Pulmonary artery catheters for adult patients in intensive care (Review)

Rajaram SS, Desai NK, Kalra A, Gajera M, Cavanaugh SK, Brampton W, Young D, Harvey S, Rowan K

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[Intervention Review]

Pulmonary artery catheters for adult patients in intensive care

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ABSTRACT

Background

Since pulmonary artery balloon flotation catheterization was first introduced in 1970, by HJ Swan and W Ganz, it has been widely disseminated as a diagnostic tool without rigorous evaluation of its clinical utility and effectiveness in critically ill patients. A pulmonary artery catheter (PAC) is inserted through a central venous access into the right side of the heart and floated into the pulmonary artery. PAC is used to measure stroke volume, cardiac output, mixed venous oxygen saturation and intracardiac pressures with a variety of additional calculated variables to guide diagnosis and treatment. Complications of the procedure are mainly related to line insertion. Relatively uncommon complications include cardiac arrhythmias, pulmonary haemorrhage and infarct, and associated mortality from balloon tip rupture.

Objectives

To provide an up-to-date assessment of the effectiveness of a PAC on mortality, length of stay (LOS) in intensive care unit (ICU) and hospital and cost of care in adult intensive care patients.

Search methods

We searched the Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2011, Issue 12); MEDLINE (1954 to January 2012); EMBASE (1980 to January 2012); CINAHL (1982 to January 2012), and reference lists of articles. We contacted researchers in the field. We did a grey literature search for articles published until January 2012.

Selection criteria

We included all randomized controlled trials conducted in adults ICUs, comparing management with and without a PAC.

Data collection and analysis

We screened the titles and abstracts and then the full text reports identified from our electronic search. Two authors (SR and MG) independently reviewed the titles, abstracts and then the full text reports for inclusion. We determined the final list of included studies by discussion among the group members (SR, ND, MG, AK and SC) with consensus agreement. We included all the studies that were in the original review. We assessed seven domains of potential risk of bias for the included studies. We examined the clinical, methodological and statistical heterogeneity and used random-effects model for meta-analysis. We calculated risk ratio for mortality across studies and mean days for LOS.

Main results

We included 13 studies (5686 patients). We judged blinding of participants and personnel and blinding of outcome assessment to be at high risk in about 50% of the included studies and at low risk in 25% to 30% of the studies. Regardless of the high risk of performance bias these studies were included based on the low weight the studies had in the meta-analysis. We rated 75% of the studies as low risk for selection, attrition and reporting bias. All 13 studies reported some type of hospital mortality (28-day, 30-day, 60-day or ICU mortality). We considered studies of high-risk surgery patients (eight studies) and general intensive care patients (five studies) separately as subgroups for meta-analysis. The pooled risk ratio (RR) for mortality for the studies of general intensive care patients was 1.02 (95% confidence interval (CI) 0.96 to 1.09) and for the studies of high-risk surgery patients the RR was 0.98 (95% CI 0.74 to 1.29). Of the eight studies of high-risk surgery patients, five evaluated the effectiveness of pre-operative optimization but there was no difference in mortality when these studies were examined separately. PAC did not affect general ICU LOS (reported by four studies) or hospital LOS (reported by nine studies). Four studies, conducted in the United States (US), reported costs based on hospital charges billed, which on average were higher in the PAC groups. Two of these studies qualified for analysis and did not show a statistically significant hospital cost difference (mean difference USD 900, 95% CI -2620 to 4420, P = 0.62).

Authors' conclusions

PAC is a diagnostic and haemodynamic monitoring tool but not a therapeutic intervention. Our review concluded that use of a PAC did not alter the mortality, general ICU or hospital LOS, or cost for adult patients in intensive care. The quality of evidence was high for mortality and LOS but low for cost analysis. Efficacy studies are needed to determine if there are optimal PAC-guided management protocols, which when applied to specific patient groups in ICUs could result in benefits such as shock reversal, improved organ function and less vasopressor use. Newer, less-invasive haemodynamic monitoring tools need to be validated against PAC prior to clinical use in critically ill patients.

PLAIN LANGUAGE SUMMARY

Pulmonary artery catheters for adult patients in intensive care

A pulmonary artery catheter (PAC) is a device utilized in intensive care units (ICU) to measure the pressures in the heart and lung blood vessels and to monitor patients. The catheter is inserted into the right side of the heart through a line placed in a large blood vessel in the neck or groin and is positioned into the pulmonary artery. Complications are uncommon and are mainly related to line insertion. Occasionally bleeding inside the lung and changes in heart rhythm have been reported, but death associated with a PAC is rare. The objective of this systematic review was to provide an up-to-date assessment of evidence on the effectiveness of PAC on death rates, days spent in ICU, days spent in hospital, and cost of care for adult ICU patients.

We identified 13 studies comparing patients treated with and without the use of a PAC that studied a total of 5686 patients. These were studies of patients undergoing routine major surgery (eight) and studies of patients who were critically ill and admitted to ICUs (five). We analysed the studies for any trial related risks and performed appropriate statistical analysis to minimize any risk of bias or errors. The quality of evidence is high from this review and further research is very unlikely to change our confidence in the estimate of effect except for cost analysis.

Our review found that there were no differences in the number of deaths during hospital stay, days spent in general ICUs, and days spent in hospital between patients who did and did not have a PAC inserted. Two US studies were analysed for hospital cost associated with or without a PAC and showed no difference in the cost. Neither group of patients studied showed any evidence of benefit or harm from using a PAC. The catheter is a monitoring tool that helps in diagnosis and is not a treatment modality. Insertion of PACs to help make treatment decisions in ICU patients should be individualized and should be done by experts in the field after adequate training

in the interpretation of data. Studies need to be conducted to identify subgroups of ICU patients who can benefit, when the device is used in combination with standardized treatment plans, in reversing shock states and improving organ function.

SUMMARY OF FINDINGS FOR THE MAIN COMPARISON *[Explanation]*

Pulmonary artery catheter for adult patients in intensive care

Patient or population: Adult patients in intensive care
Settings: Intensive care unit
Intervention: Pulmonary artery catheter

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Control	Pulmonary artery Catheter				
ICU length of stay (general intensive care patients) Follow-up: mean 10-12 days		The mean ICU length of stay (general intensive care patients) in the intervention groups was **0.5 higher** (0.44 to 0.55 higher)		2723 (4 studies)	⊕⊕⊕⊕ **high**	
Hospital length of stay (general intensive care patients) Follow-up: mean 14-22 days		The mean hospital length of stay (general intensive care patients) in the intervention groups was **0.8 lower** (2.71 lower to 1.12 higher)		1689 (2 studies)	⊕⊕⊕⊕ **high**	
Hospital length of stay (high-risk surgical patients) Follow-up: mean 10-22 days		The mean hospital length of stay (high-risk surgical patients) in the intervention groups was **0.35 higher** (0.05 lower to 0.75 higher)		503 (5 studies)	⊕⊕⊕⊕ **high**	

Cost of care (hospital charges, 1000s of US dollars)		The mean cost of care (hospital charges, 1000's of us dollars) in the intervention groups was **0.9 higher** (2.62 lower to 4.42 higher)		191 (2 studies)	⊕⊕◯◯ **low**[1]
Combined mortality of all studies Follow-up: mean 28-60 days	**Study population**		**RR 1.01** (0.95-1.08)	5686 (13 studies)	⊕⊕⊕⊕ **high**
	297 per 1000	**301 per 1000** (273 to 333)			
	Moderate				
	95 per 1000	**97 per 1000** (85 to 110)			

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% CI) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk ratio;

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1] Only 2 studies reported the hospital cost out of 5, in 1990 to 91. The applicability in present situation after 20 years is questionable. The cost cannot be compared across various countries.

BACKGROUND

Description of the condition

The concept of right heart catheterization was first introduced by Dr Warner Forrsmann in 1929 (Chatterjee 2009). It was in 1970 that Dr HJ Swan and Dr William Ganz introduced the flow-directed balloon-tipped catheter that led to a paradigm shift in the way right heart catheterizations are performed at the bedside using intracardiac pressure tracings, without utilizing fluoroscopic guidance. Since then, the pulmonary artery catheter (PAC), also called a Swan-Ganz catheter, has been utilized in the management of intensive care unit (ICU) patients for the past 42 years (Swan 1970). A PAC provides the intensivist with critical haemodynamic data that includes cardiac output, mixed venous oxygen saturation, intrapulmonary and intracardiac pressures. These variables together with additional derived variables calculated from these measurements, such as pulmonary and systemic vascular resistance, right and left ventricular stroke work indices, right and left ventricular end-systolic and end-diastolic indices, right ventricular ejection fraction, arterial and venous oxygen content, oxygen consumption, oxygen delivery and oxygen extraction ratio, are used to guide treatment of critically ill patients. On average, in the United States (US) one million PACs were used annually in the 1990s (Connors 1996).

Description of the intervention

A PAC is a diagnostic and haemodynamic monitoring tool. The PAC is used by clinicians in adult medical ICUs, cardiac catheterization laboratories and coronary care units (CCUs). It is used for pre-operative optimization of haemodynamics, intra-operative monitoring and postoperative management of critically ill patients, and in cardiothoracic surgery patients such as coronary artery bypass graft (CABG, or bypass surgery) and valvular surgeries to guide therapy and differentiate various types of shock states.

For the procedure, the balloon-tip catheter is floated through a central venous access, through the right atrium and right ventricle to the pulmonary artery and left in position to measure the filling pressures of the heart. When the balloon is inflated it measures pulmonary capillary wedge pressure or occlusion pressure, which is an indirect measure of left ventricular end-diastolic pressure. Newer PACs have the capability of measuring central venous oxygen saturation and continuous cardiac output.

Insertion of a PAC requires a central venous access and its complications are mainly related to the line placement. Advanced training and ultrasound guidance of line insertions have reduced some of these risks in recent years (Lamperti 2012). Long-term central line related complications such as infections are not attributable to PAC insertion. Additional risks of floating a PAC include possible pulmonary artery rupture and subsequent bleeding or pulmonary infarction (lung tissue loss). In an attempt to review the risk and benefits of a PAC the American Society of Anesthesiologist reviewed 860 publications. Though major morbidity related to PAC seems uncommon, minor atrial and ventricular arrhythmias (heart rhythm abnormalities) are common during catheter insertion (>20%).

Complications from PAC can be classified as:

1. those from central venous access (arterial puncture, postoperative neuropathy (pain and sensation deficit), air embolism (air in blood vessels) and pneumothorax (air outside the lungs), reported in less than 3.6%;
2. those arising from catheterization (severe dysrhythmias, right bundle branch block and complete heart block), seen in 0.3% to 3.8%; and
3. those due to prolonged catheter residence (pulmonary artery rupture, pulmonary infarction, venous thrombosis (clots in vein)), in from 0.03% to 3%.

The task force states that overall deaths attributed to a PAC are 0.02% to 1.5% (ASA task force on PAC 2003).

How the intervention might work

Pulmonary artery catheters (PACs) were initially widely used by cardiologists in the management of patients with acute heart failure or cardiac tamponade, major surgery patients with a cardiac history, and cardiogenic shock. The first data on PACs were published in 1987, in an observational study from 16 different hospitals that looked at time trends in incidence rates, on in-hospital and long-term case fatality rates in patients with acute myocardial infarction (Gore 1987). The study had 3000 patients and showed a sharp rise in the use of PACs from 1975 to 1984 (7.2% to 19.9%) with no difference in mortality in the group of patients with cardiogenic shock. There was, however, increased mortality and hospital length-of-stay (LOS) in patients with congestive heart failure and hypotension who received a PAC. Interestingly, the study showed better long-term survival in patients with cardiogenic shock who received a PAC at six months and five years. In 1990, another non-experimental study showed increased mortality in patients who received a PAC (Zion 1990). In this study only 67 patients had a PAC and the authors concluded that it was unlikely that the PAC itself had led to the increased mortality. This led to the first randomized controlled trial (RCT) of PACs in 1991 (Guyatt 1991). The European Society of Intensive Care Medicine later came out with a consensus document recommending the indications for use of PACs (ESICM 1991).

In 1996, results of a prospective, non-experimental cohort study that involved 5700 patients with nine different illnesses, of which 2100 received PACs, showed increased mortality with PAC use (Connors 1996). The publication sparked a lot of controversy primarily because it was a non-randomized comparison (Assoc. Press

1996). A Consensus Statement issued by the Society of Critical Care Medicine identified that the published evidence to support the use of PAC was paltry and scientifically very poor, and the need for clinical trials was highlighted (PAC Consensus 1997). Recent evidence suggests that use of a PAC and therapy based on the information obtained reduces surgical morbidity and mortality (Brienza 2009; Gurgel 2011; Hamilton 2011). Until now, controversy exists with the use of PACs in various clinical settings in ICUs. If clinicians acquire adequate knowledge and expertise, PAC data and monitoring may be valuable to guide therapy in critically ill patients. The device has to produce data that are reliably interpreted by attending staff. These data are usually not available from other sources and can lead to a change in therapy that is linked to improved outcomes. The therapies that might be altered or added include pressors, inotropes, vasodilators, fluids, diuretics and lusitropic agents.

Why it is important to do this review

This is an update of a Cochrane review first published in 2006 (Harvey 2006) about PAC use in adult ICU. The initial review identified 12 studies and the main findings were that PAC did not affect the mortality of patients, hospital or ICU LOS, and the cost based on charges billed to the patients were on average higher in the PAC groups.

Since the adoption of the PAC into clinical practice, several observational studies and five RCTs involving general ICU patients (Binanay 2005; Harvey 2005; NHLBI 2006; Rhodes 2002; Richard 2003) have been conducted to determine its effect on patient mortality. These studies did not show a benefit of the use of a PAC in patient outcomes. There was significant negative publicity, especially in the US, leading to a decline in the use of PACs in clinical practice. A report looking at trends in the use of PACs in the US, published in 2007 (Wiener 2007), reported a 65% reduction in its use among medical ICUs and 63% reduction in its use among surgical ICUs from 1993 to 2004. Recently, however, there has been criticism in the way the data from these studies were interpreted (Greenberg 2009). Authors have argued that the PAC is a monitoring device and that mortality must not be a basis for determining the efficacy of monitors. Patient outcomes are not dependent upon insertion of a PAC; outcomes are dependent upon appropriate interpretation of acquired data followed by administration of appropriate care. It has also been argued that studies were not adequately powered to provide conclusions on rare outcomes like patient mortality (Greenberg 2009). Also, it would have been challenging to adequately blind physicians to the PAC, as it is hard to conceal the presence of a PAC in a patient.

