

# Inhalational or total intravenous anaesthesia: is total intravenous anaesthesia useful and are there economic benefits?

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**Current Opinion in Anaesthesiology** 2011, 24:000–000

## Purpose of review

The comparison of inhalational and intravenous anaesthesia has been the subject of many controlled trials and meta-analyses. These reported diverse endpoints typically including measures of the speed and quality of induction of anaesthesia, haemodynamic changes, operating conditions, various measures of awakening, postoperative nausea and vomiting and discharge from recovery and hospital as well as recovery of psychomotor function. In a more patient-focused Health Service, measures with greater credibility are overall patient satisfaction, time to return to work and long-term morbidity and mortality. In practice, studies using easier to measure proxy endpoints dominate – even though the limitations of such research are well known.

## Recent findings

Recent study endpoints are more ambitious and include impact on survival from cancer and the possibility of differential neurotoxic impact on the developing brain and implications for neuro-behavioural performance.

## Summary

Economic analysis of anaesthesia is complex and most published studies are naive, focusing on drug acquisition costs and facility timings. Real health economics are much more difficult. Preferred outcome measures would be whole institution costs or the ability to reliably add an extra case to an operating list, close an operating room and reduce the number of operating sessions offered or permanently decrease staffing. Alongside this, however, potential long-term patient outcomes should be considered.

## Keywords

cost-benefit, economics, inhalational, intravenous, propofol, total intravenous anaesthesia

Curr Opin Anaesthesiol 24:000–000  
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0952-7907

## Introduction

In daily practice, clinicians typically choose drugs with which they are familiar, tailoring anaesthetic techniques to perceived patient benefit and personal preference rather than economic benefit. Are these aims conflicting? Are they even different? Making best use of finite resources in the face of increasing demand is a priority given the recession and public sector funding cuts in the UK and changes in the structure of healthcare provision in the USA.

The review explores the potential economic impact of choice of general anaesthetic, comparing intravenous and inhalational agents along the patient pathway from operating room to discharge and beyond. We have focused on the contemporary general anaesthetics propofol, sevoflurane, isoflurane and desflurane.

## Aspects of economics

Consideration of economics and anaesthesia is not new. Rowe [1], and Kettler and Crozier [2,3] have explored the

complexity and scope of the subject, and identified the need to analyse costs with a global perspective to properly assess cost-effectiveness. What does this imply? Different types of economic analysis [1] applicable to health-care are summarized in Table 1 [1]. The choice of analysis depends on how benefits or outputs are to be treated. A cost-identification analysis is an element of all medical economic studies but can be seen as synonymous with cost-minimization studies [4].

Costs can be described in a number of different ways (Table 2) [1,5,6]. This can include total costs (fixed and variable) and average costs (total cost divided by total number of cases). Total costs can also be direct costs and indirect costs. Health economists would refer to the latter as those from loss of productivity [5].

## Cost considerations

In the anaesthetic literature the approach to economic comparison of total intravenous anaesthesia (TIVA) and inhalational anaesthesia is often by their direct cost

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[7–10]. There is disagreement regarding the regimen with least drug cost, which may reflect differences in caseload, the use of low-flow anaesthesia [10,11], variable acquisition costs in different parts of the world [2] or the expiry of patents. On average, the use of TIVA gave higher drug costs [7,9,12–15], particularly if wastage [16] or cost of consumables such as syringes and pumps were included. This excess cost declined with longer operations [17]. Many studies looked beyond direct costs, assessing cost-effectiveness rather than minimization, recognizing that a cheaper anaesthetic that results in postoperative pain or emesis may incur additional costs and delay patient discharge [18]. Opportunities for savings in the operating room include time, cost of other consumables and operating conditions, which in turn may affect blood loss, surgical outcome and length of stay. Cole *et al.* [19] report equal haemodynamic stability with both inhalational and intravenous anaesthesia for craniotomy but suggest propofol may reduce intracranial pressure and increase cerebral perfusion pressure. There was also no haemodynamic difference found in septorhinoplasty patients, using remifentanyl in both groups [20].

In cardiac surgery volatile anaesthetics may be cardioprotective [21]. However, Flier *et al.* [22] found no benefit on cardiac morbidity and mortality or troponin concentrations after surgery. In general surgery, a faster recovery of bowel function and earlier discharge was reported when propofol was compared to desflurane for laparoscopic cholecystectomy [23].

Areas of economic impact in the recovery area or postanesthesia care unit (PACU) include length of stay, costs, drug use and the ability to ‘step down’ to a less intensive, and therefore less costly clinical area.

