Master of Medicine in Anaesthesiology

Research Submission

A cost comparison in spontaneously ventilated patients:

The Universal Anaesthesia Machine as a possible cost effective alternative.

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Submitted to: Faculty of Health Sciences, University of Cape Town

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Declaration

I, Gerhardus Petrus van Rensburg, declare that this submission is my original work unless specifically indicated otherwise. I also declare that this work, in its entirety or otherwise, has not been submitted for another qualification to this, or any another university.

It has been submitted for the degree of Master of Medicine (Anaesthesiology) and is based upon research conducted in the theatre complex of the Groote Schuur Hospital, Anzio Road, Observatory, Cape Town.

I hereby empower the University of Cape Town to reproduce this document or parts thereof in any manner they may deem necessary.

GP van Rensburg

2015-05-15

Acknowledgements

Dr Robert Nieuwveld

His support, advice and patience has been pivotal in the completion of this project.

Professor Michael James

For his help with statistical calculations and advice without which completion would have been impossible.

Suvashni

For all her fantastic and patient assistance during my literature searches.

Declaration of Interest

Neither the author nor the supervisors has any conflict of interest related to the equipment or materials used in this study.

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Abbreviations and Definitions

Universal Anaesthesia Machine (UAM)

The anaesthesia workstation manufactured and marketed by Gradian Health Systems that makes use of a draw-over vaporiser and a built-in oxygen concentrator.

Draw-over anaesthesia

An anaesthesia system where carrier gas (room air or medical air enriched with medical grade oxygen) used by the patient's spontaneous ventilatory effort is allowed to pass over a volatile anaesthetic vapour through a purpose built low resistance vaporiser. Whilst spontaneous ventilation is the most common setting in which this is described, it can also be used during positive pressure ventilation. This system does not use a carbon dioxide absorber. It will also include the group of patients that are rendered apnoeic by either the induction agent or the volatile agent itself and require temporary manual support – this makes use of the UAM's so-called "push-over" function, where the mechanism of vaporisation is retained despite the lack of ventilatory effort.

Standard Plenum System

An anaesthetic delivery system that (in our hospital) consists of a circle system containing a carbon dioxide absorber with soda lime, all the appropriate valves and a (out of circuit) plenum vaporiser. A plenum vaporiser, in contrast to a draw-over vaporiser, is a high resistance device that is dependent on positive pressure and performs predictably regardless of the mode of ventilation in use.

Spontaneous ventilation

Patients who are allowed to generate their own fresh gas flow by means of their own intrinsic ventilatory efforts. This will include the group rendered apnoeic that may require temporary manual support.

MHRA

Medicines and Healthcare products Regulatory Agency. This is an executive agency of the Department of Health in the United Kingdom that aims to protect the population it serves by

ensuring that medical devices, blood components, supply chain management and training of healthcare workers are, amongst other things, of a sufficient standard.

CE Marking

This is the symbol as depicted here. It is the abbreviation of French phrase “Conformité Européene” which literally means "European Conformity". It is the mark used by the manufacturer to indicate that it meets with legal requirements to permit its sale and movement in the European Economic Area.

The CE mark

Abstract

Background

A new appreciation of relevant risks, as well as the increased availability of technologies that facilitate the use of regional techniques, have increased the number of patients that are allowed to breathe spontaneously during their procedures. The ever-growing caseload of surgical patients in resource poor environments demands an anaesthetic service and equipment capable of meeting with these demands.

Methods

Patients were recruited to receive their general anaesthesia by means of either the Universal Anaesthesia Machine (UAM) or the standard plenum system available. Anaesthesia was administered according to a protocol and the consumption of electricity, carrier gases, volatile hypnotic agent and carbon dioxide absorbent was measured. The cost per minute was then calculated for each device respectively.

Results

Our study recruited 50 patients (25 into each group) across several surgical specialties. We found that when calculated as a total South African Rand (ZAR) per minute cost (for our centre) the UAM was statistically significantly more expensive (R 0.974/min vs. R 0.459/min, $p < 0{,}00001$). We were able to derive equations to predict the cost consumption of the respective devices, allowing the use of this data in a wide array of clinical settings.

Conclusion

Whilst our finding is by no means surprising, it allowed us to produce formulae by which individual centres can calculate the implications of each option using the specific costs of the various consumables available to them.

1. Introduction

The clearer understanding of aspiration risk as well as the ever-increasing use of regional techniques has brought about a greater proportion of patients that are allowed to breathe spontaneously during their procedures, in both resource rich and resource poor settings. Draw-over vaporisers have, however, become progressively scarcer. These factors have resulted in an increasing number of patients who ventilate spontaneously under general anaesthesia provided by means of a plenum system.

The Universal Anaesthesia Machine (UAM) is a draw-over anaesthesia system that was developed in a limited-resource setting. Its manufacturers speculate that its oxygen concentrator could render it competitive from a cost-effectiveness perspective when compared to a standard plenum system when an anaesthetised patient is allowed to breathe spontaneously.

1.1 Literature Review

Introduction

This review straddles the disciplines of health economics and clinical anaesthesia. It addresses the cost efficiency of draw-over anaesthesia when compared to anaesthesia administered by means of a plenum system and a circle circuit. The global population of surgical patients is extremely diverse and the resources to provide healthcare to these patients is just as heterogeneous and unpredictable.

Unfortunately an extreme paucity of literature exists with regard to this topic. Also, the Universal Anaesthesia Machine is a fairly new device and there is even less research available on this device. We thus draw from several topics relevant to this.

A literature search was conducted using Google Scholar and relevant articles were drawn from as far as they were relevant and applicable. A wide variety of search keywords were used to generate results and these included: UAM, Universal Anaesthesia Machine, draw-over anaesthesia, cost-efficiency etc. Also the most recent publications were incorporated

even when this appears to be very old literature. As pointed out already, the device and topic under examination is rarely studied and this rendered literature review very difficult.

Pharmaco-economics is a division of health economics and is the study of the financial costs of drugs and clinical effectiveness. This scientific discipline has facilitated a growing awareness of cost-effective medical practice with, at least sometimes, savings for hospital budgets. Cost-effectiveness impacts directly on the delivery of healthcare services and technologies as well as the provision of appropriate facilities, as their costs continue to escalate while resources are finite. [1]

Out of necessity, practitioners in under-resourced systems have resorted to (and refined) various techniques and practices that are often regarded as outdated in first-world settings. In anaesthetic circles, the classic example of this is the use of draw-over anaesthesia.

When a patient's ventilation draws ambient air (that may be supplemented by oxygen and/or nitrous oxide) over the surface of a volatile anaesthetic agent in a vaporiser, a draw-over system exists.

In contrast, a plenum system exists when the anaesthesia apparatus delivers a continuous flow of fresh pressurised gas that can then be used to deliver minute volume and/or drive ventilator bellows. [2, 3] This system is very often used in conjunction with a circle breathing system.

