NICE advice

End-tidal Control software for use with Aisys closed circuit anaesthesia systems for automated gas control during general anaesthesia

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Summary

Effectiveness

End-tidal Control is a gas delivery software option for the GE Healthcare Aisys Carestation and Aisys CS2 anaesthesia delivery systems.

- Five studies compared End-tidal Control with manual gas control: 1 randomised trial (n=200), 2 observational studies (n=3675, n=80), 1 service evaluation (n=489) and 1 audit (population size not described). Three of these 5 studies reported effectiveness outcomes.

- The randomised trial reported that using End-tidal Control resulted in a significant reduction in anaesthetic consumption compared with manual gas control.
- The randomised trial also reported that target anaesthetic concentration was reached faster using End-tidal Control than with manual gas control. One observational study reported that it took longer to reach target anaesthetic concentration with End-tidal Control, but was quicker to maintain steady concentrations.
- The service evaluation reported that the average fresh gas flow using End-tidal Control decreased significantly with increased duration of anaesthesia, resulting in reduced anaesthetic use.

Adverse events and safety

- One observational study (n=80) reported that there were no complications associated with End-tidal Control. Four studies did not report on adverse events or safety.
- Of the 5 reviewed studies, only the randomised trial recorded depth of anaesthesia. However, this was used as an exclusion criterion and not as an outcome measure.
- The audit study survey reported some issues for concern, including difficulty in changing the anaesthetic agent during surgery (not usually done during anaesthesia) and poor performance with circuit leaks.

Cost and resource use

- The End-tidal Control software is an optional addition which is compatible only with Aisys anaesthesia systems, and costs £5,000 to £5,500 depending on whether it is added to an existing system or purchased with a new system. If a new system is purchased, the initial capital cost is approximately £40,000 (list price) per system. There are no additional consumable costs for using End-tidal Control.
- Four of the reviewed studies reported cost and resource use when using End-tidal Control.
- One service evaluation, conducted in the UK, reported that when using End-tidal Control for 20 to 40 minutes, the average cost of sevoflurane reduced by £7.94 per hour (53%), and desflurane by £4.83 per hour (41%).
- One randomised trial conducted in India reported a mean reduction in oxygen, nitrous oxide and sevoflurane consumption using End-tidal Control, equivalent to a £0.64

saving per hour. One observational study conducted in Australia reported that using End-tidal Control led to a mean reduction in the use of anaesthetic (desflurane, sevoflurane, isoflurane) equivalent to a saving of £3.32 per hour. No change in fresh gas (oxygen, nitrous oxide, air) costs was identified.

- One observational study fixed fresh gas flow rates between End-tidal Control and manual gas control groups and found no difference in the consumption of sevoflurane, oxygen or air, and no difference in costs when using End-tidal Control.

Technical factors

- End-tidal Control is designed for use with the anaesthetics desflurane, isoflurane and sevoflurane.
- Three of the reviewed studies reported an overall reduction in key presses, adjustments and anaesthetist interventions when using End-tidal Control.
- One audit study reported the survey results of 18 trainee and 50 specialist anaesthetists who described some advantages of End-tidal Control. These included better control of end-tidal anaesthetic agent concentrations, allowing attention to be directed to other aspects of care.
- One observational study reported a significant reduction in greenhouse gas emissions when using End-tidal Control.

Introduction

Approximately 2.4 million patients in the UK had general anaesthesia in 2007 (NICE 2012). Most patients had a combination of intravenous and inhaled agents to induce and maintain general anaesthesia. Maintenance of inhalational anaesthesia needs an anaesthetist to continually monitor end-tidal (or expired) oxygen and anaesthetic concentrations. The anaesthetist manually adjusts the vaporiser settings, which control the concentration of anaesthetic and fresh gas (oxygen, air, and optionally, nitrous oxide) flow rates to provide adequate anaesthesia.

There are risks associated with manually controlled maintenance of inhalational anaesthesia. These include risk of hypoxia, hypercapnia (also known as hypercarbia), and over- or under-dosage of anaesthetic (Baum and Aitkenhead 1995), with the latter potentially leading to patients regaining a level of consciousness (Schober and Loer 2006).

The 5th National Audit Project by the Association of Anaesthetists of Great Britain and Ireland and the Royal College of Anaesthetists reported 153 cases of accidental awareness during general anaesthesia (including people anaesthetised by inhalational anaesthesia as well as other techniques) in the UK in 2011, representing a risk of 1 in 15,414 general anaesthesia procedures (Pandit et al. 2013).

Automating the process of monitoring and adjusting gas concentrations shortens anaesthetic induction and results in steadier arterial and brain anaesthetic concentrations, stabilising the level of anaesthesia (Sieber et al. 2000). It also minimises the amount of fresh and anaesthetic gas wasted, reducing both healthcare costs and environmental burden (Nunn 2008).

Technology overview

This briefing describes the regulated use of the technology for the indication specified, in the setting described, and with any other specific equipment referred to. It is the responsibility of healthcare professionals to check the regulatory status of any intended use of the technology in other indications and settings.

About the technology

End-tidal Control is a gas delivery software option for the GE Healthcare Aisys Carestation and Aisys CS^2 anaesthesia delivery systems. It monitors and automatically adjusts the levels of anaesthetic concentration in a closed circuit system across a specified flow range of 0.5 to 10 litres per minute. The closed circuit is currently the most widely used form of breathing system in anaesthetic machines, and usually contains integrated gas, pressure and volume-monitoring sensors.

When using End-tidal Control, the anaesthetist sets target end-tidal oxygen concentration, minimum flow rate and target end-tidal anaesthetic concentration. The system monitors these concentrations by sampling gas in the breathing circuit on a breath-by-breath basis. It applies a proprietary algorithm to automatically adjust fresh gas flow and anaesthetic concentrations to ensure that the patient's uptake of oxygen and anaesthetic are maintained at the correct level. The system contains a carbon dioxide absorber to allow the rebreathing of any anaesthetic gases in the exhaled air.

During manual gas control, the anaesthetist controls the concentration of anaesthetic by

monitoring the concentration of gases in the exhaled (end-tidal) air and manually adjusting fresh gas rates (Singaravelu and Barclay 2013).

CE marking

End-tidal Control is part of current system software versions 10 x on the Aisys CS^2 and 8 x on the Aisys Carestation, and is compatible only with the Carestation and CS^2 systems. It is available as a separate standalone software option. These software versions and compatible airway modules were CE marked to GE Healthcare in July 2013 and April 2011 respectively, as class IIb devices.

Description

End-tidal Control is a software option requiring 1 of 3 compatible GE Healthcare airway modules:

- E-series modules (E-CAiO, E-CAiOV, E-CAiOVX) for the Aisys Carestation
- M-series modules (M-CAiO, M-CAiOV, M-CAiOVX) for the Aisys Carestation
- CARESCAPE Respiratory Modules (E-sCAiOE or E-sCAiOVE) for the Aisys CS^2.

The airway module is an optional piece of hardware that slots into the main anaesthesia system and forms part of a closed-loop circuit with gas sampling of the patient's airway, circle and fresh gas concentrations, supplies (including sodalime CO_2 absorber and antibacterial filter) and water trap components. The airway modules are not required for the basic operation of the Aisys systems, but provide additional measurement and monitoring functionality, and their presence is essential for the End-tidal Control option. Module verification tests must be run to confirm correct installation. End-tidal Control is designed for use with the anaesthetics desflurane, isoflurane and sevoflurane, housed in colour-coded vaporiser cassettes. Only 1 anaesthetic cassette can be installed and active at any given time. When all hardware components are correctly installed, calibrated and warmed up, with the system measuring a patient carbon dioxide respiratory rate of 35 breaths per minute or less and registering a minute volume, End-tidal Control is ready for use. The airway module warm-up takes approximately 2 minutes.

The minimum flow rate setting for End-tidal Control provides a patient safeguard by ensuring the gas flow does not fall below the set rate. Increasing the minimum flow does not affect the speed of change to achieve target concentrations.