The most common finding is that TIVA reduces the incidence of postoperative nausea and vomiting, in the early recovery period [23–27], and the decreased requirement for antiemetics may off-set a higher initial drug cost. Further, patient dissatisfaction is often attributed to nausea and vomiting – complications that both patients and their anaesthetists wish to avoid [28,29] although Fisher warns against the use of surrogate outcomes in this regard [30].

### Key points

- There is increased scrutiny of all operating theatre costs and drug budgets are easily targeted.
- Total intravenous anaesthesia appears to provide decreased emesis and good recovery but often at higher direct costs.
- Anaesthetic agents have been implicated as affecting both long-term neurological development and cancer recurrence and survival and further investigative trials are underway.
- True health economics is complex and should include all costs and benefits relating to the health-care institution, the patient and society.

Some studies report a faster or better quality recovery with TIVA [8]; however, this seems to have little impact on subsequent patient progress [31]. Other investigators described faster recovery when inhalational agents were used [16] but without difference in recovery of cognitive function [25,32]. Some recent studies suggest increased postoperative pain following isoflurane and sevoflurane anaesthesia when compared to propofol [33,34] although the suggestion that propofol has an analgesic effect has been disputed [35] and the possibility of an antianalgesia effect of residual volatile anaesthetic proposed instead.

Although anaesthetic drugs cost can vary between TIVA and inhaled anaesthesia, any saving from cheaper drugs is minimal compared to operating room or hospital episode costs [36,37]. Despite this, although anaesthetic drug costs are comparatively small they are, from a managerial viewpoint, very visible [5,38].

### Organizational issues

Any potential reduction in cost from faster and better recovery from anaesthesia may be negated by a delay in starting theatre cases, prolonged turnover time [39] and downstream factors such as PACU staffing patterns. Staffing is typically the greatest cost for a recovery area and if a shorter recovery room stay does not result in the reduction of staff hours or numbers then there is no real economic saving [40,41]. Restructuring of PACU patient inflow may have more impact; if patients are suitable to either bypass PACU or be ‘fast-tracked’ to a nominated area for faster discharge [42].

**Table 1** Types of economic analysis applicable to anaesthesia

	Input	Output	Output examples
Cost minimization (cost identification)	Direct costs	Not applicable	Outcomes assumed equal
Cost-benefit	All costs	Economic benefits (benefits as monetary units)	Money saved, production gains or return to work
Cost-effectiveness	All costs	Natural units (measured outcomes used directly)	Numbers free from nausea, successfully treated cases
Cost-utility	All costs	Utility units (outcomes converted to common unit)	Quality adjusted life years

Adapted from [1].

**Table 2 Methods of describing costs in economic analysis**

Direct costs	Material and disposables used/wasted
Indirect costs	Resulting from event, for example loss of production
Fixed costs	Remain the same, for example building rent
Variable costs	Increases with case numbers, for example drugs
Marginal costs	Cost of one more/ fewer case
Intangible costs	Nonphysical, for example goodwill

Adapted from [1] (originally adapted from [5,6]).

### Beyond hospital discharge

Current economic pressures make explicit the requirement that healthcare should be evidence-based and delivered efficiently. Anaesthetists need to understand the economics of anaesthesia care [43] as 'medical decision-making cannot be divorced from cost' [44]. This is a complex undertaking.

Potential economic benefits may be found along the entire peri-operative track and beyond it. Improvements in patient wellbeing after discharge may impact on return to work, dependency and social functioning; however, whilst these likely have economic impact to the patient, improving them is unlikely to have financial benefits to the healthcare provider. But benefits and costs can be looked at from the different perspectives of the patient, provider or society [4]. Commonly medical studies consider patient benefits alone. So, what of the patient once they are discharged? Few data describe anaesthetic drug effects on patients' experience after discharge. Endpoints of interest would be the need to re-access healthcare including visits to primary care or emergency department attendance, perhaps re-admission.

Carvalho *et al.* [45] explored functional recovery during the week following discharge after laparoscopic sterilization. Functional recovery was slow in both inhalational and TIVA groups and not affected by anaesthetic technique [45]. Sung *et al.* [46] reported that patients anaesthetized with propofol group required less nursing care and returned to work earlier those receiving isoflurane during breast biopsy.