A circle breathing system is basically comprised of the following essential components: carbon dioxide absorber (a soda lime canister), two unidirectional valves, a fresh gas opening, a Y-piece to connect to the patient, a reservoir bag, a relief valve and low-resistance tubing. [2]

These two systems (draw-over and plenum anaesthesia) have developed largely in parallel. A draw-over system is simple to assemble and use. In contrast to a plenum system, the vaporiser has a low internal resistance making spontaneous ventilation through the circuit feasible. It is usually lightweight and portable and in further contrast to plenum systems

does not require a constant gas supply. It is therefore better suited to under-resourced settings and military or field anaesthesia. In addition, infection control is simplified - this system is inherently a non-rebreathing system, minimizing the problems of contamination and the need for disinfection. [3]

Most modern anaesthetists have very little exposure (if any) to draw-over systems and this may well skew our perceptions of the need for such systems. Many places in the world, where anaesthesia is delivered, do not even have access to compressed oxygen. Coupled to this, modern anaesthesia stations have complex technology (including electronic flow meters) that often require oxygen to drive them (e.g. ventilators), thus limiting their application outside well-funded centres. [4] This necessitates a broader view of anaesthesia and the challenges faced by anaesthetists.

"Supply and Demand"

Major improvements in the quality and safety of anaesthesia in recent decades have brought about the adoption of international standards for safe practice by the World Federation of Societies of Anaesthesiologists (WFSA) in 1992. This, inter alia, has led to a corresponding increased requirement for resources. It has been suggested that even basic requirements have not been met in large parts of the world – more than two decades later.

A significant component of this problem is attributable to a gross lack of training. A questionnaire was presented to 97 (out of approximately 350 in total) anaesthetists in public and mission practice from Uganda at a refresher course in May, 2006. Here it was found that the majority were undergoing training or had attended a training course of 1-2 years duration. One respondent had been "trained on the job". [5] Whilst clearly not material to the question of our research it does underline the importance of the fact that simple and reliable anaesthesia systems should be put in place in these settings.

Anaesthetists that are formally educated are often trained exclusively in techniques based on a continuous supply of nitrous oxide and oxygen. As was outlined above, the apparatus for use with nitrous oxide and oxygen is often available but due to lack of supplies of these gases, cannot be used. [6]

One study in Nigerian hospitals found that 44% of respondents reported an occasional lack of running water. Electricity (including generator supplies) was not always available in 80% of locations and intravenous fluids were not always available for 30% of patients. Ten percent reported never having oxygen and 25% reported occasionally having to work without oxygen. [5]

Conditions amenable to surgical correction "abound among the general population of poor countries". [6] It is believed that the main factors limiting delivery of this service are the availability of medical expertise and appropriate facilities.

Detailed and accurate statistics reflecting this are obviously virtually impossible to attain but in a 2009 systematic review the authors report that an estimated 2 to 3 billion people have no access to surgical care. They also report that surgical conditions account for 11% of total lost years of healthy life. All surgical disciplines are affected but to varying degrees. The World Health Organisation (WHO) defines surgery as an invasive intervention, but does not specifically clarify the need or place of anaesthesia. [6] In more recent literature, the Lancet Commission on Surgery and global health reaffirmed the finding that nearly 1 in 3 people worldwide do not have access to appropriate surgical care. [7] Disorders requiring surgical intervention are believed to comprise in the region of 10% (or 4.7 million) of deaths for the year 2011, in mid- and low-income countries. In the same paper, Mock et al. call for the production and dispersal of, inter alia, low-cost anaesthesia machines. They estimate that costs would amount to approximately $ 3 billion annually to diffuse surgical care such that appropriate procedures are available at primary hospitals but point out that a cost-benefit ratio of 10:1 could be gleaned from such spending. [8] At the 68th World Health Assembly, held on the 26th of May 2015, agenda item 17.1 highlighted the importance of strengthening the delivery of essential surgical care and anaesthesia. They point out that, internationally, each year more than 100 million people sustain traumatic injuries, more than 5 million people die from accidental and non-accidental trauma, and that 90% of the global burden of violence and injury mortality occurs in low- and middle-income countries. [9]

The debate has been how to safely and affordably close the gulf between supply and demand for anaesthesia in this patient population on a sustainable basis.

“Part of the solution or …”

Considering the above academic predilection to plenum systems and circle circuits and the scientific principle to move from the known to the unknown, it is easy to appreciate that experts first consider closed systems and their attendant issues: fresh gas supply, carbon dioxide absorbent, complexity of equipment and the need for electricity; all whilst being cost-effective.

A closed breathing system is, however, advised against in some texts; identifying the interruption of the oxygen supply as the chief danger. There are further difficulties with vaporisation outside the circuit with the use of basal flow rates and similarly, using artificial ventilation with the vaporiser in the circuit. The erratic supply of CO_2 absorbent additionally complicates the use of this system and adds to its cost when available. [10]

The importance of reliable availability of oxygen is clear and even as early as 1983 authors suggest a system that makes use of a “continuous flow of air by compressors with or without added oxygen, for use with continuous flow type of apparatus”. [11]

More sophisticated equipment, unfortunately, requires regular servicing which is often difficult and costly due to the large distances that need to be covered for a relatively small number of anaesthetic workstations.

Funding of healthcare operations is as fragile as any other part of the system and is often interrupted for a variety of reasons. This mandates that the provision of such a service be as cost-effective as possible.

Given the aforementioned unpredictability of oxygen supplies, an anaesthetic apparatus designed for the developing world should be economical in its consumption thereof. [10]

In one publication, authors show that electricity supplies are also frequently interrupted and even generator supply is often lost. Thus, design of an apparatus must take into account that electricity may be lost for hours at a time. [10]

In the same article, the authors also call for an apparatus that continues to function in the complete absence of compressed gases. Furthermore, they feel that it should be capable of providing anaesthesia to patients who are breathing spontaneously and those that have been paralysed pharmacologically, necessitating artificial ventilation.

When electricity is available, Ezi-Ashi et al. feel that it would optimally be used to drive an oxygen concentrator. [11]

Robustness, reliability and servicing

"Robustness, reliability and minimal servicing requirements are essential; simplicity of design is therefore implied". [12]

The next logical step would then be to describe specifications for a device theoretically capable of answering to the requirements described above.

In a two-part 1983 review Ezi-Ashi et al. investigated and discussed the delivery of inhalational anaesthesia in developing countries. In this paper, they conclude that draw-over anaesthesia is safer in such an environment and that safety is improved by even low flows of oxygen. Also, that the availability of oxygen is facilitated by the provision of reliable electricity. [12]

The same authors suggest that a compressor for use with a Boyle-type machine should be able to generate at least 25 kPa and flows of between 12 and 20 litres per minute. [11]

Oxygen concentrators are specifically discussed – even in older literature. Compressed air is usually passed over Zeolite that removes nitrogen and water vapour, leaving approximately 90% oxygen with the remainder composed of nitrogen and argon. [11]

Electricity is still, unfortunately, a necessity, being supplied from mains, generator or batteries. [12]

Several designers and manufacturers have made attempts at producing an anaesthesia workstation that meets these requirements (vide infra) but we must first consider the inherent safety implications of such a device.

