by anastomosis of stomach to jejunum NEC
G33.2	Revision of anastomosis of stomach to jejunum NEC
G33.3	Conversion to anastomosis of stomach to jejunum NEC
G33.4	Open reduction of intussusception of gastroenterostomy
G33.5	Closure of connection of stomach to jejunum NEC
G33.6	Attention to connection of stomach to jejunum
G33.8	Other specified other connection of stomach to jejunum
G33.9	Unspecified other connection of stomach to jejunum
G34.1	Creation of permanent gastrostomy
G34.2	Creation of temporary gastrostomy
G34.3	Reconstruction of gastrostomy
G34.4	Closure of gastrostomy
G34.5	Attention to gastrostomy tube
G34.8	Other specified artificial opening into stomach
G34.9	Unspecified artificial opening into stomach
G35.1	Closure of perforated ulcer of stomach
G35.2	Closure of ulcer of stomach NEC
G35.8	Other specified operations on ulcer of stomach
G35.9	Unspecified operations on ulcer of stomach
G36.1	Gastropexy NEC
G36.2	Closure of perforation of stomach NEC
G36.3	Closure of abnormal opening of stomach NEC
G36.8	Other specified other repair of stomach
G36.9	Unspecified other repair of stomach
G38.1	Open biopsy of lesion of stomach
G38.2	Open insertion of prosthesis into stomach
G38.3	Open insertion of feeding tube into stomach
G38.4	Open removal of foreign body from stomach
G38.5	Incision of stomach NEC
G38.6	Reduction of volvulus of stomach
G38.8	Other specified other open operations on stomach

OPCS 4.7 Code	Description
G38.9	Unspecified other open operations on stomach
G48.8	Other specified other operations on stomach
G48.9	Unspecified other operations on stomach
G49.1	Gastroduodenectomy
G49.2	Total excision of duodenum
G49.3	Partial excision of duodenum
G49.8	Other specified excision of duodenum
G49.9	Unspecified excision of duodenum
G50.1	Excision of lesion of duodenum
G50.2	Open destruction of lesion of duodenum
G50.8	Other specified open extirpation of lesion of duodenum
G50.9	Unspecified open extirpation of lesion of duodenum
G51.1	Bypass of duodenum by anastomosis of stomach to jejunum
G51.2	Bypass of duodenum by anastomosis of duodenum to duodenum
G51.3	Bypass of duodenum by anastomosis of duodenum to jejunum
G51.4	Bypass of duodenum by anastomosis of duodenum to colon
G51.8	Other specified bypass of duodenum
G51.9	Unspecified bypass of duodenum
G52.1	Closure of perforated ulcer of duodenum
G52.2	Suture of ulcer of duodenum NEC
G52.8	Other specified operations on ulcer of duodenum
G52.9	Unspecified operations on ulcer of duodenum
G53.1	Open biopsy of lesion of duodenum
G53.2	Closure of perforation of duodenum NEC
G53.3	Open removal of foreign body from duodenum
G53.4	Open insertion of tubal prosthesis into duodenum
G53.5	Incision of duodenum NEC
G53.6	Correction of malrotation of duodenum
G53.8	Other specified other open operations on duodenum
G53.9	Unspecified other open operations on duodenum
G57.8	Other specified other operations on duodenum
G57.9	Unspecified other operations on duodenum
G58.1	Total jejunectomy and anastomosis of stomach to ileum
G58.2	Total jejunectomy and anastomosis of duodenum to ileum
G58.3	Total jejunectomy and anastomosis of duodenum to colon
G58.5	Partial jejunectomy and anastomosis of duodenum to colon
G61.3	Bypass of jejunum by anastomosis of jejunum to colon
G69.1	Ileectomy and anastomosis of stomach to ileum
G69.2	Ileectomy and anastomosis of duodenum to ileum

OPCS 4.7 Code	Description
G69.4	Ileectomy and anastomosis of ileum to colon
G71.4	Bypass of ileum by anastomosis of ileum to transverse colon
G71.5	Bypass of ileum by anastomosis of ileum to colon NEC
G72.2	Anastomosis of ileum to transverse colon
G72.3	Anastomosis of ileum to colon NEC
H02.1	Interval appendicectomy
H02.2	Planned delayed appendicectomy NEC
H02.3	Prophylactic appendicectomy NEC
H02.4	Incidental appendicectomy
H04.8	Other specified total excision of colon and rectum
H04.9	Unspecified total excision of colon and rectum
H05.8	Other specified total excision of colon
H05.9	Unspecified total excision of colon
H06.2	Extended right hemicolectomy and anastomosis of ileum to colon
H06.8	Other specified extended excision of right hemicolon
H06.9	Unspecified extended excision of right hemicolon
H07.1	Right hemicolectomy and end to end anastomosis of ileum to colon
H07.2	Right hemicolectomy and side to side anastomosis of ileum to transverse colon
H07.8	Other specified other excision of right hemicolon
H07.9	Unspecified other excision of right hemicolon
H08.2	Transverse colectomy and anastomosis of ileum to colon
H08.5	Transverse colectomy and exteriorisation of bowel NEC
H08.8	Other specified excision of transverse colon
H08.9	Unspecified excision of transverse colon
H09.1	Left hemicolectomy and end to end anastomosis of colon to rectum
H09.2	Left hemicolectomy and end to end anastomosis of colon to colon
H09.5	Left hemicolectomy and exteriorisation of bowel NEC
H09.8	Other specified excision of left hemicolon
H09.9	Unspecified excision of left hemicolon
H10.2	Sigmoid colectomy and anastomosis of colon to rectum
H10.5	Sigmoid colectomy and exteriorisation of bowel NEC
H10.8	Other specified excision of sigmoid colon
H10.9	Unspecified excision of sigmoid colon
H11.1	Colectomy and end to end anastomosis of colon to colon NEC
H11.2	Colectomy and side to side anastomosis of ileum to colon NEC
H11.5	Colectomy and exteriorisation of bowel NEC
H11.8	Other specified other excision of colon
H11.9	Unspecified other excision of colon
H12.1	Excision of diverticulum of colon