The timeliness of institution of care with regard to PAC insertion has also been questioned. In a meta-analysis performed in 1996 (Cooper 1996) that showed no benefit of goal-directed therapy using a PAC in a general ICU population, only one study was considered of high quality (Gattinoni 1995). The study randomized 762 patients in one of three categories, cardiac index (CI) 2.5 to 3.5 ml/min/m^2; CI > 4.5 ml/min/m^2; and central venous oxygen saturation > 70%. The patients in the study, however, did not receive the PAC until up to 72 hours after development of shock. The patients in the most recent Fluid and Catheter Treatment Trial (FACTT) (NHLBI 2006) that studied the safety and efficacy of PAC-guided versus central venous pressure (CVP)-guided treatment of patients with acute lung injury also did not receive therapy until a mean of 25 hours after establishment of diagnosis. In the light of the aforementioned studies and meta-analysis, and the ongoing debate on appropriate use of the PAC, the purpose of the current systematic review was to search for all the available evidence from RCTs and to define the best evidence base for current clinical practice.

OBJECTIVES

To systematically search for and synthesize all the evidence from randomized controlled trials (RCTs) that utilized pulmonary artery catheters (PACs) in the management of critically ill patients in the intensive care units (ICUs) and analyse the effect of the PAC on mortality, length of stay and cost of care.

METHODS

Criteria for considering studies for this review

Types of studies

We included RCTs with or without blinding. We placed no limitation on the language of publication.

Types of participants

We included studies with more than 50% adult patients (16 years of age and above) where a PAC was placed in an ICU setting (see definition below) or placed during a surgical procedure leading to ICU admission.

We defined an ICU as including: an intensive care unit (ICU); a paediatric intensive care unit; a high dependency unit (HDU); a postanaesthesia care unit (PACU); or a service-specific critical care unit (CCU).

We excluded studies that included patients in whom death had been declared using brain stem death criteria and who had a PAC placed solely for organ support prior to organ donation.

We excluded studies comparing PAC with the new less invasive techniques used to measure the haemodynamic parameters, such as continuous pulse contour cardiac analysis (PiCCO).

Types of interventions

We included RCTs in which patients treated in an ICU were randomized to be managed with a PAC (of any type) in one arm of the trial and without a PAC in another arm.

Types of outcome measures

Primary outcomes

1. All types of hospital mortality (28 days, 30 days, 60 days or ICU mortality)

Secondary outcomes

1. Length of stay (LOS) in ICU
2. LOS in hospital
3. Costs of hospital care

Search methods for identification of studies

Electronic searches

We searched the Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2011, Issue 12), see Appendix 1 for the search strategy; MEDLINE (OvidSP) (1954 to January 2012), see Appendix 2; EMBASE (OvidSP) (1980 to January 2012), see Appendix 3; CINAHL (EBSCOhost) (1982 to January 2012), see Appendix 4.

Searching other resources

Grey literature search

We searched the grey literature including NYAM Grey Literature Collection, OAIster - Digital Resource from Open Archive Collections, Directory of Open Access Journals and OpenDOAR; clinical trial registers (International Standard Randomised Controlled Trial Number Register, Eur Clinical Trials Register (new 2011) and WHO International Clinical Trial Registry Platform); dissertations and theses; open access journals; meeting abstracts and conference abstracts (handsearched for original review). See Appendix 5 to see a list of all resources and terms.

Previous reviews

We reviewed the studies cited in the previously published review (Harvey 2006), now updated in 2012.

Manual searches

We handsearched conference abstracts from the four major European and North American annual critical care conferences, run by the European Society of Intensive Care Medicine, the Society of Critical Care Medicine (US), the American Thoracic Society, and the Erasme Hospital, Free University of Brussels (from 1995 to 2001). For the update we added the above grey literature search in 2012 (see Appendix 5).

Citation review

We checked the references lists of included citations and potentially relevant citations, identified from the electronic searches, for further relevant studies. We also checked the reference lists of any systematic or narrative reviews identified from the searches.

Experts

We contacted key people in the field of critical care, including clinicians and other researchers, to identify relevant studies.

Industry

We contacted relevant pharmaceutical and equipment companies for published and unpublished reports to identify relevant studies.

Data collection and analysis

Selection of studies

In the update we included all the originally selected studies (Harvey 2006) and added new studies searched for from April 2005 to January 2012. Four authors screened the updated search results independently (SR, ND, MG and AK). One author (SC) searched the grey literature. We obtained the full text articles of the studies that seemed to be relevant during our screening. We resolved discrepancies through discussion.

Data extraction and management

Two authors independently reviewed the full text reports of each included study (update in 2012 by SR or MG, AK; and original review (Harvey 2006) in 2006 by SH, DY or WB, KR) and extracted the following data:

- general information, including title, lead author, journal, publication details and name of reviewer;
- study characteristics, including verification of study eligibility, characteristics of study population, risk of bias of included studies and interventions;
- outcome measures and results, including length of follow-up, drop-outs and measures of effect.

We resolved differences in the data extracted between the two authors by discussion. We documented the reasons for excluding studies. Two authors (SH and DY) double-entered data into Review Manager in the original version (Harvey 2006). In the 2012 update two authors (SR and MG) independently extracted the data and created risk of bias tables. We resolved the discrepancies through discussion. Two authors (SR and ND) entered data into Review Manager (RevMan 5.1).

Assessment of risk of bias in included studies

We used the *Cochrane Handbook for Systematic Reviews of Interventions* (the *Handbook*) (Higgins 2011) to assess the risk of bias for each study. Two authors (SR and MG) independently assessed the risk of bias for each study considering the following seven domains for bias: random sequence generation (selection bias), allocation concealment (selection bias), blinding of participants and personnel (performance bias), blinding of outcome assessment (detection bias), incomplete outcome data (attrition bias), selective reporting (reporting bias) and other bias. For each bias we expressed our judgement as: at high risk (plausible bias that seriously weakens confidence in the results), low risk (unlikely to seriously alter the results) and unclear risk (raises some doubt about the results) of bias. We also gave the reason for our judgement. Three authors (SR, MG and AK) resolved disagreements by reviewing the data together.

We agreed that complete blinding of the treating physicians may not be feasible at the bedside, but the investigator could be blinded. If the investigator was blinded or did not participate in patient care, we agreed that those studies were at low risk for performance bias. If it was a single centre study and investigators and the treating physicians were the same person, we agreed that performance bias was at high risk. We agreed that blinding of outcome assessment was feasible in studies such as in a multicentre trial if the outcome assessor did not participate in patient care.

Measures of treatment effect

For dichotomous data (mortality), we used risk ratio (RR) as the summary measure. For continuous data (LOS, cost of care) we used mean difference as the summary measure.

Unit of analysis issues

We also combined studies that had included other interventions in addition to the PAC in a separate subgroup analysis. For studies that had two PAC intervention groups, we combined the two groups.

Dealing with missing data

We did not contact any original investigators to request information about missing data. Our search was comprehensive and missing studies was unlikely. One study (Bender 1997) did not report all the details of the outcome measures postoperatively for the control group and we judged the study as at high risk of selective reporting bias in the analysis.

Assessment of heterogeneity

We used Chi^2 test (χ^2) to assess whether observed differences in results were compatible with chance alone. A large Chi^2 statistic relative to its degree of freedom provides evidence of heterogeneity of intervention effects (variation in effect estimates beyond chance). For quantifying inconsistency we used the I^2 statistic to describe the percentage of the variability in effect estimates that was due to heterogeneity rather than sampling error (chance). An I^2 of 0% to 40% might not be important, 30% to 60% was moderate heterogeneity, 50% to 90% was substantial heterogeneity and 75% to 100% was interpreted as considerable heterogeneity (Higgins 2011). When the heterogeneity was low in the outcome measures meta-analysis was considered appropriate.

Clinical heterogeneity was explored by conducting subgroup analysis. To incorporate heterogeneity among studies random-effects model meta-analysis was used. We did not exclude any studies based on conflicting results, which minimized heterogeneity. We performed sensitivity analysis with and without any potential outlying studies. We did not perform meta-regression to investigate heterogeneity in a subgroup analysis due to low sample size of the subgroups.

Assessment of reporting biases

We tried to minimize the impact of publication bias through a thorough review of all the published data and grey literature. We dealt with location bias by searching MEDLINE, EMBASE, CENTRAL, CINAHL and grey literature using a variety of search terms. We assessed publication bias using a funnel plot for the combined mortality outcome.

Data synthesis

We summarized the aims, methods and outcome measures of interest (mortality, LOS in ICU and hospital, and costs of care). We expressed mortality as absolute numbers and percentages, and we expressed LOS as mean, median, and range for survivors and non-survivors reported separately. The primary outcome measure of interest was in-hospital mortality at any time; if this was not reported, we used the mortality at the point closest to hospital discharge. We expressed results on costs of care in a range of measures. The secondary outcome measures were ICU and hospital LOS and cost of care.

We calculated risk ratio (RR) for mortality across studies and mean days for LOS using a random-effects model in RevMan 5.1 (Higgins 2011; RevMan 5.1). All analyses were based on the intention-to-treat principle. Among the five studies that reported various costs, only two studies reported the hospital cost and a fixed-effect model was used to analyse the cost.

One study (Pearson 1989) allowed patients to cross-over to the PAC group after randomization due to ethical reasons. We combined the number of patients in the PAC group for mortality analysis and reported the hospital LOS separately. Another study (Guyatt 1991) allowed sicker patients to cross-over to the PAC group. We did not perform paired-analysis due to the low number of recruitments. The weights of these two studies were low in the meta-analysis.

Subgroup analysis and investigation of heterogeneity

Patients admitted to ICU are a heterogeneous group in terms of diagnosis, prognosis and resource utilization. This heterogeneity exists both among patients within a single ICU and among the case mix of patients admitted to medical and surgical ICUs. Therefore, we performed subgroup analysis combining data from studies that had included patient populations with similar characteristics. We did subgroup analysis of mortality separately in general intensive care patients, high-risk surgical patients, and studies of perioperative monitoring to investigate the effect of the heterogeneity of the studies. We analysed ICU LOS and hospital LOS separately for surgical and medical patients.

Sensitivity analysis

We performed sensitivity analysis to examine the impact of studies which had a high risk of bias. This was achieved by removing a study from the meta-analysis and analysing the effect of removing that study on overall mortality. We performed a similar sensitivity analysis with hospital LOS and ICU LOS with studies that had a high risk of bias.

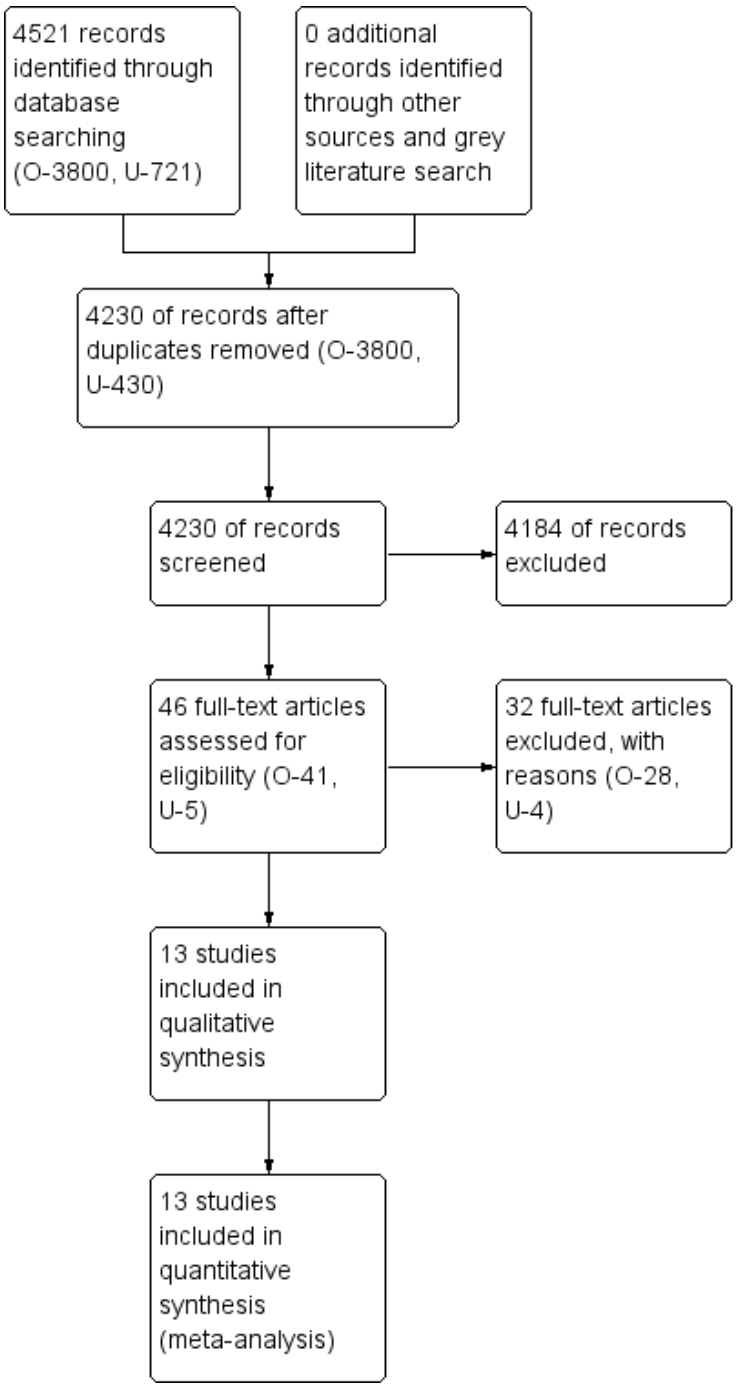
RESULTS

Description of studies

Results of the search

We identified a total of 4521 citations (3800 in 2006 (Harvey 2006) and 721 in 2012) (Figure 1). After screening by title and then abstract, we obtained full paper copies for 46 (41 in 2006 and five in 2012) citations that were potentially eligible for inclusion in the review. Of these, 28 did not fulfil our inclusion criteria and were excluded for the reasons described in the table Characteristics of excluded studies.

Figure 1. PAC for adult patients intensive care study flow diagram.O - Original review in 2006. U - Updated review in 2012.



Included studies

We included 13 RCTs. These 13 studies enrolled a total of 5686 patients. All patients were admitted to ICU and randomized to either a PAC group or control group with or without a central venous catheter (CVC) to monitor haemodynamics. All RCTs reported hospital mortality as the primary outcome (Analysis 1.1) and some reported ICU LOS and hospital LOS as secondary outcomes (Characteristics of included studies). The studies fell broadly into two groups, as follows.

1. General ICU studies: we included five studies of general intensive care patients with varying diagnoses (acute lung injury (NHLBI 2006); acute ventilatory failure (Guyatt 1991); shock (Rhodes 2002; Richard 2003)); and one study of patients admitted to the ICU requiring PAC insertion as deemed appropriate by the attending physician (Harvey 2005).

2. High-risk surgery studies: we included eight studies of patients undergoing high-risk surgery. These studies were divided into two subgroups.

a) Studies investigating the effectiveness of preoperative optimization of haemodynamics. We identified five studies in this category, for vascular surgery (Bender 1997; Berlauk 1991); abdominal, thoracic, vascular or orthopaedic surgery (Sandham 2003); abdominal reconstructive surgery (Valentine 1998); and predefined high-risk surgical patients (Shoemaker 1988).

b) Studies comparing the effectiveness of managing patients during the perioperative period where patients were admitted to the ICU following surgery. We identified three studies in this category, in aortic reconstruction (Isaacson 1990; Joyce 1990) and elective cardiac surgery patients (Pearson 1989).

