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Expert Review of Pharmacoeconomics & Outcomes Research

ISSN: 1473-7167 (Print) 1744-8379 (Online) Journal homepage: https://www.tandfonline.com/loi/ierp20

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To cite this article: Michelle Jenks, Matthew Taylor & Judith Shore (2017) Cost-utility analysis of the insufflation of warmed humidified carbon dioxide during open and laparoscopic colorectal surgery, Expert Review of Pharmacoeconomics & Outcomes Research, 17:1, 99-107, DOI: 10.1080/14737167.2017.1270759

To link to this article: https://doi.org/10.1080/14737167.2017.1270759

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EXPERT REVIEW OF PHARMACOECONOMICS & OUTCOMES RESEARCH, 2017
VOL. 17, NO. 1, 99–107
http://dx.doi.org/10.1080/14737167.2017.1270759

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ORIGINAL RESEARCH

Cost-utility analysis of the insufflation of warmed humidified carbon dioxide during open and laparoscopic colorectal surgery

Michelle Jenks, Matthew Taylor and Judith Shore

York Health Economics Consortium, Enterprise House, Innovation Way, University of York, York, UK

ABSTRACT

Background: An evaluation was conducted to estimate the cost-effectiveness of insufflation of warmed humidified CO_2 during open and laparoscopic colorectal surgery compared with usual care from a UK NHS perspective.

Methods: Decision analytic models were developed for open and laparoscopic surgery. Incremental costs per quality-adjusted life year (QALY) were estimated. The open surgery model used data on the incidence of intra-operative hypothermia and applied risks of complications for hypothermia and normothermia. The laparoscopic surgery model utilised data describing complications directly. Sensitivity analyses were conducted.

Results: Compared with usual care, insufflation of warmed humidified CO_2 dominated. For open surgery, savings of £20 and incremental QALYs of 0.013 were estimated per patient. For laparoscopic surgery, savings of £345 and incremental QALYs of 0.001 per patient were estimated. Results were robust to most sensitivity analyses.

Conclusions: Considering the current evidence base, the intervention is likely to be cost-effective compared with usual care in patients undergoing colorectal surgery.

ARTICLE HISTORY
Received 7 July 2016
Accepted 7 December 2016

KEYWORDS
Cost utility analysis; economic evaluation; colorectal surgery; hypothermia

1. Introduction

Patients requiring surgery under general and regional anesthesia are at risk of developing unintentional perioperative hypothermia, defined as a core body temperature below 36°C [1]. Heat loss can occur as a consequence of radiation of heat from the patient's body to the surrounding room as well as convection caused by the movement of air. Heat and moisture are also lost by evaporation of the serous fluid layer in both laparoscopic and open surgery (laparotomy) [2]. Exposure of the skin, internal body tissues, and organs to the atmosphere intraoperatively can increase heat loss leading to increased incidence of hypothermia during surgery and increased postoperative morbidity [3]. Studies have shown that perioperative hypothermia is linked with an increased risk of cardiac complications [4,5], surgical site infections [4,6], and an increased risk of mortality [4]. Therefore, maintaining perioperative normothermia is essential for preventing potential complications.

The National Institute for Health and Care Excellence (NICE) published clinical guidance on inadvertent perioperative hypothermia in 2008 (CG56) [7] and recommended that patients should have their temperature monitored throughout the perioperative phase. All patients having anesthesia for longer than 30 min should be warmed intraoperatively from induction of anesthesia via forced air warming. They further recommended that for those patients at increased risk of developing hypothermia, prophylactic warming via forced air warming should be carried out where anasthesia is less than 30 min. Patients defined as higher risk included those with two or more of the following characteristics: American Society of Anesthesiologists grade II–V, preoperative temperature below 36.0°C (with preoperative warming not possible due to clinical urgency), undergoing combined general and regional anesthesia, undergoing major or intermediate surgery, at risk of cardiovascular complications [7].

The NICE guidance acknowledges that multiple methods of perioperative warming exist. However, at the time of writing the guidance, limited clinical evidence was available on such methods [7].

The HumiGard™ surgical humidification system (F&P HumiGard, Fisher & Paykel Healthcare Ltd., Auckland, New Zealand) provides local insufflation of warmed (37°C), fully humidified CO_2 into the peritoneal cavity during laparoscopic surgery, as well as into the open wound during laparotomy. This is in comparison to local insufflation of room temperature, non-humidified CO_2 in laparoscopic surgery, and no intervention in open surgery. The system is used in conjunction with other heating methods, such as forced air warming blankets, and is designed to reduce the incidence of intra and postoperative hypothermia. Clinical studies have shown that, in patients undergoing elective open colorectal surgery, insufflation of warmed humidified CO_2 significantly reduces the incidence of hypothermia, in comparison to the standard insufflation of CO_2 at room temperature (20–22°C) and 0.02%

CONTACT Michelle Jenks michelle.jenks@york.ac.uk York Health Economics Consortium, Enterprise House, Innovation Way, University of York, Heslington, York YO10 5NQ, UK

