NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Medical technology guidance

Assessment report overview

HumiGard Surgical Humidification System for the Prevention of Inadvertent Perioperative Hypothermia

This assessment report overview has been prepared by the Medical Technologies Evaluation Programme team to highlight the significant findings of the External Assessment Centre (EAC) report. It includes key features of the evidence base and the cost analysis, any additional analysis carried out, and additional information, uncertainties and key issues the Committee may wish to discuss. It should be read along with the company's submission of evidence and with the EAC report. The overview forms part of the information received by the Medical Technologies Advisory Committee when it develops its recommendations on the technology.

Key issues for consideration by the Committee are described in section 6, following the summaries of the clinical and cost evidence.

Please note: additional cost analyses were carried out in response to Committee uncertainties after the ARO was prepared. This can be found in appendix E.

This report contains information that has been supplied in confidence and will be redacted before publication. This information is highlighted in yellow. This overview also contains:

- Appendix A: Sources of evidence
- Appendix B: Comments from professional bodies

- Appendix C: Comments from patient organisations
- Appendix D: Technical Evidence
- Appendix E: Additional cost analyses carried out by External Assessment Centre

1 The technology

The HumiGard system comprises a reusable humidifier and single-use tubing set and is designed to humidify and heat carbon dioxide gas which is routinely used for insufflation during surgery to create and maintain pneumoperitoneum in laparoscopic surgery. CO_2 is the choice of gas as it is colourless, noninflammable, and rapidly excreted from the circulation. The system can be used in any patient undergoing laparoscopic or open surgery with the aim of helping to reduce evaporative cooling, which can also cause tissue desiccation and prevent intra-operative hypothermia. HumiGard is designed to be used independently of intraoperative warming measures which are applied to the external body surfaces and extremities, such as forced air warming.

The system comprises a humidifier and consumable tubing set. HumiGard humidifies and warms the carbon dioxide used similarly to the warm passover humidification systems used in respiratory therapy. The passover system humidifies gas by passing heated carbon dioxide over a reservoir of water. The heated, humidified gas is then passed along a sterile tube to deliver the insufflant to the laparoscopic cavity via a needle cannula. The HumiGard system can also be applied to open surgical wounds using a bespoke patient interface diffuser to effectively immerse the open surgical wound cavity in warmed, humidified carbon dioxide. HumiGard allows the CO_2 used to be warmed and humidified further reducing potential heat loss from the exposed internal surfaces.

Minimal training is required, as the product integrates with the insufflator in the same way as the current standard of care. The HumiGard system received a Class IIa CE mark in April 2013. The HumiGard system is indicated for use in open abdominal or cardiothoracic surgical procedures where carbon dioxide (CO_2) insufflation gas is used and laparoscopic surgery where carbon dioxide (CO_2) insufflation gas is used.

2 Proposed use of the technology

2.1 Disease or condition

NICE guidance on inadvertent perioperative hypothermia (NICE guideline 65, currently being updated) states that inadvertent perioperative hypothermia is a common but preventable complication of perioperative procedures, which is associated with poor outcomes for patients. Perioperative hypothermia has been linked with cardiac dysrhythmias, immunosuppression, increased blood loss, increased surgical site infections and increased post-operative pain.

2.2 Patient group

The HumiGard system is available for all patients undergoing abdominal surgery, as an open or laparoscopic procedure. Two subgroups were identified in the scope; people receiving adjunctive warming, such as from forced air warming devices or warming mattresses, and high-risk groups as described in NICE guideline 65 (any 2 of: ASA grades II-V, preoperative temperature below 36^{o}C, combined general and regional anaesthesia, major or intermediate surgery or at risk of cardiovascular complications).

Numerous factors contribute to the risk of inadvertent perioperative hypothermia. Risk is perceived to depend on patient characteristics (such as age or BMI); surgery factors (such as magnitude of the procedure or whether body cavities are open); anaesthesia factors (such as type or duration of anaesthesia); perioperative pharmacological agents (such as premedication); environmental factors (e.g. theatre temperature) and any preventative measures (such as the use of forced air warming devices). Risk factors are not necessarily independent and combinations of risk factors may be important, for example, patient age may be a relevant factor only for long surgical procedures. Furthermore, for continuous variables, such as age, there may be thresholds above which inadvertent perioperative hypothermia (IPH) is more likely to occur.

2.3 Current management

NICE guidance on inadvertent perioperative hypothermia (NICE guideline 65, currently being updated) recommends that all patients should be assessed for their risk of perioperative hypothermia. All patients should receive warmed intravenous fluids and blood products; patients identified as higher risk should be warmed intraoperatively using a forced air warming device, as should any patient receiving anaesthesia for more than 30 minutes. 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).

NICE guideline 65 on inadvertent perioperative hypothermia relates to the prevention of perioperative hypothermia in the general surgical population and does not make any specific recommendations about the warming of insufflation gas.

2.4 Proposed management with new technology

HumiGard would be used at the same point in the care pathway as, and in combination with, current warming techniques used for all patients at a higher risk of hypothermia, all patients undergoing prolonged surgical procedures and those receiving anaesthesia for more than 30 minutes.

2.5 Equality issues

No equality issues were identified.

3 Company's claimed benefits

The benefits to patients claimed by the company are:

- Decreased incidence of intraoperative and post-operative hypothermia as a result of reduction in evaporative cooling
- Decreased incidence of surgical site infections due to improved intra-operative temperature maintenance
- Improved postoperative recovery (fewer postoperative complications and less pain) and faster discharge.

The benefits to the health system claimed by the company are:

- Reduced overall costs (due to costs no longer incurred), as a result of better patient outcomes including reduced incidence of surgical site infections, reduced length of time spent in hospital for surgery, and reduced length of time in post-operative recovery.

4 Decision problem

Table 1 Summary of the decision problem

Population	People undergoing abdominal surgery, as an open or laparoscopic procedure
Intervention	HumiGard surgical humidification system for: • Open abdominal surgery • Laparoscopic abdominal surgery
Comparator(s)	Open abdominal surgery: • No insufflant Laparoscopic abdominal surgery: • Unheated, unhumidified insufflant gas
Outcomes	The outcome measures to consider include: • Incidence of hypothermia in the intra- and post-operative period (defined as a core body temperature <36^{o}C) • Incidence of surgical site infections • Length of stay in post-operative recovery • Total length of hospital stay • Device-related adverse events • Patient-reported pain
Cost analysis	Costs will be considered from an NHS and personal social 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).
Special considerations, including issues related to equality	None

In its submission, the company proposed the following variations to the outcomes:

- 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.

The EAC agreed with the company's argument regarding a change in core temperature is the standard reported temperature measure and this could be considered a marker of temperature maintenance. However the EAC noted that the company's economic model was based on the incidence of hypothermia. The reminder of the company's submission was consistent with the scope.

