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Pre-operative optimisation employing dopexamine or adrenaline for patients undergoing major elective surgery: a cost-effectiveness analysis

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Abstract *Objective:* To compare the cost and cost-effectiveness of a policy of pre-operative optimisation of oxygen delivery (using either adrenaline or dopexamine) to reduce the risk associated with major elective surgery, in high-risk patients. *Methods:* A cost-effectiveness analysis using data from a randomised controlled trial (RCT). In the RCT 138 patients undergoing major elective surgery were allocated to receive pre-operative optimisation employing either adrenaline or dopexamine (assigned randomly), or to receive routine peri-operative care. Differential health service costs were based on trial data on the number and cause of hospital in-patient days and the utilisation of health care resources. These were costed using unit costs from a UK hospital. The cost-effectiveness analysis related differential costs to differential life-years during a 2year trial follow-up. *Results:* The mean number of inpatient days was 16 in the pre-optimised groups (19 adrenaline; 13 dopexamine) and 22 in the standard care group. The number (%) of deaths, over a 2year follow-up, was 24 (26%) in the pre-optimised groups and 15 (33%) in the standard care group. The mean total costs were EUR 11,310 in the pre-optimised groups and EUR 16,965 in the standard care group. Life-years were 1.68 in the pre-optimised groups and 1.46 in the standard care group. The probability that pre-operative optimisation is less costly than standard care is 98%. The probability that it dominates standard care is 93%. *Conclusions:* Based on resource use and effectiveness data collected in the trial, pre-operative optimisation of high-risk surgical patients undergoing major elective surgery is cost-effective compared with standard treatment.

Introduction

Clinical trials have shown pre-operative optimisation (pre-op) to reduce the risk of complications and death in high-risk patients undergoing major elective surgery [1, 2, 3]. There is also evidence that the use of pre-op results in reduced hospital costs [1, 2] and that it constitutes a cost-effective method of managing high-risk surgery [4]. However, these results have yet to have a major influence on surgical management.

A recent trial of pre-op [3] compared standard peri-operative patient management with pre-op in high-risk patients undergoing major elective surgery. In addition, the trial assessed the relative performance of the inotropes – adrenaline and dopexamine – given to enhance oxygen delivery. The study randomised 138 patients to receive standard management (n=46); pre-op employing adrenaline (n=46) or pre-op employing dopexamine (n=46) (Fig. 1). The results showed a significant reduction in hospital mortality associated with pre-op (3%) compared

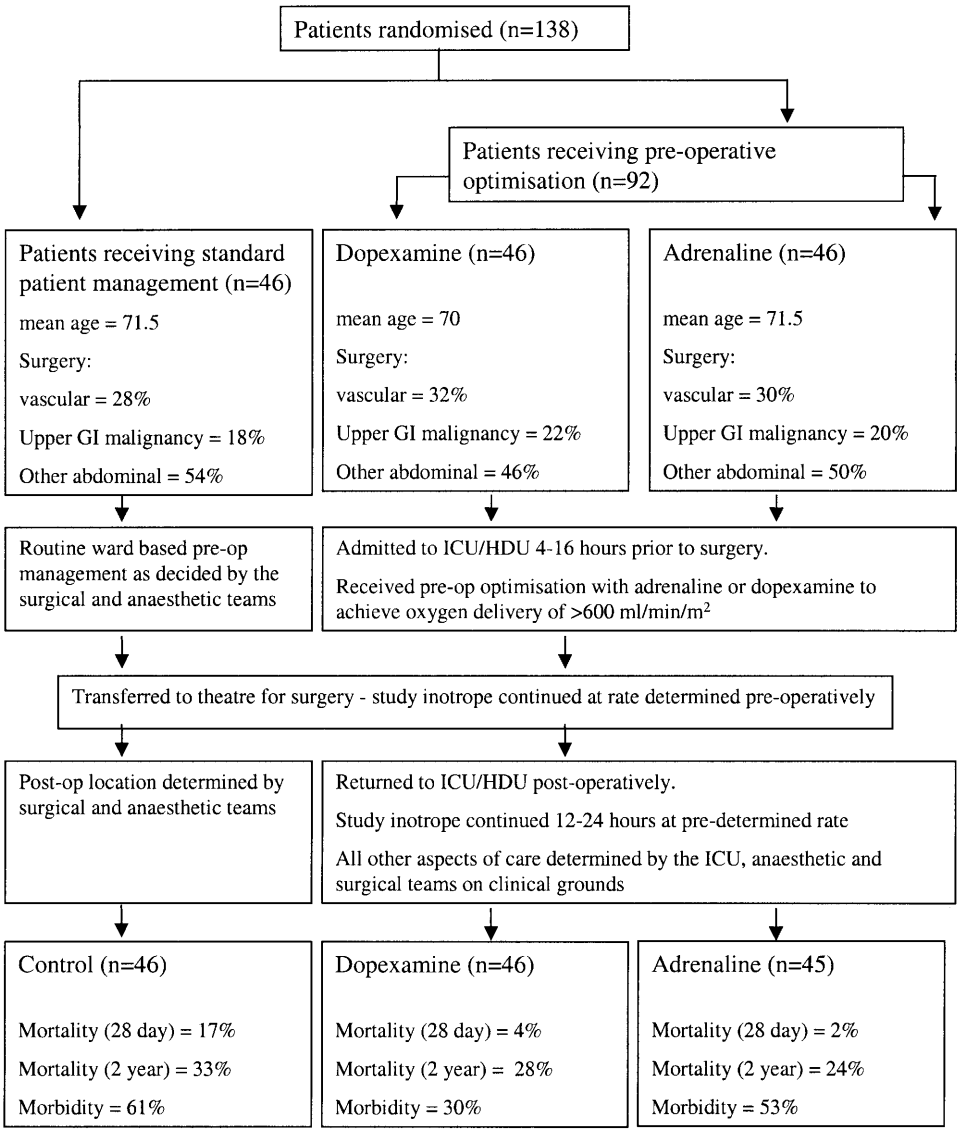

Fig. 1 Patient flows through the study. Morbidity is defined as the percent of patients developing one or more of a predefined range of complications. One patient (pre-op with adrenaline, other abdominal subgroup) was excluded from the analysis due to the absence of any data concerning resource use

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with standard patient management (17%) and a reduction in morbidity associated with pre-op employing dopexamine (30%) compared with that employing adrenaline (53%) and standard patient management (61%) [3].

