

# An evaluation of the clinical and cost-effectiveness of pulmonary artery catheters in patient management in intensive care: a systematic review and a randomised controlled trial

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## Executive summary

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## Executive summary

### Introduction

#### Background

Bedside pulmonary artery catheterisation gradually became a standard of care for critically ill patients following its introduction three decades ago. This adoption into mainstream practice occurred without any evaluation of either its clinical or cost-effectiveness. The ongoing, long-standing debate about the clinical effectiveness of pulmonary artery catheters (PACs) was rekindled in 1996 following the publication of a large, non-randomised, risk-adjusted study. The study suggested that patients had an increased odds of dying, within 30 days of admission to an intensive care unit (ICU), if a PAC was used [odds ratio (OR) 1.24, 95% confidence interval (CI) 1.03 to 1.49] and that PACs increased the use of resources. In addition, a contemporaneous, systematic review revealed that there was very little evidence from randomised controlled trials (RCTs) to support the clinical management of critically ill patients with PACs. We undertook and updated the systematic review to consider the need for an RCT.

#### Summary of systematic review

##### Objective

The objective was to search systematically for, and combine, all the evidence from RCTs relating to the effect of the clinical management of critically ill patients with a PAC both on mortality and on the costs of care.

##### Inclusion criteria

All RCTs, with or without blinding, were included where adult patients were randomised to be managed with or without (control) a PAC, the PAC was inserted in an ICU or during a surgical procedure leading to ICU admission, and either mortality, length of stay in ICU or hospital or the costs of care had been measured. There was no restriction on language. Studies were excluded if a PAC was placed solely for organ support prior to organ donation in patients declared brain dead following brain-stem death testing.

##### Outcome measures

The primary outcome measure was hospital mortality and the secondary outcome measures were length of stay in ICU and hospital and the costs of care.

#### Search strategy

The following electronic databases were searched (initially to June 2001, then updated to November 2003): Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE and CINAHL. Conference abstracts from the four major European and North American annual critical care conferences were hand-searched from 1995 to 2001. Reference lists of previous reviews, and both relevant and potentially relevant studies identified from the searches, were checked. Both experts in critical care and manufacturers of PACs were contacted for relevant literature.

#### Identification of studies

Citations were checked, with respect to the inclusion criteria, by four reviewers working in pairs and the final included studies were agreed by consensus between all reviewers.

#### Assessment of methodological quality

Included studies were assessed for possible sources of bias as recommended by the UK Cochrane Centre – no 'quality' scale was used.

#### Analysis

Separate meta-analyses were undertaken, combining data from studies that had included patient populations with similar characteristics. A weighted OR was calculated across studies using a random-effects model (Cochrane statistical package RevMan version 4.2.7). All analyses were based on the results reported on the intention-to-treat principle.

#### Results

From all searches (to November 2003), 3282 discrete citations were identified. Of these, full paper copies were obtained and reviewed for 39 and, of these, 11 studies were eligible for inclusion. These fell broadly into two groups: studies of general intensive care patients ( $n = 3$ ); and studies of high-risk surgery patients ( $n = 8$ ). The latter group could be further subdivided into those that did ( $n = 5$ ) or did not ( $n = 3$ ) include preoperative optimisation as part of the intervention. Only two studies were multi-centre (both identified from the updated search). All remaining studies were small, under-powered and in one or two centres. Potential problems of bias existed for four studies, either because the

randomisation and concealment methods were inadequate or because there was a high crossover rate from the control to the intervention group. Mortality statistics varied across studies but none reported a statistically significant difference between those managed with or without a PAC. Data pooled for the studies of general intensive care patients ( $n = 3$ ) yielded an OR of 0.97 (95% CI 0.74 to 1.26) on comparing PAC with no PAC. In the studies of high-risk surgery patients, for studies that did not include preoperative optimisation ( $n = 3$ ) the pooled OR was 1.10 (95% CI 0.13 to 9.06) and for those that did 0.98 (95% CI 0.72 to 1.33). No studies reported differences in ICU or hospital length of stay. Four studies, conducted in the USA and using hospital charges as a measure of costs of care, indicated that costs were generally higher for patients managed with a PAC, but these results were not statistically significant.

### Conclusion

Evidence from RCTs to support the clinical management of critically ill patients with PACs is scant. Initial searching of the literature (to June 2001) identified only one small RCT of general intensive care patients. This study was discontinued prematurely. The remaining seven studies were of high-risk surgery patients. Hence the initial review indicated a clear need for a large multi-centre RCT. Updated searching after the RCT had commenced revealed no conclusive evidence.

### Objectives

The objectives were to evaluate the clinical and cost-effectiveness of managing critically ill patients in adult, general intensive care with or without PACs.

### Design

The study was an open, multi-centre, RCT with economic evaluation (cost-utility and cost-effectiveness analysis).

### Setting

The setting was general (mixed medical/surgical) ICUs in the UK admitting adults.

### Participants

The participants in the trial were all adult patients in participating ICUs deemed by the responsible

treating clinician to require management with a PAC unless: less than 16 years of age; admitted to ICU electively for preoperative optimisation prior to surgery; a PAC already in place on admission to ICU; had previously been entered into the RCT; or dead using brain-stem death criteria and a PAC being placed for organ support prior to donation.

### Interventions

These were insertion of a PAC and subsequent clinical management, at the discretion of the responsible treating clinicians, using data derived from the PAC. The control group were managed without a PAC but with the option of using alternative cardiac output monitoring devices.

