A cost-effectiveness analysis of bacterial endocarditis prophylaxis for febrile children who have cardiac lesions and undergo urinary catheterization in the emergency department

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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 administration of antibiotic prophylaxis for bacterial endocarditis (BE) was compared with no prophylaxis, for febrile children with cardiac lesions undergoing urinary catheterisation (UC) in the emergency department. The antibiotics used in the study were amoxicillin 50 mg/kg, administered either orally 1 hour before the procedure, or intramuscularly or intravenously 30 minutes prior to starting the procedure, and vancomycin 20 mg/kg given over 1 to 2 hours at least 30 minutes prior to starting the procedure.

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis and cost-utility analysis.

Study population
The study population comprised a hypothetical cohort of patients aged 0 to 24 months with known moderate-risk cardiac lesions, who presented at an emergency department with a fever of unknown origin and required UC for specimen collection. Moderate-risk lesions included most congenital malformations (such as ventricular septal defects), acquired valvular dysfunction (such as rheumatic heart disease), hypertrophic cardiomyopathy, and mitral valve prolapse with valvular regurgitation and/or thickened leaflets.

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

Dates to which data relate
The effectiveness evidence was gathered from studies published between 1958 and 2000. The cost data were taken from published and electronic sources relating to 1996 to 2001, and were adjusted to 2000 prices.

Source of effectiveness data
The effectiveness data were derived from a review and synthesis of published studies and statistics, supplemented with authors' assumptions.

Modelling
A decision analysis model was used to estimate the costs and benefits of each strategy. The structure of the decision tree was presented. The time horizon for the model was patient life expectancy. The model made the following assumptions:
prophylaxis before UC prevents all BE by preventing bacteraemia (bacteria in the blood);
amoxicillin and vancomycin are equally effective in preventing bacteraemia;
in the presence of bacteraemia with organisms that cause endocarditis, the incidence of BE is constant, regardless of the cause of the bacteraemia or the type of moderate-risk cardiac lesion;
in the absence of bacteraemia or in the presence of organisms not typically associated with endocarditis, BE does not occur;
there is no increased risk of bacteraemia or BE with contaminated urine specimens; and
bacteraemia occurs immediately after instrumentation and is followed immediately by bacterial seeding of the endocardium.

**Outcomes assessed in the review**

A systematic review of the literature was undertaken to identify the following model parameters:

- the prevalence of UTI in febrile children aged 0 - 24 months;
- the prevalence of Escherichia coli, Enterococcus species, and Staphylococcus aureus causing UTI and BE;
- the prophylactic efficacy of antibiotics in preventing bacteraemia;
- the incidence of bacteraemia after UC (infected urine);
- the incidence of BE after bacteraemia;
- the mortality from endocarditis;
- the incidence of BE decompensation requiring surgical intervention;
- the incidence of congestive heart failure (CHF) with BE;
- the probability of mild reactions with penicillin;
- the probability of allergic or anaphylactic reactions with vancomycin; and
- the probability of allergic or anaphylactic reactions with gentamicin.

**Study designs and other criteria for inclusion in the review**

No inclusion criteria were reported. A randomised controlled trial and two decision analyses were used to determine the prophylactic efficacy of antibiotics in preventing bacteraemia after genitourinary procedures. Other study designs were not reported, but the authors frequently described the study population.

**Sources searched to identify primary studies**

MEDLINE was searched for articles published between 1966 and 2001.

**Criteria used to ensure the validity of primary studies**

Not reported.
Not reported.

**Number of primary studies included**
The review comprised 19 studies.

**Methods of combining primary studies**
When the estimate was based on only one study, 95% confidence intervals were calculated from the available data. If more than one study was used, a weighted mean was calculated and a range constructed from the minimum and maximum values in the studies.

**Investigation of differences between primary studies**
Not reported.

**Results of the review**
The prevalence of UTI in febrile children aged 0 - 24 months was 0.039 (range: 0.033 - 0.053).

The prevalence of Escherichia coli, Enterococcus species, and Staphylococcus aureus causing UTI and BE was 0.034 (range: 0.000 - 1.000).

The prophylactic efficacy of antibiotics in preventing bacteraemia was 0.890 (range: 0.000 - 1.000).

The incidence of bacteraemia after UC (infected urine) was 0.231 (range: 0.143 - 0.263).

The incidence of BE after bacteraemia was 0.022 (range: 0.001 - 1.000).

The mortality from endocarditis was 0.116 (range: 0.000 - 0.135).