5 The evidence

5.1 Summary of evidence of clinical benefit

The company carried out separate literature searches for laparoscopic and open surgery. Twenty (both published and unpublished) studies covering laparoscopic surgery were presented in the submission; of these, 16 were RCTs, 3 were meta-analyses and 1 cohort. For open surgery, 4 RCTs were presented (see section 7.2.2 company submission page 26). The company used a checklist to decide whether studies (both published and unpublished) were generalisable and presented 16 studies (of the total of 24) involving other humidification devices. .

Of the 3 published meta-analyses on laparoscopic surgery, 2 included studies that used devices other than HumiGard. In the third meta-analysis only 2 of the included studies used HumiGard (Manwaring et al. 2008; Sammour et al. 2010), which were already in the list of included primary studies in the sponsor's clinical evidence review. For open surgery 3 of the 4 RCTs used HumiGard (Frey et al. 2012, Frey et al in press, Weinburg et al (2014)), while

the other RCT used a different humidification device. The in press Frey et al. paper included a retrospective analysis of two RCTs, both of which were already in the list of included primary studies of the sponsor's clinical evidence review, with one being on HumiGard (Frey et al. 2012) and the other on another humidification device.

The EAC considered that humidification systems other than HumiGard were out-of-scope and therefore studies on these systems should not be included. The EAC's independent literature searches did not identify any additional studies providing relevant clinical evidence on HumiGard. The EAC judged that 7 studies provided relevant evidence, 5 on laparoscopic surgery and 2 on open surgery.

Laparoscopic surgery

Hermann and De Wilde (2015) reported on a double-blind RCT that compared HumiGard with standard gas in patients aged 18 years or over with benign uterine diseases undergoing gynaecological laparoscopic surgery. 52 patients received warm (35±2^{o}C), humidified (98% humidity) insufflant CO_2 gas via HumiGard, 52 patients in the control arm received standard cold (room temperature), dry (0% humidity) CO_2. The primary outcome was postoperative pain development at 2, 4, 6, 24, and 48 hours (all in VAS). Secondary outcome measures were morphine consumption, rejected boli, temperature change during surgery, length of time spent in the recovery room and duration of inpatient stay. The results showed a statistically significant difference in total shoulder tip pain (p=0.037). The results showed no statistically significant difference in any of the remaining outcome measures covered in the scope.

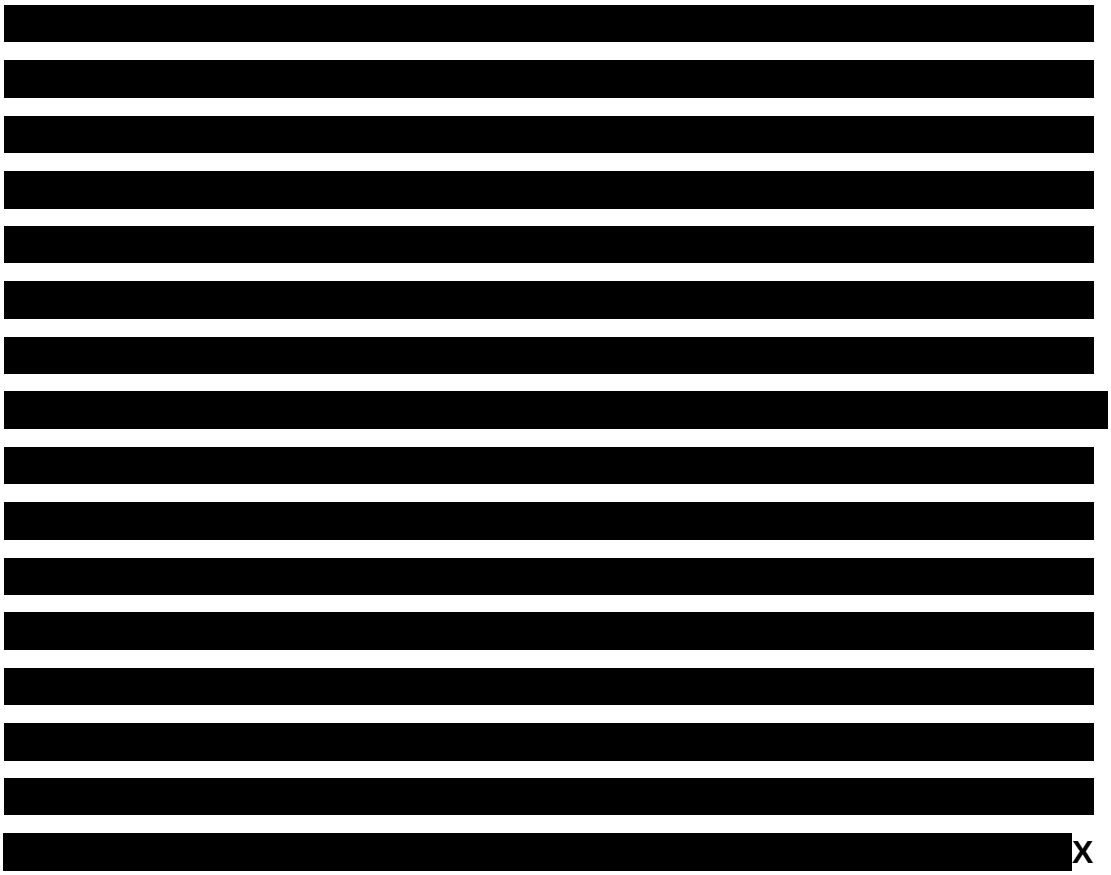
Manwaring et al. (2008) reported on a RCT that compared HumiGard with standard gas in women aged 18 to 55 years undergoing gynaecologic laparoscopy. 30 patients received warmed, humidified insufflant CO_2 gas via HumiGard, 30 patients in the control arm received standard cold, dry CO_2. The primary outcome was shoulder tip pain at four hours post-surgery.

Secondary outcome measures were time in recovery room, nausea, post-operative temperature and pelvic pain. The results showed a statistically significant difference in change in core temperature from theatre to recovery (°C) (p=0.027). The results showed no statistically significant difference in the remaining outcome measures listed in the scope.

Sammour et al. (2010) reported on a double-blind RCT that compared HumiGard with standard gas in patients aged 15 years or older undergoing elective laparoscopic colonic resection. 41 patients received warm (37^{o}C), humidified (98% humidity) insufflant CO_2 gas via HumiGard, 41 patients in the control arm received room temperature (19^{o}C), dry (0% humidity) CO_2. The primary outcome was total opiate analgesia use during the index inpatient stay. Secondary outcome measures were postoperative pain (Visual Analogue Scale (VAS) score) at 2, 4, 8, 12 hours and 1, 2, 3, 7, 14, 30, 60 days post op. Other secondary outcome measures were intra-operative core temperature, cytokine response and length of inpatient stay. Six patients in the HumiGard group and two from the control group were excluded from the analysis with reasons given. The results showed a statistical significant benefit for Humigard for post-operative pain at rest (VAS) on day 1 (p=0.01) and post-operative pain on moving (VAS) on day 1 (p=0.018). The results showed no statistically significant difference in the remaining outcome measures outlined in the scope.

