Health and economic outcomes of the detection of Klebsiella pneumoniae-produced extended-spectrum beta-lactamase (ESBL) in a hospital with high prevalence of this infection


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 compared two diagnostic methods, disk diffusion and E-test, for the detection of extended-spectrum beta-lactamase (ESBL) Klebsiella pneumoniae (K. pneumoniae). Blood cultures for disk diffusion were obtained from patients using the BACTEC 9240 blood culture system (Beckton Dickinson, USA). The E-test was performed using ESBL strips (AB BIODISK).

Type of intervention
Diagnosis.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients (mainly adults) with positive blood culture results for K. pneumoniae. Patients with false bacteraemia by K. pneumoniae (i.e. patients with presence of positive blood culture without clinical symptoms of infection) and patients with missing data in their medical charts were excluded from the study.

Setting
The setting was tertiary care. The economic study was carried out in Sao Paolo, Brazil.

Dates to which data relate
The effectiveness data were obtained from January 1996 to May 2001. The dates of the cost data and the price year were not reported.

Source of effectiveness data
The effectiveness data were derived from a single study.

Link between effectiveness and cost data
Although not explicitly stated, it seems that the costing has been carried out retrospectively on the same sample of patients as that used in the effectiveness study.

Study sample
The sample size was not determined in the planning phase and power calculations were not performed retrospectively. Patients detected with a K. pneumoniae bloodstream infection (BSI) in the authors’ setting were selected for inclusion in the study. Throughout the study period, 115 patients were identified with K. pneumonia BSI isolates, of which 7
were excluded because they did not meet the inclusion criteria. The authors did not provide any details of the study sample (e.g. age and gender distribution, co-morbidities).

Study design
The analysis was based on a single-centred retrospective cohort study. All patients with ESBL-producing strains were identified by both the disk diffusion method and the E-test. The E-test method was considered the 'gold' standard. Each patient was included only once, so in instances were more than one culture was taken and found to be positive, only the first was reviewed and recorded.

Analysis of effectiveness
The primary outcomes used in the analysis were:

- mortality due to bacteraemia, defined as death occurring within 15 days of the start of treatment and not attributable to other causes;
- the positive and negative predictive values (PPV and NPV, respectively) of disk diffusion and the E-test;
- the percentage of cases adequately treated with antibiotics;
- the percentage of cases inadequately treated with antibiotics; and
- the percentage of cases where the antibiotic treatment required adjustment.

Inadequate treatment was assumed to be therapy administered within 24 hours after blood culture to which the K. pneumoniae isolate was resistant. Treatment was considered adequate if the organism was susceptible, except when cephalosporins were used to treat ESBL. Adjusted treatment was defined as when the antimicrobial agent was altered according to the antimicrobial susceptibility test results within 48 hours after the blood culture.

Effectiveness results
With the disk diffusion method, the PPV was 94.7% (95% confidence interval, CI: 88.9 to 100) and the NPV was 96.1% (95% CI: 90.8 to 101.4) in relation to the E-test with an ESBL prevalence of 52%.

Overall, antimicrobial therapy was adequate in 63.9% of cases (69 of 108), inadequate in 27.8% of cases (30 of 108) and adjusted in 8.3% of cases (9 of 108).

The mortality rate was 24.1% (26 of 108 cases) but in 18 of these the patient's death was not caused by a K. pneumoniae BSI.

Clinical conclusions
The authors concluded that disk diffusion may lead clinicians to initiate appropriate antimicrobial treatment of BSIs in hospitals with a high prevalence of ESBL-producing K. pneumoniae.