Excluded studies

We excluded non-RCTs and systematic reviews. We also excluded RCTs that compared PACs with non-invasive haemodynamic monitoring methods and studies that had their primary outcome of interest as fluid management (see Characteristics of excluded studies).

Risk of bias in included studies

We analysed seven domains of potential risk of bias for the included studies (Figure 2). We rated blinding of participants and personnel and blinding of outcome assessment at high risk in half of the included studies and at low risk in one third of the studies. Regardless of the high risk of performance bias, these studies were included because of the low weight of the studies in the meta-analysis. We rated three quarters of the studies at low risk of selection bias, attrition bias and reporting bias (Figure 3). We performed a sensitivity analysis by removing all the trials that had high and unclear risk of bias and the results remained the same. Publication bias appeared to be unlikely as the funnel plot is symmetric, which also confirms the absence of effect of study size on the outcome (Figure 4).

Figure 2. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

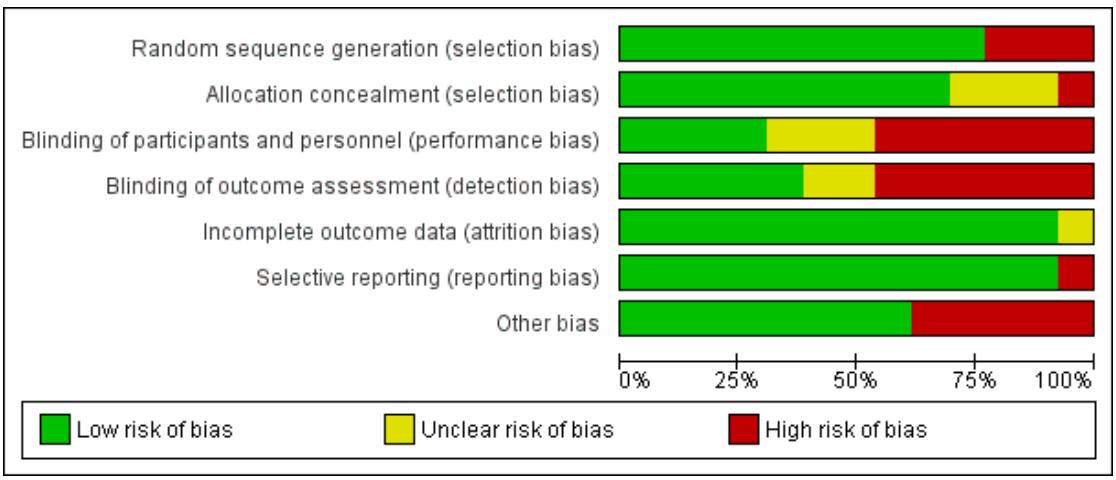


Figure 3. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

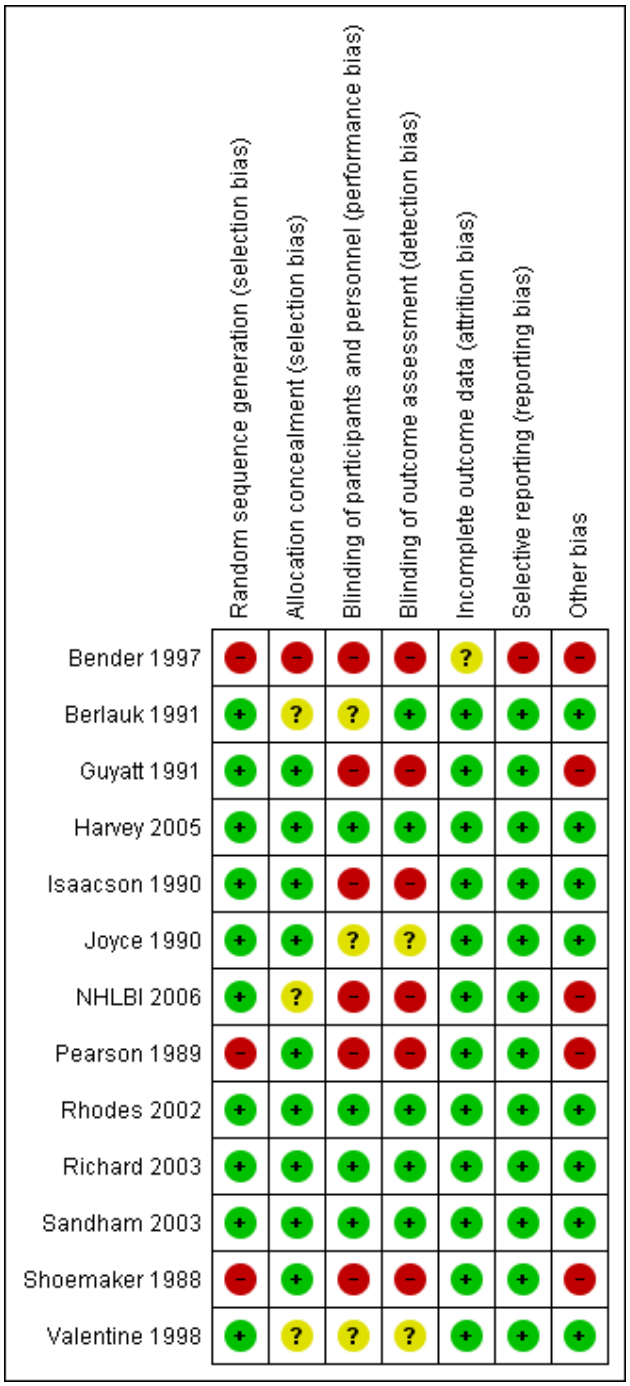
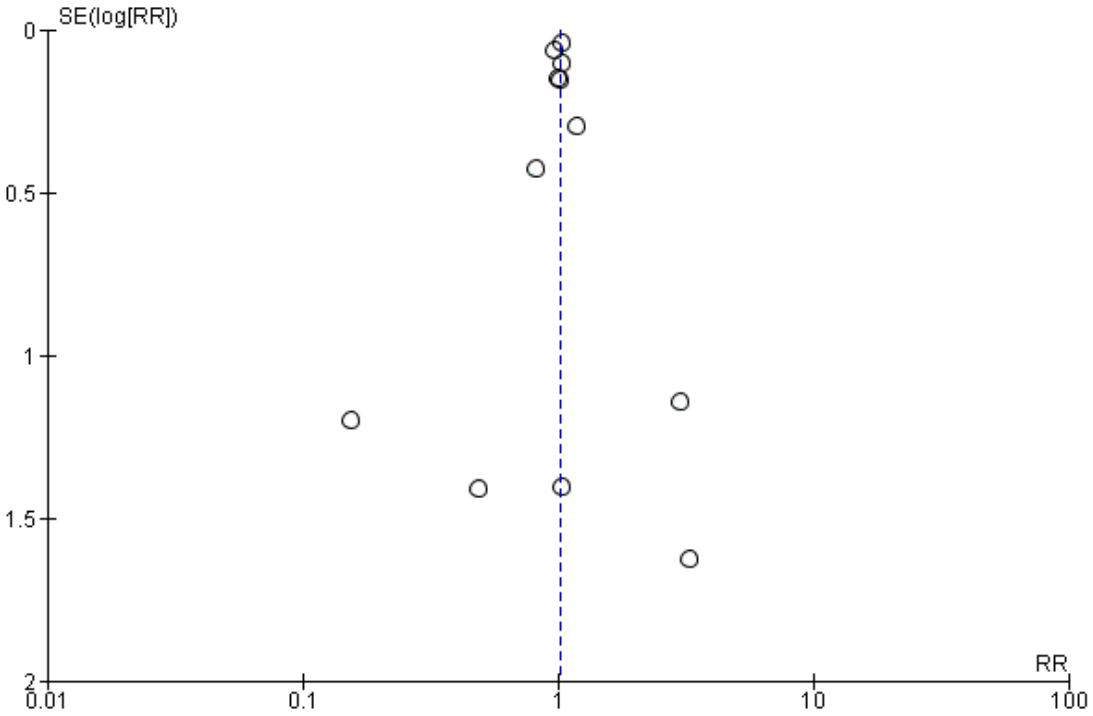


Figure 4. Funnel plot of comparison: 5 PAC versus no PAC outcome: 5.1 Combined mortality of all studies.



Allocation

Nine studies clearly used adequate randomization and concealment schemes and were classified as low risk for bias (Guyatt 1991; Harvey 2005; Isaacson 1990; Joyce 1990, Pearson 1989; Rhodes 2002; Richard 2003; Sandham 2003; Shoemaker 1988). Three studies had an unclear risk due to not reporting allocation details (NHLBI 2006; Valentine 1998) and inconsistent methods of allocation (Berlauk 1991). One high-risk study did not follow any acceptable methods (Bender 1997).

Blinding

Performance bias

The intervention under study, management with a PAC (with or without preoperative optimization), meant that it was not feasible to completely blind the study participants and some study personnel to the assigned treatment group. However, if treating physicians and patient care decision makers were not the investigators, performance bias could be minimized.

Four studies were at low risk for blinding of participants or performance bias due to the multicentre nature of the study or investigators were not the providers (Harvey 2005; Rhodes 2002; Richard 2003; Sandham 2003). Five studies were at high risk for performance bias. One study, even though a multicentre trial, was protocol driven and allowed the PAC patients to change over to a CVC at the discretion of the treating physician (NHLBI 2006). In two studies the providers were the investigators (Isaacson 1990; Shoemaker 1988) and in two other studies the providers were allowed to change the group or cross-over to PAC after randomization (Guyatt 1991; Pearson 1989).

Three studies gave insufficient information to assess performance bias (Berlauk 1991; Joyce 1990; Valentine 1998) (Figure 3).

Detection bias

The nature of the intervention under study meant that complete blinding of outcome was not feasible, however detection bias could be minimized if the investigator and treating physician were different personnel. Performance bias and detection bias shared similar high and unclear risks in all the studies except in one study. Berlauk et al (Berlauk 1991) had low risk because investigators (anaesthesiologists) were involved for a short period of the first 18 hours only and were unlikely to have influenced the mortality or hospital LOS thereafter. Two studies gave insufficient information and the risk was unclear (Joyce 1990; Valentine 1998). Four studies were at low risk (Harvey 2005; Rhodes 2002; Richard 2003; Sandham 2003). Four other studies were at high risk (Guyatt 1991; Isaacson 1990; Pearson 1989; Shoemaker 1988) however, given their low weights in the meta-analyses, the impact on the effect estimate of removing them would have been negligible. The FACTT study (NHLBI 2006) was at high risk for detection bias because only weaning of vasopressors were under protocol management and not fluid management, which may have influenced the mortality and LOS outcomes.

Incomplete outcome data

For all studies the number of patients withdrawn following randomization was low (0 to 3) and they were at low risk for attrition bias except one study, which did not report on one group of patients and the risk was unclear (Bender 1997). Another study had a higher number of withdrawals (13 in PAC group and 14 in CVC group) (Harvey 2005).

Selective reporting

All the studies were free of selective reporting bias except one (Bender 1997). We judged this study as high risk for reporting bias due to it not reporting any postoperative PAC group data. The study was of preoperative PAC monitoring, but one group of patients had a PAC postoperatively and this data may have impacted on the outcome.

Other potential sources of bias

Five studies had high risk for unknown bias. There was a high rate of cross-over from the control to the PAC group for two studies. In one study eight out of 17 patients allocated to the control group (47%) were subsequently managed with a PAC (Guyatt 1991). Allowing sicker patients to cross-over to the PAC group after randomization may have contributed to the high mortality in the PAC group. The other study had both high-risk and low-risk surgical patients, and 17 (57%) crossed-over to a PAC during the postoperative period when the physicians felt that the patient needed invasive monitoring (Shoemaker 1988). One study had three groups initially and the additional groups four and five were included after randomization (Pearson 1989). Bender et al (Bender 1997) reported that one surgical intensivist cared for 104 patients and did not report the number of patients accounting for the LOS of 27 days. The FACCT (NHLBI 2006) study randomized the patients to a PAC or CVC group and at the same time applied another strategy of randomization to the same patients to a conservative or liberal fluid therapy group.

Effects of interventions

See: **Summary of findings for the main comparison** Pulmonary artery catheter for adult patients in intensive care

Mortality

Overall, four studies (Harvey 2005; Isaacson 1990; Sandham 2003; Shoemaker 1988) reported any hospital mortality. The remaining studies reported 28-day mortality (Rhodes 2002; Richard 2003); 30-day mortality (Bender 1997; Joyce 1990); 60-day mortality (NHLBI 2006); or ICU mortality (Pearson 1989). Three studies did not specify the type of mortality statistics (Berlauk 1991; Guyatt 1991; Shoemaker 1988). The combined mortality outcome for all studies, with 5686 patients, was not significantly different (P = 0.73) between the PAC and CVC groups (RR 1.01, 95% CI 0.95 to 1.08) (heterogeneity $Tau^2 = 0.00$; $Chi^2 = 5.26$, df = 11 (P = 0.92); $I^2 = 0\%$) (Analysis 1.1; Figure 5; Figure 6). The overall outcome did not change with sensitivity analysis, by eliminating any single study. Large studies had almost similar weights and smaller studies had similar low weights, and no single study altered the weight of the analysis. To address the issue of analysing the mortality at different time points, various sensitivity analyses were conducted by removing groups of studies. Sensitivity analysis done by keeping the four studies with 1021 patients that reported only 28-day and 30-day mortality (Bender 1997; Joyce 1990; Rhodes 2002; Richard 2003) showed no difference in mortality (RR 0.98, 95% CI 0.87 to 1.10). By removing the combined 28 and 30-day mortality studies, the remaining nine studies with a total of 4665 patients also did not show any change in mortality (RR 1.03, 95% CI 0.95 to 1.11). Combining eight studies with 3665 patients that reported hospital or ICU mortality at any time point (sensitivity analysis done by removing the NHLBI study that reported 60-day mortality in combination with the four studies that reported 28 and 30-day mortality) also did not change any mortality (RR 1.03, 95% CI 0.95 to 1.11).

Figure 5. Forest plot of comparison: 5 PAC versus no PAC (combined medical and surgical patients), outcome: 5.1 Combined mortality of all studies.