In addition to the mortality and morbidity benefits, the trial also found some important differences in resource consumption between the three arms. In particular, the use of dopexamine was associated with a significantly shorter hospital stay [3].

This paper presents the results of a retrospective economic analysis of that trial. The primary aim of the analysis was to determine the cost-effectiveness of pre-op compared with standard patient management, from a health service perspective, based upon mean cost and mean effect differences. The secondary aims were to determine the cost-effectiveness of the inotropes used in the delivery of optimisation, to compare the three methods of pre-operative patient management and to estimate the probability that each method is the optimal choice for the decision maker.

Glossary of terms

Bayesian methods. Statistical framework which represents a learning process. As new information becomes available, it is combined with initial beliefs (priors), using Bayes' theorem, to provide an updated belief (posterior) which is based on all information.

Cost-effectiveness analysis. Method of comparing alternative treatments in terms of their costs and health effects, with health effects measured in natural units (e.g. life-years). Results are usually presented as an incremental cost-effectiveness ratio (ICER).

Cost-effective. A treatment is considered cost-effective, compared to an alternative, if the additional cost per unit of effect is considered worthwhile (i.e. ICER < willingness to pay for health effects).

Cost-effectiveness acceptability curve. Graph illustrating the probability that a treatment is the most cost-effective over a range of values for the decision maker's willingness to pay for health effects.

Discounting. Process of converting costs incurred and health effects received at different points in time to a common present value. This is undertaken to reduce the weight attached to future costs and health effects to reflect the time preference of individuals – that is, they prefer things now rather than in the future.

Dominance. One treatment dominates its comparator if it is associated with lower costs and greater health effects.

Incremental analysis. Analysis of the additional costs and additional effects associated with a treatment of interest, compared with the next best alternative treatment.

Incremental cost-effectiveness ratio (ICER). Ratio of the incremental cost to incremental effect associated with a treatment, when compared to the next best (non-dominated) alternative treatment.

Optimal choice. The treatment which provides the maximum health effect, from the set of cost-effective treatments, i.e. the most cost-effective. As the maximum amount that the decision maker is willing to pay for health effect alters the set of cost-effective treatments, and the optimal choice may alter.

Prior. Initial, pre-experiment belief based upon information available or opinion. For example, this may reflect results from previous trials.

Posterior. Updated, post-experiment belief incorporating new information, e.g. recent trial results. Posterior is determined by combining original prior and new information using Bayes' theorem.

Vague prior. Formed with no reference to the available information, in order to minimise the impact of the prior on the posterior distribution so that inferences are unaffected by information external to the current data. The use of a vague prior enables the data to speak for itself.

Willing to pay for health effects (λ). Maximum amount that the decision maker is prepared to pay for each unit of additional health effect. This may represent the health outcome forgone if a more costly treatment displaces other health care programmes.

Methods

Trial design

The design, baseline characteristics and clinical results of the study have been published elsewhere [3]. In brief, the trial included patients undergoing major elective surgical procedures in general surgery, vascular surgery or urology who had been identified as being at high risk of developing peri-operative complications. This prognosis was based upon surgical criteria or the presence of coexisting medical conditions. Whilst it was not possible to blind either patients or clinicians to the standard care versus pre-op status, double-blinding was employed within the pre-op groups concerning the actual inotrope received. The randomisation was stratified by three surgical sub-groups: vascular surgery; surgery for upper gastrointestinal malignancy and other abdominal surgery (which included patients from urology and general surgery). Of the patients, 30% underwent vascular surgery, 20% had surgery for an upper gastrointestinal malignancy and 50% had other abdominal surgery [3]. See Fig. 1 for a summary of the patient flows through the original study.

Patients within the pre-op groups were admitted to either an intensive care or high dependency care unit at least 4 h prior to surgery. They received haemodynamic monitoring, fluid optimisation and inotrope optimisation (employing either adrenaline or dopexamine). The inotropic support was continued for 12–24 h post surgery. Patients within the control arm of the trial received standard peri-operative patient management, as determined by the surgeon and anaesthetist. At hospital discharge, the mortality in the pre-op groups was 3% compared with 17% in the standard management group (p=0.007). There was a significant reduction in both morbidity and length of hospital stay within the pre-op group that received dopexamine (30% morbidity, 13 days per patient), compared with both the adrenaline (53%, 19 days per patient) and standard management (61%, 22 days per patient) groups.

Resource use measurement

The measurement of resource consumption of all patients in the trial is central to the process of estimating the differential cost associated with pre-op compared to standard patient management, and of pre-optimisation with dopexamine compared to adrenaline. Detailed resource use data were not collected prospectively as part of the original trial protocol, hence it was necessary to review, retrospectively, the trial case record forms and clinical notes to identify each patient's National Health Service resource use.