Primum non nocere

When administered to humans, gases should be free of oil, particulate matter, carbon dioxide, carbon monoxide, etc. This could be obtained by drawing or passing compressed air through specially designed filters. [12]

Prior to inducing anaesthesia, the Association of Anaesthetists of Great Britain and Ireland (AAGBI) recommends that an alternative means of ventilation be immediately available. [13] Clearly, this responsibility falls on the shoulders of the anaesthetist, and apparatus manufacturers cannot necessarily be expected to cater for this eventuality.

In a different section of the same guidelines, the AAGBI places "absolute responsibility for product safety on the manufacturers". [13] Suppliers are also audited on the provision of maintenance. These guidelines also demand that anaesthetists be trained to use the equipment. [14, 15] As highlighted before, a deficiency of training of this kind can, in its own right, be a significant cause of anaesthesia related morbidity and mortality.

Some authors regard capnography as an essential part of the routine monitoring during anaesthesia. The use of a vapour analyser is also regarded as essential during anaesthesia whenever a volatile agent is in use. [16]

Even in developed-world literature, authors of safety guidelines recommend that failure of the oxygen supply be addressed prior to the surgery and that a plan is in place: "Check that the apparatus is connected to a supply of oxygen and that a reserve supply is available from a spare cylinder". [17] Oxygen failure is not the only problem that clinicians face in austere

conditions. Some areas, by their very nature, predispose to hypoxia, e.g. those at significant altitude. King et al found that supplemental oxygen at an inspired fraction of 0,3 should be delivered at altitudes greater than 1 500 meters above sea level. Failing the availability of this, they regard intermittent positive pressure ventilation as necessary. [18] These 2 requirements remain central to the safety of any device to deliver anaesthesia.

Of course, arguments against draw-over techniques must be presented and relate predominantly to the benefits of a circle system.

Minimal and low-flow anaesthesia are certainly superior in terms of the preservation of temperature and humidity and the benefits of this are weighed against the potential risks of hypoxia and intra-operative awareness. [2]

Researchers investigating respiratory function and mucociliary clearance in patients receiving desflurane and nitrous oxide, found that these physiological functions are better preserved in a low-flow than in a high-flow anaesthesia technique. This is attributed to the appropriately heated and humidified air introduced into the tracheobronchial tree that limits the desiccation of secretions and increased mucous retention as well as heat loss. This is believed to cause partial occlusion in bronchioles that have undergone micro-atelectasis. All these sequelae are thus prevented by a system where exhaled gases are returned to the patient. [2] Circle systems retain exhaled water vapour and supply heat and water vapour from the absorber.

Plenum vaporisers have a constant driving pressure and predictable flow rates. Thus, they are generally more accurate than draw-over vaporisers, in addition to the above benefits.

Arguments against the use of a plenum system relate to the increased complexity (particularly the circle system, that most often accompanies it) and accompanying internal resistance, subsequently increasing the work of breathing for a spontaneously ventilated patient. [2] Draw over systems are also less accurate than plenum vaporisers at flows below 2-4 L/min or with small tidal volumes. [19]

Costs

Some regard the cost of anaesthesia care as having three main components. Direct costs (cost of agents, materials and labour), indirect costs (costs related to the consequences of an event) and intangible costs (the costs related to pain and suffering as a result of illness or treatment). The latter 2 costs, however, are clearly difficult if not impossible to quantify. [1]

The direct costs may be divided into fixed and variable costs. Fixed costs are negotiated in advance and remain relatively fixed for a particular period. Some variable costs depend on decisions made by clinicians, and this represents an opportunity to save costs. [1]

The fixed factors that contribute to the cost of inhaled anaesthetic agents include the acquisition cost per millilitre (mL), the volume of vapour produced per mL of liquid and the potency of the agent. The concentration of the agent required may vary (according to age, concurrent medications, temperature, etc.) and the depth of anaesthesia required for the invasiveness of the surgery being performed. [1]

The costs of an inhaled anaesthetic agent can be expressed as the cost per MAC hour, defined as administration of the inhaled anaesthetic agent at 1 MAC for one hour. This is calculated from the concentration of gas delivered, its minimum alveolar concentration (MAC), fresh gas flow rate, duration of inhaled anaesthetic delivery, molecular weight, cost per mL, a factor to account for the molar volume of a gas at 21°C and density. [16] The fresh gas flow rate is clearly the only parameter under the control of the anaesthetist. [1]

Indirect costs, whilst potentially a source of cost reduction, will not be reviewed here.

One study that compared low-flow anaesthesia (at 600 mL/min) to flows of 4 L/min found a 65% reduction in the amount of anaesthetic agent (Isoflurane) used. This just mathematically demonstrates a well-accepted concept but suggests that similar cost reductions may well be made elsewhere as well. [20]

Upon procuring medical devices the MHRA recommend that the following costs and issues be considered:

- Device cost and the cost of its installation
- Maintenance required and the cost thereof
- The availability of servicing insurance
- Cost of its consumables
- Value for money
- Cost of its disposal

Routine maintenance includes regular cleaning, preparing the device for its use and device calibration of the device. [21]

We have thus far considered technical requirements of an anaesthetic apparatus for the developing world. We have looked at pros and cons from a safety perspective and briefly reviewed the factors influencing the costs of administering anaesthesia in such settings.

Specific Solutions

"In austere locations, versatility of manpower and equipment are a must." This was said in reference to the Portable Anaesthesia Complete (PAC) system. It is used by the Forward Surgical Team of the US military and the British armed forces and also makes use of draw-over technology. [22]

Triservice Anaesthetic Apparatus

Many anaesthetic machines have been developed to answer the needs of the developing world. An addition to this has been the Triservice Anaesthetic Apparatus. This system incorporates a manual inflation system, two identical vaporisers, an oxygen supplementation system and an optional mechanical ventilator (that would, however, need compressed gas or electricity). The vaporiser in this system is descendant of the Oxford Miniature Vaporiser (OMV) and constructed from stainless steel, normally requiring no maintenance. The gas delivery components (circuitry etc.) is amenable to disinfection, should the need arise. The

oxygen supplementation system was purpose-built for this system and the two lowest flow rates were made available, namely 1 L and 4 L per minute. This, however, could be altered mechanically by changing the size of the apertures in the flow regulator.

The apparatus is rather meticulously reviewed but no perspective is provided in terms of its cost efficiency. Investigators in a 1981 article found respiratory rates between 11 and 24 breaths/minute with tidal volumes between 250 and 1 000 mL. They conclude that the modularity of this device improves its functionality as different components can be arranged in different sequences. [3]

The Portable Glostavent

Again, in a 2010 review of the above machine, Tully et al. call for a machine that can deliver anaesthesia safely in the absence of electronic monitors whilst using oxygen efficiently or not at all available.