The incidence of BE decompensation requiring surgical intervention was 0.186 (range: 0.000 - 0.250).

The incidence of CHF with BE was 0.27 (range: 0.145 - 0.397).

The probability of mild reactions with penicillin was 0.01 (range: 0.007 - 0.100).

The probability of allergic or anaphylactic reactions with vancomycin was 0 (range: 0).

The probability of allergic or anaphylactic reactions with gentamicin was 0 (range: 0).

**Methods used to derive estimates of effectiveness**
The authors derived two of the estimates of effectiveness from population data and made assumptions to obtain a range.

**Estimates of effectiveness and key assumptions**
The model assumed that the probability of anaphylaxis with penicillin was 0.0003 (range: 0.0002 - 0.0004). It also assumed that the probability of mortality with penicillin was 0.00002 (range: 0.00000 - 0.00004).

**Measure of benefits used in the economic analysis**
The measures of health benefit used were the number of BE cases prevented and the quality-adjusted life-years (QALYs) gained. These were obtained from the model and were discounted at a rate of 3%. Health-related quality of life scores were taken from the Years of Healthy Life Measure (Gold et al. 1998, see 'Other Publications of Related Interest' below for bibliographic details). The utility value for mitral valve disorders was used as a proxy for all...
moderate-risk lesions.

**Direct costs**
Only the direct costs of medical care were included in the analysis. These included the cost of medications, nursing time to insert an intravenous cannula and administer the antibiotic, the cost of treating mild or anaphylactic reactions to amoxicillin, and the cost of medical care preceding death from anaphylaxis. The costs averted by preventing BE were the costs of treating BE and its potential complications of cardiac surgery and CHF (including hospitalisation, tests, outpatient visits and transportation). To assess hospital costs, a cost-to-charge ratio was used. Outpatient visit costs were derived from Medicaid charges for 2000. The direct cost data were obtained from published and electronic sources relating to 2000 to 2001. These were adjusted to 2000 prices using the Consumer Price Index. The quantities and the cost parameters entered in the model were reported separately. A discount rate of 3% was applied to costs in accordance with the recommendations of the Panel on Cost-Effectiveness in Health and Medicine. The total costs per patient were reported. The authors did not include the costs of UC, as this was assumed to be the same for both groups.

**Statistical analysis of costs**
Point estimates were presented. No statistical analysis of the costs was reported.

**Indirect Costs**
The indirect costs were included, which was appropriate for the study perspective. The indirect costs reported were the hours of work missed by a parent and the opportunity costs for time in the emergency department that could have been used to attend other patients. These were derived from published and electronic sources relating to 1996 to 2001. Discounting was undertaken at a rate of 3%. The quantities and the cost data entered in the model were reported separately. The costs were adjusted to a price year of 2000.

**Currency**
US dollars ($).

**Sensitivity analysis**
A sensitivity analysis was conducted to investigate variability in the data. The methods used were not specifically described, although it appears that one-way sensitivity analyses have been performed. It would appear that all the probabilities in the model parameters were explored, and that the range used was established from the review of the literature. Uncertainty in the cost data was investigated by varying all costs between $0 and twice the value of the point estimate. The utility values for BE, no BE, and CHF were varied. The discount rate was altered between 0 and 5% for economic costs and clinical outcomes.

**Estimated benefits used in the economic analysis**
Compared with no antibiotic treatment, prophylaxis with amoxicillin or vancomycin prevented 7 BE cases per 1 million children treated.

When amoxicillin-related deaths were included, no antibiotic treatment produced greater QALY gains than giving prophylactic amoxicillin (24.91124 versus 24.91079 QALYs). When amoxicillin-related deaths were excluded, prophylaxis with amoxicillin produced a discounted QALY gain of 0.0005 (24.91129 versus 24.91124 QALYs) in comparison with no antibiotic treatment. Prophylaxis with vancomycin was also associated with a discounted QALY gain of 0.0005 in comparison with no antibiotic treatment.

**Cost results**
The discounted total cost of treatment per patient was $495.30 with amoxicillin and $667.63 with vancomycin. The discounted total cost of treatment without antibiotic prophylaxis was $1.47. The discounted incremental cost of
treatment was $493.79 with amoxicillin and $666.16 with vancomycin.

Synthesis of costs and benefits
The costs and benefits were combined by calculating the incremental cost-effectiveness ratio (ICER) to avoid one case of BE and the ICER per QALY gained.

When amoxicillin-related deaths were included, the no prophylaxis strategy was dominant.