When active, End-tidal Control includes a number of additional safety mechanisms to protect the patient. These include system checks, fresh gas sampling checks every 3 minutes, leak checks both before starting and during End-tidal Control, and the delivery of increased fresh gas flow, for example, when a leak is detected. Automatic return to active End-tidal Control resumes when the leak is resolved.

End-tidal Control supervisor is an additional safeguard included in End-tidal Control, which monitors set concentration and flow rates against actual measured values to prevent incorrect delivery of oxygen and anaesthetic. If the End-tidal Control supervisor detects any system failures, this results in automatic exit from End-tidal Control mode. Some issues, for example calibration of the airway module, need anaesthetist input. Manual re-entry into End-tidal Control mode is then needed when these issues are resolved. The system creates an End-tidal Control log that records actions, settings and measurements for later review.

Intended use

End-tidal Control is intended for use during inhalational anaesthesia and needs a controlled patient airway to be in place, for example an endotracheal tube or laryngeal mask airway.

End-tidal Control cannot be used with a face-mask airway, or with halothane as the anaesthetic agent, or while the module is in non-circle circuit, cardiac bypass, alternate oxygen, and air-only modes. It is recommended that End-tidal Control is not used during surgical procedures that cause disturbance to the lungs, such as chest surgery. The system may deliver 100% oxygen in End-tidal Control mode, therefore End-tidal Control mode should not be used when delivery of 100% oxygen may injure the patient (for example, in premature neonates in whom excessive inspired oxygen concentrations can cause retinopathy, or in patients with some forms of congenital heart disease). End-tidal Control mode stops if the anaesthetic is changed while the module is active. The manufacturer recommends exiting End-tidal Control mode before changing the anaesthetic. However, it is not routine practice to change anaesthetic agent between the anaesthetic room and the operating theatre.

The manufacturer does not specify a lower age limit for End-tidal Control, however specified respiratory rates (35 breaths per minute or less) must be met, and the system must be registering a minute volume.

Setting and intended user

End-tidal Control is intended for use by an anaesthetist in the anaesthetic room and operating theatre, depending on local facilities.

Current NHS options

General inhalational anaesthesia is delivered and monitored by an anaesthetist. This is currently performed manually by continually altering the fraction of inspired gases, fresh gas flow and vaporiser settings to ensure optimal anaesthesia delivery (Tay et al. 2013) while minimising anaesthetic waste. This approach can be automated using the GE Healthcare Aisys Carestation or Aisys CS^2.

NICE is aware of the following devices that appear to fulfil a similar function to the GE Healthcare End-tidal Control automated gas control option on Aisys anaesthesia delivery systems:

- Zeus IE anaesthesia system (Draeger Medical)
- FLOW-i Anaesthesia Delivery System (Maquet)
- FELIX AInOC anaesthetic station (Air Liquide Medical Systems).

NICE has not investigated the regulatory status of these devices; it is the responsibility of healthcare professionals to check this status for any intended use.

Costs and use of the technology

The list prices for the End-tidal Control components for use with the Aisys Carestation (excluding VAT) are:

List prices for End-tidal Control components

Anaesthetic system	System cost	Cost of purchasing End-tidal Control when ordering system	Cost of adding End-tidal Control to existing system	Cost of additional module (required for End-tidal Control)
Aisys Carestation	Supported by the manufacturer but no longer available for purchase	Not applicable	£5,091	Supported by the manufacturer but no longer available for purchase (E-series module, E-CAiOVX)
Aisys CS2	£40,837	£5,184	£5,429	£11,402 (CARESCAPE Respiratory Module series, E-sCAiOVE)

The M-series airway module is no longer commercially available, but users can still add the End-tidal Control software to existing Aisys Carestation systems fitted with an M-series airway module.

The manufacturer states there are no additional consumables, or specific checks or calibrations needed, to use End-tidal Control.

The manufacturer recommends annual maintenance checks for Aisys systems, including airway module service and calibration. Replacement parts for each annual Aisys service cost less than £10, internal battery replacement costs £180 every 4 years, and the annual airway module service kit costs £135. A fully comprehensive contract for the Aisys CS^2 and End-tidal Control fitted with an airway module is £1,562 per year. This cost can be reduced for customised contracts, tailored to individual customer requirements. The anticipated lifespan of the Aisys Carestation and Aisys CS^2 is 8 to 10 years.

The manufacturer provides training to new users as part of the initial anaesthesia system purchase, including all aspects of the Aisys systems and End-tidal Control. Training records are kept for all attendees and submitted to the hospital on completion of training. Further support is provided in theatre during the first weeks after installation. This includes providing support during the use of End-tidal Control mode in patients having anaesthesia. After initial system training, there is no cost for additional training of new users if requested.

It is anticipated that the End-tidal Control software and necessary hardware (airway module and Aisys anaesthesia delivery system) could be used for inhalational general anaesthesia for many different types of procedure. Therefore it is difficult to precisely quantify the number of patients for whom End-tidal Control could be used. The cost per patient using End-tidal Control would depend on the duration of general anaesthesia, the price of the chosen anaesthetic and the concentration of anaesthetic given.

Likely place in therapy

End-tidal Control is intended to be used in patients having general anaesthesia that is induced and/or maintained by the volatile inhalational agents isoflurane, desflurane or sevoflurane. Because the technology is embedded in existing anaesthesia delivery systems, it will be used in anaesthesia rooms or operating theatres during a surgical procedure, unless contraindicated. Some hospitals may induce anaesthesia in the operating theatre and will therefore need 1 anaesthesia machine with End-tidal Control per patient. However, other hospitals may induce anaesthesia in an anaesthesia room and then use another anaesthesia machine to maintain anaesthesia in the operating theatre, needing 2 anaesthesia machines with End-tidal Control per patient.

Specialist commentator comments

Although there are no data available to describe how many patients have inhalational agents during general anaesthesia, 2 specialist commentators estimated that less than 10% of general anaesthesia patients will have total intravenous anaesthesia, and therefore 90% have some form of inhalational anaesthesia.

Two specialist commentators considered that any clinical and resource benefits of End-tidal Control were unlikely to be realised in brief procedures, in which duration of general anaesthesia was short.

One specialist commentator felt that End-tidal Control would be of little economic benefit to hospitals already practising low-flow anaesthesia, and that it would be difficult to measure whether End-tidal Control would reduce the anaesthetist's workload sufficiently to allow the anaesthetist to focus on other areas of patient care during the course of the anaesthesia. This specialist commentator also felt that quality or depth of anaesthesia should be considered a primary outcome measure, as the ability to automate anaesthesia parameters and achieve these quickly may minimise awareness during anaesthesia,

therefore making anaesthesia safer.

One specialist commentator observed that the randomised trial was conducted in India, where anaesthetic agent costs are much lower than in developed countries. This may account for the difference in costs between this trial and that specified in other publications. A second specialist commentator, with practical experience of End-tidal Control, stated that the main economic burden comes during the wash-in phase of the anaesthetic, when high gas flows are traditionally employed. This is often a busy time clinically, with many distractions, and the anaesthetist often forgets to reduce initial high flows. Therefore the automation of End-tidal Control may be most beneficial here. A third specialist commentator felt that reducing anaesthetic agent and greenhouse gas emissions would have to result in a clear cost benefit in order for End-tidal Control to become widely used.

The use of anaesthetic rooms in UK clinical practice was referenced by 2 specialist commentators as limiting the economic benefits of End-tidal Control. Patient anaesthesia can be induced in the anaesthetic room using 1 anaesthetic (typically isoflurane, which is less costly), before being transferred to the theatre where a more expensive anaesthetic agent (typically desflurane) is used. When a single anaesthesia machine is used per patient, End-tidal Control will not work until the first agent has been washed out of the circuit (using oxygen). This operational delay reduces the economic benefit of the system.

One specialist commentator thought that there is no reason why End-tidal Control cannot be used during cardiac surgery; the user would revert to manual mode during cardiopulmonary bypass and restart End-tidal Control again when the patient was off bypass.