In this device, additional oxygen can be delivered by a cylinder or an oxygen concentrator. Its reservoir system has been modified in such a way that room air is entrained when the patient's minute volume exceeds the oxygen flow rate. This is believed to allow for the efficient use of oxygen and for effective pre-oxygenation as well as minimising the space required for its use (the concentrator is not "on-board"). It makes use of a low resistance Diamedica vaporiser that can be used for both draw-over and continuous flow anaesthesia, and a Laerdal or Ambu non-rebreathing valve. This device can be assembled in less than 2 minutes.

It has evolved into its current state over 15 years and is intended for use in rural hospitals where draw-over anaesthesia represents the standard of care as "… another concern for those administering anaesthesia in isolated environments is the difficulty in obtaining pressurised oxygen." With this apparatus in use, inhalational anaesthesia can be administered using room air if the oxygen supply should fail. It also allows for the use of manual assisted ventilation to counter the negative effects of inhalational anaesthesia. Patient safety is believed to be improved by the simple design of the apparatus, especially where sophisticated monitoring or carbon dioxide absorption systems are not available.

The authors of this article make the following claim with regards to the portable Glostavent: "In our opinion, therefore, careful clinical observation of a patient anaesthetised using a simple draw-over system is likely to be at least as safe as the use of the more complicated system that requires monitors which may be inaccurate or non-existent".

In disaster situations, an apparatus used for the delivery of oxygen should be portable, easy to use, be resistant to wear and tear and be easy to service. It should also be amenable to patients of varying sizes and should be able to deliver anaesthesia in the absence of pressurized oxygen at a sufficiently high F_IO_2 to deal with an emergency. They also call for a device that makes economical use of oxygen.

They claim that the portable Glostavent fulfils all these requirements and successfully fills the shoes of the Tri-service anaesthetic device. [10]

The Glostavent

The above devices were designed for use in austere conditions. [22] The Glostavent is a device that has evolved from its portable predecessor to deliver inhalational anaesthesia in Low or Low-Middle Income Countries (LMIC) and has met the World Federation Of Societies of Anaesthesiologists (WFSA) performance standard in this regard. [23]

It has an oxygen concentrator capable of producing 8 litres per minute oxygen (at 95%) and an equal amount of air. This rendition of the device still makes use of the Diamedica vaporiser. It is capable of functioning in the absence of electricity by means of an uninterruptible power supply and battery. This device, of all those commercially available, most closely represents the Universal Anaesthesia Machine (UAM), except that it includes an on-board minute volume divider that allows for positive pressure ventilation. [23]

The Universal Anaesthesia Machine

This device was developed as a low-cost anaesthetic machine for poorly resourced countries. Its designer and manufacturers claim ease of use and efficient consumption of oxygen in

either draw-over or continuous flow modes. It is the latest addition to the armamentarium of the anaesthetist in a resource poor environment.

The UAM combines draw-over and continuous flow systems. It is capable of working in areas without oxygen or electricity supplies. Its oxygen concentrator avoids the need for sourcing compressed oxygen. It therefore aims to deliver low cost, environmentally friendly anaesthesia. The vaporiser is manufactured by OES Medical (Oxford, UK) and of the low-resistance draw-over type, available for Isoflurane and Halothane. It has a built in oxygen concentrator and can therefore deliver supplemental oxygen even when piped or cylinder oxygen fails or runs out. Key differences from a standard Boyle's machine are the oxygen concentrator, draw-over vaporiser, bellows and balloon valve. [24]

In a 2010 publication, authors in the United Kingdom reported on initial experiences. They anaesthetised 283 patients aged 1 month to 92 years and 4 kg to 92 kg.

The authors were unable to report any machine fault but unfortunately failed to report on its efficiency. [25]

This apparatus was evaluated in the UK and was found to be as safe as generally available equipment. It was regarded as being simple and very easy to learn to use. It was, however, found to have certain limitations:

- In the case of electrical failure a generator would have to drive the oxygen concentrator or an alternative oxygen source would have to be available.
- More volatile anaesthetic agent will need to be consumed
- Where long periods of manual ventilation are required, it may become tiring. [24]

This apparatus allows a demand flow patient breathing system to receive up to 10 L/min of 95% oxygen from the concentrator. [4, 25] It incorporates a unique balloon valve that has reportedly functioned well over a period of several years in extremes of temperature, dust and humidity. It can accept and use oxygen and nitrous oxide at any pressure and has built in oxygen failure alarms. Its designer and manufacturer claim that it has lower maintenance costs. [4]

Almost most importantly, it is the only CE marked device of this nature designed for the developing world. [24]

Conclusion

Several generations of devices have been designed over recent decades in an attempt to answer the need for safe, reliable and cost-effective anaesthesia in the developing world.

Gradian Health along with Dr Paul Fenton have come forward with a possible solution and claim that the on-board oxygen concentrator is able to offset the additional costs of increased volatile agent consumption.

The researchers felt that this warranted further investigation. There were no prior studies evaluating a draw-over system against a plenum system in a prospective fashion. Thus, a research protocol was developed de novo.

2. Hypothesis

It is hypothesized that the UAM is able to deliver anaesthesia at a comparable cost to a plenum system, as it requires no gas supply. It extracts oxygen from room air by means of a built-in oxygen concentrator and uses no carbon dioxide absorbent.)

3. Methodology

The primary outcome of the study is a comparison of the total cost (in South African Rand per minute) of the two groups based on the costs of consumables at the Groote Schuur Hospital in Cape Town, South Africa. This will allow us to derive and publish equations that will allow stakeholders to determine the cost efficiency of various options in the context of their own setting.

The secondary outcomes were:

- Electricity consumed in kWh
- Volatile agents consumed in mL/min.
- Oxygen consumed in L/min (for the plenum group only)
- Medical air consumed in L/min (for the plenum group only)
- Carbon dioxide absorbent consumed in mL/min (for the plenum group only)

Costs that are identical were omitted:

- Machines are maintained by salaried in-house technologists. Specific parts can be ordered from the manufacturers when necessary and this cost, should it arise is easy to establish. Gradian offer product support but the costs relating thereto are very difficult to estimate as they are location based.
- Gradian have, thus far, established their workstations as a non-profit organisation and charge USA $ 12 000 per unit, which represents cost price. They provide on-site training for technicians upon installation at no additional cost. They offer a warranty on parts for 2 years. The plenum systems in use are purchased on a tender basis and prices are variable.

- Circuit replacement and sterilisation is identical in terms of cost as the same circuits are used.
- Humidifiers/filters are used in an identical fashion and are also disregarded.

We applied for ethics approval to the Human Research Ethics Committee and this was granted (HREC 613/2013). Patients were asked to consent based on the relevant ethical principles whilst of sound mental health and under no coercion whatsoever.

We recruited American Society of Anaesthesiologists (ASA) Class 1 and 2 patients between the ages of 18 and 75 who were scheduled for elective non-elevated risk surgery. The planned surgical procedure in all instances was amenable to patients that ventilated spontaneously through a laryngeal mask airway under general anaesthesia.