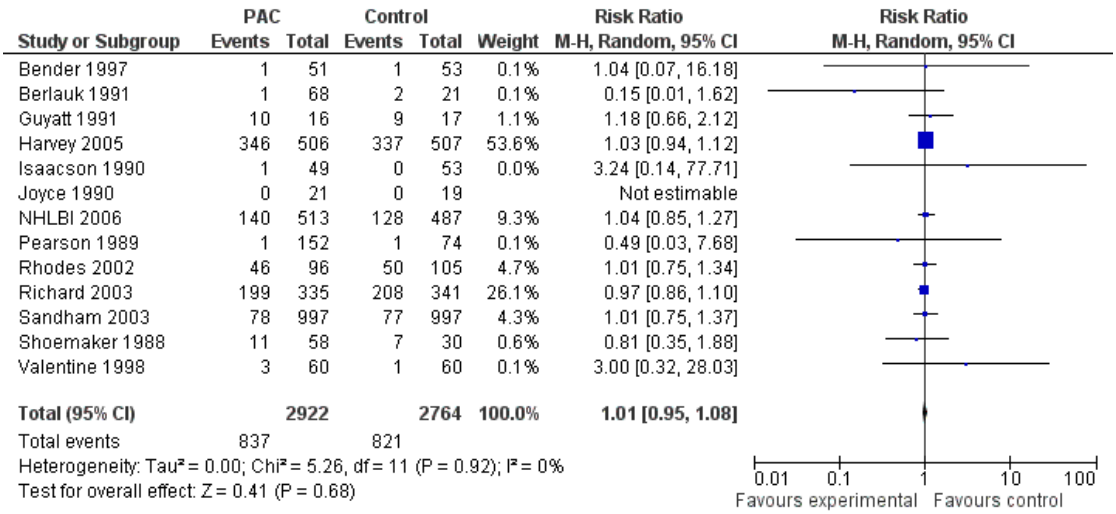
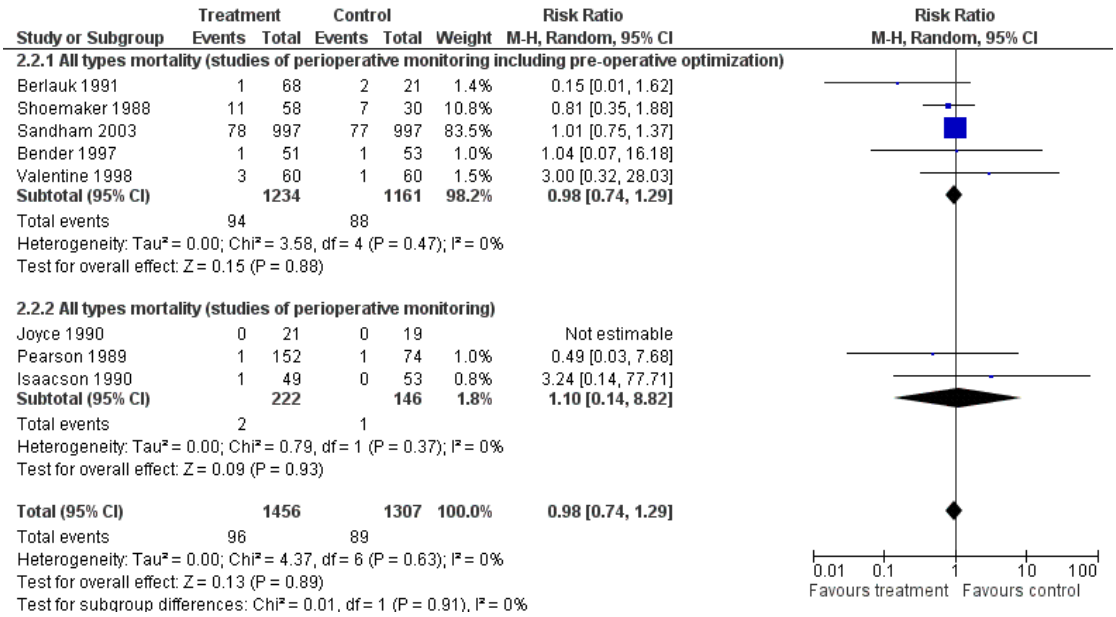


Figure 6. Forest plot of comparison: 1 PAC versus no PAC, outcome: 1.2 All types mortality (high-risk surgical patients).



Mortality: general ICU studies

Data on 2923 patients enrolled into the five studies (Guyatt 1991; Harvey 2005; NHLBI 2006; Rhodes 2002; Richard 2003) were pooled to give a RR of 1.02 (95% CI 0.96 to 1.09) comparing management with a PAC to management without a PAC (test for

heterogeneity: Tau² = 0.00; Chi² = 1.04, df = 4 (P = 0.90); I² = 0%) (Analysis 2.1).

Mortality: high-risk surgery studies

Studies comparing mortality: preoperative optimization (using a PAC) with standard preoperative care

The numbers of deaths in each group for the five studies (Bender 1997; Berlauk 1991; Sandham 2003; Shoemaker 1988; Valentine 1998) are detailed in 'All types of mortality (high-risk surgical patients)' (Figure 6). We pooled data on the 2395 patients (total number, combined PAC and control groups) enrolled into these studies, which yielded a RR of 0.98 (95% CI 0.74 to 1.29) comparing preoperative optimization with standard preoperative care (test for heterogeneity: Tau² = 0.00; Chi² = 3.58, df = 4 (P = 0.47); I² = 0%) (Analysis 2.2). Two studies (Berlauk 1991; Shoemaker 1988) had two PAC groups, which were combined for the pooled analysis.

Studies comparing mortality: PACs with CVCs for monitoring patients perioperatively

The number of deaths in each group for the three studies (Isaacson 1990; Joyce 1990; Pearson 1989) are detailed in 'All types of mortality (high-risk surgical patients)' (Figure 6). We pooled data on the 368 patients enrolled into these studies to give a RR of 1.10 (95% CI 0.14 to 8.82) comparing management with and without a PAC based on intention to treat (test for heterogeneity: Tau² = 0.00; Chi² = 0.79, df = 1 (P = 0.37); I² = 0%) (Analysis 2.2). One study (Pearson 1989) had two PAC groups, which were combined for the pooled analysis. Although a large proportion of patients in this study were reallocated from the control group to one of the two PAC groups, we analysed them as they were originally allocated, that is in the control group.

Combining data from all the high-risk surgery studies gave a pooled risk ratio of 0.98 (95% CI 0.74 to 1.29) (heterogeneity Tau² = 0.00; Chi² = 4.37, df = 6 (P = 0.63); I² = 0%) (Analysis 2.2) (Figure 6).

ICU length of stay

Most studies reported the LOS in ICU for survivors and non-survivors combined (Appendix 6). Two studies (Joyce 1990; Sandham 2003) did not report the LOS in ICU.

ICU LOS: general ICU studies

General intensive care unit studies found no significant differences between the treatment and control groups in ICU LOC. Four studies with 2723 patients (Guyatt 1991; Harvey 2005; NHLBI 2006; Richard 2003) reported the mean (standard deviation) LOS in ICU and data were pooled to give a mean difference in days spent in ICU of 0.50 (95% CI 0.44 to 0.55) comparing management with a PAC to management without a PAC (test for heterogeneity: Tau² = 0.00; Chi² = 0.66, df = 2 (P = 0.72); I² = 0%) (Analysis 3.1).

ICU LOS: high-risk surgery studies

In high-risk surgery studies, four (Bender 1997; Berlauk 1991; Shoemaker 1988; Valentine 1998) of the five studies of preoperative optimization and one (Isaacson 1990) of the three studies of perioperative monitoring only reported the mean LOS in ICU. When data were pooled to analyse the mean difference (MD) in days spent in ICU (MD 1.57 days, 95% CI 0.36 to 2.79) comparing management with PAC to without a PAC, the test of heterogeneity was extraordinarily high (heterogeneity Tau² = 1.77; Chi² = 136.51, df = 4 (P = 0.00001); I² = 97%). Such high heterogeneity suggested that the combined high-risk surgery studies were very dissimilar and therefore not appropriate for meta-analysis to compare the ICU LOS outcome in this subgroup.

Hospital length of stay

Overall, nine studies reported the LOS in hospital. Again, most studies reported the LOS in hospital for survivors and non-survivors combined (Appendix 6). None of the studies found a significant difference between the treatment groups. Shoemaker et al (Shoemaker 1988) reported more days in hospital for all groups compared with other studies of high-risk surgery patients.

Hospital LOS: general ICU studies

Two studies (Harvey 2005; Richard 2003) with a total of 1689 patients reported the mean (standard deviation) LOS in hospital. Pooled data gave a MD in days spent in hospital of -0.80 (95% CI -2.71 to 1.12) comparing management with a PAC to management without a PAC (heterogeneity Tau² = 0.34; Chi² = 1.09, df = 1 (P = 0.30); I² = 9%) (Analysis 4.1; Appendix 6).

Hospital LOS: high-risk surgery studies

Five studies with a total of 503 patients reported hospital LOS. Four (Bender 1997; Berlauk 1991; Shoemaker 1988; Valentine 1998) of them were preoperative optimizations and one (Isaacson 1990) was a study of perioperative monitoring, reporting the mean (standard deviation) LOS in hospital. Pooled data gave a MD in days spent in hospital of 0.35 (95% CI -0.05 to 0.75) comparing management with and without a PAC (heterogeneity Tau² = 0.00; Chi² = 3.54, df = 4, (P = 0.47); I² = 0%). For two studies, which had two PAC groups, a weighted mean (and standard deviation (SD)) hospital LOS was used (Berlauk 1991; Shoemaker 1988) (Analysis 4.2).

Cost

Four studies (Berlauk 1991; Isaacson 1990; Pearson 1989; Shoemaker 1988), all conducted in the US, collected data on costs of care based on hospital charges (Appendix 7) (the units shown are 1000 USD). Pearson et al (Pearson 1989) used the mean of the total cost, which was the amount actually billed to the patient. Information was also given about specific costs of arterial blood gas measurement, cardiac output measurements, and measurement of haemoglobin and haematocrit. Only the total costs have been included in this review. They reported that the mean costs per patient were significantly higher for the mixed venous oxygen saturation (SvO_2) PAC group compared with the standard PAC group, although the P value was not given. The costs given in the table (Appendix 7) for the control group excluded the 46 patients reassigned after randomization, which were as follows: reassigned to management with standard PAC (n = 33), mean total cost (SD) USD 986 (578) (USD 1068.28 for 2011, Cochrane cost converter); reassigned to management with SvO_2 PAC (n = 13), mean total cost (SD) USD 1126 (382) (USD 1219.97 for 2011, Cochrane cost converter). In addition to the hospital charges, Isaacson et al (Isaacson 1990) reported the professional fees charged by the anaesthesiologists per patient in each group and found that the fees were significantly higher per patient in the PAC group (P = 0.0001) compared with the control group.

For the meta-analysis, it was not appropriate to combine hospital costs with physician costs as there are physician charges specifically for insertion of a PAC. We excluded two studies from the subgroup analysis: the study by Pearson et al (Pearson 1989), for reasons described earlier, and the study by Shoemaker et al (Shoemaker 1988) because the SD was not reported. Therefore, data from two studies with a total of 191 patients (Berlauk 1991; Isaacson 1990) that reported hospital costs were combined with a fixed-effect model (MD 0.90, 95% CI -2.62 to 4.42) (Analysis 5.1).

DISCUSSION

Summary of main results

We identified 13 RCTs with 5686 patients assessing mortality, hospital and ICU LOS and cost effectiveness of PAC in ICUs (Summary of findings for the main comparison). Five of these studies investigated the clinical effectiveness of PACs in the management of general intensive care patients. The remaining eight studies studied high-risk surgical patients. Of these surgical patients, five trials investigated whether preoperative optimization of haemodynamics improved patient outcomes (Bender 1997; Berlauk 1991; Sandham 2003; Shoemaker 1988; Valentine 1998). In these studies, placement of a PAC was part of a package of care that also included admission to ICU preoperatively and optimization of haemodynamics to predetermined goals. Because patients admitted to ICU are a heterogeneous group, we performed subgroup analysis for studies of elective high-risk surgery patients (perioperative monitoring with and without preoperative optimization) and studies of general intensive care patients. Studies which had the potential for some aspects of high risk of bias had low weight due to small numbers of patients and were included because of their limited effect on the meta-analyses.

We could not demonstrate any beneficial or harmful effects of PACs on mortality, hospital LOS and cost of care in either patients in general ICUs or a subgroup of high-risk surgical patients. Pulmonary artery catheterization did not affect ICU LOS in general intensive care unit patients (reported by four studies) or hospital LOS (reported by nine studies).

A subgroup meta-analysis of five preoperative surgical studies suggested that preoperative optimization guided by a PAC did not improve or worsen the outcome in patients undergoing high-risk surgery. This meta-analysis was heavily weighted (85.5% weight) by the Sandham et al study (Sandham 2003) as this was the largest RCT and had low risk for bias. Sensitivity analysis did not change the mortality results. The overall mortality outcome was similar in both the PAC group and the CVC group.

Four US based studies demonstrated that the overall hospital cost billed for the PAC group was higher than for the CVC group. Two of these studies qualified for analysis and did not show statistically significant hospital cost differences.

Overall completeness and applicability of evidence

The review question is 'Does the use of PAC in ICUs lead to increased mortality, hospital or ICU LOS and cost?'. PAC is a diagnostic and monitoring tool, not a treatment intervention for any given clinical condition. Use of PAC does not increase or decrease mortality, ICU LOS or hospital LOS. It is appropriate to use in selected patients, by intensive care physicians, as a diagnostic and monitoring tool to guide patient care decisions. Cost effectiveness varies among countries with different healthcare systems. Our analysis on cost cannot be generalized or applied widely. This current evidence is a complete review of all available RCTs to date. It is unlikely that a large prospective RCT comparing PAC with CVC will be published in the future. There are several less invasive methods of haemodynamic monitoring, and their comparison with PAC is beyond the scope of this review. Regardless, the applicability of this evidence of no effect on mortality is strong in the ICUs. A PAC is however a diagnostic tool and its impact on management must not be interpreted with regard to mortality outcomes in adults in intensive care. Shock reversal, improvement in organ dysfunction and less vasopressor use are other potential outcome measures that need to be studied.

Barriers in evaluation of the PAC

One of the main barriers to an effective evaluation of the PAC in intensive care has been the lack of equipoise amongst intensive care clinicians. The training, expertise in PAC measurements, utilization of PAC data for clinical decisions and management of patients vary widely among clinicians. Iberti et al found that providers have significant gaps in their knowledge and expertise in utilizing PAC data (Iberti 1990; Iberti 1994). He reported, from a study done in US and Canada, that the physician's knowledge, understanding, use and interpretation of PAC data were 67% correct, with a range of 19% to 100%. Mean scores varied by training, frequency of insertion and use of PAC data in patient treatment (Iberti 1990). Among nurses the test scores of knowledge and use of PAC were associated with years of experience in critical care, critical care registered nurse certification, responsibility for repositioning and manipulating the catheter, frequency of use, and self-assessed adequacy of knowledge (Iberti 1994). A similar study done in Australia utilizing the same questionnaire also found that the test scores were significantly associated with years of experience in intensive care, number of PACs inserted and the physician's certification (Johnston 2008).

The evidence is clear that physicians' and nurses' understanding of PAC and its utility vary widely, making credentialing policies and competency assessments essential. Lack of clinical expertise using PACs may have played a role in patient outcomes in our meta-analysis.