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moisture content [8]. In patients undergoing elective laparoscopic colorectal surgery, insufflation of warm-humidified CO_2 into the peritoneal cavity significantly reduces the risk of surgical site infections [9]. Participants in these clinical studies typically underwent surgery of longer than 30-min duration and should, therefore, undergo prophylactic warming during their surgery according to the criteria specified within the NICE guidance. Systematic reviews, including a Cochrane review, of warmed humidified CO_2 comprising both studies relating to the HumiGard surgical humidification system and other devices within the same class suggest that the evidence relating to the impact of warmed humidified CO_2 on temperature status is mixed [10,11]. However, the Cochrane review contains an extraction error in temperature status from one of the included studies and since its publication in 2011 further studies have been published. The more recent review, by Balayssac et al., demonstrated a small beneficial effect of warmed humidified CO_2 on per procedure hypothermia [10].

The objective of this study was to estimate the cost-effectiveness of the use of warmed humidified CO_2 during open and laparoscopic surgery compared with usual care from a UK NHS perspective. A cost-utility analysis based upon quality-adjusted life years (QALYs) was conducted using data directly related to the HumiGard surgical humidification system.

2. Methods

2.1. Model: open surgery

A Microsoft Excel®-based decision analytic model was developed to estimate the cost-effectiveness of the use of warmed humidified CO_2 insufflation versus doing nothing in patients undergoing open surgery (Figure 1). The model was run based on 200 patients using the therapy in each year of the 5-year lifetime of the device. This number was informed by the likely capacity for use of the device and was varied during sensitivity analysis. All patients undergoing colorectal surgery were at risk of hypothermia and a number of complications following surgery, with the risk of each complication being dependent on the patient's temperature status. The complications were not mutually exclusive. For each complication, a cost and QALY loss, or disutility, were applied. In the base case, these were applied over a 1-year time horizon, with a 5-year time horizon considered during scenario analyses.

2.2. Model: laparoscopic surgery

A second decision analytic model was developed in Microsoft Excel® to estimate the cost-effectiveness of local insufflation of warmed humidified CO_2 versus usual care in patients undergoing laparoscopic surgery (Figure 2). In laparoscopic patients, usual care comprises local insufflation of cold (i.e. room temperature), non-humidified CO_2. Again, the model was run based on 200 patients per year using the therapy. The structure of the laparoscopic surgery model was simple, with patients undergoing surgery at risk of surgical site infection or pneumonia. The model was based on data from a recent clinical study in the NHS [9]. The risk of each complication depended on whether, or not, there had been insufflation of warmed humidified CO_2 during surgery. As with the open surgery model, the complications were not mutually exclusive and had a cost and QALY loss applied, over a 1-year time horizon in the base case. An exploratory analysis was conducted, whereby the open surgery model structure shown in Figure 1 was utilized for laparoscopic surgery in order for alternate clinical data to be included, as described under 'effectiveness parameters.'

2.3. Model input parameters and data sources

Baseline values for the model input parameters (Table 1 – supplementary material) were identified through searches of

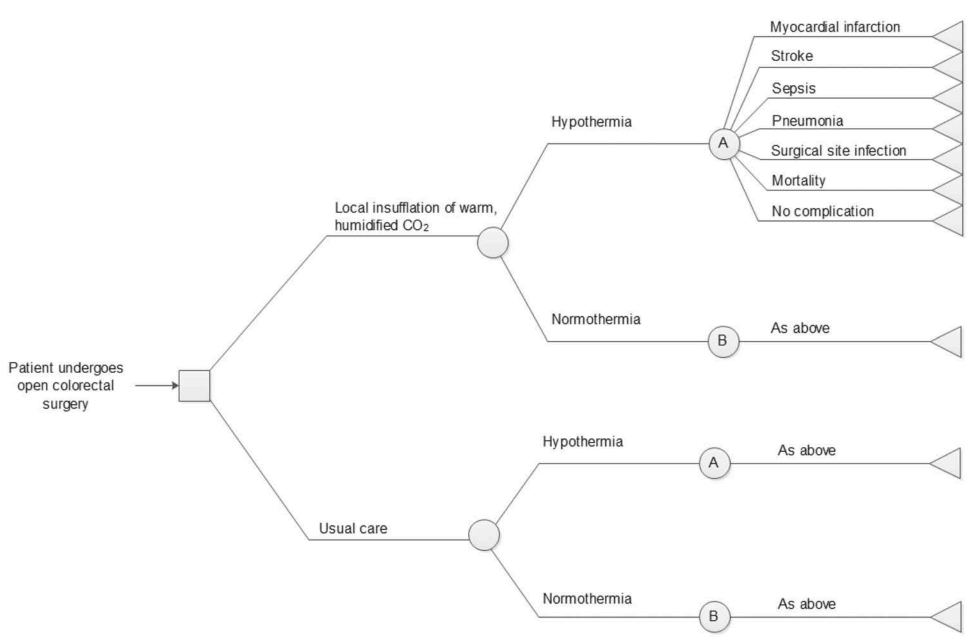

Figure 1. Decision analytic model for open surgery.

