Clinical and economic choices in anaesthesia for day surgery: a prospective randomised controlled trial

Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
The study compared four general anaesthetic agents for induction/maintenance in adult day surgery, and two general anaesthetic agents in paediatric day surgery. The anaesthetics used for adults were propofol/propofol, propofol/isoflurane, propofol/sevoflurane and sevoflurane/sevoflurane. Those used for children were propofol/halothane and sevoflurane/sevoflurane. The induction dose of anaesthetic and use of lignocaine was left to the discretion of the anaesthetist. The fresh gas flow rate was set at a rate according to a predetermined protocol. Postoperative nausea and vomiting (PONV) and pain were treated according to standardised protocols.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised adults (aged 18 years and over) and paediatric patients (aged 3 to 12 years) who were eligible for day case surgery. The inclusion criteria for the study specified patients undergoing day case surgery and patients assessed as fit for anaesthesia by one of the participating anaesthetists. The exclusion criteria specified patients undergoing a pregnancy termination, expected use of suxamethonium, or use of sedative pre-medication.

Setting
The setting for the study was secondary care in Manchester and the Wirral, UK. The economic study was carried out in Manchester, UK.

Dates to which data relate
The effectiveness evidence and resource use data were collected between October 1999 and January 2001. The price year was 2000.

Source of effectiveness data
The effectiveness data were derived from a single study.

Link between effectiveness and cost data
The costing was carried out prospectively on the same sample as that used to collect the effectiveness evidence.

Study sample
Power calculations were reported. The adult study was planned to detect a reduction in PONV from 20 to 10%, with 80% power at the 1% significance level (330 patients in each arm). The paediatric study was planned to detect a reduction in PONV from 20 to 10% with 80% power at the 5% significance level (220 patients in each arm). The study sample was recruited from consecutive day surgery patients at two hospitals. The authors reported, as evidence that the initial study sample was appropriate for the clinical study question, that the study population comprised patients eligible for day case surgery.

A chart detailed the flow of participants through the study. A total of 1,063 adults (265 in P/P group, 267 in P/I group, 280 in P/S group and 251 in S/S group) and 322 children (159 in P/H group and 163 in S/S group) were recruited. Overall, 23% of the adults and 25% of the parents approached did not wish to participate (reasons for refusal were reported) and 9% withdrew.

**Study design**

This was a double-centred, randomised controlled trial. The method of randomisation was reported in detail. A computer-generated pseudo-random number sequence was used with block allocation, stratified by anaesthetic regimens, gender and hospital site.

The duration of follow-up was reported to be 7 days. Loss to follow-up was reported for up to discharge and for 7 days postdischarge. All patients were followed up to the point of discharge. Overall, 85% of adults (86% for P/P, 87% for P/I, 84% for P/S and 85% for S/S) and 81% of paediatrics (83% for P/H and 79% for S/S) were followed up to 7 days' postdischarge.

There was no blinding of the anaesthetists, patients or researchers for the outcome assessment. Data analysts were masked to treatment allocation until the primary analysis of the data was completed. Approximately half of the patients who refused to participate in the study did so because they did not wish to undergo inhalation induction.

**Analysis of effectiveness**

The analysis of the clinical study was conducted on the basis of treatment completers only.

The primary health outcome used in the analysis was the incidence of PONV prior to hospital discharge. Research staff recorded the rate of PONV on a four-point scale ranging from zero (no nausea and vomiting) to 3 (multiple episodes of vomiting), where a score of 1 indicated nausea and a score of 2 represented one episode of vomiting.

The secondary outcome measures were recovery orientation (alert and awake, drowsy, agitated and distressed) and the number of adverse events. Postdischarge outcomes were self-reported by patients using a 10-cm visual analogue scale. These included pain, muscle pain, headache, sore throat, blurred vision, drowsiness, concentration, forgetfulness and dizziness. The outcomes reported by the parents were pain, muscle pain, headache, sore throat, drowsiness, nightmares, difficulty in sleeping and change in play.