The study focused on two key areas of resource use that were expected to affect cost differences: that employed during the initial

hospital stay and that employed in the management of subsequent related events. For the initial hospital stay, the resource use was fully detailed in clinical notes. For each patient, data were collected on the length and type of in-patient stay, and usage of drugs, interventions, infusions and investigations. Drugs that patients were taking on admission, analgesics and drugs given to help patients sleep were excluded from the resource use profile. For patients randomised to pre-op, the resource use profile included the length of the period of optimisation and the fluid employed in the process.

Some patients were re-admitted subsequent to the initial hospitalisation. Two independent clinicians, blinded to the initial randomisation, assessed whether subsequent admissions were related to the initial surgical procedure. For those that were, resource use was measured at an aggregate level, based upon length of stay. These data related to the period of 6 months following initial surgery because, beyond this period, it is assumed that re-admissions related to the original procedure would be minimal.

Valuing resource use

The cost of managing each individual patient was estimated by applying the relevant unit cost data to the detailed resource profile compiled for each patient in the study. The unit costs were obtained from a specific NHS hospital, in 1999–2000 prices. All drugs, including any consumables required to administer them, were based on the British National Formulary [5]. The costs for all infusions, investigations and interventions included overheads and all consumables required to administer them. Hotel costs for the intensive care unit, the high dependency unit and the surgical ward included fixed costs, staff costs, estate costs, overheads and the cost of monitoring equipment. The costs of all other equipment were converted into hourly rates, based on their purchase and resale prices, annual maintenance cost, expected useful life and estimated usage per annum. These were included separately on a per patient basis [6]. The additional cost of optimisation was calculated for each patient in the adrenaline and dopexamine arms, using patient-specific length of hospital stay and use of fluid, together with use of drugs and disposables set by the study protocol.

Given that the aim of the study was to cost different methods of pre-operative patient management, the cost of the original surgery was excluded from the analysis. However, the cost of any further surgery required to manage a complication or related event was included. The cost of subsequent admissions related to initial surgery was calculated on a per diem basis, using the cost of a standard surgical ward including overheads, drugs, infusions, interventions and investigations.

All costs have been translated from pounds sterling into euros at an exchange rate of £1:EUR 1.631.

Cost-effectiveness analysis

Cost-effectiveness is assessed by relating the differential cost of the alternative patient management strategies to their differential effectiveness in terms of patient life-years measured during the trial. One treatment can be defined as more cost-effective than its comparator if any of the following conditions apply: (a) it is less costly and more effective (dominance); (b) it is more costly and more effective, and its additional cost per extra unit of effectiveness is considered worth paying by decision makers and (c) it is less costly and less effective and the additional cost per extra unit of effectiveness of its comparator is *not* considered worth paying by decision makers. Figure 2 shows the incremental cost-effectiveness plane [7] on which the incremental cost and effects (survival) associated with the intervention of interest are plotted. The plane is split into four quadrants by the origin (which represents the treatment comparator). Quadrant II represents condition (a), described above. Conditions (b) and (c) are represented within quadrants I and III, respectively, with the line labelled λ determining the additional cost per unit of effect which the decision maker considers worth paying. Hence, if the incremental cost and effect of the intervention falls within the area which lies to the south-east of the line labelled λ, it is cost-effective. The area to the north-west of the line (including the whole of quadrant IV) represents the situation where the intervention of interest would not be considered cost-effective with respect to the comparator.

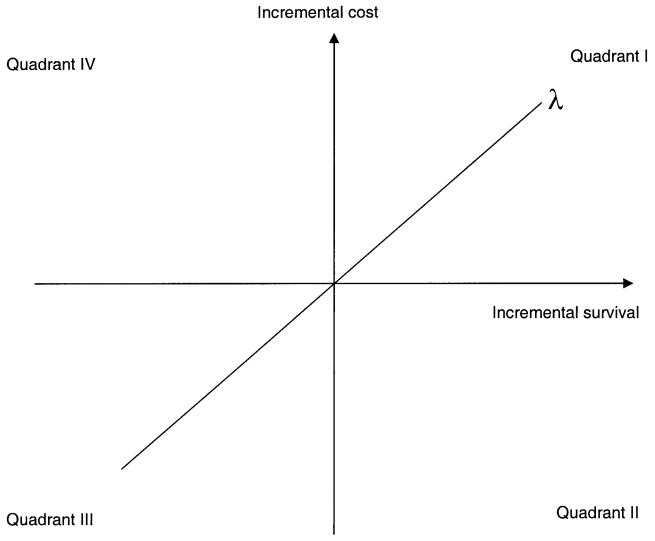

Fig. 2 Incremental cost-effectiveness plane

Mean resource use data are presented (with standard deviations), by study group, for the period of 6 months following initial surgery. Mean costs (with standard deviations) are presented, by study group, for hospitalisation (in each type of ward), drugs, interventions, infusions, investigations, pre-op and related events. In addition, the median cost and interquartile range are provided to highlight any skewness in the cost distribution. The mean and standard error, median and interquartile range are presented for the total cost for each patient management strategy.

For the cost-effectiveness analysis, estimates of the mean survival duration in the three arms of the trial are required. This was based upon the area between the survival curves over the 2 year follow-up and involves censoring all surviving patients at 2 years. Discounting has not been undertaken, due to the short-time horizon over which the resource consumption and clinical events occur.

The economic analysis was undertaken using Bayesian methods, employing vague priors concerning the effectiveness and cost of the different management strategies. This ensured that the trial results had a larger influence upon the analysis than the prior beliefs [8]. The Bayesian analysis involved repeat re-sampling from the costs and life-year data of the trial (10,000 iterations), in order to generate a posterior distribution of mean costs and mean life-years for the different management routines. The means of these distributions are used to determine the incremental cost-effectiveness ratios (ICERs) associated with the different methods of patient management. In addition, the distributions are used to calculate the probability that each of the patient management methods is the optimal choice, subject to a range of possible maximum values that a decision maker might be willing to pay for an additional life-year (λ) in this patient group. A cost-effectiveness acceptability curve is then presented, for each of the interventions, by plotting these probabilities for the various values of λ [9, 10, 11].