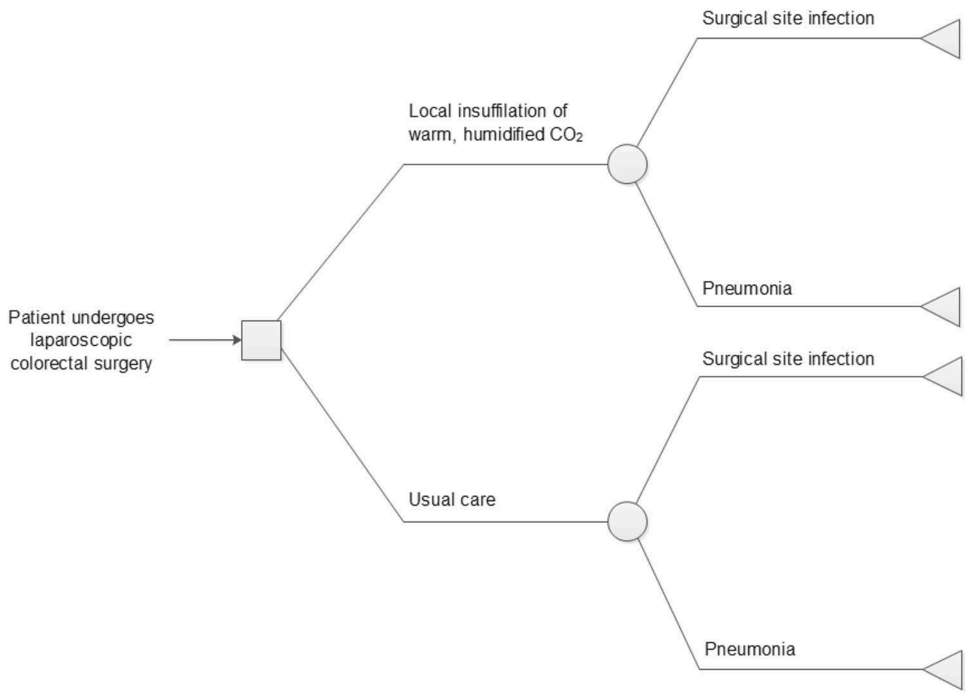

Figure 2. Decision analytic model for laparoscopic surgery.

Table 1. Base case results for open and laparoscopic colorectal surgery patients.

	Local insufflation of warmed humidified CO_2	Usual care	Difference	Incremental cost-effectiveness ratio
Open surgery patients				
Device cost per person	£102	£0	£102	
Complication costs per person	£343	£465	−£121	
Total cost per person	£445	£465	−£20	
QALYs lost per person	0.023	0.036	−0.013	Dominant
Laparoscopic surgery patients				
Device cost per person	£78	£5	£73	
Complication costs per person	£313	£739	−£427	
Total cost per person	£391	£744	−£354	
QALYs lost per person	0.0004	0.0010	−0.0006	Dominant

QALY: Quality-adjusted life year.

published literature sources. The distribution and range considered during both deterministic and probabilistic sensitivity analyses were based on reported confidence levels or conservative assumptions.

2.3.1. Effectiveness parameters

Effectiveness data around the use of warmed humidified CO_2 during both open and laparoscopic surgery were obtained from published clinical studies. Frey et al. reported on a randomized controlled trial (RCT) in which patients (n = 83) undergoing elective open colon surgery were randomized to standard warming (standard care) or standard warming plus the local insufflation of warmed humidified CO_2 during surgery. Both wound and core temperatures were recorded before, during, and after surgery. At the end of surgery, the two groups differed significantly (p = 0.005) in core temperature. None of the intervention group had a temperature below 36°C, whilst seven patients (18%, 95% CI 5–31%) in the control group had a temperature below 36°C [8]. These data on the proportion of patients who were hypothermic were used to model the risk of a number of complications following surgery.

Billeter et al. retrospectively reviewed hospital records to identify the outcomes of 707 patients who became unintentionally hypothermic during elective surgery. The majority of patients underwent open surgery. These patients were matched with 698 patients with normothermia in order to identify complications associated with hypothermia. This comparison identified significant differences in the probability of experiencing the majority of complications (including mortality, myocardial infarction, stroke, sepsis, and pneumonia) included within the model structure [4]. However, the study population is not fully applicable to the modeled population, since 10% of patients included in the study underwent colorectal surgery with a further 20% undergoing undefined general surgical procedures (personal communication with authors). Therefore, at least 70% of patients within the study did not undergo colorectal surgery. Patients undergoing open heart surgery were excluded. In the model's base case, these data have been assumed to be applicable to patient's undergoing colorectal surgery. Further, Billeter et al. defined hypothermia as a core temperature below 35°C [4], i.e. severe hypothermia, thus excluding mild hypothermia. This is inconsistent with the RCT [8] and, as such, the number of patients within the model experiencing complications may be inaccurate. The impact of both assumptions was tested through sensitivity and scenario analyses.