Measure of benefits used in the economic analysis
The authors did not derive a summary measure of benefit. In effect, a cost-consequences analysis was performed

Direct costs
The health care costs included in the analysis comprised the following:

- the cost of the disk diffusion method per K. pneumonia strain when using 12 disks per plate;
the cost of the E-test when using 2 E-test strips;

the cost of antimicrobial treatment administered for normal renal function (standard adult dose of 2.0g imipenen per
day for 14 days);

the cost of antimicrobial treatment of BSI due to a non-ESBL producing strain (2.0 g ceftriaxone daily for 14 days); and

the cost of treatment using cephalosporins (5 days of ceftriaxone followed by 14 days of imipenen).

Some costs were derived from the literature, whereas the source of other costs (e.g. for disk diffusion and E-test) were
not reported. The costs and the quantities were not reported separately and the authors provided summary costs for the
treatment costs. Since the costs were incurred during less than 2 years, discounting was not relevant. The price year was
not reported.

**Statistical analysis of costs**
The costs were treated deterministically.

**Indirect Costs**
The indirect costs were not included.

**Currency**
US dollars ($). No conversion rate from the local currency (Brazilian real) was provided.

**Sensitivity analysis**
No sensitivity analysis was carried out.

**Estimated benefits used in the economic analysis**
See the 'Effectiveness Results' section.

**Cost results**
Assuming adequate antimicrobial therapy in 108 patients, the total costs for each diagnostic strategy were reported for
different ESBL prevalence.

For the E-test methods:

when ESBL prevalence was 2%, the total cost was $37,260.36;

when ESBL prevalence was 10%, the cost was $48,332.04;

when ESBL prevalence was 25%, the cost was $70,475.40; and

when ESBL prevalence was 52%, the cost was $110,610.20.

For the disk diffusion method, for the equivalent ESBL prevalence, the costs were:

$44,484.12 at 2% prevalence;

$55,555.80 at 10% prevalence;

$76,420.90 at 25% prevalence; and
$113,893.50 at 52% prevalence.

**Synthesis of costs and benefits**
The costs and benefits were not combined.

**Authors’ conclusions**
The E-test method proved to be less costly. The authors felt that its use was "justified" and that it leads to the appropriate treatment of patients with Klebsiella pneumoniae (K. pneumoniae) bloodstream infection (BSI).

**CRD COMMENTARY - Selection of comparators**
It was unclear why the comparators used were chosen as the authors did not provide a justification for their choice. You should decide if these represent widely used health technologies in your own setting.

**Validity of estimate of measure of effectiveness**
The analysis was based on a retrospective cohort study. The study sample was representative of the study population. However, the retrospective nature of the study represents a limitation to its internal validity. The authors did not conduct any statistical analyses in order to take potential confounding factors and biases into account. In addition, no power calculations were reported. It is therefore possible that the differences observed between the two methods were due to chance.

**Validity of estimate of measure of benefit**
The authors did not derive a summary measure of benefit. The reader is referred to the comments in the 'Validity of estimate of measure of effectiveness' field (above).

**Validity of estimate of costs**
The perspective adopted in the economic analysis was not reported. However, given the costs that were included, it is likely that the perspective was narrow (i.e. that of the hospital or clinic). As the authors mainly reported summary costs it was not possible to ascertain which aspects of costs were included in the analysis. The costs and the quantities were not reported separately, which means that it would be difficult to rework the analysis in other settings. The resource use data for antimicrobial treatment were derived from public sources, but no statistical analysis of the quantities was performed. In addition, no sensitivity analysis was performed on the costs to assess the robustness of the estimates used. These factors may limit the interpretation of the study findings. Since the costs were incurred during a short time, discounting was unnecessary and was not conducted. The price year was not reported.

**Other issues**
The authors did not compare their findings with those from other studies. However, this was because of a lack of published literature in this specific area (i.e. comparison of the two methods). The authors did not directly address the issue of generalisability of the results to other settings. The authors do not appear to have presented their results selectively. The study enrolled patients with a K. pneumoniae BSI and this was reflected in the authors’ conclusions. The authors did not report any limitations to their study.

**Implications of the study**
The authors did not make explicit recommendations for changes in policy or practice, nor did they suggest areas for further research.

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