Use of the PAC in clinical practice

The PAC has been used in various clinical settings and our study did not address its use in cardiac catheterization laboratories, coronary care units or in cardiac pacing. One important use of the PAC is to differentiate various types of shock and to guide therapy. The objective of our analysis was not provider satisfaction, knowledge and comfort level on using PAC; however, these are important considerations in utilizing a diagnostic tool for accomplishing clinically significant results. Lack of any significant mortality improvement from PAC use can be attributed to several factors. A diagnostic and monitoring device that has no therapeutic applications cannot modify outcomes unless the information gathered is utilized appropriately. The aforementioned studies on physicians' and nurses' knowledge on PAC and its applicability, correct interpretation of waveforms, effective utilization of the measured and derived data, and management strategies based on the information gathered vary widely. The significant decline in the clinical utility of PAC in recent years may have caused poor training and expertise, which could lead to occasional delayed utility during the terminal stages of the disease process and improper interpretation (Weiner 2007). Proper use of a PAC depends upon a thorough understanding of factors contributing to measurement errors and data interpretation. The PAC provides a wealth of potentially useful haemodynamic information to the clinicians, and it is only if this information is utilized correctly that it may be helpful in patient management (Evans 2009).

Advantages of the PAC

During current clinical practice many clinicians still seek haemodynamic data to manage critically ill patients. For this reason, a variety of non-invasive monitoring devices have been introduced and compared with PAC as the reference standard to evaluate the test performance. PACs allow measurement of haemodynamic variables that cannot be measured reliably or continuously by less invasive monitoring devices (Evans 2009). The PAC has the added benefit of being useful as a multilumen infusion port, in addition to its utilization as a monitoring and data-gathering device. Critically ill patients require multiple drips and the current standard of practice is to provide central venous access using a CVC. A PAC is also placed through a central access and shares the same short-term complications related to line insertion; however, it has several advantages in addition to intracardiac monitoring. Newer versions of PACs (for example Swan-Ganz flow-directed catheters) provide rapid and effective monitoring of right heart pressures and have the capability to measure mixed venous oxygen saturation, perform cardiac pacing, and to assess the pulmonary vasculature by injecting contrast media to do selective angiographic studies (Edwards Lifesciences 2012). The studies included in our analysis used a standard PAC.

The PAC also has a pivotal role in the measurement of central venous oxygen saturation ($ScVO_2$). The measurement of $ScVO_2$ is crucial in the management of patients with severe sepsis and septic shock (Rivers 2001). $ScVO_2$ is obtained through the measurement of oxygen saturation in venous blood returning to the heart and is representative of the balance between oxygen delivery and consumption. A recent study showed that both low and high $ScVO_2$ values obtained in the emergency department were associated with increased mortality in sepsis patients (Pope 2010) thus underlining the importance of continuous ScVO2 monitoring via either a PAC or $ScVO_2$ catheter.

Quality of the evidence

The quality of evidence from this review for the mortality outcome in this population is robust. Using the Cochrane Grades of Recommendation, Assessment, Development, and Evaluation (GRADE) approach, the evidence was high for hospital and ICU LOS but was low for cost analysis. Only RCTs were included in the meta-analysis but many observational studies, meta-analyses and systematic reviews, cohort studies, and grey literature were examined as sources to identify RCTs. A complete risk of bias analysis and sensitivity analysis minimized uncertainties and provided concrete evidence based support. We had limitations in analysing the secondary outcomes (hospital LOS, ICU LOS and cost) because only some of the studies reported them. This was particularly so for cost effectiveness, which was reported in four studies.

We performed subgroup analysis for general intensive care patients and high-risk surgical patients, and the results did not vary significantly. Overall, the internal validity and quality of evidence is high (Summary of findings for the main comparison).

Potential biases in the review process

One potential bias is the fact that this is an update from a previous review and may have been influenced by previous conclusions. Another source of bias may be that the two groups of review authors are from the same institution and may have similar backgrounds. To overcome these potential biases four authors (SH, DY, WB and KR) from the original review participated in the update. We did not include studies that used PAC in other areas such as in heart failure patients and coronary care units due to the inclusion criteria and the different primary end points in the studies, but we have included these details in the discussion.

Agreements and disagreements with other studies or reviews

Evaluation of the clinical effectiveness of the PAC

Evaluation of the clinical effectiveness of managing general intensive care patients with a PAC was addressed by the Fluid and Catheter Treatment Trial (FACTT) (NHLBI 2006) and Pac-Man studies (Harvey 2005); both are major clinical trials with relatively low risks of bias. Both trials were adequately powered multicentre RCTs with over 1000 patients each, in North America and Europe (USA, Canada and UK). Their data on harms or complications of PAC have been conflicting. The results of the FACTT suggested an increased rate of complications from PAC insertion, as opposed to the Pac-Man study which concluded no harm from PAC insertion. The results do, however, agree with the findings of previous smaller studies (Guyatt 1991; Rhodes 2002; Richard 2003) that PACs do not appear to confer survival advantage, nor do they reduce hospital length of stay or costs of care. Both these trials disagreed with the excess mortality findings reported by Connors et al (Connors 1996) and showed that management with a PAC did not worsen the outcome in critically ill patients.

Evaluation of efficacy of the PAC

FACTT (NHLBI 2006) was the only trial which evaluated the efficacy of the PAC, but it did not address the ongoing debate as to whether the use of a PAC as a diagnostic device and monitoring tool can be responsible for adverse patient outcomes, especially because it is not a therapeutic intervention. One may argue that adverse outcomes may be related to complications of the procedure, but rather they appear to be from inadequate training and skills in utilizing the data and the lack of clinical expertise and approved treatment protocols with the use of a PAC.

PAC monitoring coupled with therapy

There is mounting evidence for the preemptive strategy of haemodynamic monitoring with a PAC coupled with therapy to reduce surgical mortality and morbidity (Hamilton 2011). Hamilton et al in their systematic review and meta-analysis of 29 trials involving 4805 patients that had perioperative haemodynamic manipulation, which included a PAC with other interventions, reported significantly reduced mortality (OR 0.43, 95% CI 0.33 to 0.78, P = 0.0002) and surgical complications. Gurgel et.al performed another meta-analysis of studies involving high-risk surgical patients with the use of a PAC to maintain tissue perfusion (Gurgel 2011). This study of 32 RCTs comprising 5056 high-risk surgical patients showed a significant reduction in mortality rate (odds ratio (OR) 0.67, 95 CI% 0.55 to 0.70, P < 0.00001) and postoperative organ dysfunction when a haemodynamic protocol was used to maintain tissue perfusion. Brienza et al published a meta-analysis of 20 studies with 4220 patients and found that perioperative haemodynamic optimization significantly reduced postoperative acute renal injury and the need for renal replacement therapy (Brienza 2009). These studies suggest that haemodynamic monitoring with a PAC and intervention in surgical subgroups of patients have significant clinical value, with improved organ dysfunction and mortality reduction.

Studies in agreement

A meta-analysis of major morbidities from 12 RCTs involving the use of a PAC showed a very small reduction in morbidity with the PAC (Ivanov 2000). Another meta-analysis that examined the relationship of outcomes and resuscitation therapies showed that in studies of severely ill patients, PAC insertion provided a mortality benefit when haemodynamic optimization was performed prior to organ failure, and that there were no differences in outcomes when the PAC was utilized in less critically ill patients or following the onset of multiorgan failure (Kern 2002). Similar results were reported in a meta-analysis by Shah et al that used wider inclusion criteria for studies including heart failure patients (mortality OR 1.04, 95% CI 0.9 to 1.2; and hospital LOS MD 0.11 days, 95% CI -0.51 to 0.74) (Shah 2005). Two RCTs included in the Shah meta-analysis were studies of perioperative monitoring. One study showed no difference in mortality (Bonazzi 2002) and the other study showed a significant reduction in mortality (2.9% in PAC group versus 29% in controls) (Schultz 1985). The ESCAPE trial had advanced heart failure patients who were admitted to coronary care units and the therapeutic goals were different, looking at the days alive out of hospital during the first six months, quality of life, biochemical and echocardiographic changes (ESCAPE 2005). These studies also concluded that PAC use did not change the overall mortality.

Cost effectiveness

Four of the 13 studies included a cost component based on hospital charges to patients, and were conducted in US hospitals. One of the problems with this approach is that specific charges vary across hospitals, and patients may not be charged the same for the cost of daily monitoring with a PAC. All the studies reported that, on average, total costs were higher for patients managed with PACs compared with those managed without. The cost effectiveness evaluation for the PAC-Man study (Stevens 2005) provided data based on UK practice. The primary outcome measure was quality-adjusted life years (QALYs) and the secondary outcome measure was hospital mortality. The authors concluded that withdrawal of PACs from routine clinical use in ICUs within the NHS may be considered cost effective. These cost effectiveness analyses of a PAC compared to CVC cannot be broadly applied to the current clinical practice. Cost varies across countries, regions, healthcare systems and types of catheters used. Cost effectiveness cannot be generalized to different populations, particularly for medical and surgical patients.

Other haemodynamic monitoring devices

Clinicians are still looking for haemodynamic monitoring tools without the known complications of the PAC. Newer cardiac output catheters are already being used in ICUs to provide haemodynamic measurements based on arterial contour power and pulse power analyses. The examples of catheters which use a different calibration scheme for measurement of cardiac output (CO) are the lithium indicator dilution calibration system (LiDCO plus ^{TM}), which uses a transthoracic lithium dilution estimate of cardiac output (CO) for calibration; PiCCO plus^{TM} uses trans-thoracic thermodilution differences in arterial compliance; whereas flow Trac^{TM} calculates CO from the pulse contour using a proprietary algorithm (Hadian 2007). These catheters cannot be used as infusion ports, available with the PAC. These catheters are preferably inserted into a large calibre artery like the femoral artery, which is again invasive and associated with complications, and are attached to monitors which perform arterial power analysis and pulse power analysis. The need for frequent recalibration is a potential disadvantage of these newer techniques. These techniques of measurement are relatively new and will require validation in comparison to PAC in large-scale randomized trials for their effectiveness in therapy in ICUs.

AUTHORS' CONCLUSIONS

Implications for practice

This review concentrated specifically on patients admitted to ICUs. This meta-analysis concluded that use of a PAC alone, without a properly designed therapeutic strategy based on haemodynamic data, did not affect mortality, ICU LOS, hospital LOS or cost in adult ICUs. It is important to note that the PAC itself is a diagnostic and haemodynamic monitoring tool and not a therapeutic intervention to achieve any major clinical outcomes. It is not a harmful tool and may be used successfully for diagnostic and haemodynamic monitoring in ICU patients by highly trained specialists (critical care physicians, cardiologists, anaesthesiologists) with appropriate training in interpretation of the PAC variables, and its applicability in specific clinical scenarios has been shown in recent studies of surgical patients.

Implications for research

Efficacy studies are needed to determine if there are optimal, PAC-guided management protocols which, when applied to specific patient groups in ICUs, could result in benefit. Shock reversal, improved organ dysfunction and vasopressor use are other potential outcome measures that need to be studied. In high-risk surgical patients, preemptive haemodynamic monitoring with PAC coupled with therapy has shown significant reduction in mortality and organ dysfunction (for example improved renal function) in recent meta-analyses (Brienza 2009; Gurgel 2011; Hamilton 2011).

One of the reasons that PAC use in general ICUs has been diminishing in recent years may be due to the increased availability of sophisticated and less invasive devices to monitor cardiac output. These are devices based on trans-oesophageal Doppler, lithium dilution, pulse contour analysis, thoracic impedance and carbon dioxide rebreathing. One explanation for the lack of benefit arising from PAC use was that there was no additional survival advantage gained from a more detailed knowledge of haemodynamics, and this was particularly true when there was no protocol driven management strategy associated with that information. Similarly, the new devices need careful scrutiny before they replace the PAC as another unevaluated 'reference standard', especially when they only serve as diagnostic tools.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by year of study]*

Shoemaker 1988

Methods	Randomized by cards arranged according to random numbers tables, by an outside person, placed in sealed opaque envelopes opened in sequence
Participants	Entry criteria: patients with one or more of 11 high risk criteria previously defined and associated with a mortality rate close to 30%. Exclusion criteria: none stated.
Interventions	PAC standard group (n = 30) - transfer to ICU. PAC placed followed by standard management to achieve normal values of haemodynamic and oxygen transport variables PAC protocol group (n = 28) - transfer to ICU, PAC placed followed by treatment to achieve supra-normal haemodynamic and oxygen transport values. Control group (n = 30) - CVC placed. Standard care. Not reported if managed in ICU preoperatively
Outcomes	Mortality and morbidity (statistic not specified). Main outcome not stated. Also reported ICU and hospital LOS
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Two series of patients in both groups and number of patients were not randomized. Series one randomization was not clear, series 2, some patients were randomized post-operatively, some preoperatively and some are not randomized
Allocation concealment (selection bias)	Low risk	Designated by cards arranged according to a random number table by an outside person, placed in opaque sealed envelope
Blinding of participants and personnel (performance bias) primary outcome	High risk	Not blinded, but providers were rotated in both control and treatment groups
Blinding of outcome assessment (detection bias) primary outcome	High risk	Not blinded

Shoemaker 1988 (*Continued*)

Incomplete outcome data (attrition bias) alloutcomes	Low risk	All outcome data are reported
Selective reporting (reporting bias)	Low risk	Reported all outcome data
Other bias	High risk	Series 1 had high-risk surgical patients and series 1 had low-risk surgical patients, but when physicians felt some patients were not candidates for invasive monitoring they were excluded from the study or included postoperatively

Pearson 1989

Methods	Randomized using a table of random numbers (no other details given)
Participants	Entry criteria: scheduled for elective cardiac surgery. Exclusion criteria: none given.
Interventions	PAC 1 group (n = 86) - standard PAC placed. PAC 2 group (n = 66) - mixed venous oxygen measuring PAC placed. Control group (n = 74) - CVC placed.
Outcomes	ICU mortality ICU LOS Costs of care. Main outcome not stated.
Notes	Of the 74 patients randomized to the control group, 46 were reassigned following randomizations to one of the PAC groups for "ethical" reasons

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	High risk	46 patients were reassigned to PAC after randomization
Allocation concealment (selection bias)	Low risk	Used a table of random numbers
Blinding of participants and personnel (performance bias) primary outcome	High risk	Not blinded in fact allowed to change the group after randomizations
Blinding of outcome assessment (detection bias) primary outcome	High risk	No blinding done

Pearson 1989 (*Continued*)

Incomplete outcome data (attrition bias) alloutcomes	Low risk	Reported all the cost, LOS and mortality outcomes
Selective reporting (reporting bias)	Low risk	None
Other bias	High risk	Additional groups 4 and 5 were included due to reassignment of groups after randomizations can cause unknown bias