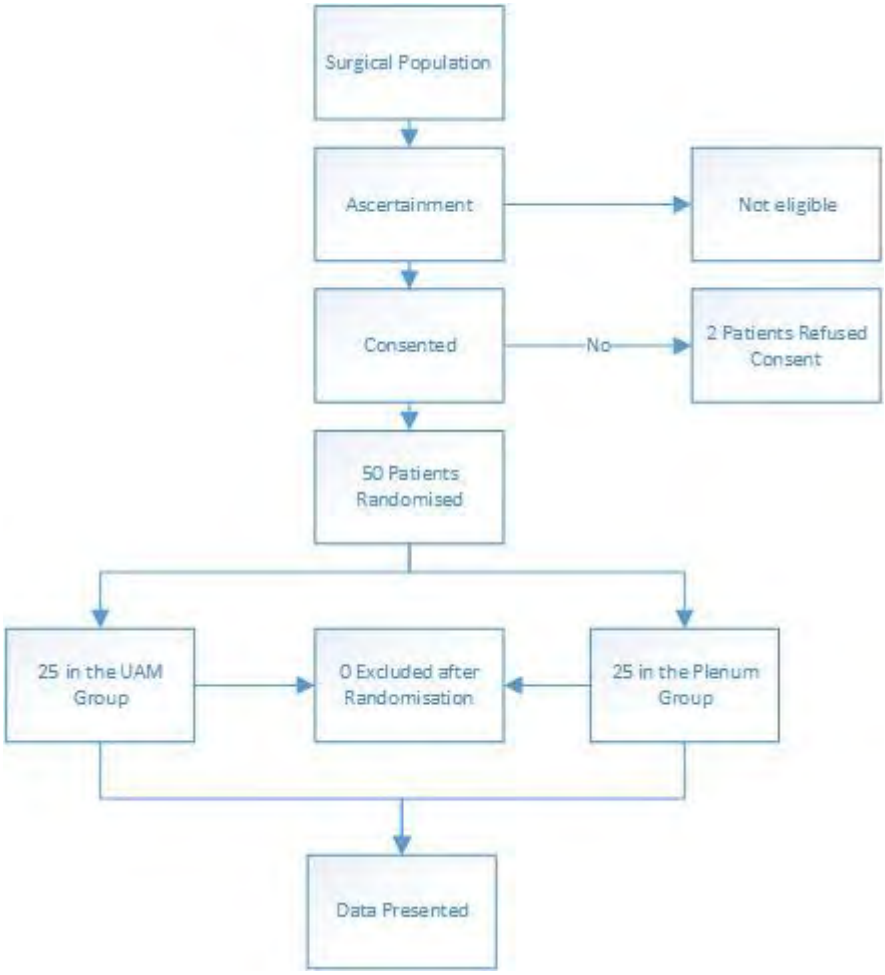
No patients were removed from the study due to surgical complications necessitating the escalation of anaesthesia care.

Specific exclusion criteria were:

- Patients younger than 18 or older than 75
- Those classified as ASA 3 or higher
- Procedures where the patient could not be rendered subjectively comfortable by means of morphine and/or local anaesthesia alone.
- Procedures where positive pressure ventilation was inherently necessary or may have become necessary during the course of the procedure.

Two groups were created, 25 patients in each: one for the UAM and the other for the standard system. Participants were allocated to either one by means of a table of random numbers that was created before initiation of the study. This table was created by means of the Excel function “randbetween”. Cells in one column were numbered 1 to 50 and in an adjacent column, cells were allocated to either group one or two and subsequently renamed “A or B”. Patients were not made aware of which group they were allocated to. Unfortunately, clinicians could not be blinded to which machine was in use. This was due to the size of the respective devices and the noise that the oxygen concentrator aboard the UAM generates. Thus, a single-blinded study was conducted.

Anaesthesia was administered and data collected by means of a predetermined protocol. Only minor deviation from this protocol was ever necessary and patient safety or data integrity were never compromised (vide infra).



CONSORT diagram. No participants were excluded once enrolled.

- The same Universal Anaesthesia Machine was used for all cases in the "UAM group". Only machines clearly marked "Datex Ohmeda Aespire" was used for the plenum group. The workstations were checked for circuit integrity and safety. The vaporisers were emptied completely by opening the sump and allowing the agent to drain into an Isoflurane bottle. Emptying was regarded as complete when no drops fell from the aperture for 10 consecutive seconds. The Isoflurane bottles were weighed using a scale, the figure recorded and then the vaporiser refilled.
- Once standard ASA monitoring was applied, patients received 0,1 mg/kg of morphine. No participant experienced adverse effects. The same Datex-Ohmeda monitor was used on both anaesthetic workstations and was plugged into the

workstation so that its electricity consumption was accounted for by our measurement device (an Efergy energy monitoring socket 2.0, commercially available).

- Patients in both groups were pre-oxygenated for 3 minutes.
    - The Plenum group received 3 L/min of oxygen and 1 L/min of air for 3 minutes.
    - The UAM group received ± 90% oxygen at ± 5 L/min.
    - The difference would not jeopardise data integrity as the UAM did not make use of piped oxygen supplies.
    - The initiation of pre-oxygenation was regarded as "Time in". The energy meter was zeroed at this time and measurement commenced.
- Anaesthesia was induced with Propofol at approximately 2 mg/kg. This was titrated such that the laryngeal mask airway (LMA) was tolerated. Where doses beyond this were required, no significant additional ventilator support ever became necessary.
- Once anaesthesia had been induced:
    - The UAM group was maintained at an F_IO_2 of 0,4 until the conclusion of surgery.
    - The Plenum group was allowed another 5 minutes of "wash-in" at the above flows. After this fresh gas flows were turned down to 0,5 L/min each of air and oxygen. Where deviations occurred, they were clearly recorded and accounted for during statistical analysis.
    - Anaesthesia was maintained by means of an end-tidal Isoflurane concentration of 1% as measured by a gas analyser for both groups.
    - The carbon dioxide absorbent was employed from the initiation of pre-oxygenation until 3 minutes after the conclusion of surgery or where the LMA was no longer tolerated.
    - Where ventilatory support became necessary, a breath was administered every 30 seconds. No patient ever required support beyond the onset of the surgery.
    - Where additional analgesia was deemed necessary, morphine was administered. The individual doses were recorded. The targeted response

was unfortunately a subjective one. If patients were not tachycardic (having had hypovolaemia ruled out), not tachypnoeic nor hypertensive (in the absence of other causes); they were regarded as pain free. The administration of local anaesthetic agents to the wound was done at the end of the procedure and represented (if applicable) the last painful stimulus. Considering the fact that patients were allowed to breathe spontaneously and subjected to procedures not characterised by large volume shifts, we used swab counts, suction bottles and (if catheterised) urine output to monitor the loss of volume.