The Bayesian analysis was undertaken using the WinBUGS (Windows-based Bayesian Inference Using Gibbs Sampling) software package, whilst the cost-effectiveness analysis was conducted within Excel.

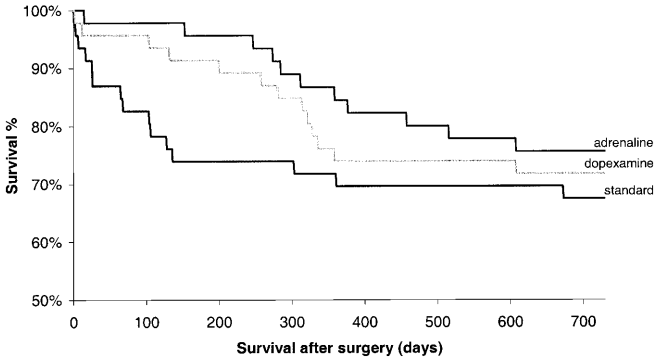

Fig. 3 Survival after surgery (proportion of the original study population)

Results

Resource use

Table 1 gives a summary of the key resources use within the alternative arms of the trial. One patient (pre-op with adrenaline, other abdominal sub-group) was excluded from the analysis due to the absence of any data concerning resource use. Patients who received pre-op spent an average (SD) of 16 days (12) in hospital at the time of surgery (19 in the adrenaline group, 13 in the dopexamine group) compared to 22 days (26) in the standard care group. In addition, patients who received pre-op tended to have lower usage of key resources (with those ran-

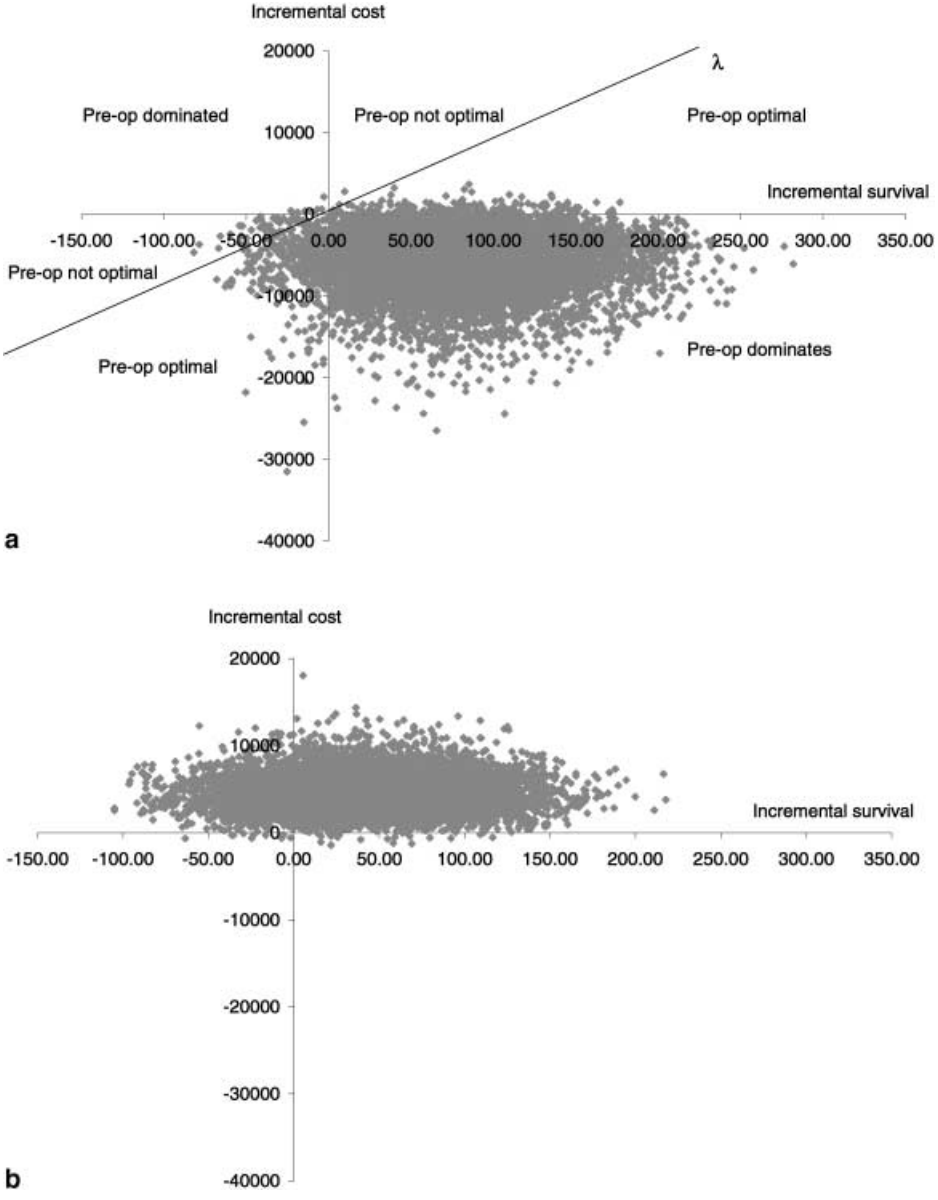

Fig. 4 **a** Cost-effectiveness plane for pre-operative optimisation (either inotrope) versus standard treatment. **b** Cost-effectiveness plane for pre-operative optimisation with adrenaline versus pre-operative optimisation with dopexamine