OPCS 4.7 Code	Description
H12.2	Excision of lesion of colon NEC
H12.3	Destruction of lesion of colon NEC
H12.8	Other specified extirpation of lesion of colon
H12.9	Unspecified extirpation of lesion of colon
H13.1	Bypass of colon by anastomosis of ileum to colon
H13.2	Bypass of colon by anastomosis of caecum to sigmoid colon
H13.3	Bypass of colon by anastomosis of transverse colon to sigmoid colon
H13.4	Bypass of colon by anastomosis of transverse colon to rectum
H13.5	Bypass of colon by anastomosis of colon to rectum NEC
H13.8	Other specified bypass of colon
H13.9	Unspecified bypass of colon
H15.8	Other specified other exteriorisation of colon
H15.9	Unspecified other exteriorisation of colon
H16.1	Drainage of colon
H16.8	Other specified incision of colon
H16.9	Unspecified incision of colon
H17.1	Open reduction of intussusception of colon
H17.3	Open reduction of volvulus of sigmoid colon
H17.4	Open reduction of volvulus of colon NEC
H17.5	Open relief of strangulation of colon
H17.6	Open relief of obstruction of colon NEC
H17.8	Other specified intra-abdominal manipulation of colon
H17.9	Unspecified intra-abdominal manipulation of colon
H18.1	Open colonoscopy
H18.8	Other specified open endoscopic operations on colon
H18.9	Unspecified open endoscopic operations on colon
H19.1	Open biopsy of lesion of colon
H19.2	Fixation of colon
H19.3	Enterorrhaphy of colon
H19.4	Open removal of foreign body from colon
H19.8	Other specified other open operations on colon
H19.9	Unspecified other open operations on colon
H29.1	Subtotal excision of colon and rectum and creation of colonic pouch and anastomosis of colon to anus
H29.2	Subtotal excision of colon and rectum and creation of colonic pouch NEC
H29.3	Subtotal excision of colon and creation of colonic pouch and anastomosis of colon to rectum
H29.4	Subtotal excision of colon and creation of colonic pouch NEC
H29.8	Other specified subtotal excision of colon
H29.9	Unspecified subtotal excision of colon
H30.3	Passage of flatus tube to reduce volvulus of sigmoid colon

OPCS 4.7 Code	Description
H30.8	Other specified other operations on colon
H30.9	Unspecified other operations on colon
H32.8	Other specified exteriorisation of colon
H32.9	Unspecified exteriorisation of colon
H33.2	Proctectomy and anastomosis of colon to anus
H33.3	Anterior resection of rectum and anastomosis of colon to rectum using staples
H33.5	Rectosigmoidectomy and closure of rectal stump and exteriorisation of bowel
H33.6	Anterior resection of rectum and exteriorisation of bowel
H40.4	Trans-sphincteric anastomosis of colon to anus
H40.8	Other specified operations on rectum through anal sphincter
H40.9	Unspecified operations on rectum through anal sphincter
H41.1	Rectosigmoidectomy and peranal anastomosis
H41.2	Peranal excision of lesion of rectum
H41.3	Peranal destruction of lesion of rectum
H41.4	Peranal mucosal proctectomy and endoanal anastomosis
H41.5	Peranal resection of rectum using staples
H42.1	Insertion of encircling suture around perianal sphincter
H42.2	Perineal plication of levator ani muscles and anal sphincters
H42.4	Removal of encircling suture from around perianal sphincter
H50.1	Posterior repair of anal sphincter
H50.2	Anterior repair of anal sphincter
H50.4	Reanastomosis of rectum to anal canal for correction of congenital atresia of rectum
H53.1	Evacuation of perianal haematoma
H54.8	Other specified dilation of anal sphincter
H54.9	Unspecified dilation of anal sphincter
H55.1	Laying open of low anal fistula
H55.2	Laying open of high anal fistula
H55.3	Laying open of anal fistula NEC
H55.4	Insertion of seton into high anal fistula and partial laying open of track HFQ
H55.5	Fistulography of anal fistula
H55.8	Other specified other operations on perianal region
H55.9	Unspecified other operations on perianal region
H56.4	Excision of anal fissure
H57.1	Placement of artificial anal sphincter NEC
H57.2	Maintenance of artificial anal sphincter NEC
H57.3	Removal of artificial anal sphincter NEC
H57.8	Other specified other operations on the anal sphincter to control continence
H57.9	Unspecified other operations on the anal sphincter to control

OPCS 4.7 Code	Description
	continence
H62.2	Mobilisation of bowel NEC
H62.3	Dilation of bowel NEC
H62.8	Other specified other operations on bowel
H62.9	Unspecified other operations on bowel
H66.1	Excision of ileoanal pouch
H66.2	Revision of ileoanal pouch
H66.8	Other specified therapeutic operations on ileoanal pouch
H66.9	Unspecified therapeutic operations on ileoanal pouch
J06.8	Other specified other transjugular intrahepatic operations on blood vessel of liver
J06.9	Unspecified other transjugular intrahepatic operations on blood vessel of liver
J10.8	Other specified transluminal operations on blood vessel of liver
J10.9	Unspecified transluminal operations on blood vessel of liver
J11.8	Other specified transjugular intrahepatic operations on blood vessel of liver
J11.9	Unspecified transjugular intrahepatic operations on blood vessel of liver
J18.1	Total cholecystectomy and excision of surrounding tissue
J18.2	Total cholecystectomy and exploration of common bile duct
J18.3	Total cholecystectomy NEC
J18.4	Partial cholecystectomy and exploration of common bile duct
J18.5	Partial cholecystectomy NEC
J18.8	Other specified excision of gall bladder
J18.9	Unspecified excision of gall bladder
J19.1	Anastomosis of gall bladder to stomach
J19.2	Anastomosis of gall bladder to duodenum
J19.3	Anastomosis of gall bladder to jejunum
J19.4	Anastomosis of gall bladder to intestine NEC
J19.5	Revision of anastomosis of gall bladder
J19.6	Closure of anastomosis of gall bladder
J19.8	Other specified connection of gall bladder
J19.9	Unspecified connection of gall bladder
J20.1	Closure of fistula of gall bladder
J20.3	Repair of perforation of gall bladder
J20.8	Other specified repair of gall bladder
J20.9	Unspecified repair of gall bladder
J21.1	Open removal of calculus from gall bladder
J21.2	Drainage of gall bladder
J21.3	Drainage of tissue surrounding gall bladder
J21.8	Other specified incision of gall bladder
J21.9	Unspecified incision of gall bladder

