Vascular catheter site care: the clinical and economic benefits of chlorhexidine gluconate compared with povidone iodine

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

Health technology
The use of chlorhexidine gluconate and povidone iodine for vascular catheter insertion site care was investigated.

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised a hypothetical cohort of hospitalised patients requiring either a peripheral or central vascular catheter for short-term use (average duration of less than 10 days). Since the risk of catheter-related infection differs for central and peripheral venous catheters, the authors analysed these two cohorts separately. The authors considered central vascular catheters to include central venous, peripherally inserted central venous, pulmonary arterial, and haemodialysis catheters and introducer sheaths. Peripheral vascular catheters included peripheral venous and peripheral arterial catheters.

Setting
The setting was secondary care. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness measures were derived from studies dating from 1991 to 2002. The resource use data were gathered from studies published between 1994 and 2001. The price year was 2001.

Source of effectiveness data
The evidence for the final outcomes was derived from a review and synthesis of published studies. The authors also made several main assumptions in their analysis.

Modelling
A decision analysis model was developed to evaluate the outcomes associated with the use of chlorhexidine gluconate and povidone-iodine solutions for catheter insertion site care. Patients with a catheter could have one of four outcomes in this model. The four outcomes were catheter-related bloodstream infection (CR-BSI), local catheter-related infection, catheter colonisation without bloodstream infection or local catheter-related infection, and no colonisation or infectious complications. The time horizon was the period of hospitalisation.
Outcomes assessed in the review
The outcomes assessed were:

- the probability of CR-BSI when povidone-iodine solution is used;
- the risk ratio of CR-BSI for chlorhexidine gluconate solution;
- the probability of catheter colonisation when povidone-iodine solution is used;
- the risk ratio of catheter colonisation for chlorhexidine gluconate solution;
- the probability of death attributable to CR-BSI; and
- the probability of local infection if colonisation occurs.

All probabilities were calculated separately for central and peripheral catheter models.

Study designs and other criteria for inclusion in the review
The probabilities of CR-BSI and catheter colonisation with povidone iodine were derived from randomised controlled trials.

Sources searched to identify primary studies
Not reported.

Criteria used to ensure the validity of primary studies
Not reported.

Methods used to judge relevance and validity, and for extracting data
Not reported.

Number of primary studies included
Approximately 16 primary studies, of which 8 were randomised controlled trials, and one was a meta-analysis, were included in the review.

Methods of combining primary studies
The probabilities of CR-BSI and catheter colonisation with povidone iodine were derived by pooling data from randomised controlled trials comparing chlorhexidine gluconate with povidone-iodine solutions for insertion site care.

The probability of CR-BSI and catheter colonisation with chlorhexidine gluconate was determined by multiplying the probability of CR-BSI when povidone iodine was used by the summary risk ratio of CR-BSI when chlorhexidine gluconate was used. This calculation was based on the results of a published meta-analysis.

Investigation of differences between primary studies
The authors reported that different types of chlorhexidine gluconate solution were used in the individual trials from which the measure of effectiveness was derived. The formulations included 0.5% to 1% chlorhexidine gluconate alcoholic solution and 0.5% or 2% chlorhexidine gluconate aqueous solution. In a meta-analysis conducted by the authors, a sub-set analysis of aqueous and non-aqueous solutions showed similar effect sizes, but only the sub-set analysis of the five studies in which alcoholic solution was used produced a statistically significant reduction in CR-BSI.

The authors concluded that the failure of chlorhexidine gluconate to achieve a significant difference, compared with
povidone iodine, might have been due to inadequate statistical power.

Results of the review
The probability of CR-BSI when povidone-iodine solution is used was 3.08% (range: 1.90 - 4.26) with central line catheters, and 0.92% (range: 0.00 - 2.32) with peripheral line catheters.

The risk ratio of CR-BSI for chlorhexidine gluconate solution was 0.49 (range: 0.28 - 0.88) for both central and peripheral line catheters.

The probability of catheter colonisation when povidone-iodine solution is used was 18.09% (range: 10.10 - 26.08) with central line catheters, and 7.91% (range: 5.53 - 10.28) with peripheral line catheters.

The risk ratio of catheter colonisation for chlorhexidine gluconate solution was 0.49 (range: 0.31 - 0.77) for both central and peripheral line catheters.

The probability of death attributable to CR-BSI infection was 15.0% (range: 4.40 - 25.0) with central line catheters, and 1.12% (range: 0.47 - 2.11) with peripheral line catheters.

The probability of local infection if colonisation occurs was 20.0% (range: 0.00 - 40.0) for both central and peripheral line catheters.

Methods used to derive estimates of effectiveness
The authors also incorporated several assumptions into their model.

Estimates of effectiveness and key assumptions
The main assumptions were:

the relative risk of death due to CR-BSI was the same for central and peripheral vascular catheters;

the relative risks for CR-BSI and catheter colonisation for chlorhexidine gluconate, compared with povidone iodine, were the same in central and peripheral vascular catheters; and

catheter colonisation without local infection had no adverse outcomes.

Measure of benefits used in the economic analysis
The outcomes used in the economic analysis were the incidence of CR-BSI and the incidence of death attributable to CR-BSI.

Direct costs
The costs and the quantities were reported separately. The direct costs included in the analysis were those of the hospital. These costs were for catheter tip cultures and antibiotic susceptibility tests, intravenous vancomycin therapy, days of oral dicloxacillin therapy, days in the intensive care unit, days on a general hospital ward, and professional fees. The increase in the length of hospital stay due to CR-BSI was estimated from current literature. The medical use costs were estimated from published sources, supplemented with expert opinion when necessary. The unit costs of each hospital day in the intensive care unit and on a regular hospital ward, of laboratory fees, and of medications, were derived from the University of Washington Medical Centre. Professional fees were based on the Health Care Financing administration fee schedules for the year 2001. Discounting was unnecessary, as all the costs were incurred during a short time, and hence was not performed. The study reported the average costs. The price year was 2001.