Equality considerations

NICE is committed to promoting equality and eliminating unlawful discrimination. We aim to comply fully with all legal obligations to:

- promote race and disability equality and equality of opportunity between men and women, and
- eliminate unlawful discrimination on grounds of race, disability, age, sex, gender reassignment, pregnancy and maternity (including women post-delivery), sexual orientation, and religion or belief, in the way we produce our guidance. (NB these are

protected characteristics under the Equality Act [2010]).

No equalities considerations were identified for the GE Healthcare End-tidal Control software.

Evidence review

Clinical and technical evidence

Five clinical studies were identified from the literature which investigated the use of End-tidal Control in Aisys anaesthesia delivery systems. These studies included 1 randomised trial (Potdar et al. 2014), 2 prospective observational studies (Tay et al. 2013, Lucangelo et al. 2014), 1 service evaluation (Singaravelu and Barclay 2013) and 1 audit (Kennedy and French 2014).

The randomised trial by Potdar et al. investigated the cost-saving potential and environmental impact of End-tidal Control (n=100) compared with manually-controlled anaesthesia (n=100). Their primary economic findings are described in the published economic evaluation section of this briefing. Analysis of secondary clinical outcomes found significant differences in the time needed to achieve an end-tidal concentration of sevoflurane of 1.5%, maximum inspired concentration of sevoflurane achieved, and the number of adjustments needed to maintain the depth of anaesthesia between End-tidal Control and manual-control groups. A summary of these results is reported in table 1.

The prospective observational study by Tay et al. was a before-and-after study in a single Australian teaching hospital, which evaluated the manual control of end-tidal gases and automated End-tidal Control after planned replacement of anaesthesia systems. Primary outcomes and parameters measured included volatile agent costs, greenhouse gas emissions, carbon dioxide absorbent costs, and fresh gas costs. Secondary outcomes included results from voluntary case reports completed by anaesthetists describing when End-tidal Control had been used, and their reasoning when they had decided against its use. The author described results as 'cases' and not 'patients' to take account of patients who had more than 1 episode of general anaesthesia during the study, that is, multiple cases. Despite 1,865 cases of general anaesthesia (having manual control of end-tidal gases in this study, only 1,036 cases (of the potential 1,810 general anaesthesia cases for whom automated gas control was considered suitable) were explicitly confirmed to have had anaesthesia with End-tidal Control. The study reports a 44% reduction in greenhouse

gas emissions when using End-tidal Control; however, fresh gas flow was different between groups and this may have affected these results. In the voluntary case reports, anaesthetists described four reasons for not choosing to use End-tidal Control which are listed in table 2. The authors discussed several concerns about automated End-tidal Control in children. These included: circle system resistance, dead space, the safety profile of low-flow anaesthesia for children, the possibility of gas leaks associated with uncuffed endotracheal tubes triggering a safety check, exit from the automated control mode, and End-tidal Control defaulting to a high fresh gas flow rate of 6 litres per minute. A summary of the clinical outcomes and results is reported in table 2.

The prospective observational study by Lucangelo et al. aimed to compare oxygen, air and anaesthetic consumption during manual and End-tidal Control anaesthesia, using the same anaesthetic system and identical fresh gas flow between groups. The study included 80 consecutive patients having elective abdominal surgery who were assigned to anaesthesia rooms equipped with anaesthesia systems with (n=40) or without (n=40) End-tidal Control, as determined by scheduling availability. The study found no difference in anaesthetic agent or fresh gas consumption between manual and End-tidal Control groups. However, in the manual-control group the researchers found that a total of 137 interventions were needed by the anaesthetist (including 50 for undershoot and 87 for overshoot, which are transient changes in dosing levels in which the closed-loop control systems overcompensate) to stabilise the end-tidal anaesthetic agent concentration, and 107 interventions to stabilise the end-tidal oxygen concentration. No interventions were reported for the End-tidal Control group. A summary of the results is reported in table 3.

The service evaluation by Singaravelu and Barclay was a UK single-centre study using retrospective information from the event log files stored in Aisys anaesthetic systems. This information was used to compare fresh gas flow rates, inhalational anaesthetic use and the need for user intervention between 168 patients having manual control and 321 patients having End-tidal Control anaesthesia. One retrospectively applied exclusion criterion removed patients from the study who had anaesthesia for less than 10 minutes. This was because insufficient data prevented a full analysis of system performance in the maintenance phase of anaesthesia. The study reported a reduction in average anaesthetic use of 40% to 55% in the End-tidal Control group, and a reduction in the average number of key presses per patient, from 13.6 key presses with manual control to 6.5 with End-tidal Control. A summary of the results is in table 4.

The study by Kennedy and French described data from an audit that monitored fresh gas flow rates within a single department in a New Zealand hospital. This study compared data

retrospectively exported from Datex (now acquired by GE Healthcare) anaesthesia delivery units (from 2001, 2006 and 2009) with detailed event logs retrospectively downloaded from Aisys anaesthesia systems, which had End-tidal Control installed (at 3 specified time periods: June 2011, December 2011, June 2012). A voluntary survey of anaesthetists using the Aisys systems was also done in 2012). Data from 2 other New Zealand hospitals (from 2007 and 2008) also using the Datex anaesthesia delivery units were described and compared. The number of patients included in the audit was not stated. The study reported a general reduction in mean fresh gas flow rates using the anaesthesia delivery units over time: 2.05 litres per minute in 2001, 1.43 litres per minute in 2006 and 1.26 litres per minute in 2009, and that fresh gas flow rates were similar for all 3 New Zealand hospitals described. However, on introduction of the Aisys systems with End-tidal Control, the mean fresh gas flow rate initially increased to 1.50 litres per minute, but dropped to 1.09 litres per minute after 12 months. A summary of the results is in table 5.

Table 1 Summary of the Potdar et al. (2014) randomised trial

Study component	Description
Objectives/ hypotheses	Hypothesis: End-tidal Control anaesthesia is an effective and safe system that would reduce consumption of gases, thus reducing cost and also environmental pollution.
Study design	Prospective, randomised, single-blind study. Randomisation was conducted using a chit-pull system, in which odd numbers were allocated to the manual-control group and even numbers allocated to the End-tidal Control group.
Setting	Single centre (Indian hospital).

Study component	Description
Inclusion/ exclusion criteria	Inclusion criteria: patients having laparoscopic abdominal and pelvic surgery, aged 15 to 75 years, ASA classification of physical health of 1 or 2, surgical procedure with a minimum of 30 minutes and a maximum of 4 hours under general anaesthesia, patient intubated with endotracheal tube and with controlled ventilation, patients maintained only on sevoflurane and not on any other agents such as propofol, midazolam or sedative infusions. Exclusion criteria: general anaesthesia with laryngeal mask airway, face mask, and spontaneous respiration, patients having cardiac, renal, and respiratory diseases, neurological or psychological illness that may interfere with entropy monitoring, ASA classification of 3 or 4, emergency surgery, patients having haemodynamic instability intraoperatively, a variation of pulse or blood pressure more than 20% of baseline or entropy values of less than 40 and more than 60 in the maintenance period of anaesthesia for more than 5 minutes.
Primary outcomes	Time needed to achieve end-tidal concentration of sevoflurane of 1.5%. Maximum inspired concentration of sevoflurane. Number of adjustments needed to maintain depth of anaesthesia (targeting entropy values between 40 and 60, monitored via an additional device).
Statistical methods	Initial sample size was not pre-determined. To ensure adequate sample size, a power calculation was performed retrospectively based on the difference in total cost of anaesthesia per hour between groups. Correlations among different measurements were assessed using Pearson's correlation coefficients. A p value <0.05 was considered statistically significant. A general linear model (ANOVA) was used to investigate and model the effect of various parameters with costs.
Participants	200 patients randomly assigned to End-tidal Control of inhalational agent (n=100), or manual control (n=100).