**Effectiveness results**

In the adult study, the presence of PONV before discharge was statistically higher in the S/S group (30%) than in the P/P group (14%), P/I group (18%) and P/S group (16%), (p<0.01).

In the paediatric study, the presence of PONV before discharge was statistically higher in the S/S group (15%) than in the P/H group (6%), (p<0.01).

There was no statistically significant difference in recovery orientation for adult day case patients.

More children in the P/H group (28%) were drowsy on recovery than those in the S/S group (12%), (p<0.001). However, more children in the S/S group (26%) were agitated and distressed on recovery than those in the P/H group (9%), (p<0.001).
There was no statistically significant difference in adverse events for adult or paediatric day case patients.

Postdischarge outcomes were obtained for 778 adult patients and 260 paediatric patients. There was no significant difference in these outcomes by day 7 postdischarge.

Clinical conclusions
The authors concluded that, in adults and paediatric day case patients, pre-discharge PONV was higher if S/S was used compared with the use of propofol for induction. There was no difference in the postdischarge outcomes at day 7.

Measure of benefits used in the economic analysis
The measure of benefit used in the economic analysis was the number of episodes of PONV avoided.

Direct costs
The quantities and the costs were not analysed separately.

The cost of the alternative anaesthetic regimens was defined in terms of intra-operative resource use, postoperative resource use and postdischarge (NHS contact). Intra-operative resource use covered induction and maintenance anaesthesia, other drugs, disposables, time in surgery, treatment of adverse events and staff time. Postoperative resource use covered PONV, pain, other drugs, other equipment, management of other adverse events, time to discharge, overnight admission and staff time. Variable costs were also reported, which were defined as the costs associated with the anaesthetic, drug, disposables, management of PONV and adverse events. Data on the length of stay (fixed costs) and staff time (semi-fixed costs) were also collected.

Neither the unit costs nor their source were reported. The quantities were estimated from actual data, which was collected by trained research staff. The time horizon for the primary economic analysis was from patient admission to the day case ward (or unit) until discharge. Patient resource use data were also collected until day 7 postdischarge. Discounting was not carried out due to the short time scale (less than one year) of the study. The price year was 2000. The resources were collected during October 1999 and January 2001. The study reported the mean variable cost, along with the standard deviation (sd).

Statistical analysis of costs
The costs were analysed using parametric statistical tests (analysis of variance for the adult study and t-tests for the paediatric study).

Indirect Costs
No indirect costs were reported as they were not appropriate to the study perspective (NHS).

Currency
UK pounds sterling (£). No currency conversion was reported.

Sensitivity analysis
The authors reported that a bootstrap estimation was used to identify the magnitude of uncertainty around the incremental cost-effectiveness ratio (ICER).

Estimated benefits used in the economic analysis
In the adult study, the proportion of patients experiencing PONV before discharge was 30% in the S/S group, 14% in the P/P group, 18% in the P/I group and 16% in the P/S group.
In the paediatric study, the proportion of patients experiencing PONV before discharge was 15% in the S/S group and 6% in the P/H group.

Cost results
In the adult study, the mean variable cost was 21.10 (sd=12.2) for the P/P group, 7.1 (sd=4.4) for the P/I group, 10.3 (sd=11.4) for the P/S group, and 8.0 (sd=10.6) for the S/S group. There was a statistically significant difference between the P/P, P/I, P/S and S/S groups, (p<0.01).

In the paediatric study, the mean variable cost was 3.5 (sd=1.9) for the P/H group and 12.4 (sd=5.9 for the S/S group. There was a statistically significant difference between the P/H and S/S groups, (p<0.0005).

Synthesis of costs and benefits
The ICERs were estimated on the principle of dominance and the interventions were ranked from highest to lowest effectiveness. Each intervention was compared with the comparator immediately below in terms of cost.

In the adult study, the ICER was 296 per PONV case avoided for the P/P group compared to the P/S group, and 333 per PONV case avoided for the P/S group compared to the P/I group. The P/I group was both cheaper and more effective than the other anaesthetic agents, and therefore, no ICER was calculated. The S/S group was dominated by the three other anaesthetic regimens in the adult study.