Table 1 Details of the key resource use collected on patients (*pre-op* pre-operative optimisation, *HDU* high dependency unit, *n/a* not applicable, *TPN* total parenteral nutrition)

Resource	Standard		Adrenaline		Dopexamine		Pre-op (either inotrope)	
	Mean (SD) *n*	Median (IQR)	Mean (SD) *n*	Median (IQR)	Mean (SD) *n*	Median (IQR)	Mean (SD) *n*	Median (IQR)
Length of stay								
Initial hospitalisation								
Ward (h)	437.33 (588.03) *44*	271.00 (168.25, 379)	387.67 (317.21) *45*	286.00 (212, 401)	248.59 (147.39) *45*	196.50 (172.75, 285.75)	317.36 (254.84) *90*	235.00 (190, 313)
ICU (h)	66.91 (137.49) *21*	0.00 (0.00, 36.25)	42.91 (97.94) *21*	0.00 (0.00, 27)	35.57 (93.03) *17*	0.00 (0.00, 24.00)	39.20 (95.03) *38*	0.00 (0.00, 25.00)
HDU (h)	25.15 (53.51) *21*	0.00 (0.00, 27.75)	25.38 (28.93) *33*	21.00 (0.00, 25.00)	24.30 (18.35) *36*	23.00 (15.00, 30.50)	24.84 (24.04) *69*	22.00 (2.00, 26.50)
Total	529.39 (624.71) *46*	323.00 (216.25, 500.75)	455.96 (363.17) *45*	311.00 (239, 505)	308.46 (194.30) *46*	249.00 (211.25, 330)	381.40 (298.09) *91*	287.00 (213, 392)
Subsequent in-patient stay								
Related to surgery (days)	0.70 (3.10) *3*	0.00 (0.00, 0.00)	3.18 (11.63) *4*	0.00 (0, 0)	0.11 (0.74) *1*	0.00 (0.00, 0.00)	1.63 (8.29) *5*	0.00 (0.00, 0.00)
Main drugs								
Cefotaximine (1 g i.v.)	10.33 (10.50) *18*	6.50 (3.00, 15.00)	9.52 (5.56) *23*	9.00 (7.00, 14.50)	8.11 (5.56) *18*	7.00 (5.25, 11.00)	8.90 (5.54) *41*	8.00 (6.00, 12.00)
Fragmin (2500 IU subcutaneously)	15.92 (12.36) *38*	12.00 (8.00, 20.00)	13.76 (11.38) *37*	11.00 (7.00, 15.00)	9.66 (3.70) *41*	9.00 (8.00, 12.00)	11.60 (8.48) *78*	9.00 (8.00, 13.00)
Metronidazole (500 mg i.v.)	11.65 (8.88) *20*	11.50 (3.00, 17.25)	8.29 (5.84) *21*	9.00 (3.00, 12.00)	9.20 (7.44) *20*	7.00) (4.50, 12.25	8.73 (6.60) *41*	8.00 (3.00, 12.00)
Main infusions								
Blood (units)	5.25 (7.15) *32*	3.00 (2.00, 6.00)	5.57 (12.27) *23*	2.00 (2.00, 4.00)	3.62 (3.28) *26*	2.00 (1.25, 4.75)	4.53 (8.69) *49*	2.00 (2.00, 4.00)
Altracurium	2.00 (n/a) *1*	2.00 (2.00, 2.00)	n/a (n/a) *0*	n/a (n/a, n/a)	n/a (n/a) 0	n/a (n/a, (n/a, n/a)	n/a (n/a) *0*	n/a (n/a, n/a)
Albumin 4.5% (250 ml)	12.22 (14.46) *18*	7.50 (3.00, 15.00)	5.63 (6.15) *19*	3.00 (1.50, 7.00)	5.41 (3.97) *27*	4.00 (3.00, 8.00)	5.50 (4.92) *46*	4.00 (2.00, 8.00)
Platelets	8.00 (n/a) *1*	8.00 (8.00, 8.00)	5.50 (2.12) *2*	5.50 (4.75, 7.25)	3.50 (3.54) *2*	3.50 (2.25, 4.75)	4.50 (2.65) *4*	5.00 (3.25, 6.25)
Cryoprecipitate	4.00 (2.83) *2*	4.00 (3.00, 5.00)	10.00 (n/a) *1*	10.00 (10.00, 10.00)	4.00 (n/a) *1*	4.00 (4.00, 4.00)	7.00 (4.24) *2*	7.00 (5.50, 8.50)
Main investigations								
Full blood count	9.13 (8.25) *46*	6.00 (3.00, 12.75)	8.71 (8.32) *45*	6.00 (4.00, 10.00)	6.51 (4.92) *45*	5.00 (3.00, 8.00)	7.61 (6.89) *90*	5.00 (3.00, 9.00)
Clotting studies	7.06 (8.26) *34*	4.00 (1.00, 9.00)	5.40 (7.31) *40*	2.50 (1.00, 5.25)	4.00 (5.31) *36*	2.50 (1.00, 4.00)	4.74 (6.44) *76*	2.50 (1.00, 4.00)
Cross match	3.70 (4.48) *46*	2.00 (2.00, 3.75)	3.23 (4.92) *43*	2.00 (1.00, 3.00)	2.48 (2.03) *44*	2.00 (1.00, 3.00)	2.85 (3.75) *87*	2.00 (1.00, 3.00)
Urea and electrolytes	9.87 (8.77) *45*	7.00 (4.00, 13.00)	9.00 (8.87) *45*	6.00 (3.00, 11.00)	6.60 (5.17) *45*	5.00 (3.00, 8.00)	7.80 (7.32) *90*	5.00 (3.00, 9.00)
Main interventions								
Surgery (h)	2.67 (0.82) *6*	2.50 (2.00, 3.00)	3.67 (0.58) *3*	4.00 (3.50, 4.00)	2.75 (0.96) *4*	2.50 (2.00, 3.25)	3.14 (0.90) *7*	3.00 (2.50, 4.00)
Arterial blood gas (number given)	25.73 (33.91) *26*	10.50 (2.25, 36.75)	14.13 (21.79) *32*	6.00 (2.75, 11.00)	11.67 (13.45) *30*	7.50 (4.00, 13.75)	12.94 (18.13) *62*	6.00 (3.00, 11.00)
TPN	9.25 (4.86) *8*	11.00 (4.00, 12.50)	6.50 (3.15) *6*	5.00 (4.25, 8.75)	8.50 (9.19) *2*	8.50 (5.25, 11.75)	7.00 (4.47) *8*	5.00 (4.00, 10.25)
Pre-operative optimisation								
Length of stay (h)	n/a (n/a) *n/a*	n/a (n/a, n/a)	9.18 (6.89) *45*	5.00 (4.00, 16.00)	10.30 (7.17) *46*	6.00 (4.00, 17.75)	9.75 (7.02) *91*	5.00 (4.00, 17.00)