### Neurological effects

True health economics considers the impact on society as a whole and this takes us from ill-health to wellbeing. Once our patients stop being patients, how long is it before they return to their normal life? Do they return to work or become a financial burden on the state? What is their quality of life? Steinmetz *et al.* [47] reported that elderly patients with cognitive dysfunction 1 week after noncardiac surgery had increased dependency on social transfer payments and increased likelihood of leaving the workforce prematurely. Those in whom the cognitive

dysfunction persisted to 3 months experienced increased mortality [47]. What we do not know is whether the type of general anaesthetic used affected the risk of this postoperative cognitive dysfunction; other risk factors may be more important [48]. Recent investigations in rats linked cognitive impairment to hippocampus pro-inflammatory cytokine release precipitated by surgery rather than anaesthesia [49] with greater effects in older animals. Inhalational general anaesthesia can lead to amyloid deposition as seen in Alzheimer's disease [50<sup>\*</sup>], but in animal studies isoflurane impacts negatively on neonatal rats rather than adult ones, by reducing neuro-genesis and causing memory deficit [51,52].

The impact of anaesthesia on long-term outcomes is an important contemporary research area and an enlarging and concerning body of evidence. Anaesthesia, as whole, is relatively well tolerated [53] and our drugs have a short duration of effect with a generally reliable swift recovery. Our impact on our patients is brief and beneficial. How uncomfortable is it then, to consider the latest articles looking at neurotoxicity from anaesthesia in children or the differential risk of cancer metastasis dependent on anaesthetic technique? Are we actually doing harm?

Emergence agitation in children after sevoflurane is well known, appears short-lived [54] and was minimally reduced by switching to propofol [55]. However, children undergoing urological surgery before the age of 2 years showed a trend towards an increased incidence of behavioural disturbance [56] and children undergoing multiple general anaesthetics before the age of 4 were more likely to develop learning disabilities later [57]. It is not clear if some anaesthetics are better tolerated than others [58<sup>\*</sup>] and separating the long-term effects of the condition necessitating surgery and the effects of the procedure itself are problematic. In any case there are times when the requirement for a general anaesthetic cannot be avoided, hence further studies are needed [59] and many are already underway [60<sup>\*\*</sup>].

### Cancer outcomes

Of serious concern are the possible interactions of anaesthetic technique and cancer recurrence [61]. Surgery for tumour removal is associated with the release of tumour cells and the balance between the ability of these to seed and the body's immune defence determines the development of clinical metastases [62<sup>\*</sup>]. The peri-operative factors that can contribute to this process are surgery which causes release of tumour cells and growth factors, reduction of antiangiogenic factors and depression of the cellular immune system, volatile anaesthesia-related impairment of natural killer (NK) cells (amongst others) and opioid-induced inhibition of both cellular and humoral immunity [63<sup>\*\*</sup>,64<sup>\*</sup>].

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Biki *et al.* [65] reported that patients undergoing radical prostatectomy showed less biochemical cancer recurrence when a general anaesthetic was combined with using an epidural in place of opioids. Similarly, the use of paravertebral block to provide analgesia for breast cancer surgery reduced the risk of tumour recurrence [66]. Gottschalk *et al.* [67\*\*] found epidural use gave no decrease in cancer recurrence after colorectal surgery but there was a potential benefit in older patients, who may have had a different tumour type.

Regional anaesthesia might improve cancer outcomes by reduction of surgical stress, decreasing need for opioids (morphine promotes angiogenesis) and by allowing the administration of lower amounts of volatile anaesthetic. In contrast to volatile agents, propofol attenuated the surgical stress response, not suppressing NK cell activity or promoting lung tumour metastases and *in vitro* inhibited breast tumour cell proliferation [68,69].

The clinical trials so far have been retrospective and descriptive but randomized trials are in progress [70].

#### Conclusion

Whilst in the past the use of total intravenous anaesthesia has appeared to incur higher drug and equipment acquisition cost, it has favourable effects such as reduced postoperative nausea and vomiting and less immunosuppression in the perioperative period. Nevertheless with only limited economic analysis of true outcome measures and at present only retrospective evidence of potentially improved cancer survival, as yet we do not have the evidence to provide a definitive answer to a complex question.

There is continuing development of novel anaesthetic compounds [71] and these need to be evaluated for cost-effectiveness and any effect on long-term outcomes. Providing robust evidence will be the challenge. In the meantime it is likely that a careful technique, tailored to the individual patient's needs, operation and outcome is unlikely to have a drastic impact on institutional spending but we should still do our part, however small. If new evidence shows that our choice of anaesthetic has real impact on postoperative function or patient survival then we will need to balance small-scale economics with the bigger picture and first, do no harm.

#### Acknowledgements

No funding or grants were received for this article.

J.R.S. acted as a paid adviser to AstraZeneca, the inventors of propofol during 2010.

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Additional references related to this topic can also be found in the Current World Literature section in this issue (pp. 000–000).

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