OPCS 4.7 Code	Description
J23.1	Excision of lesion of gall bladder
J23.2	Open biopsy of lesion of gall bladder
J23.3	Exploration of gall bladder
J23.8	Other specified other open operations on gall bladder
J23.9	Unspecified other open operations on gall bladder
J24.1	Percutaneous drainage of gall bladder
J24.2	Percutaneous fragmentation of calculus in gall bladder
J24.3	Percutaneous dissolution therapy to calculus in gall bladder
J24.8	Other specified therapeutic percutaneous operations on gall bladder
J24.9	Unspecified therapeutic percutaneous operations on gall bladder
J25.1	Percutaneous biopsy of lesion of gall bladder
J25.8	Other specified diagnostic percutaneous operations on gall bladder
J25.9	Unspecified diagnostic percutaneous operations on gall bladder
J26.1	Extracorporeal fragmentation of calculus in gall bladder
J26.8	Other specified other operations on gall bladder
J26.9	Unspecified other operations on gall bladder
J27.1	Excision of ampulla of Vater and replantation of common bile duct into duodenum
J27.2	Partial excision of bile duct and anastomosis of bile duct to duodenum
J30.1	Anastomosis of common bile duct to duodenum
J34.1	Sphincteroplasty of bile duct and pancreatic duct using duodenal approach
J34.3	Sphincteroplasty of pancreatic duct using duodenal approach NEC
J35.1	Sphincterotomy of bile duct and pancreatic duct using duodenal approach
J35.3	Sphincterotomy of pancreatic duct using duodenal approach NEC
J48.8	Other specified other therapeutic percutaneous operations on bile duct
J48.9	Unspecified other therapeutic percutaneous operations on bile duct
J54.1	Transplantation of pancreas and duodenum
J54.5	Renewal of transplanted pancreatic tissue
J56.1	Pancreaticoduodenectomy and excision of surrounding tissue
J56.2	Pancreaticoduodenectomy and resection of antrum of stomach
J56.3	Pancreaticoduodenectomy NEC
J56.4	Subtotal excision of head of pancreas with preservation of duodenum and drainage HFQ
J57.2	Left pancreatectomy and drainage of pancreatic duct
J57.4	Excision of tail of pancreas and drainage of pancreatic duct
J57.6	Pancreatic necrosectomy
J59.1	Anastomosis of pancreatic duct to stomach

OPCS 4.7 Code	Description
J59.2	Anastomosis of pancreatic duct to duodenum
J59.3	Anastomosis of pancreatic duct to transposed jejunum
J59.4	Anastomosis of pancreatic duct to jejunum NEC
J59.5	Revision of anastomosis of pancreatic duct
J59.6	Closure of anastomosis of pancreatic duct
J59.8	Other specified connection of pancreatic duct
J59.9	Unspecified connection of pancreatic duct
J60.1	Drainage of pancreatic duct
J60.2	Open removal of calculus from pancreatic duct
J60.3	Insertion of T tube into pancreatic duct
J60.4	Open insertion of tubal prosthesis into pancreatic duct
J60.5	Open dilation of pancreatic duct
J60.8	Other specified other open operations on pancreatic duct
J60.9	Unspecified other open operations on pancreatic duct
J61.1	Open cystogastrotomy of pancreas
J66.1	Percutaneous drainage of lesion of pancreas and insertion of cystogastrostomy tube NEC
J67.2	Percutaneous puncture of pancreatic duct and pancreatography
J76.8	Other specified therapeutic percutaneous operations on bile duct
J76.9	Unspecified therapeutic percutaneous operations on bile duct
J77.8	Other specified other transluminal operations on blood vessel of liver
J77.9	Unspecified other transluminal operations on blood vessel of liver
M01.1	Autotransplantation of kidney
M01.2	Allotransplantation of kidney from live donor
M01.3	Allotransplantation of kidney from cadaver NEC
M01.4	Allotransplantation of kidney from cadaver heart beating
M01.5	Allotransplantation of kidney from cadaver heart non-beating
M01.8	Other specified transplantation of kidney
M01.9	Unspecified transplantation of kidney
M02.2	Nephroureterectomy NEC
M02.4	Excision of half of horseshoe kidney
M02.6	Excision of rejected transplanted kidney
M02.7	Excision of transplanted kidney NEC
M02.8	Other specified total excision of kidney
M02.9	Unspecified total excision of kidney
M03.1	Heminephrectomy of duplex kidney
M03.2	Division of isthmus of horseshoe kidney
M03.8	Other specified partial excision of kidney
M03.9	Unspecified partial excision of kidney
M04.1	Deroofing of cyst of kidney

OPCS 4.7 Code	Description
M04.2	Open excision of lesion of kidney NEC
M04.3	Open destruction of lesion of kidney
M04.8	Other specified open extirpation of lesion of kidney
M04.9	Unspecified open extirpation of lesion of kidney
M05.4	Plication of kidney
M05.5	Repair of laceration of kidney
M05.8	Other specified open repair of kidney
M05.9	Unspecified open repair of kidney
M06.1	Open removal of calculus from kidney
M06.2	Drainage of kidney NEC
M06.8	Other specified incision of kidney
M06.9	Unspecified incision of kidney
M08.1	Open biopsy of lesion of kidney
M08.2	Open denervation of kidney
M08.3	Exploration of kidney
M08.4	Exploration of transplanted kidney
M08.8	Other specified other open operations on kidney
M08.9	Unspecified other open operations on kidney
M12.1	Percutaneous pyeloureterodynamics
M12.8	Other specified percutaneous studies of upper urinary tract
M12.9	Unspecified percutaneous studies of upper urinary tract
M13.1	Percutaneous needle biopsy of lesion of kidney
M13.2	Percutaneous drainage of kidney
M13.3	Percutaneous aspiration of kidney NEC
M13.4	Percutaneous injection of therapeutic substance into kidney
M13.5	Percutaneous injection of radiocontrast substance into kidney
M13.7	Percutaneous radiofrequency ablation of lesion of kidney
M13.8	Other specified percutaneous puncture of kidney
M13.9	Unspecified percutaneous puncture of kidney
M14.1	Extracorporeal shock wave lithotripsy of calculus of kidney
M14.8	Other specified extracorporeal fragmentation of calculus of kidney
M14.9	Unspecified extracorporeal fragmentation of calculus of kidney
M15.8	Other specified operations on kidney along nephrostomy tube track
M15.9	Unspecified operations on kidney along nephrostomy tube track
M16.1	Irrigation of kidney
M16.2	Maintenance of drainage tube of kidney
M16.8	Other specified other operations on kidney
M16.9	Unspecified other operations on kidney
M17.8	Other specified interventions associated with transplantation of