Yu et al. (2013) reported on a double-blinded RCT that compared HumiGard with standard gas in children aged 8 to 14 years undergoing acute laparoscopic appendectomy. 95 patients received warm (37^{o}C), humidified (98% humidity) insufflant CO_2 gas via HumiGard, 95 patients in the control group received room temperature (20-21^{o}C), dry (0% humidity) CO_2. The primary outcome was postoperative pain (analgesic use) in the recovery room and days 1 and 2 post op. Secondary outcome measures were pain intensity scores, intra-operative core temperature and postoperative recovery and return to normal activities. Two patients in the HumiGard group and three

from the control group were excluded from the analysis with reasons provided. The authors provided only graphical data for pain perceived at rest and on moving (VAS); however no differences at the time points (0, 2, 4, 6, 8, 10, 12, 24 and 48 hours) were reported between the two groups. The results showed no statistically significant difference in the remaining outcome measures listed in the scope.



Open surgery

Frey et al. (2012) reported on a RCT that compared HumiGard with no insufflation in patients older than 18 years (mean age 63.5 years) undergoing elective colon surgery. 42 patients received warm (37^{o}C), humidified (100% humidity) insufflant CO_2 gas via HumiGard, 41 patients in the control arm received no insufflation. The primary outcome was intra-operative core and wound temperature. The secondary outcome measure was length of hospital stay. Two patients in the HumiGard group and two from the control group were excluded from the analysis with reasons provided. The results showed a

statistically significant benefit for Humigard in: the proportion of patients with core temperature <36.0°C at end of surgery (p=0.005), the proportion of patients with core temperature <36.5°C at end of surgery (p=0.001), core temperature (°C) at end of surgery (p=<0.001), core temperature during surgery (p=<0.001), wound area temperature (°C) during surgery (p=<0.001) and wound edge temperature during surgery (p=<0.001). The results showed no statistically significant difference between groups for length of stay.

Weinberg et al. (2014) reported on a prospective pilot RCT that compared HumiGard and standard care with standard care alone in adult patients undergoing primary orthotopic liver transplantation. Standard care involved intense measures to maintain temperature homeostasis including predetermined temperatures for infused fluid, ambient air and heating mattress temperatures. No details were provided regarding number of patients in each group (abstract only); however 22 patients were randomised to receive the intervention or control. The primary outcome was intra-operative core temperature prior to reperfusion and at completion of surgery. No secondary outcomes were reported. The core temperature immediately prior to reperfusion (°C, via nasopharyngeal probe) was significantly higher in the Humigard group (p=0.02). No statistically significant differences were reported for core temperature on wound closure (°C, via nasopharyngeal probe), core temperature immediately prior to reperfusion (°C, via pulmonary artery catheter), core temperature on wound closure (°C, via pulmonary artery catheter), core temperature immediately prior to reperfusion (°C, via bladder probe) and core temperature on wound closure (°C, via bladder probe).

Table 2 Characteristics of the key studies

Abbreviations used					
Study	Study design (country)	Population	Intervention versus comparator	Outcomes considered	EAC comments on study
Laparoscopic surgery					
Herrmann and De Wilde (2015)	RCT at a university clinic for gynaecology in Germany. Full article in peer reviewed journal.	Patients aged 18 years or over with benign uterine diseases undergoing gynaecological laparoscopic surgery (N=104) Mean age 47 years	HumiGard (n=52) vs. Standard gas (n=52)	Postoperative pain development at 2, 4, 6, 24, and 48 hours (all in VAS) Morphine consumption Rejected boli Temperature change during surgery Length of time spent in the recovery room Duration of inpatient stay	Adequate sample size which was based a statistical power analysis. Appropriate randomization and concealment. There was inadequate blinding as the surgeon was not blinded to the group assignment. However participants, personnel and outcome assessors were blinded to treatment allocation
Manwaring et al. (2008)	RCT at a university hospital in Australia. Full article in peer reviewed journal.	Women aged 18 to 55 years undergoing gynaecologic laparoscopy (N=60) Mean age 30 years	HumiGard (n=30) vs. Standard gas (n=30)	Shoulder-tip pain at 4 hours post-surgery Time in recovery room Nausea Post-operative temperature Pelvic pain	Adequate sample size which was based a statistical power analysis. Appropriate randomization and concealment. There was inadequate blinding as operating staff were not blind to the group assignment. All nursing staff were blinded to the nature of insufflation gas used. Unclear whether patients and

Abbreviations used					
Study	Study design (country)	Population	Intervention versus comparator	Outcomes considered	EAC comments on study
					outcome assessors were blinded. The study was unclear in terms of dropout rates and intention to treat analysis.
Sammour et al. (2010)	RCT at three public hospitals in New Zealand. Full article in peer reviewed journal.	Patients aged over 15 years or older undergoing elective laparoscopic colonic resection for any indication (N=82) Median age 70 years	HumiGard (n=41) vs. Standard gas (n=41)	Total opiate analgesia use during the index inpatient stay Post-operative pain at 2 hours, 4 hours, 8 hours, 12 hours, day 1, day 2, day 3, day 7, day 14, day 30, and day 60 postoperatively (in VAS) Intra-operative core temperature Cytokine Response Days of hospital stay	Adequate sample size which was based a statistical power analysis. Appropriate randomisation and adequate concealment, with a computerised, stratified by hospital. Allocations were concealed in opaque numbered envelopes until interventions were assigned on the day of surgery. Drop outs were reported and an intention to treat analysis was carried out. There was evidence of selective reporting as the intra-operative core temperature was measured at 15 minutes intervals but only the change in temperature between the start and end of the procedure, as well as the minimum, maximum, and

Abbreviations used					
Study	Study design (country)	Population	Intervention versus comparator	Outcomes considered	EAC comments on study
					mean/median temperatures were reported. Data on morphine equivalent usage per kilogram of patient weight and data on the core body temperature at all-time points were not shown.
Yu et al. (2013)	RCT at children's hospital in New Zealand. Full article in peer reviewed journal.	Children aged 8–14 years undergoing acute laparoscopic appendectomy (N=195) Median age (IQR): 12 (3)	HumiGard (n=97) vs. Standard gas (n=98)	Postoperative pain (analgesic use: recovery, day 1, day 2). Pain intensity scores Intra-operative core temperature Postoperative recovery and return to normal activities	Adequate sample size which was based a statistical power analysis. Appropriate randomisation and adequate concealment. Three nurses from an independent hospital department generated the random allocation sequence and they were kept uninformed of all other parts of the study. The baseline characteristics of the two groups were comparable with no significant differences were found between the groups.
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