Study component	Description
Results	Cost saving potential of End-tidal Control results are presented in the published economic evaluation section. **Consumption of oxygen, nitrous oxide and sevoflurane gases** Consumption of nitrous oxide was significantly less in the End-tidal Control group (0.70 litre/minute) than in the manual-control group (0.83 litre/minute), p=0.001. Consumption of sevoflurane was statistically significantly less in the End-tidal Control group than in the manual-control group (0.17 litre/minute vs 0.20 litre/minute), p=0.0001. Oxygen consumption was also less in the End-tidal Control group than in the manual-control group (1.74 litre/minute vs 1.83 litre/minute) but was not statistically significantly different, p=0.21. **Time needed to achieve end-tidal concentration of sevoflurane of 1.5%** There was a statistically significant difference between the 2 groups (3.08 minutes for End-tidal Control vs 13.40 minutes for manual control), p=0.0001. **Maximum inspired concentration of sevoflurane** There was a statistically significant difference between the 2 groups (2.66% for End-tidal Control vs 2.11% for manual control), p=0.0001. **Number of adjustments needed to maintain the depth of anaesthesia** The number of drug delivery adjustments was 3 per patient in the End-tidal Control group. The number of adjustments in the manual-control group varied from 5 to 12. There was a statistically significant difference between the average number of adjustments between the 2 groups, p=0.0001.
Conclusions	The authors concluded that End-tidal Control is a good system for conserving the consumption of gases, and reducing the number of adjustments needed to maintain depth of anaesthesia.

Abbreviations: ANOVA, analysis of variance; ASA, American Society of Anesthesiologists.

Table 2 Summary of the Tay et al. (2013) prospective before-and-after observational study

Study component	Description
Objectives/ hypotheses	Compared with the conventional practice of using manual control in the delivery of volatile agents, the automated control of end-tidal anaesthetic gases in a clinical setting would produce a significant difference in volatile agent consumption cost and the rate of greenhouse gas emissions.
Study design	Prospective before-and-after observational study.
Setting	A single tertiary hospital (teaching hospital in Australia), which included a 12 week manual phase (January to April 2011), followed by a preparation and education phase of 2 months (April to May 2011) to introduce the Aisys Carestation with End-tidal Control to all medical, nursing and technical assistance staff. A 12 week End-tidal Control phase (July to October 2011) was then implemented for comparison.
Inclusion/ exclusion criteria	Inclusion criteria: all patients needing elective or emergency surgery involving general anaesthesia with a volatile agent. Exclusion criteria: patients needing cardiac or neuro surgery, total intravenous anaesthesia, electroconvulsive therapy, sedation and regional anaesthesia without a volatile agent general anaesthetic.
Primary outcomes	Voluntary case report from anaesthetists in End-tidal Control phases. Greenhouse gas emissions.
Statistical methods	Patient baseline characteristics and categorical variables were compared by the chi-squared test and continuous variables were tested for normality and compared by a 2-sample Wilcox on rank-sum (Mann–Whitney) test. Mean differences and 95% confidence intervals were reported. P values <0.05 were considered statistically significant.
Participants	3,675 cases of general anaesthesia. Of these, 1,865 were in the manual phase (age range: 2 months to 94 years), and 1,810 in the End-tidal Control phase (age range: 6 months to 91 years). Of the 1,810 cases in the End-tidal Control phase, 1,169 had voluntary case report forms returned, which indicated End-tidal Control was used in 1,036 cases (and not used in 133 cases).

Study component	Description
Results	Volatile agent cost per hour, carbon dioxide absorbent use/costs and fresh gas costs are presented in the published economic evaluation section. **Voluntary case reports** Reasons reported for not using End-tidal Control included anaesthetists not being aware that End-tidal Control was available to them, quick surgical cases, leaks in the breathing system often as a result of inadequately placed airway device and use in children 6 years or younger. **Greenhouse gas emissions** The rate of greenhouse gas emissions was 13.0 kg/hour (SD 6.2) in the End-tidal Control phase and 23.2 kg/hour (SD 10.8) in the manual phase, an absolute reduction of 10.2 kg/hour (95% CI: 2.7 to 17.7 kg/hour, p=0.0179) or a relative reduction of 44% when using End-tidal Control.
Conclusions	The authors concluded that the use of End-tidal Control increases participation in low-flow anaesthesia with environmental benefits.

Table 3 Summary of the Lucangelo et al. (2014) prospective observational study

Study component	Description
Objectives/ hypotheses	To compare oxygen, air and anaesthetic consumption during manual and End-tidal Control low-flow anaesthesia provided by the same anaesthetic machine using identical fresh gas flow (1 litre/min).
Study design	Prospective observational study of consecutive patients admitted to operating rooms that either had the End-tidal Control feature present or absent on the anaesthetic machine.
Setting	Operating rooms in a single hospital (hospital name and dates of study were not stated in the paper).
Inclusion/ exclusion criteria	Inclusion criteria: 18 to 80 years of age, ASA classification of physical health of 1 or 2, expected duration of surgery exceeding 1 hour. Exclusion criteria: BMI exceeding 30, chronic use of opioids, contraindication to any component of the anaesthesia protocol, neurological disorders, and arterial hypertension.

Study component	Description
Primary outcomes	Anaesthetic machine characteristics. Amount of consumed gases. Oxygen and sevoflurane efficiencies. Number of interventions by the anaesthetist.
Statistical methods	Normality was assessed by the Kolmogorov–Smirnov–Lilliefors test. Non-normal data were described as medians [IQR]. The Mann–Whitney test was used to compare data between groups. The adjusted p value was calculated according to Dineen and Blakesley method. The significance level was set at 5%.
Participants	80 consecutive patients admitted to the operating room in need of elective abdominal surgery under general anaesthesia, 40 of whom were anaesthetised with the End-tidal Control feature present on the anaesthetic machine and 40 with End-tidal Control absent. No difference in patient characteristics was found between groups. No patient was excluded from the trial.

Study component	Description
Results	No clinical complications were observed. **Anaesthetic machine characteristics** Tidal volume, respiratory rate, duration of anaesthesia, sevoflurane delivery, and awakening time did not differ significantly between End-tidal Control and manual-control anaesthesia groups. The median [IQR] time to reach target end-tidal anaesthetic agent concentration was 145 [130 to 171] seconds with End-tidal Control and 71 [43 to 98] seconds with manual control (P<0.00001). The median [IQR] time to maintain steady end-tidal anaesthetic oxygen concentration was 145 [130 to 171] seconds with End-tidal Control and 360 [278 to 531] seconds with manual control (P<0.00001). **Amount of consumed gases** The median [IQR] oxygen delivery was 87 [48 to 120] litres with End-tidal Control, and 74 [52 to 105] litres with manual control. The median [IQR] sevoflurane delivery was 15 [11–23] ml with End-tidal Control and 17 [12 to 23] ml with manual control. The median [IQR] oxygen uptake was 260 [231 to 275] ml/minute with End-tidal Control and 252 [226 to 277] ml/minute with manual control. The median [IQR] sevoflurane uptake was 3.7 [2.3 to 4.4] ml/minute with End-tidal Control and 3.8 [3.0 to 4.4] ml/minute with manual control. The delivery and uptake of oxygen and sevoflurane were not significantly different between manual and End-tidal Control groups. **Oxygen and sevoflurane efficiencies** The median [IQR] oxygen efficiency was 47% [34% to 60%] with End-tidal Control and 51% [44% to 62%] with manual control. The median [IQR] sevoflurane efficiency was 21% [12% to 39%] with End-tidal Control and 22% [14% to 40%] with manual control. The oxygen and sevoflurane efficiencies were not significantly different between manual and End-tidal Control groups. **Number of interventions by the anaesthetist** To reach the pre-established end-tidal anaesthetic agent concentration, the median number of interventions in the manual-control group was 4 (with a total of 137, including 50 for undershoot and 87 for overshoot of end-tidal anaesthetic agent concentration). No interventions were

Study component	Description
	needed for the End-tidal Control group. To maintain the end-tidal oxygen concentration, 107 interventions were needed in the manual-control group with all patients needing at least 1 intervention. No interventions were needed for the End-tidal Control group.
Conclusions	The authors concluded that low-flow anaesthesia delivered with an anaesthetic machine able to automatically control end-tidal anaesthetic and oxygen concentrations provided the same clinical stability as that of manually-controlled anaesthesia. Similar oxygen and sevoflurane consumption was reported between groups; however End-tidal Control avoids the continuous manual adjustment of delivered sevoflurane and oxygen concentrations.