### Outcome measures

The main outcome measure was hospital mortality. Secondary outcome measures were length of stay in the ICU, length of stay in an acute hospital and organ-days of support in the ICU. For the economic evaluation, the main outcome measure was quality-adjusted life-years (QALYs) and the secondary outcome measure was hospital mortality.

### Results

Sixty-five ICUs in the UK participated. Of these, 43 (66%) used alternative cardiac output monitoring devices in control group patients. A total of 1263 patients were identified as being eligible for the trial. Of these, 1041 (82.4%) were randomised and allocated to management with ( $n = 519$ ) or without ( $n = 522$ ) a PAC. There were no losses to follow-up. However, 27 patients (13 in the PAC group and 14 in the control group) were withdrawn from the trial because either the patient withdrew consent on recovering mental competency or the relatives withdrew agreement following randomisation. Data on 1014 patients were included in the analysis. Participants in the two groups had similar baseline characteristics. There was no difference in hospital mortality for patients managed with (68.4%) or without (65.7%) a PAC. The adjusted hazard ratio (PAC versus no PAC) was 1.09 (95% CI 0.94 to 1.27). There was no difference in the median length of stay in ICU, the median length of stay in an acute hospital or mean organ-days of support in ICU between the two groups. The economic evaluation found that the expected cost per QALY gained from the withdrawal of PAC was £2985. The expected cost per life gained from the withdrawal of PAC was £22,038. ►

## Conclusions

Clinical management of critically ill patients with a PAC, as currently practised in the UK, neither improves hospital survival for adult, general intensive care patients nor reduces length of stay in hospital. The lack of demonstrable benefit from a device previously believed to be beneficial could be explained by statistical chance, by misinterpretation of PAC-derived data, by ineffective treatment strategies based on data correctly interpreted using the current paradigm or by subsequent inaction following insertion of the device. It is also possible that detailed data on haemodynamics, however used, cannot modify the disease process sufficiently to influence outcome. The economic evaluation, using decision analysis techniques rather than conventional hypothesis testing, suggests that the withdrawal of the PAC from routine clinical practice in the NHS would be considered cost-effective in the current decision-making climate, and might result in lives or life-years being saved at modest cost.

## Future research

The use of PACs is declining in the UK, predominately because other, less invasive technologies for measuring cardiac output are now

becoming available. As it is unclear whether deriving detailed haemodynamic data, from a PAC or from any other means, affects outcome in critically ill patients, these new devices must be subjected to proper evaluation. Ideally, it needs to be determined whether the lack of effectiveness seen in this study is unique to PACs or is a 'class effect' of all haemodynamic monitors measuring cardiac output. This study examined the effectiveness of clinical management of critically ill patients with a PAC (a package of pulmonary artery catheterisation and subsequent unprotocolised management) in a heterogeneous population of critically ill patients. By indicating no overall benefit from management with a PAC, it should now be possible to examine protocolised management with a PAC in selected groups of critically ill patients against appropriate controls, something that was difficult while PACs were the considered standard of care.

## Publication

Harvey S, Stevens K, Harrison D, Young D, Brampton W, McCabe C, *et al.* An evaluation of the clinical and cost-effectiveness of pulmonary artery catheters in patient management in intensive care: a systematic review and a randomised controlled trial. *Health Technol Assess* 2006;**10**(29).

# NHS R&D HTA Programme

The research findings from the NHS R&D Health Technology Assessment (HTA) Programme directly influence key decision-making bodies such as the National Institute for Health and Clinical Excellence (NICE) and the National Screening Committee (NSC) who rely on HTA outputs to help raise standards of care. HTA findings also help to improve the quality of the service in the NHS indirectly in that they form a key component of the 'National Knowledge Service' that is being developed to improve the evidence of clinical practice throughout the NHS.

The HTA Programme was set up in 1993. Its role is to ensure that high-quality research information on the costs, effectiveness and broader impact of health technologies is produced in the most efficient way for those who use, manage and provide care in the NHS. 'Health technologies' are broadly defined to include all interventions used to promote health, prevent and treat disease, and improve rehabilitation and long-term care, rather than settings of care.

The HTA Programme commissions research only on topics where it has identified key gaps in the evidence needed by the NHS. Suggestions for topics are actively sought from people working in the NHS, the public, service-users groups and professional bodies such as Royal Colleges and NHS Trusts. Research suggestions are carefully considered by panels of independent experts (including service users) whose advice results in a ranked list of recommended research priorities. The HTA Programme then commissions the research team best suited to undertake the work, in the manner most appropriate to find the relevant answers. Some projects may take only months, others need several years to answer the research questions adequately. They may involve synthesising existing evidence or conducting a trial to produce new evidence where none currently exists.

Additionally, through its Technology Assessment Report (TAR) call-off contract, the HTA Programme is able to commission bespoke reports, principally for NICE, but also for other policy customers, such as a National Clinical Director. TARs bring together evidence on key aspects of the use of specific technologies and usually have to be completed within a short time period.

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Reviews in *Health Technology Assessment* are termed 'systematic' when the account of the search, appraisal and synthesis methods (to minimise biases and random errors) would, in theory, permit the replication of the review by others.

The research reported in this monograph was commissioned by the HTA Programme as project number 97/08/03. The contractual start date was in January 2000. The draft report began editorial review in December 2004 and was accepted for publication in January 2006. As the funder, by devising a commissioning brief, the HTA Programme specified the research question and study design. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the referees for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

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