Statistical analysis of costs
The cost data were treated as point estimates (i.e. the data were deterministic).

**Indirect Costs**
The indirect costs were not included in the analysis.

**Currency**
US dollars ($).

**Sensitivity analysis**
To assess the overall uncertainty associated with the results, the authors used a Monte Carlo simulation to conduct a multivariate sensitivity analysis. The distributions of the parameters were fitted so that the means were similar to the base-case, and so that the 95% central ranges corresponded with the ranges derived from the literature. The decision analysis model was simulated 10,000 times. The authors also conducted a series of one-way sensitivity analyses to evaluate the effect of varying individual parameters on the outcomes. They also estimated the incremental cost of chlorhexidine gluconate over povidone iodine under a variety of clinical situations, as different packages and amounts of povidone-iodine solution are used for catheter site care, and alcohol solution is sometimes applied before the catheter site is disinfected with povidone iodine.

**Estimated benefits used in the economic analysis**
The use of chlorhexidine gluconate rather than povidone iodine for central line catheter site care led to an absolute decrease in the incidence of CR-BSI of 16 cases per 1,000 catheters (from 31 to 15 cases per 1,000 catheters; number-needed-to-treat, NNT of 64 patients). It also led to a decrease in the incidence of death attributable to CR-BSI of 2 cases per 1,000 catheters (from 4 to 2 cases per 1,000 catheters; NNT 435 patients).

The use of chlorhexidine gluconate rather than povidone iodine for peripheral line catheter site care led to an absolute decrease in the incidence of CR-BSI of 5 cases per 1,000 catheters (from 9 to 4 cases per 1,000 catheters; NNT 213 patients). It also led to a decrease in the incidence of death attributable to CR-BSI of 0.05 cases per 1,000 catheters (from 0.10 to 0.05 cases per 1,000 catheters; NNT 21,277 patients).

**Cost results**
Compared with the use of povidone iodine in central line catheter site care, chlorhexidine gluconate resulted in expected cost-savings of $113 for each catheter used (cost decreased from $224 to $111 for each catheter used).

Compared with the use of povidone iodine in peripheral line catheter site care, chlorhexidine gluconate resulted in expected cost-savings of $8 for each catheter used (cost decreased from $16 to $8 for each catheter used).

**Synthesis of costs and benefits**
As chlorhexidine gluconate was dominant over povidone iodine (i.e. it was more effective and less expensive), a synthesis of the costs and benefits was not relevant. In the Monte Carlo analysis, the use of chlorhexidine gluconate produced cost-savings in over 99% of the simulations. The results were found to be robust in one-way sensitivity analyses.

**Authors' conclusions**
The use of chlorhexidine gluconate for patients requiring short-term vascular catheterisation, either with central or peripheral catheters, would reduce the incidence of vascular catheter-related infection. It would also decrease the health care costs.
CRD COMMENTARY - Selection of comparators
A justification was given for using povidone iodine as the comparator. It represented the current standard solution for vascular catheter insertion site care in the authors’ setting. You should decide if this is a widely used health technology in your own setting.

Validity of estimate of measure of effectiveness
The authors did not report that a systematic review of the literature was undertaken to identify all relevant research and minimise biases. They also did not report the sources searched for relevant research. Despite this, the review and synthesis of the literature were based on up-to-date studies, the oldest being published in 1991, with a majority of studies being randomised controlled trials. The effectiveness estimates were combined using a meta-analysis and, where appropriate, the authors considered the impact of differences between the primary studies on the effectiveness estimates. In addition, uncertainty in the model was evaluated using a probabilistic sensitivity analysis based on all of the outcomes derived from the literature.

Validity of estimate of measure of benefit
The estimation of benefits was modelled. The decision analytic model used to derive these estimates appears to have been appropriate.

Validity of estimate of costs
All the categories of cost relevant to the perspective adopted were included in the analysis. As such, all the relevant costs appear to have been included. The costs and the quantities were reported separately, which will enhance the generalisability of the authors' results. Resource use and costs were derived from a number of published sources. Uncertainty in these parameters was appropriately evaluated in a probabilistic sensitivity analysis. Discounting was unnecessary since all the costs were incurred during a short time. The price year was reported, which will aid any inflation exercises.

Other issues
The authors made appropriate comparisons of their findings with those from other studies that found that the incidence of CR-BSI was significantly lower among patients whose catheter sites were disinfected with chlorhexidine gluconate rather than povidone iodine. However, it does appear that no study has quantified the cost-effectiveness of chlorhexidine gluconate. The issue of generalisability to other settings was appropriately addressed in the sensitivity analysis. The authors do not appear to have presented their results selectively and their conclusions reflected the scope of the analysis.

The authors reported several further limitations to their study. First, the study did not consider the impact of antibiotic resistance or hypersensitivity reactions with chlorhexidine gluconate in the analysis, although the authors stated that the effect was likely to be small. Second, the indirect costs were not included in the analysis (the authors stated that this would have resulted in even greater cost-savings for the chlorhexidine gluconate strategy). Third, the data were not generalisable for patients requiring long-term catheterisation, as the meta-analysis of trials only included patients requiring short-term catheterisation (i.e. less than 10 days). Finally, the study did not examine the cost-effectiveness of chlorhexidine gluconate with other preventive measures.

Implications of the study
The authors concluded that the use of chlorhexidine gluconate could be relatively easily implemented to improve patient safety, and thus should, perhaps, take priority in efforts to prevent vascular catheter-related infection.

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