    - Haemodynamic parameters where maintained within autoregulatory limits (i.e. a mean arterial blood pressure of more than 65 mmHg) and 20% of baseline in hypertensive patients. This was achieved by means of phenylephrine boluses (50 µg) and/or ephedrine (5 mg) boluses.

- At the conclusion of the surgery:
    - The vaporiser was switched off (both groups).
    - The fresh gas flows were turned up to 3 L/min of air and 1 L/min of oxygen in the Plenum group. Erroneously, some cases were allowed 3 minutes and others 5 minutes of washout. The average duration of washout was 4 minutes. Each individual case was recorded separately and the duration of the case calculated. This does not impact on the final cost per minute.
- At the conclusion of the anaesthetic:
    - The amount of electricity consumed was recorded (both groups), the soda lime canister was dropped from the circle circuit and the fresh gas flows increased to meet the requirement of the leak in the circuit. The "time out" was recorded at this stage. This presented a data point when the anaesthetic was over and its duration could be calculated. Data collection had ceased prior to high flows necessitated by the circuit leak. Once the LMA had been removed, the flows were closed and the patient transferred to the recovery area.
    - The same soda lime canister was used as described until the inspired partial pressure of CO_2 (P_ICO_2) was 1,0 kPa for 10 minutes. The amount of absorbent was then averaged out over the number of minutes that it took to be saturated (calculated from the "time in" and "time out" fields. The

randomisation and participant identification unfortunately necessitated periods of time between cases in the Plenum group. This meant that, to an unquantifiable extent, the absorbent was allowed to regenerate. This will almost certainly underestimate the consumption of the absorbent.

- Once the patient had been handed over to the recovery staff, the vaporiser was emptied into the same bottle from which it had been filled. The bottle was then weighed and the figure recorded (both groups). To quantify the amount of volatile that may have spilled and/or vaporised is virtually impossible.

4. Results

50 Participants were enrolled into one of two groups and subjected to the following surgical procedures:

Procedure	UAM	Plenum
General Surgery:		
Lymph node biopsy	2	
Incision & drainage abscess	7	5
Split skin graft	2	
Microductectomy	1	
Excision breast mass		1
Rectal biopsy		1
Orthopaedic Surgery:		
Wound debridement	1	
Removal of orthopaedic hardware	1	2
Open reduction & internal fixation (ORIF) – Calcaneum	1	
ORIF – Distal radius fracture	1	
Metacarpal joint release or ORIF – Finger	1	1
Bunion correction		1
Orthopaedic open biopsy	2	
ORIF & bone graft - Tibia		1
Multiple nerve transfers		1
Percutaneous ORIF – Distal femur		1
Urology:		
Transurethral cystoscopy, lithotripsy & stent insertion	1	4
Extra-corporeal shock-wave lithotrypsy	2	4
Gynaecology:		
Operative hysteroscopy and IUCD insertion	1	3
Cervical cone biopsy	2	
Totals	**25**	**25**

Table 1. Detail of the distribution of procedures between the respective groups.

A fairly heterogeneous group of procedures are thus seen. This is believed to realistically simulate the surgical stimulus that may be encountered in a resource-poor setting, in that neurosurgical, thoracic and major intra-abdominal procedures were excluded.

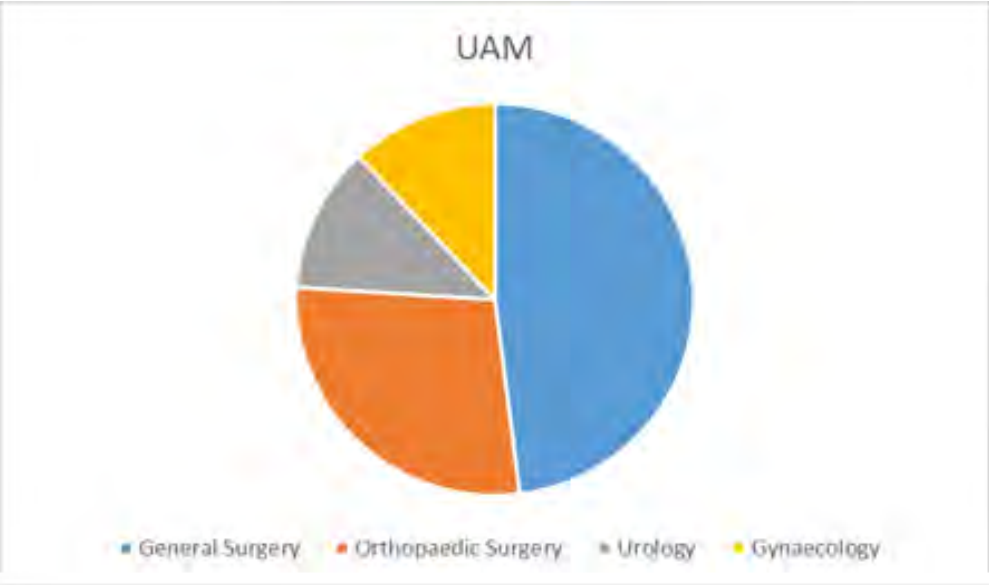


Fig. 1. Graphic presentation of procedures for which the UAM was used.

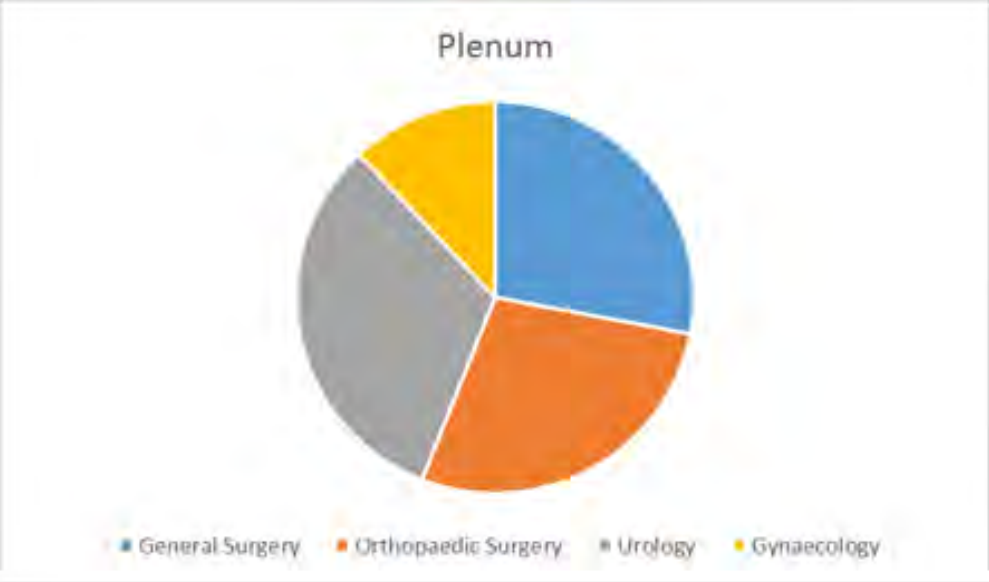


Fig. 2. Graphic presentation of procedures for which the plenum system was used.