Abbreviations: ASA, American Society of Anesthesiologists; CI, confidence interval; IQR, interquartile range

Table 4 Summary of the Singaravelu and Barclay (2013) service evaluation

Study component	Description
Objectives/ hypotheses	To evaluate End-tidal Control in clinical practice by measuring inhalation anaesthetic use and the need for user intervention and comparing this with contemporaneous surgeries done using manual control of fresh gas flow.
Study design	Service evaluation.
Setting	Gynaecology theatres within a single UK centre (Liverpool Women's Hospital) between June and October 2010.
Inclusion/ exclusion criteria	Because of the study design, initial inclusion and exclusion criteria were not explicitly described in the paper. Subsequent exclusions, applied retrospectively, included patients with duration of anaesthesia of less than 10 minutes.
Primary outcomes	Inhalation anaesthetic use. User intervention.

Study component	Description
Statistical methods	Data were compared using Spearman correlation and t-tests.
Participants	321 patients were anaesthetised using End-tidal Control (n=181 sevoflurane, n=140 desflurane). 168 patients were anaesthetised using manual control of fresh gas (n=143 sevoflurane, n=25 desflurane).
Results	Inhalation anaesthetic use Average fresh gas flow during End-tidal Control decreased significantly with increased duration of anaesthesia (Spearman r=-0.88, p=0.0016). When comparing anaesthetics of the same duration, the average volatile anaesthetic use was consistently reduced by 40% to 55% in the End-tidal Control group. User intervention The mean number of key presses was 6.5 (95% CI 6.0 to 7.0) with End-tidal Control, and 13.6 (95% CI 12.8 to 14.4) with manual control. Secondary outcomes With End-tidal Control, the measured end-tidal concentration was within 10% of the set target for 98% of the total time spent in steady state, allowing 5 minutes for equilibration after each change in the set target. The mean difference between measured end-tidal concentration and target end-tidal concentration using End-tidal Control was 1.47% (95% CI: 1.29% to 1.66%).
Conclusions	The authors concluded that automatic implementation of low-flow anaesthesia using End-tidal Control allows the user to set and maintain a desired end-tidal volatile concentration while using less anaesthetic and reducing the number of interventions needed by the clinician.

Table 5 Summary of the Kennedy and French (2014) audit

Study component	Description
Objectives/ hypotheses	To describe the effect of the introduction of the Aisys anaesthesia machine with automated control of end-tidal vapour concentration on fresh gas flow rates.

Study component	Description
Study design	Audit study.
Setting	Single theatre suite (comprising 11 operating theatres) in a New Zealand (Christchurch) hospital using Datex ADUs (during 2009), and from Aisys machines with End-tidal Control (in June 2011, December 2011 and June 2012). Comparative data from the same hospital using ADUs (from 2001 and 2006) were described, as well as data from 2 other major tertiary (Middlemore hospital) and secondary (North Shore hospital) care metropolitan public hospitals in New Zealand also using ADUs (in 2007 and 2008 respectively).
Inclusion/ exclusion criteria	Because of the study design, no inclusion or exclusion criteria were described. However, the authors do state that the theatres in the Christchurch hospital had a broad mix of adult elective and acute surgery, but that data were not collected from operating theatres with significant paediatric practice or from cardiothoracic or neurosurgery operating theatres.
Primary outcomes	Mean fresh gas flow rates. Online voluntary survey results.
Statistical methods	Not reported.
Participants	Population size and demographics not described.

Study component	Description
Results	Mean fresh gas flow rates End-tidal Control: • Christchurch Aisys June 2011: 1.50 litre/minute • Christchurch Aisys Dec 2011: 1.29 litre/minute • Christchurch Aisys June 2012: 1.09 litre/minute Manual gas control: • Christchurch ADU 2001: 2.05 litre/minute • Christchurch ADU 2006: 1.43 litre/minute • Middlemore ADU 2007: 1.24 litre/minute • North Shore ADU 2008: 1.27 litre/minute • Christchurch ADU 2009: 1.26 litre/minute The overall proportion of time spent in End-tidal Control mode with the Aisys machines was 34% in June 2011, 60% in December 2011 and 61% in June 2012. There is an association between reduction in flow rates and increasing proportion of time spent in End-tidal Control mode. Online voluntary survey results The survey was completed by 68/90 anaesthetists (75%), including 18 trainees and 50 specialist anaesthetists. End-tidal Control was used 'often' or 'most of the time' by 67% of respondents. The reasons most commonly selected for not using End-tidal Control were the need to teach trainees (47.7% 'relevant' or 'very relevant') and when using total intravenous anaesthesia (34.9% of respondents). Major issues reported with End-tidal Control were: • difficulty in changing agent during surgery (39.7%) • poor performance with circuit leaks, such as ill-fitting laryngeal mask airway (40.5%).

Study component	Description
	Major advantages reported for End-tidal Control were: • better control of agent concentrations (75.3%) • allowing attention to be directed to other aspects of anaesthesia care (71%) • perception of reduced workload (55.8%).
Conclusions	The authors concluded that automatic control of anaesthetic agent concentration can lead to reduction in overall fresh gas flows.

Abbreviations: ADU, anaesthesia delivery units.

Recent and ongoing studies

No ongoing or in-development trials of End-tidal Control for general anaesthesia were identified.

Costs and resource consequences

The manufacturer stated that as of May 2014, 401 Aisys Carestation units have been sold to 55 UK hospitals and 37 Aisys CS2 units have been sold to 9 UK hospitals, giving a total of 438 systems across the UK. End-tidal Control has been purchased for 425 (97%) of these systems.

Approximately 2.4 million people had general anaesthesia in 2007 in England (NICE 2012), but there are no data available to quantify how many of these general anaesthesia patients had inhalational anaesthetic agents compared with intravenous anaesthesia (noting the potential overlap of patients having both inhalational and intravenous anaesthetic agents). Two specialist commentators have estimated that less than 10% of patients will have total intravenous anaesthesia, leaving approximately 90% having some form of inhalational anaesthesia. However it is difficult to precisely estimate the total UK population for whom End-tidal Control could be used.

Published economic evaluation

Four of the 5 reviewed studies included an economic evaluation of End-tidal Control compared with manual control of anaesthetic gases. In all studies, this economic evaluation was limited to consumption of gases. Only 1 of these was done in the UK, and only 1 standardised fresh gas flow between groups to eliminate a potential confounding factor.

The service evaluation by Singaravelu and Barclay, the only reviewed study done in the UK, found that for surgery of 20 to 40 minutes duration, the average cost of volatile anaesthetic per hour was reduced from £14.92 to £6.98 (saving £7.94 per hour) for sevoflurane and £11.91 to £7.08 (saving £4.83 per hour) for desflurane with End-tidal Control.

The prospective observational study by Lucangelo et al. was the only published study specifically designed to use identical fresh gas flow between groups. This reported no significant difference in gas consumption between manual and End-tidal Control, and therefore no difference in cost.

For the 2 studies set in India and Australia, the reported costs have been converted to £GBP (pounds sterling).

The randomised trial by Potdar et al. stated that the total cost of oxygen, nitrous oxide and sevoflurane consumption decreased from 417.76 Indian rupees per hour in the manual-control group (n=100) to 353.95 Indian rupees per hour in the End-tidal Control group (n=100), p=0.0001. This translated to a saving of £0.64 per hour (using exchange rates on 6 June 2014 as stated on XE, because dates of inclusion were not reported in the study).

