Preoperative use of mupirocin for the prevention of healthcare-associated Staphylococcus aureus infections: a cost-effectiveness analysis

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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 study examined three strategies for the prevention of healthcare-associated Staphylococcus aureus (S. aureus) infections. The strategies were to screen with nasal culture and give treatment to carriers (screen-and-treat); to give treatment to all patients without screening (treat-all); and to neither screen nor treat (no intervention). Treatment consisted of preoperative intranasal mupirocin.

Type of intervention
Screening and treatment.

Economic study type
Cost-effectiveness analysis

Study population
The study population comprised a hypothetical cohort of adult patients undergoing non-emergent cardiothoracic, neurologic, general or gynaecologic surgery requiring postoperative hospitalisation.

Setting
The setting was a hospital. The economic study was carried out in the USA.

Dates to which data relate
The clinical data were derived from studies published between 1995 and 2003. Data on resource use and costs came from studies published between 1996 and 2004. The price year was 2003.

Modelling
A decision tree analysis was performed in order to evaluate the clinical and economic impact of the two strategies based on intranasal mupirocin treatment (screen-and-treat and treat-all) over no intervention. The time horizon of the model was 90 days. The structure of the tree was depicted. The model allowed for a number of ultimate clinical outcomes, such as recovery from surgery without infection, death due to underlying illness, death due to pneumonia or infections, and recovery from infection. The model also included the possibility of readmission and the need for home health care service after discharge.

Study designs and other criteria for inclusion in the review
The clinical data used in the model were:

- prevalence of infection;
- health care associated infection rates, i.e. bloodstream infections (BSIs) and surgical site infections (SSIs);
- the rate of pneumonia due to S. aureus or due to pathogens other than S. aureus;
- the effectiveness of mupirocin (reduction in S. aureus infection among carriers given mupirocin treatment);
- the mortality rate due to health care-associated BSI or SSI, or underlying disease;
the rate of readmission among patients with SSI; and

the rate of patients requiring home-health services for health care-associated infections.

Sources searched to identify primary studies
These clinical estimates were derived from published data. The authors stated that, whenever possible, data from randomised clinical trials (RCTs) were used. Most of the probability estimates came from a large randomised trial involving 3,864 surgical patients. Otherwise, prospective studies were used in particular to assess infection-attributable mortality.

Methods used to derive estimates of effectiveness
Clinical data were identified through a review of MEDLINE. Some details of the search criteria, such as the period covered and keywords used, were reported.

Measure of benefits used in the economic analysis
Several model outputs were reported. These included the total number of S. aureus infections, the number of S. aureus infections prevented with the two strategies (screen-and-treat and treat-all), the number of deaths due to infection, and deaths prevented. In the sensitivity analysis, life-years saved and infection prevented with respect to a no intervention strategy were considered as summary benefit measures. These were combined with the costs.

Direct costs
The analysis was carried out from a societal perspective. Two main categories of costs were included in the analysis: costs associated with the intervention and excess hospitalisation costs. The former covered mupirocin treatment, nasal bacterial culture without drug-susceptibility testing, and compensation for registered nursing; the latter covered health care-associated BSI, SSI, health care-associated pneumonia, and home health care and durable equipment. The unit costs and the quantities of resource use were not reported separately, and only a few estimates of cost items were presented. The costs and quantities were derived from published studies reporting cost estimates since 1990. Some information on the sources used to derive the costs was provided. For example, health care costs associated with BSI were obtained from a prospective multi-centre cohort study of 1,028 patients with sepsis syndrome. Charges were adjusted using a state- and year-specific cost-to-charge ratio. Discounting was not relevant as the costs were incurred over a 3-month period. The costs were inflated to 2003 values using the Consumer Price Index.

Statistical analysis of costs
The costs and quantities appear to have been treated deterministically.

Indirect Costs
The study was conducted from a societal perspective and the opportunity cost to patients participating in the intervention was considered. Specifically, the hourly compensation rate for workers was derived from the US Department of Labour, Bureau of Labor Statistics. Half an hour was assumed to have been required for nasal swab screening and one hour for the application of mupirocin.

Currency
US dollars ($).

Sensitivity analysis
A one-way sensitivity analysis was undertaken to evaluate the robustness of the model results to variations in both the clinical and economic inputs of the model. Alternative values for probability estimates were based on published confidence intervals. Otherwise, the authors defined ranges (50 to 200% of the base-case value). Great attention was given to the uncertainty around the efficacy of mupirocin in the sensitivity analyses. Some scenario analyses and two-way sensitivity analyses were also performed.

Estimated benefits used in the economic analysis
In a hypothetical cohort of 10,000 patients, the total number of S. aureus infections was 178 with no intervention and 92 with both interventional strategies. Thus, the two strategies prevented 86 infections compared with no intervention.
In a hypothetical cohort of 10,000 patients, the total number of deaths due to infection was 3 with no intervention and 1 with both interventional strategies. Thus, the two strategies prevented 2 infections compared with no intervention.