Table 2 Unit costs of the key resources used within the trial (see text for source of data) (*ICU* intensive care unit, *HDU* high dependency unit, *TPN* total parenteral nutrition)

Resource	Unit cost (euros)
Length of stay	
Ward (per h)	16.80
ICU (per h)	57.90
HDU (per h)	41.59
Related stay (per day)	419.17
Main drugs (per dose)	
Cefotaximine (1 g i.v.)	11.43
Fragmin (250 IU subcutaneously)	3.73
Metronidazole (500 mg i.v.)	8.46
Main infusions	
Blood (per unit)	130.14
Altracurium infusion (ml/h)	58.96
Albumin 4.5% (250 ml per dose)	34.14
Platelets (per unit)	231.49
Cryoprecipitate (per unit)	39.36
Main investigations (per test)	
Full blood count	6.61
Clotting studies	11.87
Cross match	14.22
Urea and electrolytes	5.76
Main interventions	
Surgery (h)	631.20
Arterial blood gas	11.60
TPN	100.16
Pre-operative optimisation	
Adrenaline (per patient)	390.07
Dopexamine (per patient)	130.02
Hotel costs (per hour)	1.80
Disposables (per patient)	3.83
Cost of fluid (per unit)	32.51

domised to dopexamine having the lowest usage overall).

Costs

The unit costs of key resources are detailed in Table 2. Table 3 details the estimated costs for the standard care group and the pre-op patients, both for the entire group and separately for each inotrope. The additional costs of administering pre-op were more than offset by reductions in the costs of the initial in-patient stay and in the costs of resources used in post-operative patient care. The mean cost associated with patients receiving pre-op was EUR 11,310 (EUR 13,820 adrenaline, EUR 9,247 dopexamine) whilst the mean cost for patients receiving standard management was EUR 16,965.

Life expectancy

In the paper reporting the clinical results of the study [3], an 8% lower absolute risk of in-hospital mortality was reported in the pre-op groups at hospital discharge. At 2 years post-surgery, standard patient management is associated with a mortality of 33% (15 deaths) compared with 26% in the pre-optimisation groups (24 deaths – 11 adrenaline, 13 dopexamine) (see Figure 3). Translating 2 year mortality into mean survival duration generates 1.68 years post-surgery for patients in the pre-op groups (1.74 – adrenaline, 1.62 – dopexamine), compared with 1.46 for patients receiving standard care.

Cost-effectiveness

Figure 4a illustrates the simulated values of mean incremental costs and life-years for the comparison between pre-op (using either inotrope) and standard care. Each point represents one simulation result of mean cost and life-year difference. Pre-op (using either inotrope) dominates standard patient management based upon the mean of these points. On average, pre-op is both cheaper (saving of EUR 5,655) and more effective (additional life-years of 0.22). The majority of the points are located below the horizontal axis (negative incremental cost), indicating that the probability that pre-op is cost-saving is high (98%). In addition, a considerable proportion of the points are located within quadrant II, where pre-op involves both reduced costs and higher survival duration than standard care, indicating a considerable probability that pre-op dominates standard patient management (93%).

Figure 4b illustrates the simulated values of mean incremental cost and effect for the comparison between the inotropes. The majority of the points are located within quadrant I, where adrenaline involves higher costs and higher survival duration than dopexamine. Based upon the mean of these points, pre-op employing adrenaline is associated with an ICER of EUR 38,108 per life-year gained when compared to pre-op employing dopexamine (incremental cost = EUR 4,573; incremental effect =0.12 life-years).

Figure 5a illustrates the probability that pre-op (using either inotrope) is the optimal choice, compared with standard patient management, for a range of maximum values that a decision maker might be willing to pay for an additional life-year (λ). The figure shows that the probability that pre-op is optimal when the decision maker is unwilling to pay anything for an additional life-year (i.e. the probability that it is less costly than standard care) is 98%. If the decision maker is willing to pay EUR 32,620 (£20,000) per life-year gained, the probability that pre-op is optimal is 99.35%, hence the probability that standard patient management is optimal is 0.65%.