The prospective observational study by Tay et al. stated that the mean volatile anaesthetic (isoflurane, desflurane, sevoflurane) cost per hour (in Australian dollars) decreased from $18.87 (SD $6.15) in the manual-control group (n=1865) to $13.82 (SD $3.27) in the End-tidal Control group (n=1036), an absolute reduction of $5.05 (95% CI: $0.88 to $9.22, p=0.0243), or a relative reduction of 27%. This translated to an overall cost saving in volatile anaesthetic agent through the use of End-tidal Control of approximately £3.32 (95% CI: £0.58 to £6.06) per hour (using exchange rates on 1 November 2011 as stated on XE). Carbon dioxide absorbent usage was 144 kg in the End-tidal Control phase ($4050) and 156 kg in the manual phase ($4108); the differences between groups for usage and costs were not statistically significant. Consumption savings of fresh gases (oxygen, air,

nitrous oxide) from the medical gas supplier were not clinically significant between groups.

Strengths and limitations of the evidence

Four of the 5 reviewed studies were conducted outside the UK; therefore it is unclear how generalisable the results would be to the UK NHS. Additionally, none of the 5 reviewed clinical studies reported results from a paediatric population, with 1 study describing anaesthetists choosing not to use End-tidal Control in patients under 6 years. Therefore the applicability of End-tidal Control to a paediatric population was not identified from the literature.

The best quality evidence identified by literature review was the randomised single-blind study by Potdar et al. that included 200 patients. This trial appropriately randomised patients using a chit-pull system of 200 labelled chits (or tickets) with odd numbers allocated to manual control and even numbers to End-tidal Control anaesthesia. Single blinding was appropriate in this study as anaesthetists cannot be blinded to the use of manual or End-tidal Control of anaesthetic gases. This was the only reviewed study that took into account depth of anaesthesia as an outcome measure of both manual and End-tidal Control groups. However, the study and its reporting had several weaknesses. None of the figures or table numbers were referred to correctly in the text, incorrect statistical tests were applied, and contradictory p values were stated in the results and discussion sections. The intervention and control arms were uneven at baseline, with patients in the End-tidal Control group being significantly younger (mean age 38.9 years compared with 43.0 years), suggesting a possible weakness in the chosen method of randomisation. The authors described a power calculation to confirm adequate sample size to detect the difference in total costs between arms, but this was performed retrospectively, rather than prospectively (which would have been more appropriate). This trial may also lack external validity to the NHS in general because of the extensive exclusion criteria, in which only patients having laparoscopic abdominal or pelvic surgery, aged between 15–80 years, with surgery lasting 30 minutes to 4 hours, were considered.

The largest study identified was the prospective before-and-after observational study by Tay et al., which included 1,865 cases of manually controlled anaesthesia and 1,810 cases eligible for End-tidal Control. However, of this group of eligible cases, only 1,036 cases (57.2%) were confirmed as using End-tidal Control via voluntary case report forms. The authors noted the intrinsic increased risk of bias caused by non-randomisation of patients to manual or automated control in their study. Although the study included patients of all ages who were having elective or emergency general anaesthesia with a volatile agent, it

excluded patients having cardiac surgery (in line with manufacturer's stated contraindications) or neurosurgery procedures, which could increase the risk of selection bias and limit the generalisability of the data. The End-tidal Control and manual-control results were recorded during different time periods, which meant that the results could be influenced by seasonal variation. Whereas the characteristics of the 1,810 cases eligible for manual and End-tidal Control were described and were not statistically different, the demographics of the 1,036 End-tidal Control cases were not described or compared with the manual-control group. It was unclear whether the results stated in this study referred to the 1,810 cases eligible for End-tidal Control, or the 1,036 cases confirmed as having End-tidal Control anaesthesia.

The prospective observational study by Lucangelo et al. included 80 consecutive patients. The authors attempted to reduce bias by assigning patients to anaesthetic rooms with or without End-tidal Control on the anaesthetic machine based on an operating schedule prepared by a surgeon who was unaware of the study design, although randomisation was not attempted. This was the only study reviewed that maintained identical fresh gas flow between groups, thus removing 1 potential confounding factor of analysis. The study was at risk of selection bias by excluding patients with expected surgery duration of less than 1 hour. This may have resulted in an overestimation of End-tidal Control benefits, because the same study also stated that End-tidal Control takes longer to reach the target end-tidal anaesthetic concentration than manual control. Although the study recorded the number of key presses for the manual-control group, the authors failed to record the initial setting of target end-tidal anaesthetic agent concentration, starting and stopping the End-tidal Control mode as equivalent key presses in the End-tidal Control arm. This was the only identified study that addressed the safety of End-tidal Control, by stating there were no clinical complications reported during the study. However this statement must be considered with caution given that only 40 patients had anaesthesia with End-tidal Control on the anaesthetic machine in this study.

The service evaluation by Singaravelu and Barclay included 321 patients anaesthetised using End-tidal Control and 168 with manual control, and was the only identified UK study. The study may be subject to reporting bias because it retrospectively excluded patients having anaesthesia for less than 10 minutes, and therefore may have overestimated the benefit of End-tidal Control. The authors did not describe the characteristics of the patients involved in this study, so therefore it was not possible to assess the risk of selection bias or study generalisability. The authors identified the lack of information to describe each anaesthetist's reasons for the choice of manual or End-tidal Control mode as a limitation of their study. The proportion of patients having sevoflurane and desflurane

was different between the 2 groups (44% of the End-tidal Control group had desflurane compared with 15% in the manual-control group); therefore any difference in average costs would be subject to performance bias.

The audit described by Kennedy and French compared the Aisys anaesthesia system with End-tidal Control used in a hospital in New Zealand, with historical data collected from a different anaesthesia system (the Datex anaesthesia delivery unit with manual control) from 3 hospitals across New Zealand. The difference in anaesthesia systems and time periods used in this study resulted in significant potential for bias in the results. Additionally, there was likely to be selection bias, because paediatric and neurosurgery patients were not included in the End-tidal Control group but were included for the manual-control groups at 2 different hospitals. The number of patients included and their characteristics were not described, which limited interpretation of the study. Results from the audit were analysed at 3 specified time points for the End-tidal Control group only and resulted in a change to default settings of the Aisys system during the audit. It was unclear whether similar feedback was provided to the manual-control group resulting in any change to clinical practice, thus introducing another potential source of performance bias. Although the authors reported an association between a reduction in flow rates and increasing proportion of time spent in End-tidal Control mode, it was unclear how this association was statistically tested.

Relevance to NICE guidance programmes

NICE has issued diagnostics guidance on depth of anaesthesia monitors – Bispectral Index (BIS), E-Entropy and Narcotrend-Compact M, as well as a guideline on sedation in children and young people, but this guidance does not specifically cover the choice of manual or automated control of inhalational general anaesthesia.

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Tay S, Weinberg L, Peyton P et al. (2013) Financial and environmental costs of manual versus automated control of end-tidal gas concentrations. Anaesthesia and Intensive Care 41(1): 95–101

Search strategy and evidence selection

Search strategy

In order to maximise sensitivity, the search strategy included 1 concept only: the intervention. Text word and subject heading searches were designed to retrieve records which named the device or the manufacturer in the title and abstract of the record, or explicitly discussed the automated control of tidal volume or gas flow. The strategy excluded animal studies and non-English language publications. The results were limited to studies published from 2008 to the current day; this reflects that the earliest clinical trials described on the manufacturer's webpages took place in 2009.

The final strategy was peer-reviewed by an independent information specialist.

The following databases were searched:

- Cochrane Central Register of Controlled Trials (Cochrane Library, Wiley)
- Cochrane Database of Systematic Reviews (Cochrane Library, Wiley)
- Database of Abstracts of Reviews of Effect (Cochrane Library, Wiley)
- Embase (Ovid SP)
- Health Technology Assessment Database (Cochrane Library, Wiley)
- MEDLINE and MEDLINE in Process (Ovid SP)
- NHS Economic Evaluation Database (Cochrane Library, Wiley).

The search strategies used for each of the databases are presented below (A1 to A7). The manufacturer's webpages were additionally browsed for published evidence not retrieved by the database searches. This returned no additional studies.