OPCS 4.7 Code	Description
	kidney
M17.9	Unspecified interventions associated with transplantation of kidney
M18.1	Total ureterectomy
M18.2	Excision of segment of ureter
M18.3	Secondary ureterectomy
M18.4	Excision of duplex ureter
M18.8	Other specified excision of ureter
M18.9	Unspecified excision of ureter
M19.2	Creation of urinary diversion to intestine NEC
M19.3	Revision of urinary diversion
M19.4	Cutaneous ureterostomy NEC
M19.5	Revision of ureterostomy stoma
M19.6	Percutaneous tunnelled kidney to bladder bypass using prosthesis
M19.8	Other specified urinary diversion
M19.9	Unspecified urinary diversion
M20.1	Bilateral replantation of ureter
M20.2	Unilateral replantation of ureter
M20.3	Replantation of ureter after urinary diversion
M20.8	Other specified replantation of ureter
M20.9	Unspecified replantation of ureter
M21.1	Direct anastomosis of ureter to bladder
M21.2	Anastomosis of ureter to bladder using flap of bladder
M21.3	Ileal replacement of ureter
M21.4	Colonic replacement of ureter
M21.5	Revision of anastomosis of ureter NEC
M21.6	Ureteroureterostomy
M21.8	Other specified other connection of ureter
M21.9	Unspecified other connection of ureter
M22.1	Suture of ureter
M22.2	Removal of ligature from ureter
M22.3	Closure of ureteric fistula
M22.8	Other specified repair of ureter
M22.9	Unspecified repair of ureter
M23.1	Open ureterolithotomy
M23.8	Other specified incision of ureter
M23.9	Unspecified incision of ureter
M25.1	Excision of ureterocele
M25.2	Open excision of lesion of ureter NEC
M25.3	Ureterolysis
M25.4	Open biopsy of lesion of ureter
M25.5	Open exploration of ureter
M25.8	Other specified other open operations on ureter

OPCS 4.7 Code	Description
M25.9	Unspecified other open operations on ureter
M26.1	Nephroscopic laser fragmentation of calculus of ureter
M26.2	Nephroscopic fragmentation of calculus of ureter NEC
M26.3	Nephroscopic extraction of calculus of ureter
M26.4	Nephroscopic insertion of tubal prosthesis into ureter
M26.8	Other specified therapeutic nephroscopic operations on ureter
M26.9	Unspecified therapeutic nephroscopic operations on ureter
M27.1	Ureteroscopic laser fragmentation of calculus of ureter
M27.2	Ureteroscopic fragmentation of calculus of ureter NEC
M27.3	Ureteroscopic extraction of calculus of ureter
M27.4	Ureteroscopic insertion of ureteric stent
M27.5	Ureteroscopic removal of ureteric stent
M27.6	Ureteroscopic endoluminal balloon rupture of stenosis of ureter
M27.7	Ureteroscopic dilation of ureter
M27.8	Other specified therapeutic ureteroscopic operations on ureter
M27.9	Unspecified therapeutic ureteroscopic operations on ureter
M30.4	Nephroscopic ureteroscopy
M31.1	Extracorporeal shockwave lithotripsy of calculus of ureter
M31.8	Other specified extracorporeal fragmentation of calculus of ureter
M31.9	Unspecified extracorporeal fragmentation of calculus of ureter
M32.8	Other specified operations on ureteric orifice
M32.9	Unspecified operations on ureteric orifice
M33.1	Percutaneous insertion of metallic stent into ureter
M33.2	Percutaneous insertion of plastic stent into ureter
M33.3	Percutaneous replacement of metallic stent into ureter
M33.4	Percutaneous replacement of plastic stent into ureter
M33.5	Percutaneous insertion of ureteric stent into ureter NEC
M33.6	Percutaneous removal of ureteric stent from ureter NEC
M33.8	Other specified percutaneous ureteric stent procedures
M33.9	Unspecified percutaneous ureteric stent procedures
M34.3	Cystectomy NEC
M34.4	Simple cystectomy
M48.8	Other specified operations on bladder
M48.9	Unspecified operations on bladder
M49.8	Other specified other operations on bladder
M49.9	Unspecified other operations on bladder
M54.3	Removal of artificial urinary sphincter from outlet of female bladder
M54.8	Other specified open operations on outlet of female bladder

OPCS 4.7 Code	Description
M54.9	Unspecified open operations on outlet of female bladder
M55.2	Implantation of artificial urinary sphincter into outlet of female bladder
M55.6	Insertion of retropubic device for female stress urinary incontinence NEC
M55.8	Other specified other open operations on outlet of female bladder
M55.9	Unspecified other open operations on outlet of female bladder
M60.3	Removal of artificial urinary sphincter from outlet of male bladder
M60.8	Other specified open operations on outlet of male bladder
M60.9	Unspecified open operations on outlet of male bladder
M64.2	Implantation of artificial urinary sphincter into outlet of male bladder
M64.8	Other specified other open operations on outlet of male bladder
M64.9	Unspecified other open operations on outlet of male bladder
M70.8	Other specified other operations on outlet of male bladder
M70.9	Unspecified other operations on outlet of male bladder
M71.8	Other specified other operations on prostate
M71.9	Unspecified other operations on prostate
M83.3	Removal of foreign body from urinary tract NEC
M83.8	Other specified other operations on urinary tract
M83.9	Unspecified other operations on urinary tract
N34.8	Other specified other operations on male genital tract
N34.9	Unspecified other operations on male genital tract
O11.1	Gastro-oesophageal junction
O14.1	Pelvic lymph node
O15.8	Other specified operations on blood vessel
O15.9	Unspecified operations on blood vessel
O30.8	Specified other large intestine NEC
O30.9	Other large intestine NEC
P21.8	Other specified plastic operations on vagina
P21.9	Unspecified plastic operations on vagina
P32.1	Reconstruction of vagina using bowel interposition
P32.2	Reconstruction of vagina using pelvic peritoneal graft
P32.8	Other specified other plastic operations on vagina
P32.9	Unspecified other plastic operations on vagina
Q13.8	Other specified introduction of gametes into uterine cavity
Q13.9	Unspecified introduction of gametes into uterine cavity
Q21.8	Other specified other introduction of gametes into uterine cavity
Q21.9	Unspecified other introduction of gametes into uterine cavity