Joyce 1990

Methods	Preoperative randomization into two groups.
Participants	Entry criteria: elective infra-renal aortic reconstructive surgery. Exclusion criteria: unstable angina; recent myocardial infarction (last 6 months); left ventricular ejection fraction less than 50%
Interventions	PAC group (n = 21) - PAC placed (no management protocol). Control group (n = 19) - CVC placed (no management protocol)
Outcomes	Main outcome was postoperative cardiac complications (defined). Also reported 30-day postoperative mortality
Notes	A non-randomized group (n = 11) were included in the analyses

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Used "sealed envelope technique"
Allocation concealment (selection bias)	Low risk	Sealed envelopes are concealed allocation
Blinding of participants and personnel (performance bias) primary outcome	Unclear risk	Insufficient information to judge
Blinding of outcome assessment (detection bias) primary outcome	Unclear risk	Insufficient information to judge
Incomplete outcome data (attrition bias) alloutcomes	Low risk	Reported all data

Joyce 1990 (*Continued*)

Selective reporting (reporting bias)	Low risk	Reported all outcomes
Other bias	Low risk	None

Isaacson 1990

Methods	Randomized using marked cards.
Participants	Entry criteria: elective aortic reconstructive surgery. Exclusion criteria: uncorrectable coronary artery disease; cor pulmonale; severe heart failure; cardiomyopathy; left ventricular ejection fraction less than 40%; symptomatic valvular disease; renal failure; severe restrictive/obstructive pulmonary disease
Interventions	PAC group (n = 49) - PAC placed before induction of general anaesthesia. Control group (n = 53) - CVC placed before induction of general anaesthesia
Outcomes	Hospital mortality, ICU LOS, hospital LOS, costs of care. Main outcome not stated
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Used marked cards, shuffled
Allocation concealment (selection bias)	Low risk	Used faced down cards and made sure investigator would not know which monitor patient would receive
Blinding of participants and personnel (performance bias) primary outcome	High risk	Not blinded same group who did the study made the patient care decision as well
Blinding of outcome assessment (detection bias) primary outcome	High risk	Not blinded
Incomplete outcome data (attrition bias) alloutcomes	Low risk	No missing out come data
Selective reporting (reporting bias)	Low risk	Followed prespecified protocol
Other bias	Low risk	None

Guyatt 1991

Methods	Randomization blocked according to a computer-generated list of random numbers in groups of four for each unit. Participating physicians were not aware of the blocking. Envelopes were prepared in sequential order for each unit and were checked daily
Participants	Entry criteria: assisted ventilation; hypotension with CVP of 10cm H2O or more; oliguria with CVP 10cm H2O or more; oliguria with hypoxaemia; hypoxaemia and CVP less than 10cm H2O; physician believed patient might benefit from a PAC. Exclusion criteria: PAC ethically contraindicated; PAC an ethical imperative; PAC placed preoperatively for intraoperative monitoring; organ transplant surgery; receiving high frequency jet ventilation; consent from a close relative not obtained.
Interventions	PAC group (n = 16) - PAC placed and used at the discretion of the attending physician (no management protocol). Control group (n = 17) - standard care without a PAC.
Outcomes	Main outcome mortality (mortality statistic not specified). Secondary outcome ICU LOS
Notes	Trial stopped early because of poor recruitment.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer generated sequence
Allocation concealment (selection bias)	Low risk	Physicians were not aware of blocks and used envelopes
Blinding of participants and personnel (performance bias) primary outcome	High risk	Not blinded and allowed to cross-over to PAC group
Blinding of outcome assessment (detection bias) primary outcome	High risk	Not blinded and allowed to change the group if physician felt ethically need PAC
Incomplete outcome data (attrition bias) alloutcomes	Low risk	Reported all data including cross-over data

Guyatt 1991 (*Continued*)

Selective reporting (reporting bias)	Low risk	Reported all outcomes
Other bias	High risk	High risk of contaminating the randomized group by allowing the sicker patients to cross-over to PAC group may have contributed to high mortality reported

Berlauk 1991

Methods	Randomized using random number generator. Patients entered consecutively in order of appearance on the surgical schedule. No other details given
Participants	Entry criteria: scheduled to receive an in situ vein graft bypass for lower limb vascular insufficiency. Exclusion criteria: myocardial infarction within 3 months; coronary artery bypass graft within 6 weeks; uncompensated congestive heart failure; severe valvular disease; unstable angina
Interventions	PAC 1 group (n = 45) - transfer to ICU, PAC placed followed by "tune-up" treatment (using predefined end points) at least 12 hrs preoperatively. PAC 2 group (n = 23) - transfer to anaesthetic holding area, PAC placed followed by "tune-up" treatment (using predefined end points) at least 3 hrs preoperatively. Control group (n = 21) usual care without a PAC. Arterial catheters and CVCs placed
Outcomes	Main outcome cardiovascular complications. Secondary outcomes were immediate postoperative graft thrombosis and adverse intra-operative events. Also reported mortality (not specified), ICU LOS, hospital LOS
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Used random number generator (Statworks)
Allocation concealment (selection bias)	Unclear risk	Eligible patients were entered consecutively in order of the surgical schedule, no central allocation used, anaesthesiologist may have foreseen allocation while screening for eligibility
Blinding of participants and personnel (performance bias) primary outcome	Unclear risk	Appears to be the study group treated the patients postoperatively

Berlauk 1991 (*Continued*)

Blinding of outcome assessment (detection bias) primary outcome	Low risk	Anesthesioloist cared for initial 18 hours and unlikely to influence LOS and mortality
Incomplete outcome data (attrition bias) alloutcomes	Low risk	Reported all outcome data
Selective reporting (reporting bias)	Low risk	Reported all predefined outcome data
Other bias	Low risk	None

Bender 1997

Methods	Randomized but methods not described.
Participants	Entry criteria: scheduled for elective infrarenal aortic reconstruction or lower limb revascularize (by a single surgeon). Exclusion criteria: anticipated need before surgery for suprarenal or supra-coeliac aortic clamping; myocardial infarction within 3 months or inadequately controlled angina; poorly compensated congestive heart failure; coronary artery bypass surgery within 6 weeks; symptomatic aortic/mitral valvular disease
Interventions	PAC group (n = 51) - transfer to ICU, PAC placed followed by "optimizations" preoperatively using a treatment algorithm. Control group (n = 53) - standard care without a PAC. Arterial catheter and CVC placed
Outcomes	Adverse outcomes (defined) including 30-day mortality, ICU LOS, hospital LOS. Main outcome not stated
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	High risk	Patients were assigned randomly by the surgical intensivist
Allocation concealment (selection bias)	High risk	Intensivist assigned patients, not concealed at all
Blinding of participants and personnel (performance bias) primary outcome	High risk	Not blinded. Patients were chosen.
Blinding of outcome assessment (detection bias) primary outcome	High risk	Same physician analysed data and cared for all patients, not blinded for any outcome

Bender 1997 (*Continued*)

Incomplete outcome data (attrition bias) alloutcomes	Unclear risk	Did not report about patients who did not get PAC postoperatively in group 2
Selective reporting (reporting bias)	High risk	Postoperative non-PA catheter group data is not reported and no tables or number of patients
Other bias	High risk	One surgical intensivist cared for all 104 patients reported and the unreported group of patients for the LOS of 27 days at times reported is likely to create several unknown bias

Valentine 1998

Methods	Randomized using sealed envelopes. No other details given.
Participants	Entry criteria: elective abdominal aortic reconstruction. Exclusion criteria: myocardial infarction within 3 months; coronary artery bypass surgery within 6 weeks; severe aortic/mitral valve disease; unstable angina/recent change in angina symptoms; clinically overt congestive cardiac failure; advanced chronic renal insufficiency; repeat aortic operations; additional procedures, e.g. renal artery bypass grafting performed
Interventions	PAC group (n = 60) - transfer to ICU, PAC placed followed by "tune-up" treatment (using predefined end points used be Berlauk et al) at least 14 hrs preoperatively. Control group (n = 60) not transferred to ICU, CVC placed and no specific preoperative treatment
Outcomes	Adverse postoperative events (defined), duration of ventilation, ICU LOS and hospital LOS, hospital mortality. Main outcome not stated.
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Used sealed envelopes
Allocation concealment (selection bias)	Unclear risk	Not mentioned how allocation was done
Blinding of participants and personnel (performance bias) primary outcome	Unclear risk	Not mentioned if the study group also treated the patients

Valentine 1998 (*Continued*)

Blinding of outcome assessment (detection bias) primary outcome	Unclear risk	Not mentioned study reviewers were blinded from knowing or altering the outcome
Incomplete outcome data (attrition bias) alloutcomes	Low risk	Reported all predefined outcome data
Selective reporting (reporting bias)	Low risk	No selective reporting
Other bias	Low risk	Two control group patients were transferred over to PAC but did not include them in analysis

Rhodes 2002

Methods	Randomized using computer generated random numbers stored in sealed envelopes
Participants	Entry criteria: either circulatory shock (definition given); oliguria (definition given); requirement for vasoactive infusion; need for mechanical ventilation. Exclusion criteria: less than 18 yrs of age; admitted to ICU for preoperative optimizations
Interventions	PAC group (n = 96) - PAC placed (no management protocol). Control group (n = 105) - standard care without a PAC or any other form of cardiac output monitoring
Outcomes	Main outcome 28-day mortality. Secondary outcomes ICU LOS, hospital LOS and morbidity.
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Quirk of computer generated sequence
Allocation concealment (selection bias)	Low risk	Sealed envelopes
Blinding of participants and personnel (performance bias) primary outcome	Low risk	Double blinding of the study was not feasible, but treating physicians were not prelocalized to follow a path, allowed to treat clinically and remove PAC if felt the need does not exist, less likely to influence the outcome

Rhodes 2002 (*Continued*)

Blinding of outcome assessment (detection bias) primary outcome	Low risk	Study outcome assessment was done later on and treating physicians were not given instructions to follow a protocol and end result
Incomplete outcome data (attrition bias) alloutcomes	Low risk	All data are reported including the PAC group who did not get the catheter, included in the analysis
Selective reporting (reporting bias)	Low risk	None
Other bias	Low risk	Well covered without any bias

Sandham 2003

Methods	Randomized using computer generated sequence concealed in sealed, opaque consecutively numbered envelopes. Stratified according to type of surgery, ASA class and blocked according to centre
Participants	Entry criteria: Age >60; American Society of Anesthesiologists class III or IV risk; scheduled for urgent/elective major abdominal, thoracic, vascular or orthopaedic surgery. Exclusion criteria: none stated.
Interventions	PAC group (n = 997) - PAC placed prior to surgery, followed by treatment directed to predefined physiological goals. Control group (n = 997) - standard care without a PAC. Placement of CVC permitted
Outcomes	Main outcome hospital mortality. Secondary outcome hospital LOS
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer generated sequence
Allocation concealment (selection bias)	Low risk	Sealed envelopes used
Blinding of participants and personnel (performance bias) primary outcome	Low risk	Single blind, not double, not feasible but large multicentre trial unlikely to introduce bias
Blinding of outcome assessment (detection bias) primary outcome	Low risk	Blinded assessment of outcome done

Incomplete outcome data (attrition bias) alloutcomes	Low risk	None
Selective reporting (reporting bias)	Low risk	Well reported
Other bias	Low risk	None

Richard 2003

Methods	Randomized using 24-hour, 7 day-a-week, central telephone service
Participants	Entry criteria: circulatory shock (definition given) for less than 12 hours and/or acute respiratory distress syndrome (definition given) for more than 24 hours. Exclusion criteria: less than 18 years; haemorrhagic shock; myocardial infarction complicated by cardiogenic shock; thrombocytopaenia (platelets <10,000 mm-3); participated in other trials in the last 30 days; were moribund; physician refused to agree with use of full life support
Interventions	PAC group (n = 335) - PAC placed (no management protocol). Control group (n = 341) - standard care without a PAC.
Outcomes	Main outcome 28-day mortality. Secondary outcomes 14-day mortality, 90-day mortality, ICU LOS, hospital LOS.
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Permuted block algorithm with stratification of each centre
Allocation concealment (selection bias)	Low risk	Central randomizations by telephone 24 hours a day 7 days a week
Blinding of participants and personnel (performance bias) primary outcome	Low risk	No standardized protocols and analysis was not done by treating physicians
Blinding of outcome assessment (detection bias) primary outcome	Low risk	Outcome assessment was blinded to study personal and unbinding of others is not likely to induce bias, multi-entered nature

Richard 2003 (*Continued*)

Incomplete outcome data (attrition bias) alloutcomes	Low risk	None missing
Selective reporting (reporting bias)	Low risk	Reported specifically
Other bias	Low risk	None

Harvey 2005

Methods	Randomized using a 24-hour, 7 day-a-week, central telephone randomization service and minimized by unit, age group, presumptive clinical syndrome, surgical status
Participants	Entry criteria: deemed to require management with a PAC by the treating clinician. Exclusion criteria: less than 16 years; admitted electively for preoperative optimizations; PAC already in situ on admission to ICU; previously enrolled into the trial; declared brain dead with PAC placed prior to organ donation
Interventions	PAC group (n = 506) - PAC placed (no management protocol). Control (n = 508) - standard care without a PAC but with the option to use alternative cardiac output monitoring devices if the unit had opted to be in stratum B
Outcomes	Primary outcome hospital mortality. Secondary outcomes ICU LOS, hospital LOS, organ-days of support in ICU, costs of care
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Minimization was described
Allocation concealment (selection bias)	Low risk	Used a central 24 hour telephone service
Blinding of participants and personnel (performance bias) primary outcome	Low risk	Not blinded, not likely influence the results due to multicentre trial and investigators are not providers
Blinding of outcome assessment (detection bias) primary outcome	Low risk	Investigators were blinded
Incomplete outcome data (attrition bias) alloutcomes	Low risk	None
Selective reporting (reporting bias)	Low risk	None

Harvey 2005 (*Continued*)

Other bias	Low risk	None

NHLBI 2006

Methods	Randomized multicentre factorial study, patients with acute lung injury for 48 hours or less, randomly assigned in permuted blocks of eight to receive a PAC or a CVC with the use of an automated system Patients were simultaneously randomly assigned to a strategy of either liberal or conservative use of fluids guided by a protocol
Participants	Inclusion criteria: patients receiving positive pressure ventilation by tracheal tube and had a ratio of the partial pressure of arterial oxygen (PaO_2) to the fraction of inspired oxygen (FiO_2) below 300 and bilateral infiltrates on chest radiography consistent with the presence of pulmonary edema not due to left atrial hypertension Exclusion criteria: presence of a PA catheter after the onset of acute lung injury, presence of acute lung injury for more than 48 hours, inability to obtain consent, presence of chronic conditions that could independently impair survival or weaning or compliance with protocol such as dialysis, severe lung or neuromuscular disease, irreversible conditions and estimated six month mortality rate exceeded 50% such as cancer
Interventions	All patients received low tidal volume ventilation according to ARDS network protocol within one hour after randomizations and continued until day 28 or until breathing without assistance PAC or CVC was inserted within 4 hours after randomizations. Haemodynamic management as dictated by the protocol was started within the next 2 hours and continued for 7 days or until 12 hours after the patient was able to breathe without assistance. PAC was allowed to be replaced by a CVC if haemodynamic stability defined by the absence of protocol directed interventions for > than 24 hours was achieved after day 3
Outcomes	Four main protocol variables were measured. Blood pressure and urinary output guided management was in both groups. PAOP and CI in the PAC group and CVP and clinical assessment (skin temperature and appearance, rate of capillary refilling) in the CVC group guided management. Outcome measures were reversal of hypotension, oliguria and ineffective circulation. Fluid therapy either crystalloids or colloids and vasopressors were used as per the judgement of the physician, but weaning from vasopressors was done as per protocol
Notes	Lactate levels, mixed venous or superior vena cava oxygen saturation were not used