Given the potential limitations outlined above with the applicability of the data from Billeter et al. [4], scenarios were run using surgical site infection data from three additional sources identified through a targeted review of the literature. In each of these scenarios, the model was run using surgical site infection data only, meaning that the probability of all other complications was 0% for both normothermic and hypothermic patients. Data from three studies were used, in which patients were categorized by hypothermia or normothermia and the number of surgical site infections in each group quantified. No other complications were considered. First, Kurz et al. included patients undergoing colorectal surgery (n = 200); in the hypothermia group, 19% developed surgical site infections, whilst in the normothermia group, 6% developed surgical site infections (p = 0.009) [6]. Second, Flores-Maldonado et al. included patients undergoing cholecystectomy primarily through open surgery (n = 261), finding in the hypothermia group 11.5% developed surgical site infections, compared with 1.9% in the normothermia group (p = 0.004) [12]. Finally, Anannamcharoen et al. included patients undergoing open colon and rectal resections (n = 229) and found that 17.6% of normothermia patients developed a surgical site infection compared with 30.8% of hypothermia patients (p = NR) [13].

Effectiveness data regarding the use of local insufflation of warmed humidified CO_2 during laparoscopic surgery were obtained from a retrospective cohort study of 246 patients reported by Mason et al. [9]. The incidence of surgical site infections and pneumonia was analyzed before and after the introduction of the therapy. Following the introduction of the warm-humidified CO_2 for insufflation, the incidence of surgical site infections was significantly reduced from 13.0% to 5.1% (odds ratio = 0.34; p = 0.04) [9]. There was also a nonsignificant reduction in the incidence of pneumonia from 3.2% to 0.8% (p = 0.21) [14]. Due to the before and after nature of this study, it is subject to potential bias and, therefore, extensive sensitivity analyses were carried out. These analyses included using data obtained from Sammour et al. [15] on temperature status and using the open surgery model structure. Whilst Sammour et al. did not report the number of patients who were hypothermic post-surgery (the study was primarily pain based), the data were provided following direct communication with the authors [15]. At a cutoff of 36°C, 5 of 35 patients in the warmed humidified CO_2 arm were hypothermic versus 9 of 39 in the control group. At a cutoff of 35°C, 0 of 35 patients in the warmed humidified CO_2 arm was hypothermic versus 3 of 39 in the control group. Data from Mason et al. show the incidence of hypothermia to be significantly higher in the control arm compared with the warmed humidified CO_2 arm (57% vs. 13.0%; p < 0.001) [9].

2.3.2. Disutilities

Disutilities were applied within the model to those patients experiencing complications. For myocardial infarction, stroke, and mortality, the reduction in quality of life was deemed to be permanent, and as such, an annual disutility was applied in each year of the model's duration (1 year in the base case) for patients experiencing these complications. For the remaining complications, a one-off disutility was applied regardless of the model time horizon, such that after an initial decrement, quality of life returned to normal. All disutilities were derived from the published literature except for mortality. In the base case, this was assumed to be 0.5 per year, given that patients undergoing colorectal surgery are likely to have diseases such as cancer and bowel disease [8], meaning their quality of life is lower than that of the average person. This assumption was varied during sensitivity analysis.

2.3.3. Costs

Complication costs were obtained primarily from 2013/14 NHS reference costs. Because complications may have occurred either during the initial hospital stay or during a second visit, total HRG costs were utilized. Costs obtained from older sources were inflated to 2013/14 prices using the hospital and community health services index [16].

For stroke and myocardial infarction, both an initial cost for hospital stay and treatment, and a cost for longer term management of the condition, were applied. The longer term management cost was an annual cost so that in scenarios where a longer time horizon is considered, the management cost was discounted and applied each year. In the first year, both the initial cost and the annual management costs were applied. The remaining complications incurred initial costs only.

The cost of a surgical site infection was taken from a recent study conducted in one NHS hospital comprising data on 282 surgical site infections [17]. Whilst costs were categorized by wound type, the average overall cost was used in the model given the small sample size in many of the categories.

It was conservatively assumed that no cost should be attributed to mortality, as advice from clinical experts suggested that these patients were already likely to be in hospital following their colorectal surgery or a subsequent complication. All complication costs were varied during sensitivity analyses.

The HumiGard system comprises both a multiuse humidifier with a life span of at least 5 years and a consumable gas-conducting circuit used during open and laparoscopic surgery. The cost of the humidifier was applied based upon the number of patients using the device each year over its 5-year lifetime. Nurses using the device require training which typically involves a 7.5-h training course for one senior nurse per hospital. More recently, short training sessions to a number of nurses at hospital audit days have been provided. In the base case, 25 h of nurse time per device was included for training; this was varied in sensitivity analysis to capture the different methods of training delivery.