A1. Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R). Ovid SP. 1946 to Present. Search date: 20/05/14.

1 Anesthesiology/is [Instrumentation] (3319)

2 Anesthetics, Inhalation/ad [Administration & Dosage] (2670)

3 Anesthesia, Inhalation/is or Anesthesia, General/is (3182)

4 Anesthetics/ad [Administration & Dosage] (2162)

5 Anesthetics/is [Instrumentation] (1)

6 Anesthesia, Closed-Circuit/ (730)

7 Intraoperative Monitoring/ (14995)

8 or/1-7 (25941)

9 Tidal Volume/ or Feedback/ or Feedback, Physiological/ (40365)

10 Automation/ or Software/ or Decision Making, Computer-Assisted/ (92169)

11 9 or 10 (132116)

12 8 and 11 (655)

13 (anesthes* or anesthet* or anaesthes* or anaesthet*).ti,ab,kf. (306733)

14 (ge healthcare* or gehealthcare* or ge health care* or general electric).ti,ab,kf,in. (1813)

15 14 and (13 or 8) (61)

16 (et control* or etcontrol* or end-tidal control* or endtidal control* or etca or eto2 or etaa or aisys*).ti,ab,kf. (116)

17 ((end-tidal or endtidal or eto2 or etaa or etca or tidal volume or gas flow*1 or fresh gas* or gas* control or volatile agent*) adj5 (automat* or target control* or closed-loop or closed-circuit or negative feedback or negative feed-back or feedback control* or feed-back control* or feedback system*1 or feed-back system*1)).ti,ab,kf. (82)

18 ((anesthe* or anaesthe*) adj5 (automatic* or automate* or automation or

automating)).ti,ab,kf. (366)

19 12 or 15 or 16 or 17 or 18 (1220)

20 exp animals/ not humans/ (3936735)

21 19 not 20 (1110)

22 limit 21 to english language (958)

23 limit 22 to yr="2008 -Current" (273)

A2. Database: Embase. Ovid SP. 1974 to 2014 May 19. Search date: 20/05/14.

1 anesthesiology general device/ or *anesthesiology/ or anesthesiology monitoring device/ (12645)

2 *general anesthesia/ or *inhalation anesthesia/ (23333)

3 anesthetic equipment/ (3954)

4 anesthesiology software/ (5)

5 or/1-4 (39414)

6 tidal volume/ (12487)

7 automation/ or autoanalysis/ (52108)

8 feedback system/ or negative feedback/ (65577)

9 decision support system/ (12776)

10 or/6-9 (141874)

11 10 and 5 (599)

12 (anesthes* or anesthet* or anaesthes* or anaesthet*).ti,ab. (374008)

13 (ge healthcare* or gehealthcare* or ge health care* or general electric).ti,ab,in. (5458)

14 13 and (5 or 12) (178)

15 (et control* or etcontrol* or end-tidal control* or endtidal control* or etca or eto2 or etaa or aisys*).ti,ab. (180)

16 ((end-tidal or endtidal or eto2 or etaa or etca or tidal volume or gas flow*1 or fresh gas* or gas* control or volatile agent*) adj5 (automat* or target control* or closed-loop or closed-circuit or negative feedback or negative feed-back or feedback control* or feed-back control* or feedback system*1 or feed-back system*1)).ti,ab. (113)

17 ((anesthe* or anaesthe*) adj5 (automatic* or automate* or automation or automating)).ti,ab. (446)

18 11 or 14 or 15 or 16 or 17 (1445)

19 exp animals/ not humans/ (4374090)

20 18 not 19 (1265)

21 limit 20 to yr="2008 -Current" (579)

22 limit 21 to english language (556)

A3. Database: Cochrane Database of Systematic Reviews. The Cochrane Library, Wiley. Issue 5 of 12, May 2014. Search date: 20/05/14.

#1 MeSH descriptor: [Anesthesiology] this term only 277

#2 MeSH descriptor: [Anesthetics, Inhalation] this term only 2176

#3 MeSH descriptor: [Anesthetics] this term only 549

#4 MeSH descriptor: [Anesthesia, Inhalation] this term only 1658

#5 MeSH descriptor: [Anesthesia, General] this term only 3930

#6 MeSH descriptor: [Anesthesia, Closed-Circuit] this term only 84

#7 MeSH descriptor: [Monitoring, Intraoperative] this term only 1315

#8 #1 or #2 or #3 or #4 or #5 or #6 or #7 8211

#9 MeSH descriptor: [Tidal Volume] this term only 646

#10 MeSH descriptor: [Feedback] this term only 960

#11 MeSH descriptor: [Feedback, Physiological] this term only 68

#12 MeSH descriptor: [Automation] this term only 213

#13 MeSH descriptor: [Software] this term only 769

#14 MeSH descriptor: [Decision Making, Computer-Assisted] this term only 144

#15 #9 or #10 or #11 or #12 or #13 or #14 2746

#16 #8 and #15 182

#17 (ge next healthcare* or gehealthcare* or ge next health next care* or "general electric"):ti,ab,kw 27

#18 (et next control* or etcontrol* or end-tidal next control* or endtidal next control* or etca or eto2 or etaa or aisys*):ti,ab,kw 7

#19 (("end-tidal" or endtidal or eto2 or etaa or etca or "tidal volume" or gas next flow* or fresh next gas* or gas* next control or volatile next agent*) near/5 (automat* or target next control* or "closed-loop" or "closed-circuit" or "negative feedback" or "negative feedback" or feedback next control* or feed-back next control* or feedback next system* or feed-back next system*)):ti,ab,kw 19

#20 ((anesthe* or anaesthe*) near/5 (automatic* or automate* or automation or automating)):ti,ab,kw 33

#21 #16 or #17 or #18 or #19 or #20 258

#22 #21 in Cochrane Reviews (Reviews and Protocols) 0

A4. Database: Database of Abstracts of Reviews of Effect. The Cochrane Library, Wiley. Issue 2 of 4, April 2014. Search date: 20/05/14.

#1 MeSH descriptor: [Anesthesiology] this term only 277

#2 MeSH descriptor: [Anesthetics, Inhalation] this term only 2176

#3 MeSH descriptor: [Anesthetics] this term only 549

#4 MeSH descriptor: [Anesthesia, Inhalation] this term only 1658

#5 MeSH descriptor: [Anesthesia, General] this term only 3930

#6 MeSH descriptor: [Anesthesia, Closed-Circuit] this term only 84

#7 MeSH descriptor: [Monitoring, Intraoperative] this term only 1315

#8 #1 or #2 or #3 or #4 or #5 or #6 or #7 8211

#9 MeSH descriptor: [Tidal Volume] this term only 646

#10 MeSH descriptor: [Feedback] this term only 960

#11 MeSH descriptor: [Feedback, Physiological] this term only 68

#12 MeSH descriptor: [Automation] this term only 213

#13 MeSH descriptor: [Software] this term only 769

#14 MeSH descriptor: [Decision Making, Computer-Assisted] this term only 144

#15 #9 or #10 or #11 or #12 or #13 or #14 2746

#16 #8 and #15 182

#17 ge next healthcare* or gehealthcare* or ge next health next care* or "general electric"

74

#18 et next control* or etcontrol* or end-tidal next control* or endtidal next control* or etca or eto2 or etaa or aisys* 21

#19 ("end-tidal" or endtidal or eto2 or etaa or etca or "tidal volume" or gas next flow* or fresh next gas* or gas* next control or volatile next agent*) near/5 (automat* or target next control* or "closed-loop" or "closed-circuit" or "negative feedback" or "negative feed-back" or feedback next control* or feed-back next control* or feedback next system* or feed-back next system*) 21

#20 (anesthe* or anaesthe*) near/5 (automatic* or automate* or automation or automating) 36

#21 #16 or #17 or #18 or #19 or #20 323

#22 #21 Publication Date from 2008 to 2014, in Other Reviews 4

A5. Database: Cochrane Central Register of Controlled Trials. The Cochrane Library, Wiley. Issue 4 of 12, April 2014. Search date: 20/05/14.