The demographic and general properties of the 2 groups were as follows:

Parameter	UAM	Plenum
Average age	40,6 years	41,6 years
Males	12	9
Females	13	16

ASA 1	13	17
ASA 2	12	8
Average weight	75,7 kg	76,0 kg

Table 2. Demographic data of the 2 groups

Parameter	UAM	Plenum
Average morphine dose	7,60 mg	7,83 mg
Average morphine dose per kg	0,101	0,103
Average duration of surgery	52,0 minutes	61,6 minutes

Table 3. General data of the 2 groups

It is seen here then that the 2 groups were sufficiently similar to regard patient factors as being controlled for as far as reasonably possible. The cases in the plenum group were, on average, longer and this was accounted for by calculating the cost per minute of administering the anaesthetic.

The cost of consumables at our centre (Groote Schuur Hospital, Anzio Road, Observatory, Cape Town, South Africa) are in South African Rand (ZAR):

Consumable	Cost
Electricity	R 0.80 per kWh
Carrier gas: Oxygen	R 0.0072 per litre
Carrier gas: Air	R 0.0072 per litre
Isoflurane	R 216.18 per 250 mL
Carbon dioxide absorbent (soda lime)	R 169.12 per 5 litre container

Table 3. Cost of consumables

The statistical analysis was done by means of an electronic package, Statistica Version 12. The total cost per anaesthetic was calculated. The data were subjected to a test for normality of distribution and found to be non-parametric in distribution.

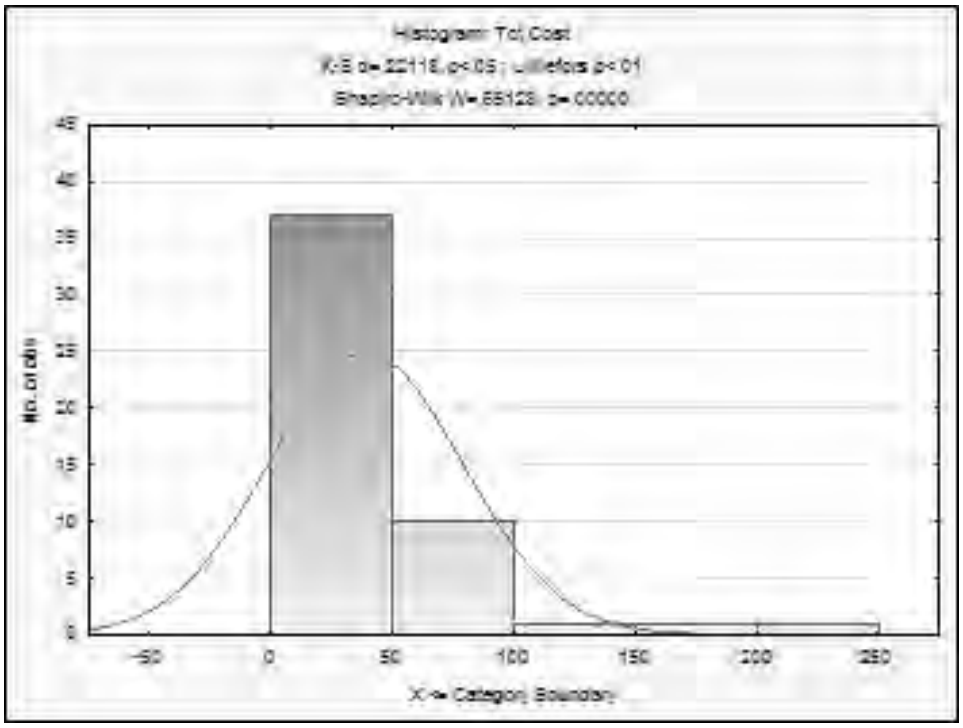


Fig. 3. The non-parametric distribution of the data

Data were subjected to a Man-Whitney-U test with continuity correction. The findings were as follows:

Group	Mean	Confidence Interval	p value
UAM	R 0.974/min	R 0.860/min to R 1.087/min	< 0,00001
Plenum	R 0.459/min	R 0.384/min to R 0.534/min	

Table 4. Comparative cost of anaesthesia

The finding is thus that a statistically significant difference exists between the 2 groups.

This is, however, not surprising, and represents only the preliminary part of our question. The next part relates to the generation of equations that may allow healthcare managers to predict the cost effectiveness of a device of this nature.

Total Cost per minute for the Plenum System is calculated as follows:

$$\frac{\textbf{Volatile Cost + Electricity Cost + Gas Cost + Soda lime Cost}}{\textbf{Duration of Anaesthesia}}$$

If this is then expanded upon:

$$\frac{[(\text{Volatile} \times 1{,}496) \times (\text{cost}_V \div \text{vol}_V)] + [\text{Elect} \times \text{cost}_E] + [\text{Gas}_1 \times \text{cost}_{G1} \times \text{Time}] + [(0{,}5076 \times \text{Time}) \times (\text{cost}_S \div \text{vol}_S)]}{\text{Time}}$$

Legend

- Volatile = Amount of volatile consumed in grams. If the volume in millilitres (mL) is known, the correction factor 1,496 is omitted.
- $cost_V$ = Cost per unit as the volatile is issued by the pharmacy. i.e. cost per bottle
- vol_V = Volume of volatile agent as issued by the pharmacy. i.e. bottle volume in mL
- Elect = Amount of electricity consumed in kilowatt hour.
- $cost_E$ = Cost of electricity as provided by the supplier per kilowatt hour.
- Gas_1 = Averaged fresh gas flow in L/min. This term needs to be expanded if more than one gas is used. For each additional carrier gas the term:

  (Gas_2 x $cost_{G2}$ x Time)

  is included and summed.

- $cost_{G1}$ = Cost of the gasses (per litre) as provided by the hospital.
- 0,5076 = Consumption (mL) of soda lime per minute from our data.
  Canister volume of 667 mL that lasted 1 314 minutes to reach an inspired fraction of carbon dioxide equal to 1 percent (F_ICO_2 of 0,01).
- $Price_S$ = Purchase price of a container of carbon dioxide absorbent as issued by the pharmacy.
- vol_S = Volume of carbon dioxide absorbent container as provided by the pharmacy.
- Time = Duration of the anaesthetic in minutes

For a draw-over system, the term relating to carbon dioxide absorbent can be omitted and, if only an oxygen concentrator is used the terms relating to fresh gas flow can similarly be omitted:

$$\frac{[(\text{Volatile} \times 1{,}496) \times (\text{cost}_V \div \text{vol}_V)] + [\text{Elect} \times \text{cost}_E] + [\text{Gas}_1 \times \text{cost}_{G1} \times \text{Time}]}{\text{Time}}$$

Draw-over with non-concentrator Oxygen or Nitrous oxide

$$\frac{[(\text{Volatile} \times 1{,}496) \times (\text{cost}_V \div \text{vol}_V)] + [\text{Elect} \times \text{cost}_E]}{\text{Time}}$$

Draw-over with only concentrator Oxygen

Legend:

- Volatile = Amount of volatile consumed in grams. If the volume in millilitres (mL) is known, the correction factor for grams to millilitres of 1,496 is omitted.
- cost_V = Cost per unit as the volatile is issued by the pharmacy. i.e. cost per bottle
- vol_V = Volume of volatile agent as issued by the pharmacy. i.e. bottle volume in mL
- Elect = Amount of electricity consumed in kilowatt hour.
- cost_E = Cost of electricity as provided by the supplier per kilowatt hour.
- Gas_1 = Averaged fresh gas flow in L/min. This term needs to be expanded if more than one gas is used. For each additional carrier gas the term:

  $(\text{Gas}_2 \times \text{cost}_{G2} \times \text{Time})$

  is included and summed.
- cost_{G1} = Cost of the gasses (per litre) as provided by the hospital.