2.4. Model outcomes

The primary outcome of the model is the incremental cost-effectiveness ratio (ICER). This was determined by calculating the incremental costs (total expected costs with insufflation of warmed humidified CO_2 minus total expected costs with standard care) and dividing these by the incremental QALYs (total expected QALYs with insufflation of warmed humidified CO_2

minus total expected QALYs with standard care). The information used to generate the ICER was combined with the cost-effectiveness threshold (cost per QALY) to determine net monetary benefit. A cost-effectiveness threshold of £20,000 per QALY was used.

2.5. Sensitivity analyses

Sensitivity and scenario analyses were conducted to test the impact on the results of the assumptions used within the model. Extensive univariate deterministic sensitivity analyses were conducted around the inputs from both models. This involved varying model inputs individually and assessing their impact on the results of the model. Probabilistic sensitivity analysis based on 2000 iterations of each model was conducted to explore combined model parameter uncertainty. During each model iteration, a random set of inputs was drawn based upon statistical distributions around the mean value of each parameter. The statistical distributions used reflected the extent of uncertainty in each input parameter and are shown in Table 1 – supplementary material.

A number of scenario analyses were conducted: (1) the time horizon of the costs and QALY loss associated with each of the complications was varied, with results reported at 5 years; (2) the open surgery model was run using the data from three alternative clinical event data sources as detailed previously [6,12,13]; and (3) the impact of not attributing QALY loss and costs to all complications for the open surgery model was investigated through multiway sensitivity analysis. This involved setting the majority of costs and disutilities to zero and identifying threshold values for the model's key drivers and (4) a scenario combining 70% laparoscopic surgery patients and 30% open surgery patients was considered where 75 and 200 patients use the humidifier each year. Finally, the open surgery model structure (Figure 1) was utilized to conduct an exploratory analysis for laparoscopic surgery patients in order to make use of alternate clinical data pertaining to their hypothermia status [15]. Authors of further studies reporting on temperature change in patients undergoing laparoscopic surgery with or without warmed humidified CO_2 were contacted to provide data on the proportion of patients classified as being hypothermic, but no responses were received [18,19].

3. Results

3.1. Base case results

Local insufflation of warmed humidified CO_2 during surgery dominates usual care for patients undergoing either open or laparoscopic colorectal surgery (Table 1). Estimated cost savings of £20 per open surgery patient and £354 per laparoscopic surgery patient are generated with local insufflation of warmed humidified CO_2 compared with standard care due to decreased incidence of complications. Fewer QALYs are lost when using the therapy compared to usual care. Specifically, use of local insufflation of warmed humidified CO_2 led to an increase of 0.013 QALYs per patient for open surgery patients and 0.001 QALYs per patient for laparoscopic surgery patients. Based on a cost-effectiveness threshold of £20,000 per QALY, the average net monetary benefit per patient is estimated to be £282 per open surgery patient and £366 per laparoscopic surgery patient.

3.2. Deterministic sensitivity analysis results

Univariate deterministic analyses were conducted based on the ranges shown in Table 1 – supplementary material and the analyses indicated that the direction of results is robust to changes in most inputs (Figure 3). The model's results in open surgery patients are sensitive to the proportion of patients with hypothermia in each group and the probability of mortality with hypothermia. Two-way sensitivity analysis showed that in order for local insufflation of warmed humidified CO_2 to be cost-effective at a £20,000 per QALY threshold, there must be an absolute reduction

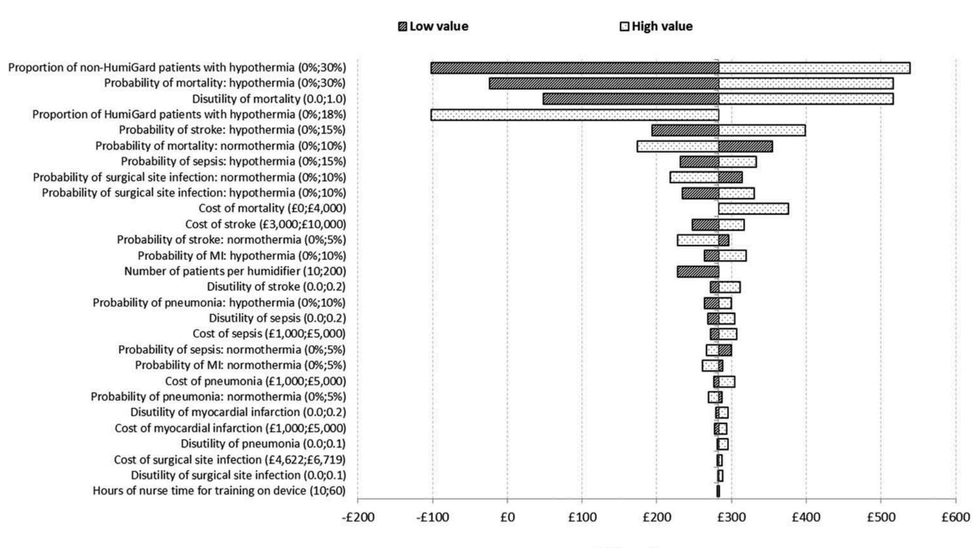

Figure 3. Univariate sensitivity analyses in open surgery patients.
MI, Myocardial infarction.