Abbreviations used					
Study	Study design (country)	Population	Intervention versus comparator	Outcomes considered	EAC comments on study
	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Open surgery					
Frey et al. (2012)	RCT at a university hospital in Sweden. Full article in peer	Patient older than 18 years undergoing elective colon surgery (N=83) Mean age 63.5	HumiGard (n=42) vs. No insufflation (n=41)	Intra-operative temperature: core and wound (°C) Days of hospital stay	The sample size was adequate and based on a statistical power analysis. No significant differences between the groups' baseline characteristics regarding clinical

Abbreviations used					
Study	Study design (country)	Population	Intervention versus comparator	Outcomes considered	EAC comments on study
	reviewed journal.	years.			variables (age, gender, weight, height, and body mass index), patient diagnoses, operation codes, and intraoperative variables. The blinding was inadequate with the operating team including nurse measuring patients' temperature was not blinded to type of treatment. Unclear whether other personnel, patients and outcome assessors were blinded.
Weinberg et al. 2014	RCT pilot trial in Australia. Abstract only.	Adult patients undergoing primary orthotopic liver transplantation (N=22) Age not stated	HumiGard plus standard care vs. Standard care alone (number of patients in each are not stated)	Intraoperative core temperature prior to reperfusion and at completion of surgery	Only an abstract available. The study was described as randomized however no details were stated. It is unclear from the abstract if there was adequate blinding. Difficult to critique.

EAC critical appraisal of the clinical evidence

The EAC concluded that the clinical evidence on HumiGard for laparoscopic surgery was relatively robust in that it came from four RCTs and one retrospective cohort study in appropriate patients, all of which compared HumiGard with standard unhumidified insufflant gas. The retrospective cohort study was submitted as academic in confidence at draft stage and has not yet been submitted for publication and undergone peer review. The clinical evidence submitted for open surgery was based on two small RCTs, one of which was a small pilot study published as abstract only.

From the EAC's evidence synthesis, the incidence of hypothermia was derived from one RCT which found no statistically significant differences between the groups

[redacted]

and one retrospective cohort study which found a statistically significant decrease in the HumiGard group compared with the control

[redacted]

Pooled estimate on this outcome appears to favour HumiGard

[redacted]

however, due to the difference between the studies in the designs and the effects observed, this pooled result should be interpreted with caution.

Three studies presented outcomes using median (range) or median (interquartile range) which suggests that the data are not normally distributed. The EAC converted medians, ranges and interquartile ranges into means and standard deviations but noted that the additional meta-analyses using converted values should be interpreted with caution.

Some studies reported the same outcome measure but at different or multiple time-points. The company pooled these studies to estimate an overall effect size for the time period covering all the time-points. It is inappropriate to combine such studies for the different time-points to produce an overall effect size. Such an estimated overall effect size is not clinically useful in relation to

the effect size at each individual time point. Some studies were counted more than once as they reported the outcome at more than one time-point invalidating the analyses. Humidification systems other than HumiGard are outside scope for this assessment report. For this reason, the EAC focussed on the seven studies that used HumiGard.

The EAC extracted data on all outcomes of interest from relevant studies using HumiGard and produced meta-analyses based on only studies on HumiGard. The incidence of hypothermia was derived from one RCT which found no statistically significant differences between the groups (14% vs 23%; risk ratio 0.62; 95% CI 0.23 to 1.67), and one retrospective cohort study which found a statistically significant decrease in the HumiGard group compared with the control (13% vs 57%; risk ratio 0.23; 95% CI 0.14 to 0.37). Pooled estimate on this outcome appears to favour HumiGard (risk ratio 0.34; 95% CI 0.13 to 0.89; p=0.03); however, due to the difference between the studies in the designs and the effects observed, this pooled result should be interpreted with caution.

Adverse events

Two RCTs on laparoscopic surgery mentioned adverse events (Herrmann and De Wilde 2015; Sammour et al. 2010); both found no adverse events specific to the intervention device. No studies on open surgery reported device-related adverse events.

5.2 Summary of economic evidence

The company identified two studies from the clinical evidence search which incorporated a cost-effectiveness analysis. The EAC judged that the company's search strategy was highly sensitive and well-constructed and the selection criteria reflected the NICE scope. The EAC carried out their own economic search and found no additional studies.

Both studies were published as conference abstracts and assessed the HumiGard system compared with standard care in the UK. The company

provided unpublished academic in confidence unfinished study reports related to both abstracts.

Jenks et al. (2015) reported on a cost-utility analysis using a decision analytic model of the HumiGard system compared with standard care in patients undergoing open or laparoscopic colorectal surgery. The results showed that the HumiGard system dominated over standard care in both open and laparoscopic surgery patients.

The clinical aspects of the Mason et al. (2015) study have already been outlined in section 5 of this report. The study also reported on the cost-benefit analysis of the HumiGard system compared with standard care in patients undergoing laparoscopic colorectal surgery. The results showed that the HumiGard system dominated over standard care, with a cost saving of £1,226 per SSI avoided. This cost saving already includes the offset costs of the avoided SSI.

De novo analysis

The company submitted a *de novo* analysis evaluating HumiGard compared with standard care. The model was based on an analysis presented in one of the published abstracts. It models both laparoscopic and open surgery and presents combined results assuming a 70:30 split in usage of HumiGard. Both take the form of a simple decision tree (see figures 1 and 2), and incorporate the probability of complications associated with hypothermia and related NHS costs accrued. The time horizon was 1 year in the base case, with a 5 year time horizon considered in the scenario analysis. In the scenario analysis complications including stroke and myocardial infarction had longer term follow-up costs applied. These costs were discounted at a rate of 3.5% per year. The analysis was considered from an NHS and personal social services perspective.