OPCS 4.7 Code	Description
Q41.6	Recanalisation of fallopian tube
Q54.3	Division of uteropelvic ligament
Q55.1	Examination of female genital tract under anaesthetic and Papanicolau smear
Q55.2	Examination of female genital tract under anaesthetic NEC
Q55.5	Transvaginal ultrasound examination of female genital tract
Q55.8	Other specified other examination of female genital tract
Q55.9	Unspecified other examination of female genital tract
Q56.8	Other specified other operations on female genital tract
Q56.9	Unspecified other operations on female genital tract
R01.2	Fetoscopic insertion of tracheal plug for congenital diaphragmatic hernia
R04.6	Percutaneous insertion of fetal tracheal plug for congenital diaphragmatic hernia
T16.4	Repair of congenital diaphragmatic hernia
T19.1	Bilateral herniotomy
T19.2	Unilateral herniotomy
T19.8	Other specified simple excision of inguinal hernial sac
T19.9	Unspecified simple excision of inguinal hernial sac
T20.1	Primary repair of inguinal hernia using insert of natural material
T20.2	Primary repair of inguinal hernia using insert of prosthetic material
T20.3	Primary repair of inguinal hernia using sutures
T20.4	Primary repair of inguinal hernia and reduction of sliding hernia
T20.8	Other specified primary repair of inguinal hernia
T20.9	Unspecified primary repair of inguinal hernia
T21.1	Repair of recurrent inguinal hernia using insert of natural material
T21.2	Repair of recurrent inguinal hernia using insert of prosthetic material
T21.3	Repair of recurrent inguinal hernia using sutures
T21.4	Removal of prosthetic material from previous repair of inguinal hernia
T21.8	Other specified repair of recurrent inguinal hernia
T21.9	Unspecified repair of recurrent inguinal hernia
T22.1	Primary repair of femoral hernia using insert of natural material
T22.2	Primary repair of femoral hernia using insert of prosthetic material
T22.3	Primary repair of femoral hernia using sutures
T22.8	Other specified primary repair of femoral hernia
T22.9	Unspecified primary repair of femoral hernia
T23.1	Repair of recurrent femoral hernia using insert of natural material
T23.2	Repair of recurrent femoral hernia using insert of prosthetic material
T23.3	Repair of recurrent femoral hernia using sutures

OPCS 4.7 Code	Description
T23.4	Removal of prosthetic material from previous repair of femoral hernia
T23.8	Other specified repair of recurrent femoral hernia
T23.9	Unspecified repair of recurrent femoral hernia
T24.1	Repair of umbilical hernia using insert of natural material
T24.2	Repair of umbilical hernia using insert of prosthetic material
T24.3	Repair of umbilical hernia using sutures
T24.4	Removal of prosthetic material from previous repair of umbilical hernia
T24.8	Other specified primary repair of umbilical hernia
T24.9	Unspecified primary repair of umbilical hernia
T25.1	Primary repair of incisional hernia using insert of natural material
T25.2	Primary repair of incisional hernia using insert of prosthetic material
T25.3	Primary repair of incisional hernia using sutures
T25.8	Other specified primary repair of incisional hernia
T25.9	Unspecified primary repair of incisional hernia
T26.1	Repair of recurrent incisional hernia using insert of natural material
T26.2	Repair of recurrent incisional hernia using insert of prosthetic material
T26.3	Repair of recurrent incisional hernia using sutures
T26.4	Removal of prosthetic material from previous repair of incisional hernia
T26.8	Other specified repair of recurrent incisional hernia
T26.9	Unspecified repair of recurrent incisional hernia
T27.1	Repair of ventral hernia using insert of natural material
T27.2	Repair of ventral hernia using insert of prosthetic material
T27.3	Repair of ventral hernia using sutures
T27.4	Removal of prosthetic material from previous repair of ventral hernia
T27.8	Other specified repair of other hernia of abdominal wall
T27.9	Unspecified repair of other hernia of abdominal wall
T28.1	Closure of gastroschisis
T34.2	Open drainage of pelvic abscess
T37.1	Excision of lesion of mesentery of small intestine
T37.2	Destruction of lesion of mesentery of small intestine
T37.3	Biopsy of lesion of mesentery of small intestine
T37.4	Repair of mesentery of small intestine
T37.8	Other specified operations on mesentery of small intestine
T37.9	Unspecified operations on mesentery of small intestine
T38.1	Excision of lesion of mesentery of colon
T38.2	Destruction of lesion of mesentery of colon