5. Shortcomings

The fairly novel nature of the UAM has meant that there are no prospective data considering its cost-efficiency. This coupled to the fact that the question of cost-efficiency in the context of draw-over anaesthesia has never been addressed prospectively has made both literature review and protocol development particularly challenging.

The filling of the UAM vaporiser necessitates that volatile agent be poured into it. This, even if no agent is spilt, inherently means that some of the agent vaporises. The plenum vaporiser, in contrast, is almost a sealed system where virtually no vapour is lost during filling. This difference skews data in favour of the plenum system. We are not aware of a sustainable solution to control for this situation and believe that it represents a problem that exists when the device is used in clinical practice.

The randomisation process unfortunately required that there were periods of time (days) between the enrolment of cases in the plenum group. To avoid the soda lime canister being used during non-research cases, it had to be removed and kept away from the theatre complex. This led to the carbon dioxide that had been absorbed being liberated to an unquantifiable extent, allowing regeneration of the soda lime. This would have skewed data in favour of the plenum system in that the amount of soda lime consumed was underestimated over the total duration of time that it was used.

6. Conclusion

We present mathematical relationships that aim to aid responsible persons to predict the cost efficiency of the Universal Anaesthesia Machine and a circle system for their particular environment. These equations hope to accommodate factors that influence the acquisition price of carrier gas and other consumables. We are unfortunately not able to account for all the relevant costs, as is the case when a workstation has its battery charged and is then used or the influence of oil and fuel prices, distances between sites where oxygen is dispensed and anaesthesia is delivered etc. These costs may vary between different health environments and our equations hope to allow for these variations. Costs relating to the installation and maintenance of these devices are also highly variable and often determined by factors that are extremely difficult to account for. It is our belief that the safety and robustness of draw-over anaesthesia systems will continue to render it a very attractive option in a resource-poor setting and the data presented here may well strengthen the argument for the acquisition of the appropriate equipment.

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Participant Information Document

The Universal Anaesthesia Machine (UAM) is a newly developed anaesthesia machine, specifically designed for patients that breathe on their own during their operations.

The study we aim to conduct is titled: "A cost comparison of spontaneously ventilated patients: the UAM as a possible cost effective alternative."

Our study will compare the costs incurred by the use of the Universal Anaesthesia Machine to the costs incurred by the use of a standard anaesthesia machine. We will simply record the amount of oxygen, medical air, anaesthetic drugs, electricity and carbon dioxide absorbent used during the anaesthetic.

We are planning to pay for our own research.

You will not be paid for if you decide to participate in this study.

The research question was originally suggested by the machine's manufacturers (Gradian Health). That is, however, the extent of their involvement. Neither of the investigators holds any personal interest in this company. Therefore, no conflict of interest exists.

The information gathered from this study will hopefully help health managers (particularly in 3rd world systems) to buy the most appropriate anaesthetic machines.

There are no particular benefits, harm or additional risks to you as participant. We will use anaesthesia machines already in active daily use according to the standard of care at our hospital. All the machines in use have been tested, checked and certified as safe.

The University of Cape Town (UCT) undertakes that in the event of you suffering any significant deterioration in health or well-being, or from any unexpected sensitivity or toxicity, that is caused by your participation in the study, it will provide immediate medical care. UCT has appropriate insurance cover to provide prompt payment of compensation for any trial-related injury according to the guidelines outlined by the Association of the British Pharmaceutical Industry, ABPI 1991. Broadly-speaking, the ABPI guidelines recommend that the insured company (UCT), without legal commitment, should compensate you without you having to prove that UCT is at fault. An injury is

considered trial-related if, and to the extent that, it is caused by study activities. You must notify the study doctor immediately of any side effects and/or injuries during the trial, whether they are research-related or other related complications.

UCT reserves the right not to provide compensation if, and to the extent that, your injury came about because you chose not to follow the instructions that you were given while you were taking part in the study. Your right in law to claim compensation for injury where you prove negligence is not affected. Copies of these guidelines are available on request.

Consent Document

You can freely choose to participate or not to participate in this study. You will suffer no harm or discrimination and will still receive care according to the standard at our facility.

Your participation in this study will not have any influence on the standard of care that you will receive, regardless of whether you decide to participate or not.

We will pay for our own research and neither of the researchers hold any interest in the company that makes the UAM. There is, therefore, no conflict of interest.

You will not be paid to participate in this study.

If you should decide to consent, you are welcome to withdraw consent before or after your operation. You will continue to receive care according to the usual standard of our facility. If you do decide to take part, you will not be expected to do or say anything beyond what is expected of any other patient.

If you choose to participate, you will be assigned to one of the two groups: either the group where a standard machine will be used or the group where the UAM will be used.

We will record your weight, the amount of electricity, pain medication received, anaesthetic drug, oxygen, medical air and carbon dioxide absorbent used during your anaesthetic. We will also record the duration of your anaesthetic. After your anaesthetic is over, your involvement in the study will end.

Should you wish to see the results of the research on your anaesthetic, this information can be made available to you.

The University of Cape Town (UCT) undertakes that in the event of you suffering any significant deterioration in health or well-being, or from any unexpected sensitivity or toxicity, that is caused by your participation in the study, it will provide immediate medical care. UCT has appropriate insurance cover to provide prompt payment of compensation for any trial-related injury according to the guidelines outlined by the Association of the British Pharmaceutical Industry, ABPI 1991. Broadly-speaking, the ABPI guidelines recommend that the insured company (UCT), without legal commitment, should compensate you without you having to prove that UCT is at fault. An injury is considered trial-related if, and to the extent that, it is caused by study activities. You must notify the

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If you have any questions or complaints about your welfare or rights as participant, you can contact any of the researchers:

Dr. G.P. van Rensburg: 082 554 1405 or 021 404 5001

Dr. R.W. Nieuwveld: 021 404 5445 or 021 404 5001

Or the Human Research Ethics Committee:

Prof. Marc Blockman (Chairman): 021 406 6338

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Participant Investigator