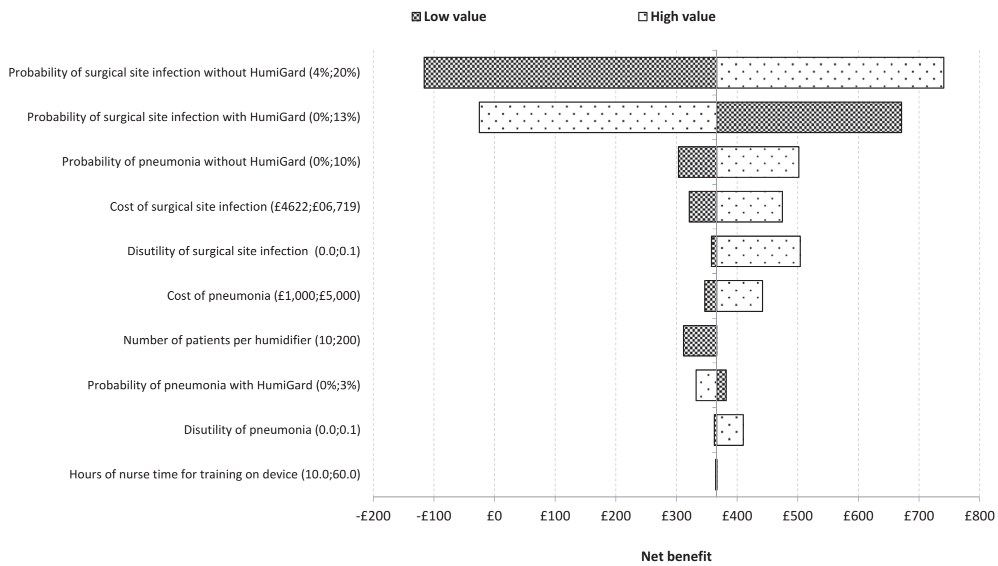

Figure 4. Univariate sensitivity analyses in laparoscopic surgery patients.

in hypothermia of at least 5%. Where the probability of mortality in patients with hypothermia is at an extreme value of 1.3% (well below the baseline value of 4% in normothermia patients), local insufflation of warmed humidified CO_2 is not cost-effective at a £20,000 per QALY threshold.

Univariate sensitivity analyses results for laparoscopic patients indicate that the model's results are robust to changes in all parameters except the probability of surgical site infection with either intervention at a threshold of £20,000 per QALY (Figure 4). Where the absolute difference in the probability of surgical site infection between the treatment and comparator is at 0.5% or below, local insufflation of warmed humidified CO_2 is not cost-effective.

3.3. Probabilistic sensitivity analyses results

Probabilistic sensitivity analyses were conducted for both open and laparoscopic surgery patients. At a threshold of £20,000 per QALY, local insufflation of warmed humidified CO_2 was cost-effective in 99.6% of iterations for open surgery patients. Of the 2000 iterations, 62.5% fell in the southeast quadrant (indicating the intervention is both more effective and less costly) and 37.6% in the northeast quadrant (indicating the intervention is more effective, but more costly). For laparoscopic surgery patients, local insufflation of warmed humidified CO_2 was cost-effective in 97.0% of iterations at a £20,000 threshold with 96.8% of iterations falling in the southeast quadrant (indicating the intervention is both more effective and less costly), 2.6% in the northeast quadrant (indicating the intervention is more effective, but more costly), 0.0% in the southwest quadrant (indicating the intervention is less effective, but less costly) and 0.7% in the northwest quadrant (indicating the intervention is both less effective and more costly). Note: values do not add to exactly 100% due to rounding.

3.4. Scenario analyses results

3.4.1. Time horizon

Extending the time horizon of the model, i.e. extending the length of time that the costs and disutilities associated with certain complications were applied for, results in the use of local insufflation of warmed humidified CO_2 in open surgery patients becoming increasingly cost-effective. Where a 5-year time horizon was considered, a net benefit of £1338 per open surgery patient was generated (at a £20,000 per QALY threshold). Probabilistic analyses found warmed humidified CO_2 to be cost-effective in 100% of iterations at a £20,000 threshold. All iterations fell either in the southeast (96.9%) or northeast (3.1%) quadrant. Changing the time frame did not impact on the results of the model for laparoscopic patients as there were no long-term costs and disutilities incorporated for pneumonia or surgical site infection.