#1 MeSH descriptor: [Anesthesiology] this term only 277

#2 MeSH descriptor: [Anesthetics, Inhalation] this term only 2176

#3 MeSH descriptor: [Anesthetics] this term only 549

#4 MeSH descriptor: [Anesthesia, Inhalation] this term only 1658

#5 MeSH descriptor: [Anesthesia, General] this term only 3930

#6 MeSH descriptor: [Anesthesia, Closed-Circuit] this term only 84

#7 MeSH descriptor: [Monitoring, Intraoperative] this term only 1315

#8 #1 or #2 or #3 or #4 or #5 or #6 or #7 8211

#9 MeSH descriptor: [Tidal Volume] this term only 646

#10 MeSH descriptor: [Feedback] this term only 960

#11 MeSH descriptor: [Feedback, Physiological] this term only 68

#12 MeSH descriptor: [Automation] this term only 213

#13 MeSH descriptor: [Software] this term only 769

#14 MeSH descriptor: [Decision Making, Computer-Assisted] this term only 144

#15 #9 or #10 or #11 or #12 or #13 or #14 2746

#16 #8 and #15 182

#17 ge next healthcare* or gehealthcare* or ge next health next care* or "general electric" 74

#18 et next control* or etcontrol* or end-tidal next control* or endtidal next control* or etca or eto2 or etaa or aisys* 21

#19 ("end-tidal" or endtidal or eto2 or etaa or etca or "tidal volume" or gas next flow* or fresh next gas* or gas* next control or volatile next agent*) near/5 (automat* or target next control* or "closed-loop" or "closed-circuit" or "negative feedback" or "negative feed-back" or feedback next control* or feed-back next control* or feedback next system* or feed-back next system*) 21

#20 (anesthe* or anaesthe*) near/5 (automatic* or automate* or automation or automating) 36

#21 #16 or #17 or #18 or #19 or #20 323

#22 #21 Publication Date from 2008 to 2014, in Trials 90

A6. Database: Health Technology Assessment Database. Cochrane Library, Wiley. Issue 2 of 4, April 2014. Search date: 20/05/14.

#1 MeSH descriptor: [Anesthesiology] this term only 277

#2 MeSH descriptor: [Anesthetics, Inhalation] this term only 2176

#3 MeSH descriptor: [Anesthetics] this term only 549

#4 MeSH descriptor: [Anesthesia, Inhalation] this term only 1658

#5 MeSH descriptor: [Anesthesia, General] this term only 3930

#6 MeSH descriptor: [Anesthesia, Closed-Circuit] this term only 84

#7 MeSH descriptor: [Monitoring, Intraoperative] this term only 1315

#8 #1 or #2 or #3 or #4 or #5 or #6 or #7 8211

#9 MeSH descriptor: [Tidal Volume] this term only 646

#10 MeSH descriptor: [Feedback] this term only 960

#11 MeSH descriptor: [Feedback, Physiological] this term only 68

#12 MeSH descriptor: [Automation] this term only 213

#13 MeSH descriptor: [Software] this term only 769

#14 MeSH descriptor: [Decision Making, Computer-Assisted] this term only 144

#15 #9 or #10 or #11 or #12 or #13 or #14 2746

#16 #8 and #15 182

#17 ge next healthcare* or gehealthcare* or ge next health next care* or "general electric" 74

#18 et next control* or etcontrol* or end-tidal next control* or endtidal next control* or etca or eto2 or etaa or aisys* 21

#19 ("end-tidal" or endtidal or eto2 or etaa or etca or "tidal volume" or gas next flow* or fresh next gas* or gas* next control or volatile next agent*) near/5 (automat* or target

next control* or "closed-loop" or "closed-circuit" or "negative feedback" or "negative feed-back" or feedback next control* or feed-back next control* or feedback next system* or feed-back next system*) 21

#20 (anesthe* or anaesthe*) near/5 (automatic* or automate* or automation or automating) 36

#21 #16 or #17 or #18 or #19 or #20 323

#22 #21 Publication Date from 2008 to 2014, in Technology Assessments 1

A7. Database: NHS Economic Evaluation Database. Cochrane Library, Wiley. Issue 2 of 4, April 2014. Search date: 20/05/14.

#1 MeSH descriptor: [Anesthesiology] this term only 277

#2 MeSH descriptor: [Anesthetics, Inhalation] this term only 2176

#3 MeSH descriptor: [Anesthetics] this term only 549

#4 MeSH descriptor: [Anesthesia, Inhalation] this term only 1658

#5 MeSH descriptor: [Anesthesia, General] this term only 3930

#6 MeSH descriptor: [Anesthesia, Closed-Circuit] this term only 84

#7 MeSH descriptor: [Monitoring, Intraoperative] this term only 1315

#8 #1 or #2 or #3 or #4 or #5 or #6 or #7 8211

#9 MeSH descriptor: [Tidal Volume] this term only 646

#10 MeSH descriptor: [Feedback] this term only 960

#11 MeSH descriptor: [Feedback, Physiological] this term only 68

#12 MeSH descriptor: [Automation] this term only 213

#13 MeSH descriptor: [Software] this term only 769

#14 MeSH descriptor: [Decision Making, Computer-Assisted] this term only 144

#15 #9 or #10 or #11 or #12 or #13 or #14 2746

#16 #8 and #15 182

#17 ge next healthcare* or gehealthcare* or ge next health next care* or "general electric" 74

#18 et next control* or etcontrol* or end-tidal next control* or endtidal next control* or etca or eto2 or etaa or aisys* 21

#19 ("end-tidal" or endtidal or eto2 or etaa or etca or "tidal volume" or gas next flow* or fresh next gas* or gas* next control or volatile next agent*) near/5 (automat* or target next control* or "closed-loop" or "closed-circuit" or "negative feedback" or "negative feed-back" or feedback next control* or feed-back next control* or feedback next system* or feed-back next system*) 21

#20 (anesthe* or anaesthe*) near/5 (automatic* or automate* or automation or automating) 36

#21 #16 or #17 or #18 or #19 or #20 323

#22 #21 Publication Date from 2008 to 2014, in Economic Evaluations 10

Evidence selection

A total of 934 records were retrieved from the literature search. After de-duplication, 733 remained. An initial 292 records were excluded at first pass as being animal or plant studies, bench research and obviously irrelevant interventions. The 441 remaining records were sifted against the inclusion criteria at title and abstract.

The first-sift removed 395 records based on the following exclusion criteria:

- Articles of poor relevance against search terms

- Publication types that were out of scope
  - non-English language studies
  - conference abstracts
  - review articles (for example, Cochrane review protocols)
  - articles if neither the abstract nor full text is freely available online.

Full articles were retrieved for the remaining 46 records, with full text assessment undertaken at second sift to identify relevant primary research addressing the use of the medical technology within the defined indication under review. The conventional evidence hierarchy was applied and the best available evidence was selected for inclusion within the evidence tables and for critical appraisal.

During the second sift, 41 records were excluded for the following reasons: 34 were not relevant to the medical technology, 5 were conference abstracts not previously identified from the title and abstract, 1 was a general review article and 1 was only available with full-text in non-English language.

This left 5 articles on the End-tidal Control mode for inclusion within evidence tables and critical appraisal (1 randomised study, 2 prospective observational studies, 1 service evaluation and 1 audit, tables 1 to 5 respectively).

About this briefing

Medtech innovation briefings summarise the published evidence and information available for individual medical technologies. The briefings provide information to aid local decision-making by clinicians, managers, and procurement professionals.

Medtech innovation briefings aim to present information and critically review the strengths and weaknesses of the relevant evidence, but contain no recommendations and are not formal NICE guidance.

Development of this briefing

This briefing was developed for NICE by Newcastle and York External Assessment Centre. The Interim Process & Methods Statement sets out the process NICE uses to select topics,

and how the briefings are developed, quality assured and approved for publication.

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Newcastle and York External Assessment Centre

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Specialist commentators

The following specialist commentators provided comments on a draft of this briefing:

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