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Used an automated system in permuted blocks of eight
Allocation concealment (selection bias)	Unclear risk	Not mentioned

Blinding of participants and personnel (performance bias) primary outcome	High risk	Not blinded
Blinding of outcome assessment (detection bias) primary outcome	High risk	Not blinded
Incomplete outcome data (attrition bias) alloutcomes	Low risk	Only one lost to follow-up in control group
Selective reporting (reporting bias)	Low risk	Published reports included all outcomes
Other bias	High risk	Two different randomizations were done simultaneously (conservative and liberal fluid therapy and PAC versus CVC)

PAC - pulmonary artery catheter
CVC - central venous catheter
CVP - central venous pressure
LOS - length of stay
ICU - intensive care unit
FACTT - Fluid And Catheter Treatment Trial

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Bach 1992	Not an RCT of management with PAC compared with management without a PAC
Barone 2001	Review and meta-analysis
Boldt 1995	Not an RCT of management with PAC compared with management without a PAC
Bonazzi 2002	Patients assigned to the control group were not transferred to ICU of HDU following surgery
Boyd 1993	Not an RCT of management with PAC compared with management without a PAC
Brazzi 1995	Not an RCT of management with PAC compared with management without a PAC
Cobb 1992	Not an RCT of management with PAC compared with management without a PAC
Cohen 1998	Not an RCT of management with PAC compared with management without a PAC

(*Continued*)

Eyer 1990	Not an RCT of management with PAC compared with management without a PAC
Girbes 1999	Study end point was the commencement of surgery
Holmes 1997	Not an RCT
Kearns 1993	Summary of a previously reported RCT
Latour-Perez 1997	Not an RCT
Mermel 1991	Not an RCT
Mitchell 1992	Not an RCT of management with PAC compared with management without a PAC
Orlando 1985	Conference abstract only
Raybin 1989	Letter
Schultz 1985	Not all patients assigned to the control group were transferred to ICU or HDU following surgery
Senagore 1987	Not an RCT of management with a PAC compared with management without PAC
Shoemaker 1990	Patients were randomly allocated in the second part of the study only. In addition, there was no clear data on mortality in the two groups
Sola 1993	Review article
Stewart 1998	Not an RCT
Stout 2006	Randomized part of this trial is to be cardiac output (CO) (indocyanine green (ICG)) or not and didn't include PACs. PACs and CO (TD) are only referred to in the literature review part of the study
Stubbig 1992	Not an RCT of management with PAC compared with management without a PAC
Suttner 2006	Not an RCT, PAC compared with thoracic electrical bioimpedance, non-invasive method
Takala 2011	Not an RCT of use of PACs - both groups had some use of PAC, the randomization was to MICO or not
Tuman 1989	Not an RCT
Wilson 1999	Not all patients assigned to the control group were transferred to ICU or HDU following surgery
Yu 1993	Not an RCT of management with PAC compared with management without a PAC
Yu 1995	Not an RCT of management with PAC compared with management without a PAC
Yu 2011	Tested the intervention of blood volume measurement and both groups had PACs

(*Continued*)

Ziegler 1997	Not an RCT of management with PAC compared with management without a PAC

ICU - intensive care unit
HDU - high dependency unit
MICO - minimally invasive cardiac output
PAC - pulmonary artery catheter
RCT - randomized controlled trial

DATA AND ANALYSES

Comparison 1. Combined mortality: PAC versus no PAC

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Combined mortality of all studies	13	5686	Risk Ratio (M-H, Random, 95% CI)	1.01 [0.95, 1.08]

Comparison 2. PAC versus no PAC

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 All types mortality (general intensive care patients)	5	2923	Risk Ratio (M-H, Random, 95% CI)	1.02 [0.96, 1.09]
2 All types mortality (high-risk surgical patients)	8	2763	Risk Ratio (M-H, Random, 95% CI)	0.98 [0.74, 1.29]
2.1 All types mortality (studies of perioperative monitoring including pre-operative optimization)	5	2395	Risk Ratio (M-H, Random, 95% CI)	0.98 [0.74, 1.29]
2.2 All types mortality (studies of perioperative monitoring)	3	368	Risk Ratio (M-H, Random, 95% CI)	1.10 [0.14, 8.82]

Comparison 3. ICU length of stay PAC versus no PAC

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 ICU length of stay (general intensive care patients)	4	2723	Mean Difference (IV, Random, 95% CI)	0.15 [-0.74, 1.03]

Comparison 4. Hospital length of stay: PAC versus no PAC

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Hospital length of stay (general intensive care patients)	2	1689	Mean Difference (IV, Random, 95% CI)	-0.80 [-2.71, 1.12]
2 Hospital length of stay (high-risk surgical patients)	5	503	Mean Difference (IV, Random, 95% CI)	0.35 [-0.05, 0.75]

Comparison 5. Cost of care: PAC versus no PAC

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Cost of care (hospital charges, 1000's of US dollars)	2	191	Mean Difference (IV, Fixed, 95% CI)	0.90 [-2.62, 4.42]

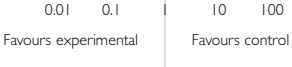
Analysis 1.1. Comparison 1 Combined mortality: PAC versus no PAC, Outcome 1 Combined mortality of all studies.

Review: Pulmonary artery catheters for adult patients in intensive care

Comparison: 1 Combined mortality: PAC versus no PAC

Outcome: 1 Combined mortality of all studies

Study or subgroup	PAC n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Bender 1997	1/51	1/53		0.1 %	1.04 [0.07, 16.18]
Berlauk 1991	1/68	2/21		0.1 %	0.15 [0.01, 1.62]
Guyatt 1991	10/16	9/17		1.1 %	1.18 [0.66, 2.12]
Harvey 2005	346/506	337/507		53.6 %	1.03 [0.94, 1.12]
Isaacson 1990	1/49	0/53		0.0 %	3.24 [0.14, 77.71]
Joyce 1990	0/21	0/19			Not estimable
NHLBI 2006	140/513	128/487		9.3 %	1.04 [0.85, 1.27]
Pearson 1989	1/152	1/74		0.1 %	0.49 [0.03, 7.68]



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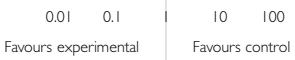
Study or subgroup	PAC n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Rhodes 2002	46/96	50/105		4.7 %	1.01 [0.75, 1.34]
Richard 2003	199/335	208/341		26.1 %	0.97 [0.86, 1.10]
Sandham 2003	78/997	77/997		4.3 %	1.01 [0.75, 1.37]
Shoemaker 1988	11/58	7/30		0.6 %	0.81 [0.35, 1.88]
Valentine 1998	3/60	1/60		0.1 %	3.00 [0.32, 28.03]
Total (95% CI)	**2922**	**2764**		**100.0 %**	**1.01 [0.95, 1.08]**

Total events: 837 (PAC), 821 (Control)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 5.26$, df = 11 (P = 0.92); $I^2 = 0.0\%$

Test for overall effect: Z = 0.41 (P = 0.68)

Test for subgroup differences: Not applicable



Analysis 2.1. Comparison 2 PAC versus no PAC, Outcome 1 All types mortality (general intensive care patients).

Review: Pulmonary artery catheters for adult patients in intensive care

Comparison: 2 PAC versus no PAC

Outcome: 1 All types mortality (general intensive care patients)

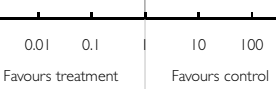
Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Guyatt 1991	10/16	9/17		1.2 %	1.18 [0.66, 2.12]
Harvey 2005	346/506	333/507		56.0 %	1.04 [0.95, 1.14]
NHLBI 2006 (1)	140/513	128/487		9.9 %	1.04 [0.85, 1.27]
Rhodes 2002	46/96	50/105		5.0 %	1.01 [0.75, 1.34]
Richard 2003	199/335	208/341		27.8 %	0.97 [0.86, 1.10]
Total (95% CI)	**1466**	**1457**		**100.0 %**	**1.02 [0.96, 1.09]**

Total events: 741 (Treatment), 728 (Control)

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 1.04$, df = 4 (P = 0.90); $I^2 = 0.0\%$

Test for overall effect: Z = 0.64 (P = 0.52)

Test for subgroup differences: Not applicable



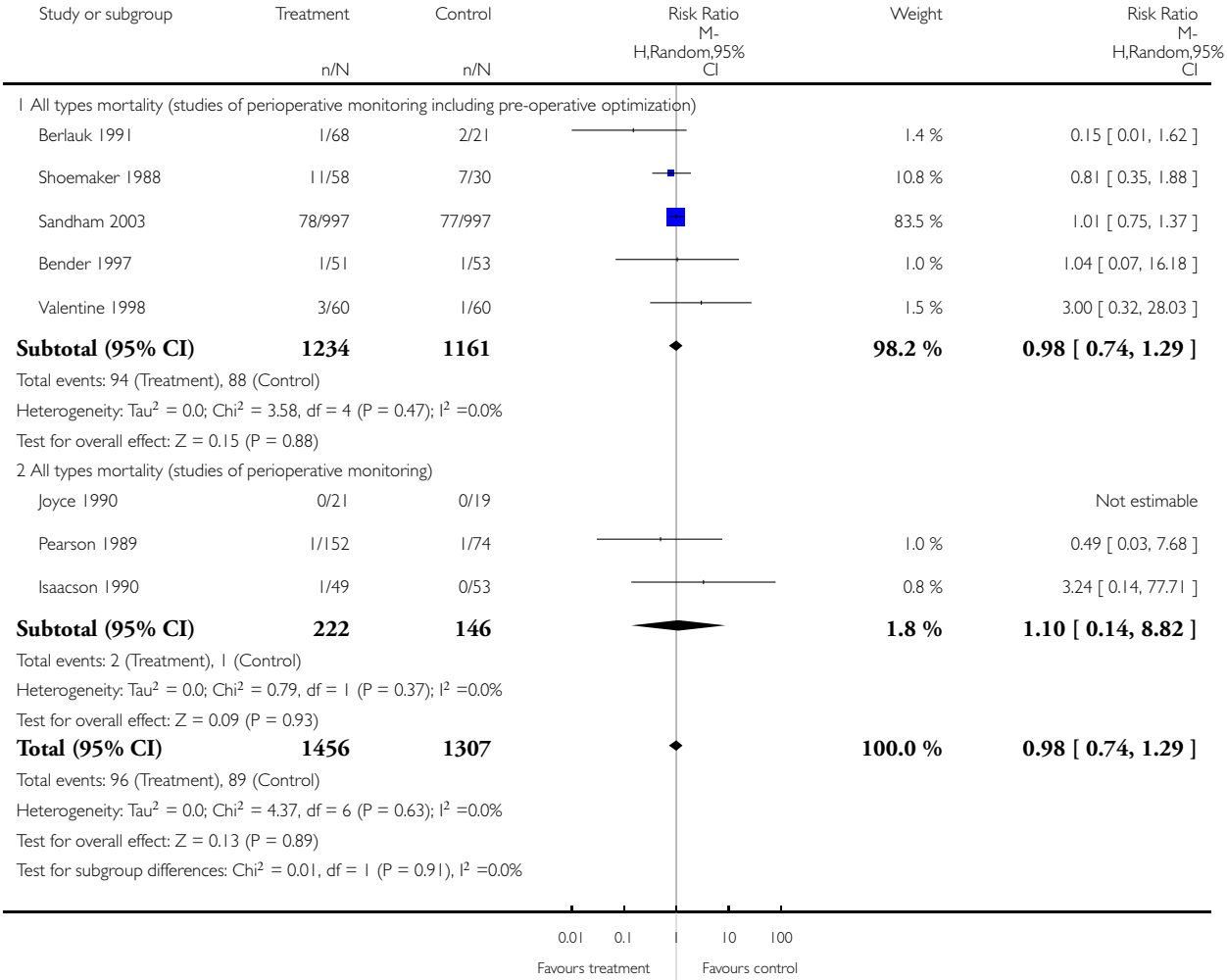
(1) 60 day mortality calculated number of events from the percent reported 27.4% for PAC and 26.3% for CVC

Analysis 2.2. Comparison 2 PAC versus no PAC, Outcome 2 All types mortality (high-risk surgical patients).

Review: Pulmonary artery catheters for adult patients in intensive care

Comparison: 2 PAC versus no PAC

Outcome: 2 All types mortality (high-risk surgical patients)



Analysis 3.1. Comparison 3 ICU length of stay PAC versus no PAC, Outcome 1 ICU length of stay (general intensive care patients).

Review: Pulmonary artery catheters for adult patients in intensive care

Comparison: 3 ICU length of stay PAC versus no PAC

Outcome: 1 ICU length of stay (general intensive care patients)

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Guyatt 1991	16	10.3 (0)	17	8.1 (0)			Not estimable
Harvey 2005	506	10.7 (16.1)	508	10.7 (20.1)		15.7 %	0.0 [-2.24, 2.24]
NHLBI 2006	513	12.5 (11.32)	487	12 (8.82)		50.0 %	0.50 [-0.75, 1.75]
Richard 2003	335	11.6 (10.1)	341	11.9 (10)		34.3 %	-0.30 [-1.82, 1.22]
Total (95% CI)	**1370**		**1353**			**100.0 %**	**0.15 [-0.74, 1.03]**

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.66$, df = 2 (P = 0.72); $I^2 = 0.0\%$

Test for overall effect: Z = 0.33 (P = 0.74)

Test for subgroup differences: Not applicable

Analysis 4.1. Comparison 4 Hospital length of stay: PAC versus no PAC, Outcome 1 Hospital length of stay (general intensive care patients).

Review: Pulmonary artery catheters for adult patients in intensive care

Comparison: 4 Hospital length of stay: PAC versus no PAC

Outcome: 1 Hospital length of stay (general intensive care patients)

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Harvey 2005	506	22.9 (34.3)	507	26.1 (45.4)		14.2 %	-3.20 [-8.15, 1.75]
Richard 2003	335	14 (11.6)	341	14.4 (11.3)		85.8 %	-0.40 [-2.13, 1.33]
Total (95% CI)	**841**		**848**			**100.0 %**	**-0.80 [-2.71, 1.12]**

Heterogeneity: $Tau^2 = 0.34$; $Chi^2 = 1.09$, df = 1 (P = 0.30); $I^2 = 9\%$

Test for overall effect: Z = 0.82 (P = 0.41)

Test for subgroup differences: Not applicable

Analysis 4.2. Comparison 4 Hospital length of stay: PAC versus no PAC, Outcome 2 Hospital length of stay (high-risk surgical patients).