Figure 1 Model structure for laparoscopic patients

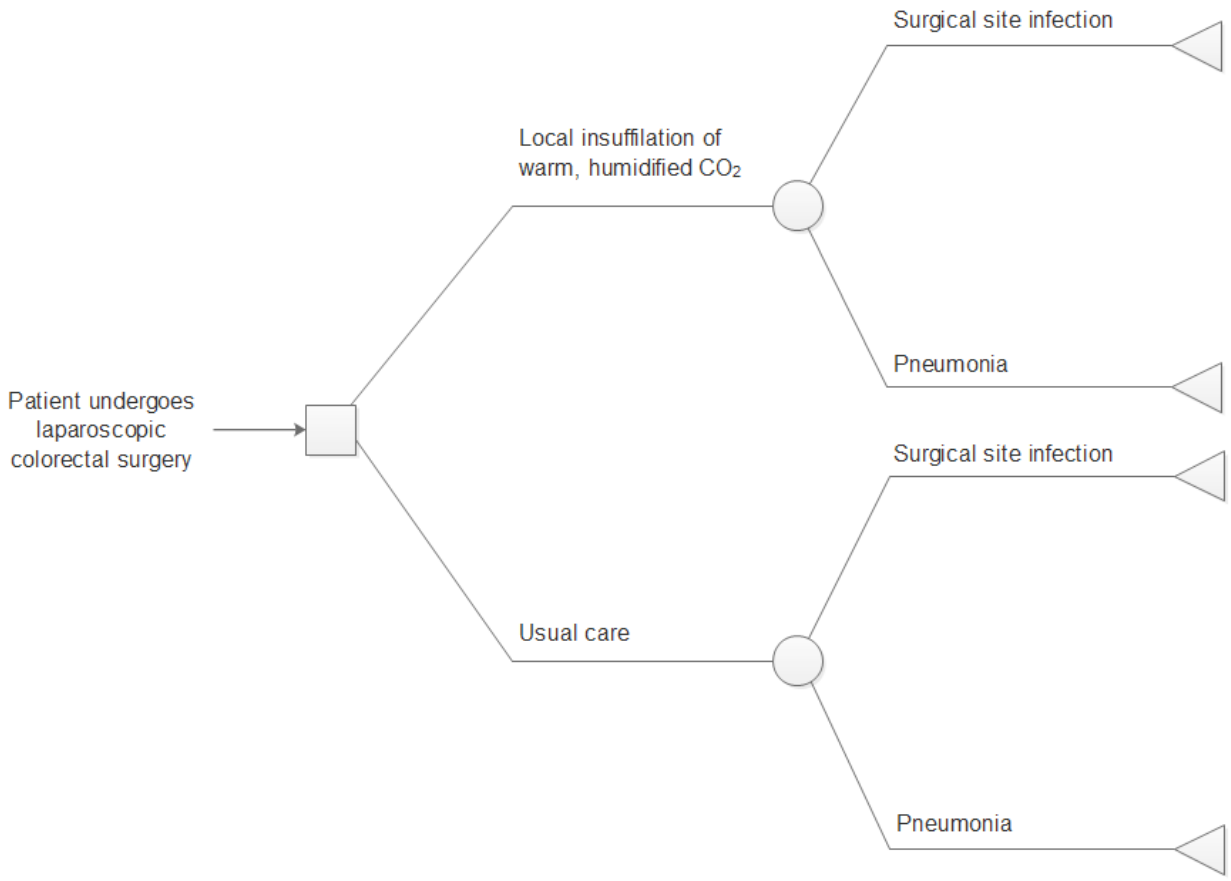
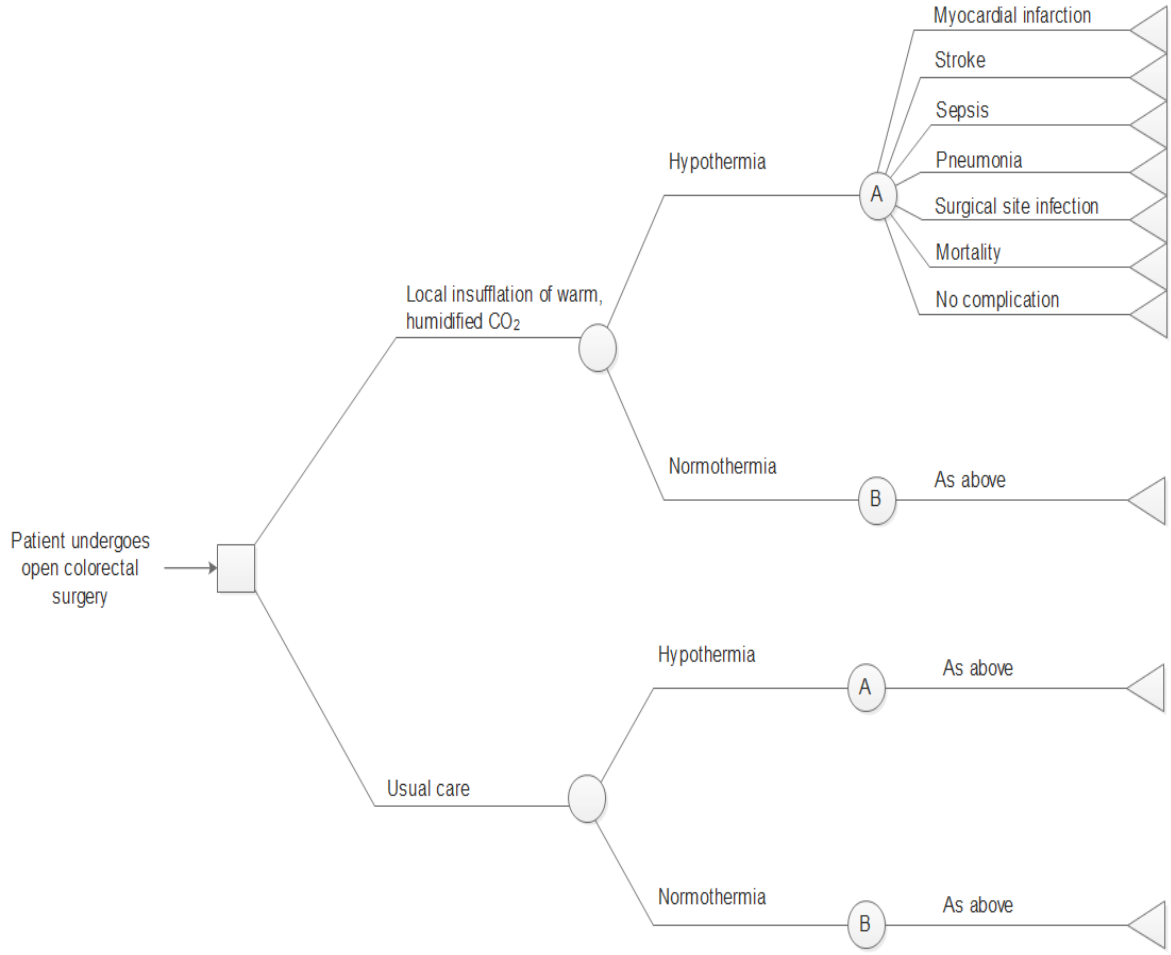


Figure 2 Model structure for open patients



Clinical parameters and variables

Table 3 shows the model input parameters and values used in the base case.