When amoxicillin-related deaths were excluded, the discounted ICER for amoxicillin compared with no prophylaxis was $70 million per BE prevented and $10 million per QALY gained.

The discounted ICER for vancomycin compared with no prophylaxis was $95 million per BE prevented and $13 million per QALY gained.

The results were sensitive to the inclusion of amoxicillin-associated deaths, which made the amoxicillin strategy less effective and more costly than no prophylaxis. The sensitivity analysis showed that the findings were robust to variations in the model parameters. Even when the prevalence of UTIs was 100%, the use of prophylactic antibiotics was not cost-effective. Removing the high opportunity cost of the emergency department from the analysis did not alter the cost-effectiveness findings.

Authors' conclusions
Antibiotic prophylaxis for bacterial endocarditis (BE) prior to urinary catheterisation (UC) in febrile children who are aged 0 to 24 months, and who have moderate-risk cardiac lesions, is not a cost-effective use of health care resources in the emergency department.

CRD COMMENTARY - Selection of comparators
No explicit justification was provided for the comparator used. The authors noted the uncertain benefits and undesirable health and economic consequences of the intervention in the absence of a UTI. By using a no-treatment strategy as the comparator, the active value of the treatment was able to be evaluated. You should decide if the comparator represents current practice in your own setting.

Validity of estimate of measure of effectiveness
A systematic review was undertaken but the authors did not fully describe their methodology, particularly the inclusion criteria and selection process. The estimates of effectiveness were arrived at by the use of meta-analytic techniques. The authors reported the methods used to derive estimates of effectiveness and adopted a weighting scheme, although it was unclear which differences between the studies this was reflecting. When estimates were unavailable from the literature, the authors' assumptions were justified by reference to population data.

Validity of estimate of measure of benefit
The measures of benefit used were the BE cases avoided and QALYs gained. These were estimated from the model. The health state utility values were taken from the Years of Healthy Life Measure. The utility value for mitral valve disorders was used as a proxy for all moderate-risk lesions. However, this was varied in the sensitivity analysis to encompass values for other moderate-risk lesions.

Validity of estimate of costs
The cost analysis was performed from a societal perspective. It appears that all the relevant categories of costs have been included in this analysis. Some relevant costs were excluded from the analysis. The authors did not include the costs of UC, as this was assumed to be the same for both groups and would not have affected the findings. The quantities and the unit costs were reported separately, thus enhancing the reproducibility of the study in other settings.
A sensitivity analysis was conducted on all of the model input parameters, using ranges that appear to have been appropriate. The costs were treated deterministically, but sensitivity analyses were conducted to assess the robustness of the estimates used. Discounting was applied correctly and at an appropriate rate. Costs, rather than charges, were reported using a cost-to-charge ratio. This practice is methodologically superior to reporting charges and it enhances the generalisability of the study findings. The cost data were derived from published and electronic sources relating to 1996 to 2001, and were adjusted to a single price year. The price year was reported, which increases the generalisability of the results.

Other issues
The authors compared their findings with those from other studies and found them to be in agreement with other published results. The authors did not directly address the issue of the generalisability of the results to other settings. However, the extensive sensitivity analysis explored the effect of factors such as antibiotic efficacy, bacterial prevalence, the incidence of bacteraemia and BE, and costs, which increases the generalisability of the results. The authors do not appear to have presented their results selectively. The study population comprised children with moderate-risk cardiac lesions and this was reflected in the authors’ conclusions.

The authors discussed several limitations to their study that were associated with the reliance on data from the literature. First, many of the studies were undertaken on adult rather than paediatric populations. Second, the estimate of the incidence of BE with bacteraemia was derived from a single study. Third, the patient population with moderate-risk lesions was heterogeneous. The authors addressed these weaknesses by varying values in the sensitivity analyses and found that the cost-effectiveness outcome was unchanged.

Implications of the study
The authors stated that there are no data to support the practice of prophylactically administering antibiotics to prevent endocarditis from instrumentation during UC.

Source of funding
None stated.

Bibliographic details

PubMedID
15121944

Other publications of related interest


Indexing Status
Subject indexing assigned by NLM
MeSH
Antibiotic Prophylaxis /economics; Bacteremia /etiology /prevention & control; Cost-Benefit Analysis; Decision Trees; Emergency Medical Services /economics; Endocarditis, Bacterial /economics /epidemiology /etiology /prevention & control; Fever /complications; Heart Diseases /complications; Humans; Infant; Probability; Quality-Adjusted Life Years; Risk; Urinary Catheterization /adverse effects; Urinary Tract Infections /complications /diagnosis

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