In the paediatric study, the P/H group was cheaper and more effective, and therefore, dominated the S/S group. No ICER was calculated.

The authors reported the results of bootstrap estimations of sampling distributions of the ICERS. In the adult study, the results showed that the rank ordering was not stable and the differences between arms could be negative or positive in terms of net PONV and costs. In the paediatric study, the ICERs were all in the South East quadrant indicating that P/H is more effective and less costly than S/S and the result is stable.

Authors' conclusions
The S/S group (sevoflurane induction and sevoflurane maintenance with nitrous oxide) was more costly with higher rates of postoperative nausea and vomiting (PONV) in both adult and paediatric day case surgery patients. In adults, the cost per extra episode of PONV avoided was 296 (propofol/propofol versus propofol/sevoflurane) and 333 (propofol/sevoflurane versus propofol/isoflurane).

CRD COMMENTARY - Selection of comparators
This study compared four alternative anaesthetic regimens for adult day case surgery and two anaesthetic regimens for paediatric day case surgery. The comparators used were justified on the grounds that they reflected current or emerging models of anaesthetic practice in the UK, as found from the results of a literature review and national survey. You should decide if these are widely used health technologies in your own setting.

Validity of estimate of measure of effectiveness
This study used the rate of PONV as its primary outcome measure and the number of PONV cases avoided as the measure of health benefit.

The analysis used a randomised controlled trial, which was appropriate for the study question. The study sample was representative of the study population. Adult and paediatric patient groups were shown to be comparable at analysis. Although a randomised controlled trial was conducted, the outcomes were analysed for treatment completers only. No patients were lost to follow-up pre-discharge. Therefore, using treatment completers in the analysis would not have affected the results for the primary outcome measure and measure of benefit in the economic evaluation.
Validity of estimate of measure of benefit
The number of PONV cases avoided was used as the measure of benefit in the economic analysis. The study therefore assumed that the presence or absence of PONV would directly impact on the patients' health status. This assumption seems valid, but the authors did not provide any published evidence in support.

Validity of estimate of costs
All the categories of variable cost relevant to the perspective adopted (NHS) were included in the analysis. The analysis did not include fixed or semi-fixed costs, but the authors reported that these did not differ between the groups in the adult or paediatric study, and they are therefore unlikely to have affected the authors' conclusions. The authors did not report the unit costs or source of unit costs. The costs and the quantities were not reported separately for the pre-discharge costs, but were reported for the patient resource use costs. Resource use was collected prospectively alongside a randomised controlled trial. A statistical analysis of the costs was performed, and bootstrap estimations of sampling distributions of the ICERs were used as a sensitivity analysis. However, no sensitivity analysis of the prices was conducted. Discounting was irrelevant since all the costs were incurred over one year.

Other issues
The authors made some appropriate comparisons of their findings with those from other studies. The issue of generalisability to other settings was addressed by the use of bootstrap estimations. The eligibility criteria and willingness of patients to participate in a trial was mentioned as a limiting factor for external validity, although the case-mix of the trial reflected the case-mix of UK day surgery. The authors did not report their results selectively. The study enrolled patients eligible for day case surgery and this was reflected in the authors' conclusions. The authors reported further limitations to their study. First, the problems of recruitment and achieving the target sample size (final power was 70% in adult study and 66% in paediatric study). Second, the anaesthetists, researchers and patients were not masked to the allocated anaesthetic regimen, although the data analysts were. Finally, the use of P/H as a comparator in the paediatric study.

Implications of the study
The authors suggest that the important results from this study for decision-makers are that there are differences in variable costs between the study arms, indicating that the choice of anaesthetic agents will translate into secondary care budget differences. The main conclusions are that S/S is not a cost-effective regimen for day case surgery in adults or children when pre-discharge PONV is used as the primary outcome measure. In adults, P/I provided the lowest cost without significantly higher PONV rates. In children, P/H provided the lower cost with a significantly lower PONV rate. The PONV rate was low despite no patients receiving prophylactic anti-emetics.

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Other publications of related interest

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