**Cost results**
In a hypothetical cohort of 10,000 patients, the total costs saved in comparison with the no intervention strategy were $1,019,207 and $877,052 with the screen-and-treat and treat-all strategies, respectively.

**Synthesis of costs and benefits**
The costs and benefits were not combined in the base-case analysis since the two interventional strategies (screen-and-treat and treat-all) dominated the no intervention option.

The sensitivity analysis showed that the model results were robust to variations in most inputs, except for the mupirocin efficacy rate (reduction in S. aureus infections with mupirocin). If this rate was less than 16.1% (51% in the base-case), the screen-and-treat strategy would no longer be cost-saving: for example, when the mupirocin efficacy rate was 8% (lowest value), the incremental cost per infection prevented was $17,317 and the incremental cost per life-year gained was $247,626 with the screen-and-treat strategy. The corresponding figures with the treat-all strategy were $27,257 and $389,782, respectively.

In general, the cost-effectiveness of screen-and-treat ranged from cost-saving in the best-case scenario to $304,350 per life-year gained in the worst-case scenario. The cost-effectiveness of the treat-all strategy ranged from cost-saving in the best-case scenario to $296,900 per life-year gained in the worst-case scenario. However, both best- and worst-case scenarios were based on extreme values and do not represent very realistic situations.

When the two interventional strategies were compared, the authors stated that the incremental cost-effectiveness ratio of the screen-and-treat strategy over the treat-all strategy was very sensitive to S. aureus colonisation rates, cost of mupirocin and nursing compensation (results not reported).

**Authors’ conclusions**
The authors concluded that the use of preoperative intranasal mupirocin for patients undergoing non-emergent surgery requiring postoperative hospitalisation was a cost-effective alternative to no treatment. Specifically, both the screen-and-treat and treat-all strategies were more effective and less expensive than no treatment given the high cost of health care-associated infections.

**CRD COMMENTARY - Selection of comparators**
The choice of the comparator (i.e. no intervention) was appropriate. Both a screening strategy and a treat-all patients strategy were included, and these should cover most of the available options for preventing S. aureus infections among surgical patients. You should decide whether this is a valid comparator in your own setting.

**Validity of estimate of measure of effectiveness**
The authors reviewed literature in order to identify relevant clinical estimates, and some information on the method of the review and the design of the primary studies was provided. The authors used the best available evidence (RCTs) whenever possible, which should ensure the validity of the clinical data. Some uncertain estimates were subjected to extensive variation in the sensitivity analysis, and it was shown that the results of the analysis were sensitive to variations in key model inputs such as the efficacy of mupirocin treatment.

**Validity of estimate of measure of benefit**
Cases of infections avoided and life-years saved are commonly used outcomes of screening and treatment options. Life-years represent a valid benefit measure as they can be compared with the benefits of other health care interventions. However, it was not clear how life-years saved were calculated given the short time horizon of the model.

**Validity of estimate of costs**
The analysis of the costs was consistent with the perspective adopted. It appears that all the relevant categories of costs have been included in the analysis, regardless of who paid for them. Most of the costs were not broken down into single
items and were presented only as macro-categories. This may limit the possibility of replicating the analysis in other settings. Furthermore, economic data were derived from published studies, few details of which were provided. The authors pointed out that, when true costs of health care services were not available, charges were used but were then converted into costs using specific cost-to-charge ratios. The price year was reported, which will facilitate reflation exercises in other time periods. Key cost estimates were varied in the sensitivity analysis.

Other issues
The authors reported the findings from another study, the results of which were comparable with those achieved in the current analysis. In terms of the issue of the transferability of the study results, the authors noted that caution will be required if extrapolating their results to patients with few co-morbidities undergoing low-risk procedures. Similarly, the study findings should not be applied to non-surgical patients. The authors acknowledged some limitations of their analysis, primarily the fact that the model did not consider the issue of mupirocin resistance over time, which may have the effect of reducing treatment efficacy.

Implications of the study
The study results support the preoperative use of mupirocin in patients undergoing a broad range of surgical procedures. However, the cost-effectiveness results are highly sensitive to the mupirocin efficacy rate.

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MeSH
Anti-Bacterial Agents /administration & dosage /economics /therapeutic use; Cost Savings; Cost-Benefit Analysis; Cross Infection /prevention & control; Decision Trees; Mupirocin /administration & dosage /economics /therapeutic use; Nose /microbiology; Sensitivity and Specificity; Staphylococcal Infections /economics /prevention & control; Staphylococcus aureus /isolation & purification; Surgical Wound Infection /prevention & control

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