OPCS 4.7 Code	Description
T38.3	Biopsy of lesion of mesentery of colon
T38.4	Repair of mesentery of colon
T38.8	Other specified operations on mesentery of colon
T38.9	Unspecified operations on mesentery of colon
T45.2	Image controlled percutaneous drainage of pelvic abscess
T52.8	Other specified excision of other fascia
T52.9	Unspecified excision of other fascia
T56.8	Other specified other excision of other fascia
T56.9	Unspecified other excision of other fascia
T85.6	Block dissection of pelvic lymph nodes
T97.1	Repair of recurrent umbilical hernia using insert of natural material
T97.2	Repair of recurrent umbilical hernia using insert of prosthetic material
T97.3	Repair of recurrent umbilical hernia using sutures
T97.8	Other specified repair of recurrent umbilical hernia
T97.9	Unspecified repair of recurrent umbilical hernia
T98.1	Repair of recurrent ventral hernia using insert of natural material
T98.2	Repair of recurrent ventral hernia using insert of prosthetic material
T98.3	Repair of recurrent ventral hernia using sutures
T98.8	Other specified repair of recurrent other hernia of abdominal wall
T98.9	Unspecified repair of recurrent other hernia of abdominal wall
Y51.2	Approach to organ through gastrostomy
Y51.8	Other specified approach to organ through artificial opening into gastrointestinal tract
Y51.9	Unspecified approach to organ through artificial opening into gastrointestinal tract
Y62.3	Harvest of flap of skin and gastrocnemius muscle
Y64.3	Harvest of flap of gastrocnemius muscle NEC

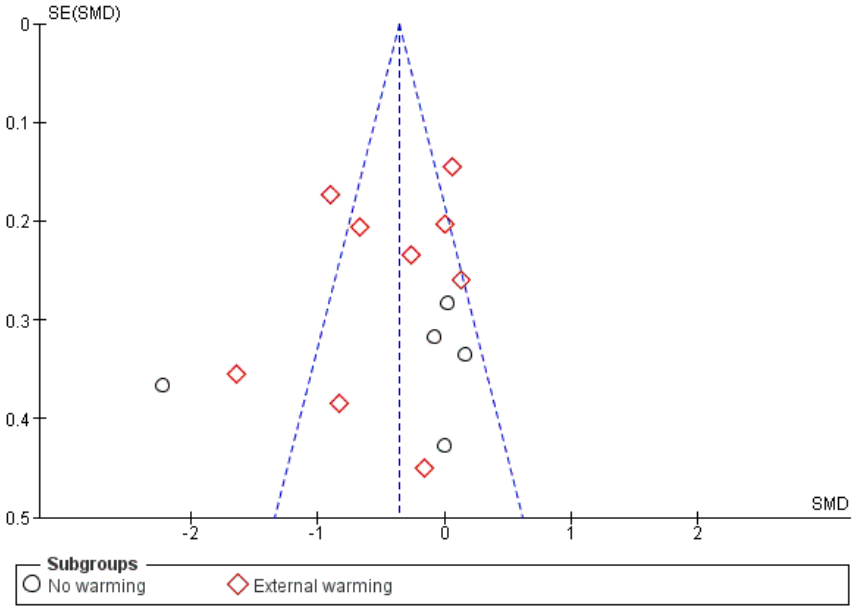
11.6 Appendix 5: Supporting evidence

Funnel plots (risk of bias analysis)

The following funnel plots correspond to the meta-analyses carried out in section 7.8.

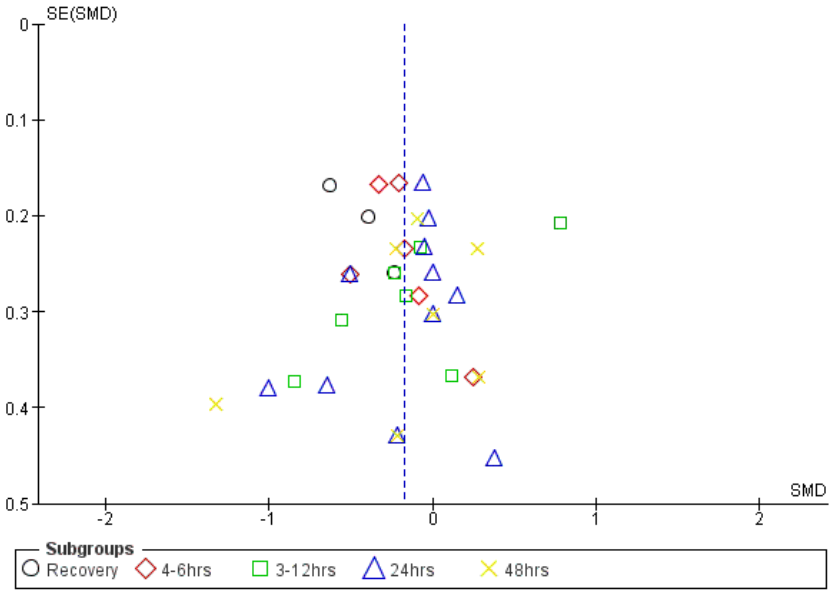
Laparoscopic surgeries

Temperature change



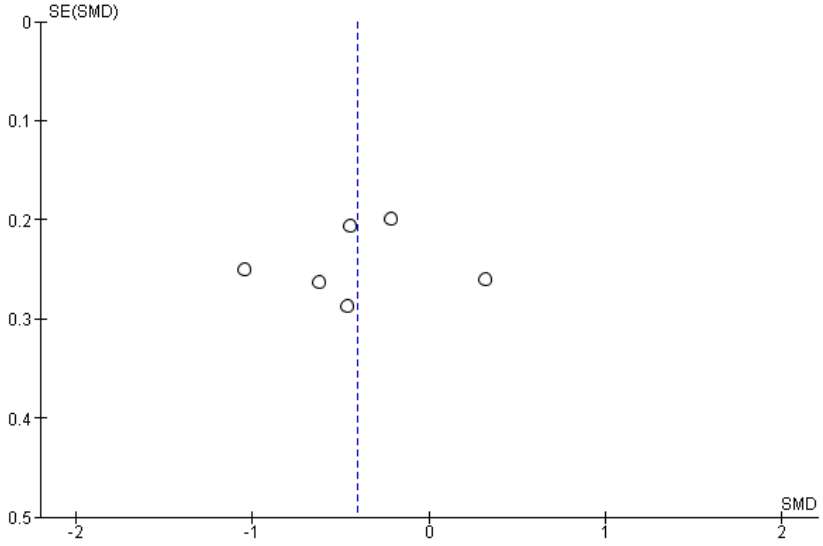
Funnel plot of core temperature change studies

Pain (VAS)