Review: Pulmonary artery catheters for adult patients in intensive care

Comparison: 4 Hospital length of stay: PAC versus no PAC

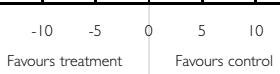
Outcome: 2 Hospital length of stay (high-risk surgical patients)

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Bender 1997	51	12.5 (1.4)	53	12 (1.3)		58.9 %	0.50 [-0.02, 1.02]
Berlauk 1991	68	18.93 (11.8)	21	15.4 (7.5)		0.9 %	3.53 [-0.73, 7.79]
Isaacson 1990	49	10.2 (8.4)	53	9.4 (6.8)		1.8 %	0.80 [-2.18, 3.78]
Shoemaker 1988	58	22.35 (4.18)	30	22.2 (2.8)		7.4 %	0.15 [-1.32, 1.62]
Valentine 1998	60	13 (2)	60	13 (2)		31.1 %	0.0 [-0.72, 0.72]
Total (95% CI)	**286**		**217**			**100.0 %**	**0.35 [-0.05, 0.75]**

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 3.54$, df = 4 (P = 0.47); $I^2 = 0.0\%$

Test for overall effect: Z = 1.72 (P = 0.085)

Test for subgroup differences: Not applicable



Analysis 5.1. Comparison 5 Cost of care: PAC versus no PAC, Outcome 1 Cost of care (hospital charges, 1000's of US dollars).

Review: Pulmonary artery catheters for adult patients in intensive care

Comparison: 5 Cost of care: PAC versus no PAC

Outcome: 1 Cost of care (hospital charges, 1000's of US dollars)

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Berlauk 1991	68	27.3 (0)	21	23.4 (12.3)			Not estimable
Isaacson 1990	49	16.7 (9.1)	53	15.8 (9)		100.0 %	0.90 [-2.62, 4.42]
Total (95% CI)	**117**		**74**			**100.0 %**	**0.90 [-2.62, 4.42]**

Heterogeneity: not applicable

Test for overall effect: Z = 0.50 (P = 0.62)

Test for subgroup differences: Not applicable

APPENDICES

Appendix 1. Search strategy for CENTRAL, *The Cochrane Library*

#1 MeSH descriptor Catheterization, Swan-Ganz explode all trees
#2 MeSH descriptor Heart Catheterization explode all trees
#3 pulmonary artery catheter*
#4 (pulmonary arter*) near (flotation or cathet*)
#5 (right heart) near catheter*
#6 right-heart near catheter*
#7 swan-ganz near catheter*
#8 swanganz near catheter*
#9 (#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8)
#10 MeSH descriptor Critical Care explode all trees
#11 MeSH descriptor Intensive Care Units explode all trees
#12 (intensiv* or critical or postanesthesia or postanaesthesia) near care
#13 high dependency unit*
#14 (#10 OR #11 OR #12 OR #13)
#15 (#9 AND #14)

Appendix 2. Search strategy for MEDLINE (OvidSP)

1 . exp Catheterization-Swan-Ganz/ or Heart-Catheterization/ or pulmonary art?ery catheter*.ti,ab. or (pulmonary arter* adj5 (flotation or cathet*)).mp. or (right?heart and catheter*).mp. or swan?ganz*.ti,ab.
2 . exp Critical care/ or exp Intensive-Care-Units/ or critical care unit*.mp. or ((intensiv* or critical or post?an?esthesia) adj5 care unit).mp. or high dependency unit*.mp. or critical care.ti,ab.
3 . 1 and 2
4 . (adolescent* or child* or preschool* or infant* or newborn).mp.
5 . Adult.mp.
6 . 4 not (5 and 4)
7 . 3 not 6
8 . ((randomised controlled trial or controlled clinical trial).pt. or randomized.ab. or placebo.ab. or drug therapy.fs. or randomly.ab. or trial.ab. or groups.ab.) not (animals not (humans and animals)).sh.
9 . 7 and 8

Appendix 3. Search strategy for EMBASE (OvidSP)

1 . exp swan-ganz-catheter/ or exp heart-catheterization/ or pulmonary art?ery catheter*.ti,ab. or (pulmonary arter* adj5 (flotation or cathet*)).mp. or (right?heart and catheter*).mp. or swan?ganz*.ti,ab. (
2 . exp intensive-care/ or critical care unit*.mp. or ((intensiv* or critical or post?an?esthesia) adj5 care unit).mp. or high dependency unit*.mp. or critical care.ti,ab.
3 . 1 and 2
4 . (placebo.sh. or controlled study.ab. or random*.ti,ab. or trial*.ti,ab. or ((singl* or doubl* or trebl* or tripl*) adj3 (blind* or mask*)).ti,ab.) not (animals not (humans and animals)).sh.
5 . 3 and 4

Appendix 4. Search strategy for CINAHL (EBSCOhost)

S1 (MM "Swan-Ganz Catheterization")
S2 (MH "Heart Catheterization+")
S3 TX pulmonary arter* and TX (flotation or cathet*)
S4 TX (swan-ganz or right-heart) and TX catheter*
S5 S1 or S2 or S3 or S4
S6 (MH "Critical Care")
S7 (MM "Intensive Care Units")
S8 TX high dependency unit*
S9 AB (intensiv* or critical or postanesthesia or postanaesthesia) and AB care
S10 S6 or S7 or S8 or S9
S11 S5 and S10

Appendix 5. Search strategy for grey literature

Several combinations of the following search terms where used. Truncation was used when available	
pulmonary artery catheter	random

(*Continued*)

pulmonary arterial catheter pulmonary artery catheterization pulmonary arterial catheterization right heart catheterization swan ganz	randomised randomizations randomised randomizations

Grey Literature Sources

www.nyam.org/library/pages/grey˙literature˙report
NYAM Grey Literature Collection

http://oaister.worldcat.org
OAIster - Digital Resource from Open Archive Collections

www.doaj.org
Directory of Open Access Journals

www.opendoar.org
OpenDOAR

Clinical Trial Registers

www.isrctn.org
Int Standard Randomized Controlled Trial Number Reg

https://www.clinicaltrialsregister.eu
Eur Clin Trials Register
(new 2011)

http://apps.who.int/trialsearch
WHO ICTRP

Dissertations and Theses

www.ndltd.org
Networked Digital Library of Theses and Dissertations

(*Continued*)

ProQuest Dissertations & Theses
Open Access Journals
www.doaj.org Directory of Open Access Journals
www.opendoar.org OpenDOAR
http://roar.eprints.org Registry of Open Access Repositories
Meeting Abstracts
http://gateway.nlm.nih.gov/gw/Cmd Meeting Abstracts thru NLM Gateway
Conference Abstracts (hand-searched in the original review)
European Society of Intensive Care Medicine *Intensive Care Medicine* http://xa.yimg.com/kq/groups/19299193/148298693/name/ISICEM+abstracts+2011.pdf 31st International Symposium on Intensive Care and Emergency medicine
Society of Critical Care Medicine *Critical Care Medicine*
American Thoracic Society *The American Journal of Respiratory and Critical Care Medicine* *Proceedings of the American Thoracic Society*

Appendix 6. ICU and hospital length of stay

Study ID	Measure	ICU LOS, PAC	ICU LOS, no PAC	P value	Hosp LOS, PAC	Hosp LOS, no PAC	P value
Guyatt 1991	Mean, days (survivors)	10.3	8.1	0.58			
Rhodes 2002	Median (IQR), days (survivors)	10 (2, 14)	6 (2, 13)	0.27	29 (15, 54)	25 (15, 53)	0.81
Rhodes 2002	Median (IQR), days (all patients)	5.7 (2, 12)	4 (2, 10)	0.47	13 (5, 32)	14 (3, 32)	0.81
Isaacson 1990	Mean (SD), days (all patients)	2.7 (2.6)	2.1 (1.0)	0.13	10.2 (8.4)	9.4 (6.8)	0.60
Richard 2003	Mean (SD), days (all patients)	11.6 (10.1)	11.9 (10.0)	0.72	14.0 (11.6)	14.4 (11.3)	0.67
Pearson 1989	Mean (SD), days (all patients)	PAC 1: 1.6 (1.1), PAC 2: 2.1 (4.1)	1.35 (1.1)				
Bender 1997	Mean (SD), days (all patients)	2.7 (0.2)	2.6 (0.5)		12.5 (1.4)	12.0 (1.3)	
Berlauk 1991	Mean (SD), days (all patients)	PAC 1: 3.5 (2.0), PAC 2: 2.5 (1.3)	2.6 (2.1)		PAC 1: 19.4 (11.6), PAC 2: 18.0 (12.0)	15.4 (7.5)	
Sandham 2003	Median (IQR), days (all patients)				10 (7, 15)	10 (7, 15)	0.41
Shoemaker 1988	Mean (SD), days (all patients)	PAC control: 15.8 (3.1), PAC protocol: 19.3 (2.4)	11.5 (1.7)	<0.05 (PAC protocol vs PAC control)	PAC control: 25.2 (3.4), PAC protocol: 19.3 (2.4)	22.2 (2.8)	
Valentine 1998	Mean (SD), days (all patients)	8 (1)	7 (1)		13 (2)	13 (2)	

(*Continued*)

Harvey 2005	Median (IQR), days (survivors)	12.1 (6.2, 22.3)	11.0 (5.7, 21.0)	0.26	34 (23, 61)	40 (21, 70)	0.43
Harvey 2005	Median (IQR), days (non-survivors)	2.6 (0.7, 8.4)	2.5 (0.8, 7.2)	0.71	3 (1, 11)	3 (1, 11)	0.90
NHLBI 2006	Mean ICU free days at day 28	12.5 +/-0.5	12.0+/- 0.4	0.40			

Appendix 7. Costs of care

Study	Measure	Cost, PAC 1	Cost, PAC 2	Cost, no PAC	P value
Isaacson 1990	Mean (SD) total hospital charges per patient	$16,680 (9,108)	N/A	$15,813 (9,028)	
Isaacson 1990	Mean (SD) Anesthesiologists fee per patient	$1,739 (225)	N/A	$1,551 (252)	0.0001
Pearson 1989	Mean (SD) total costs (billed to patient)	$855.51 (231)	$1128.38 (759)	$591.19 (68)	
Berlauk 1991	Mean (SD) total hospital charges	$29,102 (13,207)	$23,770 (12,418)	$23,386 (12,303)	
Shoemaker 1988	Average (not specified) hospital charges	PAC control: $37,335	PAC protocol: $27,665	$30,748	
Stevens 2005	Mean (SEM) total cost per patient (converted to US $, reported in UK £18,612 for PAC and £19,211 for no, PAC Cochrane cost converter)	$28,677.97 (1627.12)		$ 29,600.92 (1987.67)	

WHAT'S NEW

Last assessed as up-to-date: 31 January 2012.

Date	Event	Description
24 April 2012	New citation required and conclusions have changed	This review is an update of a previous Cochrane systematic review (Harvey 2006) that included 12 RCTs. The previous authors Harvey S, Young D, Brampton W, Cooper A, Doig GS, Sibbald W and Rowan K decided not to update the review In this updated version, we found five new large trials and chose to include one large trial which met our inclusion criteria (NHLBI 2006). Additionally three RCTs were excluded due to a different patient population and end points (Bonazzi 2002; ESCAPE 2005; Schultz 1985). In general our review reaches the same conclusions as Harvey 2006. However, we included one large new trial (NHLBI 2006) and thus have more precise estimates on hospital mortality. We applied several additional sensitivity and subgroup analyses which supported the overall results. We graded the quality of evidence of our outcomes. In our discussion we have cited several additional studies which are both in agreement and disagreement with our results. We have reported the review with several additional subheadings and background information. We modified some of the conclusions
24 April 2012	New search has been performed	In the previous version (Harvey 2006) the databases were searched until 2002. In this updated version, we reran the searches until 31 January 2012. We included risk of bias tables, graph and summary graph, study flow diagram, funnel plot, grey literature appendix and summary of finding tables. We have extended our search strategy to include additional electronic databases

HISTORY

Protocol first published: Issue 1, 2002

Review first published: Issue 3, 2006

Date	Event	Description
28 May 2010	Amended	Contact details updated.
7 August 2008	Amended	Minor edit to text

(*Continued*)

31 July 2008	Amended	Converted to new review format.

CONTRIBUTIONS OF AUTHORS

S Rajaram (SR): lead author on meta-analysis, reviewed the papers, coordinated the review, screened search results, extracted data, assessed risk of bias, conducted the analysis, entered data into RevMan, interpreted the data and drafted the full review, edited and critically revised the report.

N Desai (ND): author on meta-analysis, reviewed the papers, drafted the background, edited references in RevMan, added clinical and consumer perspective in discussion, created summary of finding table and critically revised the report.

M Gajera (MG): author on meta-analysis, reviewed the papers, screened search results and selected articles, assessed risk of bias, appraised quality of papers, selected references, provided clinical perspective,and critically revised the report.

A Kalra (AK): author on meta-analysis, reviewed the papers and drafted part of the background, edited discussion and critically revised the report.

S Cavanaugh (SC): author on meta-analysis, assisted with literature search, drafted the grey literature report, organized the retrieval of papers, screened retrieved papers against eligibility criteria, provided additional data about papers, screened data on unpublished studies and critically revised the report.

W Brampton (WB): author on meta-analysis, provided advice on retrieved papers eligibility, performed previous work that was the foundation of the current review and critically revised the report.

S Harvey (SH): author on meta-analysis, performed previous work that was the foundation of the current review and critically revised the report.

D Young (DY): author on meta-analysis, performed previous work that was the foundation of the current review and critically revised the report.

K Rowan (KR): author on meta-analysis, performed previous work that was the foundation of the current review.

DECLARATIONS OF INTEREST

S Harvey, K Rowan, D Young and W Brampton are authors on one of the citations included in the original review and update (Harvey 2005).

All other authors: none known.

SOURCES OF SUPPORT

Internal sources

- University of Oxford (Young), UK.

For original review (Harvey 2006)

- Gloucestershire Hospitals NHS Trust (Brampton), UK.

For original review (Harvey 2006)

External sources

- National Health Service Health Technology Assessment Programme (Project Number 97/08/03), UK.

For original review (Harvey 2006)

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

None

NOTES

None

INDEX TERMS

Medical Subject Headings (MeSH)

*Length of Stay; Catheterization, Swan-Ganz [adverse effects; economics; *mortality]; Cost-Benefit Analysis; Critical Illness [*mortality]; Hospital Mortality; Intensive Care [economics; *methods]; Intensive Care Units; Randomized Controlled Trials as Topic

MeSH check words

Adult; Humans