The clinical effectiveness and cost-effectiveness of central venous catheters treated with anti-infective agents in preventing bloodstream infections: a systematic review and economic evaluation


CRD summary
This well-conducted review assessed the use of central venous catheters treated with anti-infective agents (AI-CVCs) in preventing catheter-related bloodstream infection (CRBSI). The authors concluded that use of AI-CVCs reduced CRBSI rates for durations of five to 12 days and greater than 20 days with femoral or jugular vein insertion. The conclusions were likely to be reliable.

Authors’ objectives
To assess the clinical and cost effectiveness of central venous catheters (CVCs) treated with anti-infective agents (AI-CVCs) in preventing catheter-related bloodstream infection (CRBSI).

Searching
The following databases were searched without language restrictions from 1985 to August 2005: MEDLINE, EMBASE, SCI/Web of Science, SCI/ISI Proceedings and The Cochrane Library. Search terms were reported. References of articles and reviews were checked and companies manufacturing AI-CVCs were contacted.

Study selection
Randomised controlled trials (RCTs) comparing AI-CVCs with standard CVCs in patients with a CVC requirement were eligible for inclusion. The primary review outcome was CRBSI. Secondary outcomes were clinical symptoms, colonisation and local clinical signs. Studies reporting only interim data were excluded from the review, as were studies of AI-CVCs which required in-house preparation.

Included studies used AI-CVCs treated with an antibiotic, coated extra-luminally with an anti-infective or coated both intra- and extra-luminally with an anti-infective. The treating agents used were chlorhexidine and silver sulfadiazine (CHSS), silver impregnation, benzalkonium chloride impregnation, minocycline rifampin, miconazole and rifampicin or silver carbon and platinum. Some trials compared different AI-CVCs. Most trials used triple-lumen CVCs, single-, double- and four-lumen CVCs were also used. The mean duration of insertion ranged from 3.8 to 66.21 days where reported. Patients had mean ages ranging from 45 to 66 years. Trials had an average of 62.7 per cent male participants.

A minimum of two reviewers independently selected the studies for the review. Disagreements were resolved through discussion.

Assessment of study quality
Two reviewers independently assessed the studies for validity using criteria based on CRD Report 4, which assesses randomisation, allocation concealment, baseline comparability, reporting of study protocol, blinding, follow-up, treatment of withdrawals and use of intention-to-treat (ITT) analysis. Disagreements were resolved through discussion.

Data extraction
One reviewer extracted the data using a pre-tested extraction form, another reviewer checked the extraction. Some authors were contacted for additional data as a result of a related research project. If multiple diagnostic methods for CRBSI were reported, the most reliable was used to structure the analysis. Odds ratio (ORs) were calculated for CRBSI. Relative Risks (RRs) were calculated for colonisation data.

Methods of synthesis
The studies were combined in fixed-effect meta-analyses with sub-group analyses based on whether the AI-CVCs were treated with an antibiotic, coated extra-luminally with an anti-infective, or coated both intra- and extra-luminally with an anti-infective. Statistical heterogeneity was assessed by visual examination of forest plots and by use of the X² and I².
tests. Where statistically significant heterogeneity was detected a DerSimonian and Laird random-effects model was used. Additional subgroup analyses based on type of treated catheter, outcome categorisations, duration and insertion site were also used to investigate heterogeneity. Sensitivity analyses were used to investigate the effect of study randomisation and blinding, and the impact of analysis by person rather than CVC. This last analysis controlled for clustering effects in trials with more than one catheter per patient. Publication bias was assessed using a funnel plot.

**Results of the review**

Thirty-two RCTs (n between 6,634 and 7,371 analysed; three RCTs did not report n) were included in the review. Overall methodological quality was poor. Only 19 trials reported appropriate randomisation. Only 10 reported appropriate allocation concealment. Fourteen used blinded outcome assessment. Twenty five had follow-up of at least 80 per cent.

There was a significant reduction in CRBSI in the AI-CVC groups (OR 0.45, 95% CI: 0.34, 0.60, 24 RCTs). Subgroup analysis found significant effects in antibiotic treated AI-CVCs (OR 0.26, 95% CI: 0.15, 0.46, six RCTs) and in catheters treated both intra- and extra-luminally (OR 0.43, 95% CI: 0.26, 0.70, nine RCTs), but not in those treated only extra-luminally.

Subgroup analysis found statistically significant reductions in CRBSI for all treatment types assessed by more than one RCT except CHSS extra-luminally treated CVCs.

CRBSI was statistically significantly lower in AI-CVCs in trials with catheter duration between five and 12 days (OR 0.40, 95% CI: 0.27, 0.58; 16 RCTs) and more than 20 days (OR 0.25, 95% CI: 0.09, 0.65; one RCT), but not between 13 and 20 days.

Statistically significant benefits in CRBSI for AI-CVC use were found in the following insertion subgroups: femoral (OR 0.12, 95% CI: 0.03, 0.54, one RCT), jugular (OR 0.23, 95% CI: 0.11, 0.50, three RCTs) and mixed (OR 0.42, 95% CI: 0.28, 0.62; 16 RCTs), but not in the subclavian groups.

There was no evidence of statistically significant heterogeneity between the trials for any analysis of CRBSI incidence. Results for secondary outcomes and results of further sensitivity and sub-group analyses were also reported.

**Cost information**

An economic evaluation found a cost saving of £138.20 for every patient who received an AI-CVC instead of a standard CVC.

**Authors' conclusions**

The use of AI-CVCs reduced CRBSI rates for durations of five to 12 days and for greater than 20 days with femoral or jugular vein insertion. The best clinical effect was found in CVCs treated with minocycline rifampicin or intra- and extra-luminally with CHSS.

**CRD commentary**

The review question and inclusion criteria were clear. The search was reasonably extensive and the lack of language restrictions together with the attempt to locate unpublished studies reduced chances that relevant studies were missed and bias introduced. The authors used appropriate methods to reduce reviewer bias and error throughout the review process. An appropriate validity assessment was conducted and was used to inform the synthesis. The use of meta-analysis was appropriate. Extensive assessment and investigation of heterogeneity was undertaken. It may not have been appropriate, however, to use the detection of statistical heterogeneity to determine the use of a fixed- or random-effects analysis. The authors' conclusions reflected the results of the review accurately and were likely to be reliable.

**Implications of the review for practice and research**

Practice: The authors stated that AI-CVCs were clinically effective and relatively inexpensive, and that their integration into standard care was justified. They noted that use of AI-CVCs without other practical care initiatives would have only a limited impact on CRBSI prevention.

Research: The authors stated that further evidence was required to determine the benefits of externally treated
catheters, particularly those treated with CHSS. More research was required to assess the effectiveness of AI-CVCs for durations of 13 to 20 days, for CVCs inserted in the subclavian vein and to compare catheters with different treatments.

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This report has been updated in the following paper, but the conclusions have not changed.


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