3.4.2. Use of alternative effectiveness data for open surgery

The model was run using data from the three alternative data sources reporting on the impact of hypothermia or normothermia on surgical site infections in people undergoing either colorectal or gall bladder surgery (none of the three sources reported on other complications of hypothermia) [6,12,13]. Local insufflation of warmed humidified CO_2 remained dominant versus standard care in open surgery patients in two of the three scenarios. Using data from Kurz et al. [6] result in a net monetary benefit of £23 per patient. Probabilistic analysis shows that local insufflation of warmed humidified CO_2 is cost-effective in 56.2% of iterations at a £20,000 threshold and dominant in 54.7% of iterations. Where alternate data from Flores-Maldonado et al. [12] are used, a net benefit of −£9 per patient is generated and probabilistic analyses demonstrate that the intervention is cost-effective in 35.9% of iterations at a £20,000 threshold and dominant in 34.4% of iterations. When data from

Anannamcharoen et al. are used [13], a net monetary benefit of £25 per patient is generated. Probabilistic analyses found that local insufflation of warmed humidified CO_2 is cost-effective in 58.6% of iterations at a £20,000 threshold and dominant in 57.2% of iterations.

3.4.3. Complication costs and disutility

Multiway sensitivity analyses of costs and disutilities of complications were conducted. In open surgery patients, provided that a disutility of mortality of at least 0.22 is included within the model, the ICER remains below the £20,000 threshold. This is the case where the costs and disutilities associated with all other complications are set to zero.

The model's results are robust to changes in the disutilities and costs of complications for laparoscopic surgery patients. Provided that a cost of at least £1000 is incurred for a surgical site infection, no disutilities or costs for other complications need to be incurred for the humidifier to remain dominant over usual care. A cost of £1000 is below the value identified for any surgical site infection resulting from any surgical category [17]. Therefore, for both open and laparoscopic patients, the model was robust to any potential double counting of loss of quality of life or costs incurred from complications.

Finally, throughout the base case modeling, complications were not mutually exclusive. From the raw data set of the retrospective cohort study in laparoscopic patients [9], it could be determined that one patient in the usual care arm experienced both pneumonia and a surgical site infection. When this patient was excluded from the probability of surgical site infection, the therapy remained dominant over usual care. As this information was not available for open surgery, the same analysis could not be conducted in this patient group.

3.4.4. Combined open and laparoscopic patient group

The results of the two models were combined to estimate the cost-effectiveness of the use of the humidifier in a patient population, whereby 70% underwent laparoscopic surgery and 30% underwent open surgery. Based on 200 patients using the device each year, use of the humidifier dominated usual care, with a net monetary benefit of £341 per patient. The probabilistic results showed the humidifier to be cost-effective at a £20,000 threshold in 99.5% of iterations. Where only 75 patients used the humidifier each year, it remained dominant with a net monetary benefit of £336 per patient and was cost-effective in 98.9% of iterations.

3.4.5. Use of open surgery model structure for laparoscopic surgery patients

The open surgery model structure was utilized to make use of RCT data reporting on the temperature status of laparoscopic surgery patients from Sammour et al. [15]. These data were obtained from the author directly, given that the required data were not included within the publication of the study which was primarily focused on pain. Further, no clinical evidence sources reporting on clinical events in patients undergoing laparoscopic patients specifically were identified; hence, the sources used in the open surgery model had to be utilized, resulting in a further limitation of this analysis [4,6,12,13]. The costs and disutility assigned to each of the complications were also in line with those used in the open surgery model as reported in Table 1 – supplementary material. Running the model using data from Billeter et al. [4] and temperature data specific to laparoscopic patients at a 35°C cutoff resulted in a net monetary benefit of £91 over a 1-year time horizon and £542 over a 5-year time horizon (based on a £20,000 per QALY threshold). Probabilistic sensitivity analysis estimates an 81.4% probability of being cost-effective at 1 year and 98.4% probability at 5 years. Running the model using data limited to surgical site infections (hence a worst case scenario) and temperature data specific to laparoscopic patients at a 36°C cutoff results in a net monetary benefit of between −£11 and −£27 depending on the data source used [6,12,13]. These results are highly uncertain, with probabilistic results demonstrating cost-effectiveness in around 38% of model iterations, due to the small differences in both incremental QALYs and costs. Where data on hypothermia incidence from Mason et al. [9] are used, warmed humidified CO_2 consistently dominates over usual care.

4. Discussion

Prior clinical studies have demonstrated that local insufflation of warmed humidified CO_2 during colorectal surgery is effective at reducing the incidence of perioperative hypothermia [8,15]. This study expands on this finding by estimating the cost-effectiveness of the use of a humidifier compared with standard care (i.e. insufflation with cold-dry CO_2) in patients undergoing colorectal surgery. The humidifier was found to dominate over standard care, with an estimated net monetary benefit per patient of £282 per open surgery patient and £366 per laparoscopic surgery patient. This finding is consistent with a previous cost-effectiveness analysis of an alternate method of perioperative warming [20]. Consistent with current guidance (CG65) [7], the results of this study highlight the need to carry out prophylactic measures to avoid unintentional perioperative hypothermia during colorectal surgery.