Table 3 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)
HumiGard: pneumonia	0.79%	NR	Noor *et al.* (2015)
Standard care: SSI	12%	NR	Noor *et al.* (2015)
Standard care: pneumonia	3.17%	NR	Noor *et al.* (2015)
Open surgery			
HumiGard: Proportion of patients with hypothermia post-surgery	0%	NR	Frey *et al.* (2012)
Standard care: Proportion of patients with hypothermia post-surgery	18%	95% CI: 5-31%	Frey *et al.* (2012)
Probability of myocardial infarction: normothermia	1.1%	NR	Billeter *et al.* (2014)

Probability of myocardial infarction: hypothermia	3.3%	NR	Billeter *et al.* (2014)
Probability of stoke: normothermia	1.0%	NR	Billeter *et al.* (2014)
Probability of stroke: hypothermia	6.5%	NR	Billeter *et al.* (2014)
Probability of sepsis: normothermia	2.6%	NR	Billeter *et al.* (2014)
Probability of sepsis: hypothermia	7.5%	NR	Billeter *et al.* (2014)
Probability of SSI: normothermia	3.3%	NR	Billeter *et al.* (2014)
Probability of SSI: hypothermia	5.0%	NR	Billeter *et al.* (2014)
Probability of pneumonia: normothermia	1.3%	NR	Billeter *et al.* (2014)
Probability of pneumonia: hypothermia	5.1%	NR	Billeter *et al.* (2014)
Probability of mortality: normothermia	4.0%	NR	Billeter *et al.* (2014)
Probability of mortality: hypothermia	17.0%	NR	Billeter *et al.* (2014)
CI, confidence interval; NR, Not reported			

Costs and resource use

With the exception of long term costs of MI and stroke, and the cost of SSIs, the clinical management of patients undergoing abdominal surgery was costed using NHS reference costs. Table 4 outlines the weighted average costs per patient for possible postoperative hypothermia related complications. Further details of the costs can be found in the assessment report (pg. 63).

Table 4 Calculation of complication costs

Complication	Weighted average
Post MI	£43.25
Inpatient stay for MI	£1468.51
Inpatient stay for pneumonia	£1798.59
SSI	£1857.92
Inpatient stay for sepsis	£2149.02
Inpatient stay for stroke	£2833.76

The costs of the HumiGard technology are shown in Table 5. The costs include the cost of purchasing the equipment, tubing kits for each patient and the costs of training nurse staff.

Table 5 Costs per treatment associated with the HumiGard system and standard care

	HumiGard		Comparator*	
Items	**Value**	**Source**	**Value**	**Source**
Price of the technology per treatment	£1,600 (per humidifier with 5 year life span)	Fisher and Paykel Healthcare Ltd	£5	NHS Supply chain (Dry line tubing kit – reported in briefing note to cost between £5 and £10)
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	N/A	
Maintenance cost Provided annually	£0	Fisher and Paykel Healthcare Ltd	N/A	
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	N/A	
Other costs (staff) None	£0	Fisher and Paykel Healthcare Ltd	N/A	
Total cost per treatment	Laparoscopic: £75+£5.63 = £80.63 Open:	£1,600 cost of device and £510 of training spread among 75 patients per	£5-10	A cost of £5 has been used within the model.

	£99+£5.63 = £104.63	year for 5 years plus the cost of consumables.		

* The cost of the comparator technology applies to laparoscopic surgery patients only.

The company estimates the cost of the comparators to be:

- For laparoscopic surgery: £5 per patient (dry line tubing kit)
- For open surgery: no additional cost

Sensitivity analysis

The company conducted a range of sensitivity analyses. These include scenario analysis to explore the use of alternative sources of clinical effectiveness, univariate deterministic sensitivity analysis and a probabilistic analysis of the base case results. Scenario analyses using alternative time horizons (up to 5 years) are also presented. Tables 6-8 highlight the variables used in the company's sensitivity analysis for open and laparoscopic surgery.

Table 6 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 (see Table C5.1 of the company's economic submission).
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 (see Table C5.2 of the company's economic submission) 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 (see Table C5.3 of the company's economic submission) 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 (see Table C5.4 of the company's economic submission).
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 7 Variables used in multi-way scenario-based sensitivity analysis – Open surgery

Variable	*Base case (normothermia/hypothermia)*	*Open surgery: Kurz et al. (1996) data*	*Open surgery: Anannamcharoen et al. (2012) data*	*Open surgery: Flores-Maldonado et al. (2001) data*	*Use of multiplier (m) on Billeter hypothermia data (m = 0.1, 0.5 and 0.8)*
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 8 Variables used in multi-way scenario-based sensitivity analysis – Laparoscopic surgery

Variable	*Base case*	*Temperature data: Sammour Clinical event data: Billeter*	*Temperature data: Sammour Clinical event data: Kurz*	*Temperature data: Sammour Clinical event data: Flores-Maldonado*	*Temperature data: Mason Clinical event data: Billeter*	*Temperature data: Mason Clinical event data: Kurz*	*Temperature data: Mason Clinical event data: Flores-Maldonado*
Proportion of HumiGard patients with hypothermia post-surgery	N/A	14.3%	14.3%	14.3%	13.0%	13.0%	13.0%
Proportion of non HumiGard patients with hypothermia post-surgery	N/A	23.1%	23.1%	23.1%	57.0%	57.0%	57.0%
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

Results

The base case results of the company's submission state that HumiGard costs £419 per patient compared to usual care of £724, saving of £305. The majority (69%) of the cost savings are derived from a reduction in SSIs. The company's base case combines laparoscopic and open surgery, and the cost savings are largely driven by laparoscopic surgery. The results of the company's analysis, separating open and laparoscopic surgeries are presented in Table 9.

Table 9 The company base case results for open, laparoscopic and combined surgeries

Type of surgery	HumiGard	Usual Care	Increment
Open	£483	£503	-£20
Laparoscopic	£391	£819	-£428
Combined (company base case)	£419	£724	-£305

The company noted that the base case analysis included only patients who used forced-air warming blankets; therefore the base case analysis reflects this subgroup. The company also noted that insufficient detail was provided to enable a subgroup analysis for high risk groups to be conducted.

The results of the sensitivity analysis were presented as a Tornado diagram by the company, which showed the impact of varying specific parameters in univariate sensitivity analyses (see assessment report, Figure 7, page 75). The results were sensitive to the probability of SSI in the control group. When

the absolute difference in risk of SSI reduces to around 0.3% (e.g. 4.7% versus 5%) the HumiGard system becomes cost increasing. The company also presented the results of the scenario analyses for laparoscopic and open surgery separately. HumiGard remained cost saving for open surgery for all analyses using alternative clinical effectiveness data. For open surgery, the use of the data from the RCT (Sammour et al, 2010) substantially reduced the cost savings, and HumiGard was associated with a modest additional cost when these data were combined with data on complications from the studies by Billeter et al. (2014) or Flores-Maldonado et al. (2001).

The company's probabilistic sensitivity analysis found that HumiGard was cost saving in 97.4% of iterations and the average probabilistic cost savings were £302 per patient. The company noted that the results of the PSA have a skewed distribution (see the company's submission, Figure C7) and state that this is due to the distribution of costs of complications within the model which have a gamma distribution bounded by 0, but no upper limit.