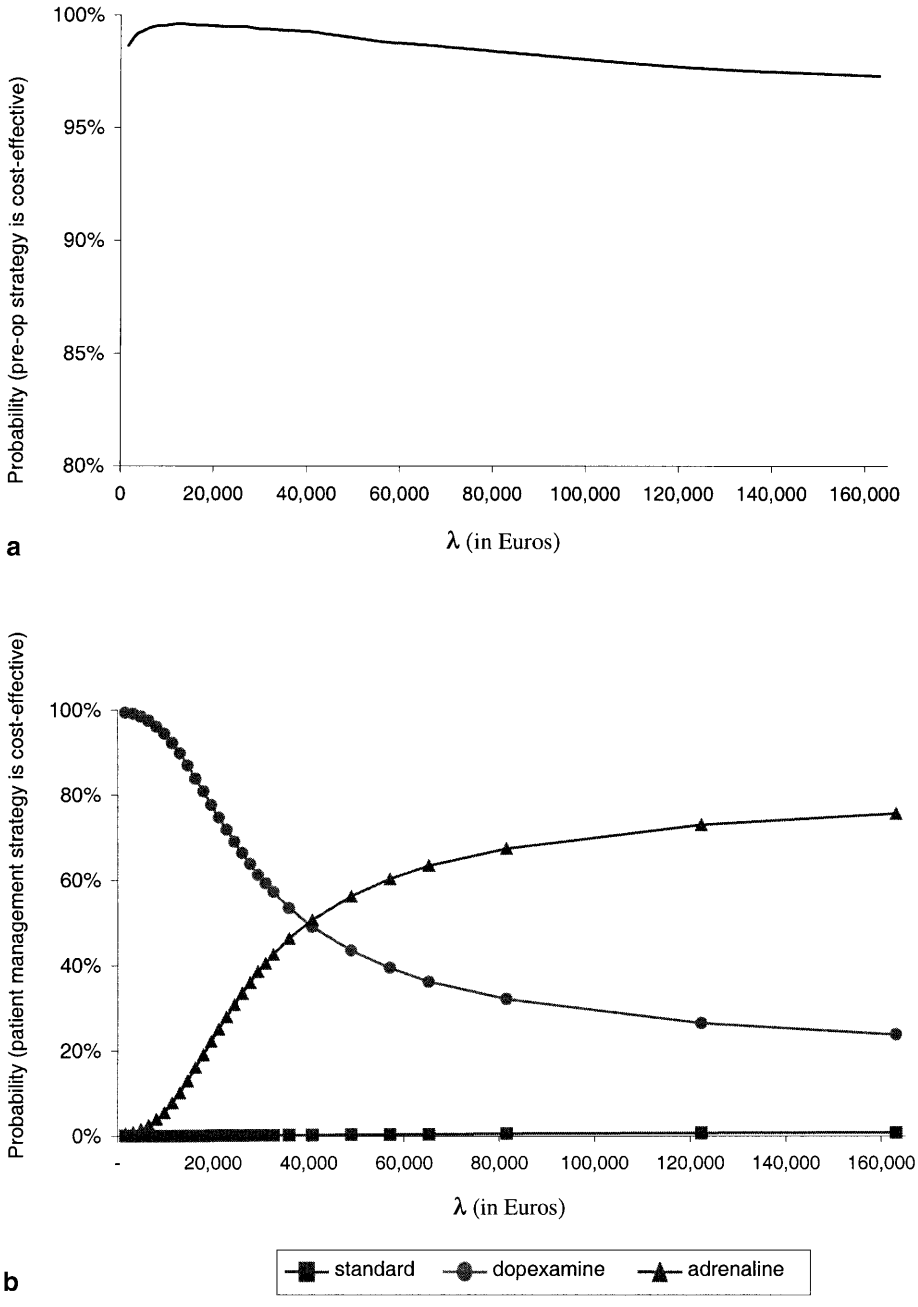

Fig. 5 **a** Cost-effectiveness acceptability curve showing the probability that pre-operative optimisation (either inotrope) is optimal, compared with standard patient management, for a given willingness to pay for an additional life-year (λ). **b** Cost-effectiveness acceptability curves showing the probability that each management option is optimal for a given willingness to pay for an additional life-year (λ)

This value is consistent with funding decisions made in the UK NHS (for example by the National Institute for Clinical Excellence).

Figure 5b compares all three patient management strategies, illustrating the probability that each is the optimal choice, for a range of λ values. When the decision maker is unwilling to pay anything for an additional life-year, the probability that pre-op with dopexamine is optimal (i.e. dopexamine is cost-saving) is 99.6%. If the decision maker is willing to pay EUR 32,620 (£20,000) per life-year gained, the probability that pre-op with dopexamine is optimal is 57.2%, compared with probabilities of 42.6% and 0.2% for pre-op with adrenaline and standard patient management, respectively. Further discussion of the results of the analysis, in particular the choice between adrenaline and dopexamine, appears within the discussion section.

Discussion

The analysis presented here suggests that we expect pre-op to dominate standard management (probability

Table 3 Costs in the trial groups – euros (*ICU* intensive care unit, *HDU* high dependency unit)