Based on sensitivity and scenario analyses, the results in open surgery patients are sensitive to the incidence of perioperative hypothermia in patients in each group. In order for local insufflation of warmed humidified CO_2 to be cost-effective, a 5% absolute reduction in postoperative hypothermia is required. A study in open surgery patients (18%, 95% CI 6–30%) found the absolute reduction in hypothermia (defined as temperature below 36°C) to be significantly greater than 5% [8]. However, hypothermia was defined by Billeter et al. as a temperature below 35°C (i.e. severe hypothermia) in their analysis of complications [4], and hence this discrepancy is a limitation of this analysis. This limitation was explored through the use of alternative complication data, based on surgical site infections only [6,12,13]. The direction of the results changed in one of the three scenarios. However, all three sources omitted relevant clinical consequences of hypothermia and thus would be expected to underestimate cost savings and QALY gains.

A second limitation of both the laparoscopic and open surgery analyses was that a cost and disutility associated with each complication was applied independently, due to a paucity of identified data reporting the cost and utilities of patients with multiple complications. Therefore, the potential exists for double counting of costs and quality-of-life decrement in patients who experienced multiple complications. For open surgery patients, the incidence of multi-complication patients is unknown. However, for laparoscopic patients, this was determined from the data set and only affected one patient; hence, any impact of double counting on the model's results was negligible. A scenario analysis for open surgery patients showed that the model's results were highly robust to multiway sensitivity analyses around the costs and disutilities of complications. Both analyses were limited, in that the follow-up period during which the incidence of complications was measured exceeded 1 year [4,9]. Within the model, it was assumed that complications occurred soon after surgery with a cost and QALY loss applied immediately. Therefore, costs and disutilities were not discounted. This simplifying assumption was made given that the time point for each complication incidence was unknown. From the sensitivity analyses undertaken, the model's results appear robust to changes in complication costs and disutilities and, therefore, it is anticipated that this simplification would have a negligible impact on results.

Third, univariate sensitivity analysis conducted on the laparoscopic model identified the probability of surgical site infection in usual care patients to be the key driver of the analysis. Where the absolute difference between treatment groups is equal to or less than 0.5%, local insufflation of warmed humidified CO_2 is no longer cost-effective. Data from four studies show that perioperative hypothermia is associated with increased risk of surgical site infection [4,6,12,13] and, therefore, the plausibility of the absolute difference in probability of surgical site infections being just 0.5% is likely to be low. Scenario analyses conducted on the structure of the laparoscopic model demonstrated uncertainty in the model's results. These analyses were limited by the generalizability of the clinical evidence to patients undergoing laparoscopic colorectal surgery within the UK NHS.

Finally, the robustness of all economic models is dependent upon the internal and external validity of the clinical studies used to populate the model. RCT data were used as far as possible in order to mitigate against confounding factors influencing temperature status with or without warmed humidified CO_2. However, within these studies, some nonstatistically significant differences between group characteristics remained. Extensive sensitivity and scenario analysis were conducted to assess any potential bias introduced by these variations and by any potential bias introduced through the use of data from less optimal clinical study designs. These analyses showed that warmed humidified CO_2 remained cost-effective throughout the majority of analyses conducted.

From a UK NHS perspective, local insufflation of warmed humidified CO_2 during open and laparoscopic colorectal surgery using the HumiGard surgical humidification system is estimated to dominate over usual care since lower costs and greater QALYs are generated in the majority of scenarios considered.

Key issues

- Previous guidance from the National Institute for Health and Clinical Excellence published in 2008 recommended that patients should have their temperature monitored throughout the perioperative phase. They further recommended that for those patients at increased risk of developing hypothermia, prophylactic warming via forced air warming should be carried out.
- The guidance acknowledged that multiple methods of perioperative warming exist, but at the time of writing limited clinical evidence was available on such methods.
- Several clinical studies conducted since 2008 have shown that insufflation of warmed humidified CO_2 (using the HumiGard^{TM} surgical humidification system) during open and laparoscopic colorectal surgery is effective in reducing peri-operative hypothermia and other post-operative complications including surgical site infections.
- This paper demonstrates that insufflation of warmed humidified CO2 during open and laparoscopic colorectal surgery is likely to be cost-effective from a NHS perspective.
- The authors are not aware of any other studies that consider the full cost-effectiveness of this intervention in both open and laparoscopic surgery patients.
- The paper provides information relating to the cost-effectiveness of insufflation of warmed humidified CO2 during open and laparoscopic colorectal surgery.

Acknowledgments

The authors are grateful to The ICENI Centre (Colchester Hospital University Foundation Trust and Anglia Ruskin University) for providing clinical data to populate the economic model.

Disclosure statement

In accordance with Taylor & Francis policy and my ethical obligation as a researcher, I am reporting that I receive funding from a company that may be affected by the research reported in the enclosed paper. I have disclosed those interests fully to Taylor & Francis, and I have in place an approved plan for managing any potential conflicts arising from that involvement.

Funding

This manuscript was funded by Fisher & Paykel Healthcare Ltd.

Declaration of interest

All authors are employed by York Health Economics Consortium Ltd. and received funding for health economics consultancy from Fisher & Paykel Healthcare, manufacturers of the HumiGard device. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

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