The EAC reviewed the assumptions built into the company's model in relation to available evidence and expert opinion and verified that there were no identifiable errors in the coding of the company's model.

EAC revisions to the company's model

The EAC re-ran the company's base case and univariate sensitivity analyses for open and laparoscopic surgery separately, and conducted additional analyses using its preferred estimates (see assessment report Figure 8 and Figure 9, page 76).

The key amendments included in the EAC revisions to the company's model were:

- Inclusion of updated NHS reference costs of pneumonia, acute myocardial infarction and sepsis using NHS reference costs
- Annuitizing the capital cost of the HumiGard system

- Re-estimating the costs of post-MI to reflect current drug prices
- Use of alternative costs of treating stroke and SSIs
- Use of a five year time horizon
- Inclusion of the data on hypothermia from the RCT in laparoscopic surgery linked to data on complications from the retrospective cohort study (laparoscopic surgery only).

Additional sensitivity analyses conducted by the EAC included the use of a one-year time horizon, an alternative source for the costs of SSIs and (for laparoscopic surgery only) the direct data on complications reported in the abstract of the RCT in laparoscopic surgery. The EAC also reprogrammed the company's model to allow a probabilistic sensitivity analysis to be conducted for the amended model.

For open surgery, the results of the EAC reanalysis suggest that HumiGard is cost saving compared to standard care with an average saving per patient of £209. This increase in cost saving compared to the company's base case was due to the longer time horizon. The probability that HumiGard is cost saving was 98% in the probabilistic sensitivity analysis for the longer time horizon. The results for a one year time horizon were broadly similar to those reported by the company (an average cost saving of £28 per patient).

The EACs reanalysis found lower cost savings for laparoscopic surgery than reported by the company (an average cost saving of £77 per patient). This was largely due to the use of data from the RCT of HumiGard rather than the unpublished retrospective study. The probabilistic analysis found that HumiGard was cost saving in 67.5% of iterations. When a one year time horizon was used HumiGard was associated with a small additional cost of £11 per patient.

The EAC considered that the study by Sammour et al. (2010) is a well-designed prospective double blinded RCT and presented more robust evidence than the incomplete Mason et al. study. The EAC therefore revised

the model structure combining (Sammour et al., 2010) and complications modelled according to Billeter et al. (2014) as their preferred analysis for laparoscopic surgery.

EAC critical appraisal of the economic evidence

The EAC considered that the company's de novo model reflected the NICE scope. The model was well presented and the EAC's model verification checks did not identify any coding errors. In the base case analysis the results for laparoscopic and open surgery are combined. These different types of surgery are associated with different risks and resource consequences. The EAC considered that the results for the two types of patients/surgeries should be considered as separate analyses.

The EAC noted discrepancies between the published abstract and unpublished manuscript (see assessment report pg. 61). The current manuscript and correspondence with the company/authors highlighted that the manuscript is a work in progress and emphasises the importance of the peer review process for journal articles before the study and findings can be considered robust.

The EAC noted that the study by Billeter et al. (2014) was a large study (N=707) and designed to match cases and controls for a range of characteristics. One of NICE clinical experts considered the data from the USA would be generalisable to a UK population. The study has, however, several limitations. Firstly, it was not limited to patients undergoing abdominal surgery; it included a large proportion of patients undergoing general surgery (25%) in addition to patients undergoing surgery for a variety of other reasons. The study also excluded patients with mild hypothermia (35 to 36^{o}C) from their definition of hypothermia (the definition of normothermia was not explicitly stated), whereas the other studies of clinical effectiveness included patients with mild hypothermia within their definitions. It is not possible to directly estimate the impact of this on the results; however, if the rates of compilations are expected to be lower in patients with mild hypothermia

compared to moderate/severe hypothermia, the use of these data would underestimate the cost savings associated with reducing rates of hypothermia. The EAC further notes that the difference in the proportions of patients experiencing SSIs was not statistically significant.

The EAC sought expert advice on the estimates of training time. One Expert Adviser considered that the amount of time was broadly correct, but considered that pairs of team leaders would be trained. The other expert considered that the training time for nurses may have been overestimated. The EAC concluded that the estimates of training time to be broadly correct and unlikely to have a significant impact on the overall estimates of total costs.

The EAC also considers it necessary to annuitize the capital cost of the humidifier, taking into account the opportunity cost of purchasing equipment and its lifespan, applying a discount rate of 3.5% over 5 years. Given the cost per patient was already low; this adjustment had only a small effect, increasing the humidifier cost per patient from £4.27 to £4.57.

The EAC considered that the economic evidence submitted by the company reflected the NICE final scope with the exception of the inclusion of specified subgroup analyses. The EAC agrees with the company's justification for not providing subgroup analyses and that data were not available to model the use of HumiGard for high risk patients, and that the base case results apply only to patients with adjunct warming.

5.3 Technical evidence

Following the Committee's decision to select HumiGard for evaluation, a few areas of uncertainty were identified in the Committee discussions. The areas of uncertainty regarded tissue discolouration in open surgery being of a similar appearance to tissue ischaemia, the ergonomics of using HumiGard, possible infection control issues and is the mechanism of action of heated, humidified carbon dioxide different for open surgery compared to laparoscopic surgery? In order to address these issues a short technical report was commissioned

by NICE to help contribute to the Medical Technology Advisory Committee's decision-making in their evaluation of the HumiGard device (please see appendix D for the full report). The summary of the findings are as follows:

- There may be some tissue discolouration visible when using HumiGard in open surgery, but trained users do not find this problematic.
- There is no reason to believe that HumiGard adds undue complexity or restricts the field of vision during open surgery.
- The single use nature of the administration set and the use of filters make it unlikely that HumiGard will cause bacterial contamination during surgery. The administration set is not entirely sterile, meaning that there is a possibility of contamination entering the system during setup. The company has submitted a test report to demonstrate that bacteria are not transmitted from the reservoir or sensor to the patient. No evidence has been identified that indicates any increase in infection rates.
- The device works in the same way for each type of surgery. The differences are the delivery method to the operative site. For open surgery the heated, humidified CO2 is delivered by a diffuser device that is placed at the edge of the wound area.

6 Ongoing research

Details of ongoing studies can be found below.