Resource	Standard		Adrenaline		Dopexamine		Pre-op (either inotrope)	
	Mean (SE)	Median (IQR)	Mean (SE)	Median (IQR)	Mean (SE)	Median (IQR)	Mean (SE)	Median (IQR)
Length of stay								
Ward	7347 (9879)	4553 (2826, 6367)	6513 (5329)	4805 (3561, 6737)	4176 (2476)	3301 (2902, 4800)	5331 (4281)	3948 (3192, 5258)
ICU	3874 (7960)	0 (0, 2099)	2485 (5671)	0 (0, 1563)	2059 (5386)	0 (0, 1390)	2270 (5502)	0 (0, 1448)
HDU	1046 (2225)	0 (0, 1154)	1055 (1203)	873 (0, 1040)	1011 (763)	957 (624, 1269)	1033 (1000)	915 (83, 1102)
Total excluding related	12267 (13579)	7197 (3978, 13156)	10053 (9188)	6624 (4822, 10541)	7246 (6621)	5499 (4107, 7614)	8634 (8074)	5861 (4299, 9083)
Related in-patient stay	606 (3380)	0 (0, 0)	1332 (4875)	0 (0, 0)	46 (309)	0 (0, 0)	682 (3477)	0 (0, 0)
All drugs	367 (496)	169 (62, 470)	243 (307)	126 (51, 255)	215 (296)	103 (60, 240)	229 (300)	115 (52, 252)
All infusions	1124 (1989)	400 (162, 1100)	777 (1888)	256 (99, 551)	611 (984)	296 (76, 546)	693 (1495)	287 (98, 557)
All investigations	416 (419)	268 (125, 552)	344 (380)	211 (118, 327)	244 (221)	173 (128, 279)	293 (312)	184 (125, 320)
All interventions	856 (1762)	90 (0, 1008)	474 (1073)	46 (12, 293)	337 (855)	52 (0, 131)	405 (966)	46 (0, 206)
Pre-optimisation	n/a (n/a)	n/a (n/a, n/a)	770 (250)	699 (537, 1013)	839 (267)	751 (603, 1086)	805 (260)	701 (573, 1033)
Total cost	16,965 (3,338)	16,440 (14,640, 18,675)	13,820 (1,743)	13,638 (12,603, 14,823)	9,247 (847)	9,171 (8,667, 9,758)	11,310 (889)	11,236 (10,686, 11,856)

93%). In addition, regardless of the value placed upon a life-year gained, the probability of pre-op being optimal, compared with standard care, is high (>97%). Hence, the decision maker should choose to adopt pre-op for these patients. However, this comparison does not inform the decision maker as to which inotrope to employ within the optimisation process and so decision makers will be interested in a comparison of the three methods of patient management. For this comparison, we expect standard management to be dominated by both pre-op management strategies, with pre-op employing adrenaline being more effective and expensive than pre-op employing dopexamine (with each additional life-year costing EUR 38,108 – £23,367). In this situation, the decision as to which method of patient management to employ and the probability that this method is optimal, depends crucially on the value that the decision maker is willing to pay for additional life-years in this patient group.

If decision makers are only interested in costs, and they do not value improvement in patients' life expectancy, they should adopt pre-op employing dopexamine (probability of there being a cost-saving >99%). However, we know that decision makers do value additional life-years, and while no monetary value for incremental health gain has officially been stated in the UK, values of between Can$20,000 (EUR 14,385) and Can$100,000 (EUR 71,927) per quality-adjusted life-year gained were suggested in Canada in 1992 [12]. Further, the National Health Service has funded many interventions with implied values within this range. For example, implantable cardioverter defibrillators had an estimated cost per life-year gained of £26,000–30,000 (EUR 42,400–48,930), and was recommended for use by the National Institute for Clinical Excellence [13].

The analysis shown in Fig. 5b indicates that if decision makers value additional life-years at a minimum of EUR 32,620, they should adopt pre-op employing dopexamine. At this value of λ the probability that this is the optimal choice falls to 57%. This reflects the fact that as decision makers are willing to pay more for a life-year gained, pre-op employing adrenaline (which is both more expensive and more effective than dopexamine) becomes more attractive to them. That is, the additional effects are considered worth the additional costs. On the other hand, if the maximum willingness-to-pay for additional life-years exceeds EUR 38,108, the decision maker should adopt pre-op employing adrenaline, with a probability that this is the optimal choice of at least 50%.

The results of our study corroborate the cost and cost-effectiveness analyses undertaken in previous studies [1, 14]. Shoemaker [1] concluded that average hospital charges and patient expenditures were reduced for pa-

tients receiving pre-op, but did not undertake a formal cost-effectiveness analysis. Guest et al. [4] provided a detailed analysis of the cost of resources associated with pre-operative optimisation and standard patient management pre-operatively, intra-operatively, post-operatively and employed in treating complications. They concluded that the median cost per patient and per survivor was lower for the group receiving pre-op [4]. However, the use of medians rather than means reduces the impact of any extreme values on the results, and where data are likely to be highly skewed (as costs typically are) the use of medians will not facilitate an estimate of the total cost impact across a sample of patients [14] In addition, the use of the number of survivors, at 28 days post-surgery, as the measure of effectiveness limits the analysis through the implicit assumption that life expectancy for survivors is identical between the groups. Our study has attempted to capture the life-years gained associated with pre-op patient management through the survival duration data. However, the survival duration data has been censored at 2 years post-surgery and so underestimates the life expectancy of patients in all of the different patient management arms.

There are other limitations to this study. First, it concentrates upon the health care costs that directly affect the hospital, and ignores costs that fall upon other sectors, either directly or indirectly. For example, earlier discharge from hospital may impact upon resource use at a general practitioner or patient level, as patients receive care at home rather than in hospital. Second, the study utilised local costs applicable in one centre that may not be representative of costs at other UK hospitals. Hence, the study may not be generalisable to other settings without some modification. Third, retrospective collection of resource data can be a limitation to studies. However, in this study the patient notes had been well maintained and over 70% of the costs related to in-patient stay, about which hospital information systems are generally accurate and complete.

This study has shown that decision makers can be confident that pre-op is a cost-effective method of managing high-risk surgical patients undergoing major elective surgery. The study has also shown that, given current levels of information, the decision concerning which inotrope to employ, to achieve optimisation, depends crucially upon the value that the decision maker is willing to pay for additional life-years in this patient group. In addition, there is considerable uncertainty surrounding the choice between inotropes and further research is likely to be good value for money.

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