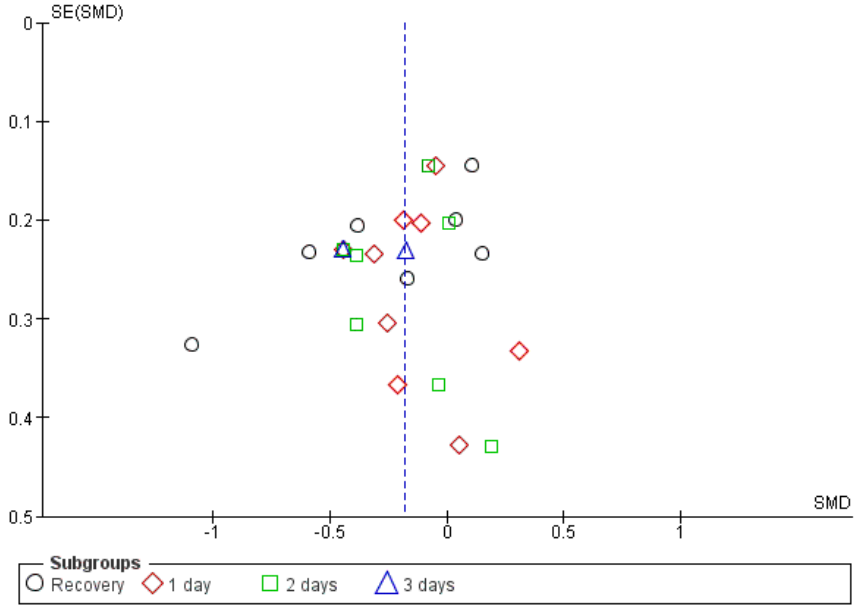
Funnel plot for total pain VAS studies.

Shoulder-tip VAS



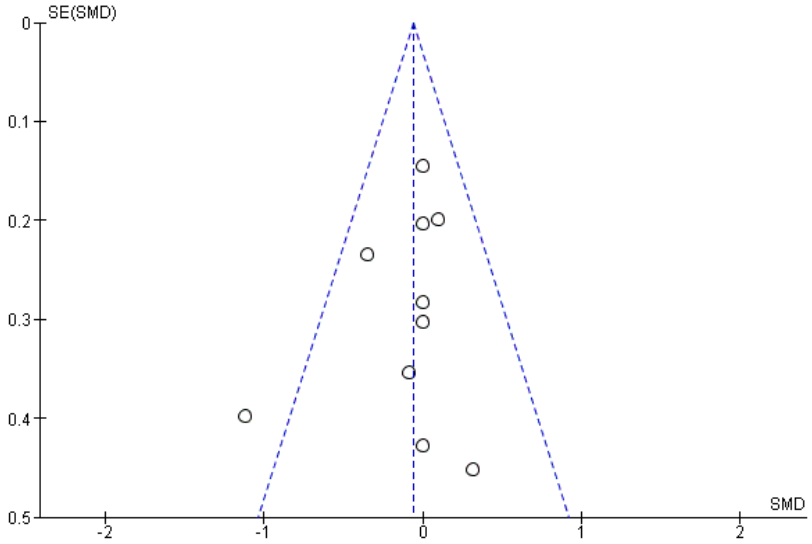
Funnel plot for shoulder tip pain (VAS 12-24hrs) studies.