Study ID	Type of study	Comparison	Status	Completion date
The company identified ongoing studies				
NCT01098175	Case control study	Humidified gas at 31-32 °C or exposure of the surgical wound to the air	Unknown	December 2011
NCT01887028	Crossover RCT	Warmed, humidified CO_2 or cool, dry	Unknown	September 2015

		CO_2		
NCT02319902	Parallel RCT	Heated humidified CO_2 or cold CO_2	Currently recruiting participants	December 2015
Additional ongoing studies identified by the EAC				
ACTRN12606000287538	Parallel RCT	Humidified, heated CO_2 or use of cold, dry CO_2	Not yet recruiting	Unclear
ACTRN12615001231538	Crossover RCT	Heated humidified gas on or gas off (standard care) for 30 minute intervals	Not yet recruiting	Unclear
NCT02586974	Parallel RCT	Warmed, humidified CO_2 or standard CO_2 insufflation	Currently recruiting participants	August 2016

7 Issues for consideration by the Committee

Clinical evidence

- The company's submission included evidence based on other humidification systems which the EAC excluded as it was out of scope
- Individual studies show benefit for different specific outcomes, but not consistently across all outcomes in the scope.
- The evidence on open surgery is limited in quantity, however based on the cost modelling there are higher potential cost savings to me made.

Cost evidence

- The cost modelling relies on estimates of the reduction in surgical site infection based on limited quality clinical data (Mason et al).

8 Authors

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Paul Dimmock, Technical Analyst (Evaluation)

NICE Medical Technologies Evaluation Programme

February 2016

Appendix A: Sources of evidence considered in the preparation of the overview

A Details of assessment report:

- Darte, R. et al HumiGard Surgical Humidification System for the prevention of inadvertent perioperative hypothermia. January 2016.

B Submissions from the following Company's:

- Fisher and Paykel Healthcare

C Related NICE guidance

D Hypothermia: prevention and management in adults having surgery. NICE clinical guideline 65(2015). Available from www.nice.org.uk/guidance/CG65

E Inditherm patient warming mattress for the prevention of inadvertent hypothermia. NICE medical technology guidance 7(2011). Available from www.nice.org.uk/guidance/MTG7

F References

Anannamcharoen S, Vachirasrisirkul S, Boonya-Assadorn C. (2012) Incisional surgical site infection in colorectal surgery patients. Journal of the Medical Association of Thailand; 95: 42-47.

Billeter A, Hohmann S, Druen D, et al. (2014) Unintentional perioperative hypothermia is associated with severe complications and high mortality in elective operations. Surgery; 156: 1245-1252.

Flores-Maldonado A, Medina-Escobedo E, Rios-Rodrigues H, et al. (2001) Mild perioperative hypothermia and the risk of wound infection. Archives of Medical Research; 32: 227-231.

Frey JM, Janson M, Svanfeldt M, et al. (2012) Local insufflation of warm humidified CO_2 increases open wound and core temperature during open

colon surgery: a randomized clinical trial. Anesthesia and Analgesia; 115: 1204-1211.

Herrmann A, De Wilde RL. (2015) Insufflation with humidified and heated carbon dioxide in short-term laparoscopy: a double-blinded randomized controlled trial. BioMed Research International: 412618.

Jenks M, Taylor M, Shore J. Cost-utility Analysis of the Provision of Warmed Humidified Carbon Dioxide During Open and Laparoscopic Colorectal Surgery. Unpublished.

Kurz A, Sesslet D, Lenhardt R. (1996) Perioperative normothermia to reduce the incidence of surgical-wound infection and shorten hospitalization. Study of Wound Infection and Temperature Group. New England Journal of Medicine; 334: 1209-1215.

Luengo-Fernandez R, Gray A, Rothwell, P. (2012) A population-based study of hospital care costs during 5 years after transient ischemic attack and stroke. Stroke; 43: 3343–3351.

Manwaring JM, Readman E, Maher PJ. (2008) The effect of heated humidified carbon dioxide on postoperative pain, core temperature, and recovery times in patients having laparoscopic surgery: a randomized controlled trial. Journal of Minimally Invasive Gynecology; 15: 161-165.

Mason SE, Kinross JM, Hendricks J, et al. 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. Unpublished.

Noor N, Reynecke D, Hendricks J, et al. (2015) PTH-309 Use of warmed humidified insufflation carbon dioxide to reduce surgical site infections in laparoscopic colorectal surgery: a cohort study. Gut; 64.

Sammour T, Kahokehr A, Hayes J, et al. (2010) Warming and humidification of insufflation carbon dioxide in laparoscopic colonic surgery: a double-blinded randomized controlled trial. Annals of Surgery; 251: 1024-1033.

Weinberg L, Alban D, Pearce B, et al. (2014) 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. Austin LifeSciences Research Week: 52.

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

Appendix B: Comments from professional bodies

Expert advice was sought from experts who have been nominated or ratified by their Specialist Society, Royal College or Professional Body. The advice received is their individual opinion and does not represent the view of the society.

Mr Tan Arulampalam
General Surgeon, Association of Surgeons of Great Britain and Ireland

Dr Jonathan M Cousins
Consultant Anaesthetist Intensivist, Royal College of Anaesthetists

Ms Jane Hendricks
Laparoscopic nurse practitioner, Royal College of Nursing

Dr Mark Harper
Consultant Anaesthetist, Association of Anaesthetists of Great Britain and Ireland

Dr John Andrzejowski
Consultant Anaesthetist, Association of Anaesthetists of Great Britain and Ireland

4 of the 5 experts have used the device in question and all four thought it a significant modification of existing technology (one expert ticked thoroughly novel as well). All agreed that there was no current comparator in the NHS. The experts with experience of HumiGard had used it in laparoscopy and all claimed better outcomes using HumiGard. The experts indicated that outcomes to support its use may be difficult to quantify (e.g. pain measures) but all said its use would be uncontroversial and all appeared unaware of any published research evidence to support the heating and humidification of insufflant gas in laparoscopy.

Appendix C: Comments from patient organisations

The following patient organisations were contacted and no response was received.

- Beating Bowel Cancer
- Bowel Cancer UK
- British Cardiac Patients Association (BCPA)
- British Heart Foundation
- British Obesity Surgery Patients Association (BOSPA)
- Cardiac Risk in the Young (CRY)
- Cardiovascular Care Partnership (UK)
- Colostomy Association
- Crohn's and Colitis UK (NACC)
- IA (Ileostomy and Internal Pouch Support Group)
- Pumping Marvellous
- Royal College of Surgeons of England
- The Somerville Foundation (Previously Grown Up Congenital Heart Patients Association)

Appendix D: Technical evidence

Appendix E: Additional cost analyses carried out by External Assessment Centre

Specification for further work as agreed with Amber Young (MTAC lead), Alan Wailoo, Cynthia Iglesias and Peter Groves:

Undertake sensitivity analyses on the de novo economic model varying the following parameters:

Surgery type	**Source of complications**	**Source of effectiveness**	**Estimate of SSI cost**	**Difference in stroke risk (%)**
Open	Billeter	Frey	£9,141.60 £1,080.69	A range will be provided
Lap	Billeter	Mason	As above	As above
Lap	Mason	Mason	As above	NA