Analgesic use



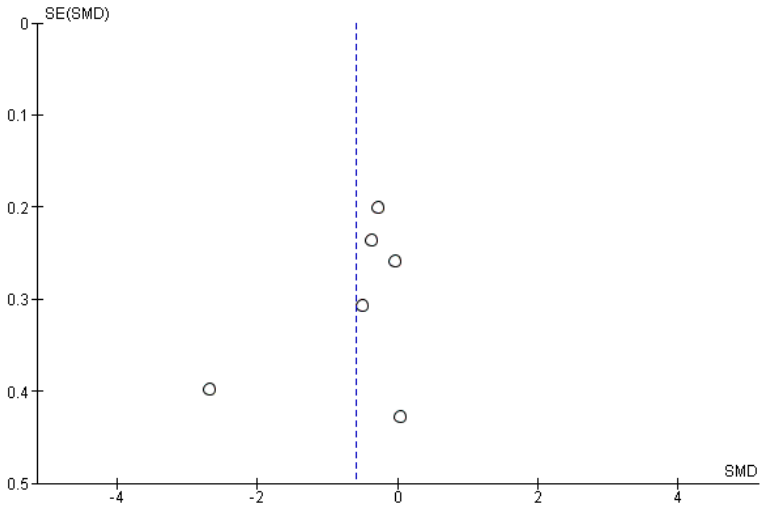
Funnel plot of analgesic use studies

Hospital stay



Funnel plot total length of hospital stay studies

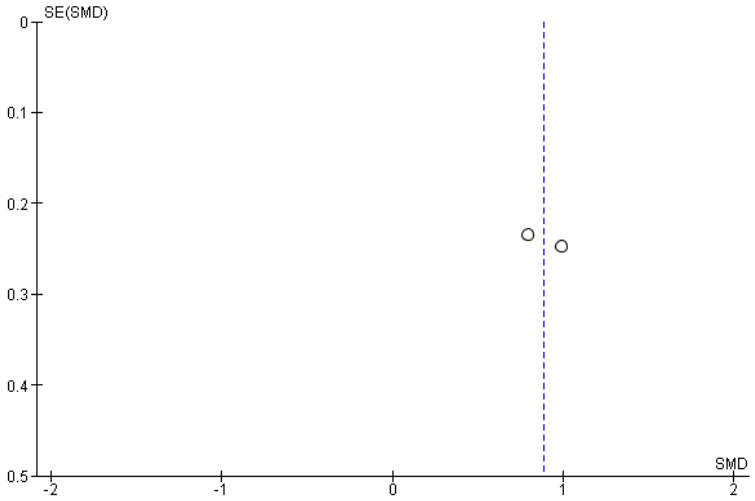
Recovery



Funnel plot time spend in recovery room time studies

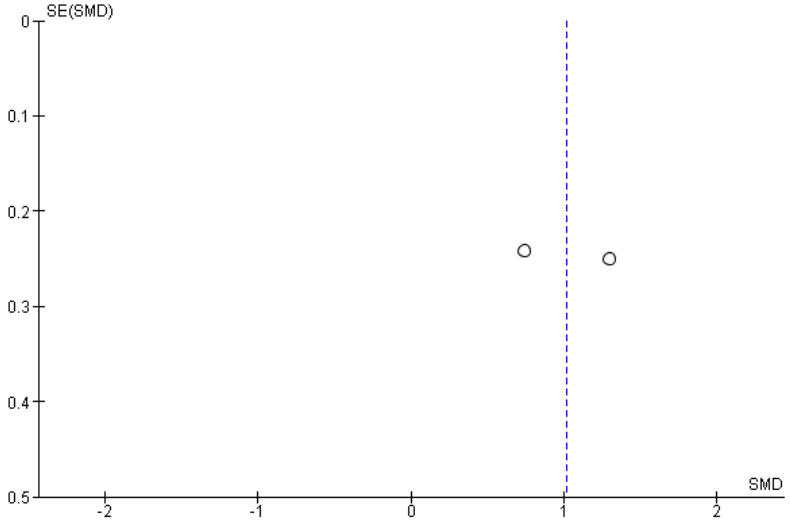
Open surgeries

Core temperature



Funnel plot core temperature studies

Wound temperature



Funnel plot wound temperature studies

12 Related procedures for evidence submission

12.1 Cost models

An electronic executable version of the cost model should be submitted to NICE with the full submission.

NICE accepts executable cost models using standard software – that is, Excel, TreeAge Pro, R or WinBUGs. If you plan to submit a model in a non-standard package, NICE should be informed in advance. NICE, in association with the External Assessment Centre, will investigate whether the requested software is acceptable, and establish if you need to provide NICE and the External Assessment Centre with temporary licences for the non-standard software for the duration of the assessment. NICE reserves the right to reject cost models in non-standard software. A fully executable electronic copy of the model must be submitted to NICE with full access to the programming code. Care should be taken to ensure that the submitted versions of the model programme and the written content of the evidence submission match.

NICE may distribute the executable version of the cost model to a consultee if they request it. If a request is received, NICE will release the model as long as it does not contain information that was designated confidential by the model owner, or the confidential material can be redacted by the model owner without producing severe limitations on the functionality of the model. The consultee will be advised that the model is protected by intellectual property rights, and can be used only for the purposes of commenting on the model's reliability and informing comments on the medical technology consultation document.

Sponsors must ensure that all relevant material pertinent to the decision problem has been disclosed to NICE at the time of submission. NICE may request additional information not submitted in the original submission of evidence. Any other information will be accepted at NICE's discretion.

When making a full submission, sponsors should check that:

- an electronic copy of the submission has been given to NICE with all confidential information highlighted and underlined
- a copy of the instructions for use, regulatory documentation and quality systems certificate have been submitted
- an executable electronic copy of the cost model has been submitted
- the checklist of confidential information provided by NICE has been completed and submitted.

- A PDF version of all studies (or other appropriate format for unpublished data, for example, a structured abstract) included in the submission have been submitted

12.2 Disclosure of information

To ensure that the assessment process is as transparent as possible, NICE considers it highly desirable that evidence pivotal to the Medical Technologies Advisory Committee's decisions should be publicly available at the point of issuing the medical technology consultation document and medical technology guidance.

Under exceptional circumstances, unpublished evidence is accepted under agreement of confidentiality. Such evidence includes 'commercial in confidence' information and data that are awaiting publication ('academic in confidence').

When data are 'commercial in confidence' or 'academic in confidence', it is the sponsor's responsibility to highlight such data clearly, and to provide reasons why they are confidential and the timescale within which they will remain confidential. The checklist of confidential information should be completed: if it is not provided, NICE will assume that there is no confidential information in the submission. It is the responsibility of the manufacturer or sponsor to ensure that the confidential information checklist is kept up to date.

It is the responsibility of the sponsor to ensure that any confidential information in their evidence submission is clearly underlined and highlighted correctly. NICE is assured that information marked ‘academic in confidence’ can be presented and discussed during the public part of the Medical Technologies Advisory Committee meeting. NICE is confident that such public presentation does not affect the subsequent publication of the information, which is the prerequisite allowing for the marking of information as ‘academic in confidence’.

Please therefore underline all confidential information, and highlight information that is submitted under ‘commercial in confidence’ in blue and information submitted under ‘academic in confidence’ in yellow.

NICE will ask sponsors to reconsider restrictions on the release of data if there appears to be no obvious reason for the restrictions, or if such restrictions would make it difficult or impossible for NICE to show the evidential basis for its guidance. Information that has been put into the public domain, anywhere in the world, cannot be marked as confidential.

Confidential information submitted will be made available for review by the External Assessment Centre and the Medical Technologies Advisory Committee. NICE will at all times seek to protect the confidentiality of the information submitted, but nothing will restrict the disclosure of information by NICE that is required by law (including in particular, but without limitation, the Freedom of Information Act 2000).

The Freedom of Information Act 2000, which came into force on 1 January 2005, enables any person to obtain information from public authorities such as NICE. The Act obliges NICE to respond to requests about the recorded information it holds, and it gives people a right of access to that information. This obligation extends to submissions made to NICE. Information that is designated as ‘commercial in confidence’ may be exempt under the Act. On receipt of a request for information, the NICE secretariat will make every effort to contact the designated company representative to confirm the status of any

information previously deemed ‘commercial in confidence’ before making any decision on disclosure.

12.3 Equality

NICE is committed to promoting equality and eliminating unlawful discrimination, including paying particular attention to groups protected by equalities legislation. The scoping process is designed to identify groups who are relevant to the evaluation of the technology, and to reflect the diversity of the population. NICE consults on whether there are any issues relevant to equalities within the scope of the evaluation, or if there is information that could be included in the evidence presented to the Medical Technologies Advisory Committee to enable them to take account of equalities issues when developing guidance.

Evidence submitters are asked to consider whether the chosen decision problem could be impacted by NICE’s responsibility in this respect, including when considering subgroups and access to recommendations that use a clinical or biological criterion.

For further information, please see the NICE website (www.nice.org.uk/aboutnice/howwework/NICEEqualityScheme.jsp).