Cost-effectiveness analysis of linezolid compared with vancomycin for the treatment of nosocomial pneumonia caused by methicillin-resistant Staphylococcus aureus


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 linezolid and vancomycin for the treatment of nosocomial pneumonia (NP) caused by methicillin-resistant Staphylococcus aureus (MRSA). The linezolid regimen included linezolid 600 mg plus aztreonam every 12 hours (q12h), while the vancomycin regimen was vancomycin 1,000 mg plus aztreonam q12h.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Patients were included in the study if it was likely that they had NP only and no other forms of non-NP. As there was no International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9CM) code that differentiated NP from community-acquired pneumonia, an algorithm was created to narrow the universe of patients with any diagnosis of pneumonia on admission to hospital, to a sample of patients who were most likely to have NP only. Admissions associated with a principal diagnosis of pneumonia were excluded, as were certain secondary diagnoses of pneumonia. Patients were excluded if their length of stay was less than 7 days or more than 21 days. Admissions for immunocompromised states and admissions of patients younger than 16 years of age were also excluded.

Setting
The setting was secondary care. The economic study was carried out in the mid-Atlantic region of the USA.

Dates to which data relate
The effectiveness data were taken from a study published in 2003. The dates to which the resources and prices related were not reported.

Source of effectiveness data
The effectiveness data were derived from a review of the literature.

Modelling
A decision-analytic model was used to compare the costs and effectiveness of linezolid and vancomycin.

Outcomes assessed in the review
The outcomes assessed were survival with and without bacteraemia, and non-survival with and without, for each
treatment regimen.

**Study designs and other criteria for inclusion in the review**
The measures of effectiveness were derived from prospective, double-blind, randomised controlled trials (RCTs).

**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**
Two studies, reported in one paper (Wunderink et al. 2003, see 'Other Publications of Related Interest' below for bibliographic details) were included.

**Methods of combining primary studies**
The study used was a pooled analysis of two RCTs.

**Investigation of differences between primary studies**
Not reported, but details may have been provided in the study used (Wunderink et al. 2003).

**Results of the review**
For the linezolid regimen, the probabilities were:

- 0.09 for survival with bacteraemia and 0.71 for survival without bacteraemia; and
- 0.01 for non-survival with bacteraemia and 0.19 for non-survival without bacteraemia.

For the vancomycin regimen, the probabilities were:

- 0.11 for survival with bacteraemia and 0.53 for survival without bacteraemia; and
- 0.06 for non-survival with bacteraemia and 0.31 for non-survival without bacteraemia.

**Measure of benefits used in the economic analysis**
The measure of benefit used was lives saved.

**Direct costs**
The costs included in the analysis were hospital charges and drug costs. The hospital charges information was obtained from the billed hospital claims database, while average wholesale prices (less 15%) were used for drug costs. The costs and the quantities were not reported separately. Discounting was not performed, but it was not necessary given the relatively short duration of follow-up. The price year was not stated.
Statistical analysis of costs
Point estimates were used for the costs and no statistical analyses were reported.

Indirect Costs
No indirect costs were included.

Currency
US dollars ($).

Sensitivity analysis
The following variables were subject to sensitivity analysis:

the costs (median billed charges were replaced with mean billed charges, median allowed charges and median payments);

the treatment duration (1 standard deviation around the means for 11.3 days for linezolid and 10.7 days for vancomycin); and

the mortality rate (used absolute mortality rates observed in the hospitals claims data).

A multi-factorial sensitivity analysis, in which several of the input parameters were varied simultaneously, was also performed by means of Monte Carlo simulation.

Estimated benefits used in the economic analysis
The unadjusted survival rates observed in the linezolid and vancomycin treatment regimens were significantly different, (p=0.03). The rate was 80% (60/75) in the linezolid-treated patients and 63.5% (54/85) in the vancomycin-treated patients.

Adjustment for baseline clinical and co-morbidity variables resulted in 2.2-times higher odds of survival with linezolid compared with vancomycin.

Cost results
Expected median daily billed hospital charges for the typical patient with NP caused by MRSA were $2,888 with linezolid treatment and $2,993 with vancomycin treatment.

Mean treatment durations of 11.3 days for linezolid and 10.7 days for vancomycin resulted in expected total billed hospital charges for the typical patient with NP caused by MRSA of $32,636 (linezolid) and $32,025 (vancomycin), respectively.

Synthesis of costs and benefits
The costs and benefits were combined using an incremental cost-effectiveness ratio (ICER).

The ICER for linezolid compared with vancomycin per life saved was $3,600.

The 95% confidence interval around the ICER per life saved due to linezolid therapy ranged from a $5,765 cost-saving to a $12,965 cost per life saved.

In all instances of the sensitivity analysis, the ICER for linezolid per life saved was below the conventional cost-effectiveness benchmark of $50,000.
Authors' conclusions
Linezolid was a cost-effective alternative to vancomycin for the treatment of nosocomial pneumonia (NP) caused by methicillin-resistant Staphylococcus aureus (MRSA).

CRD COMMENTARY - Selection of comparators
The reason for the choice of the comparator was clear. It was chosen because it reflected standard practice in the authors' setting. You should consider whether this is a widely used technology in your own setting.

Validity of estimate of measure of effectiveness
The authors did not state that a systematic review of the literature had been undertaken, which means it is not possible to rule out selection bias. Only one paper, which had combined two RCTs, was used in the estimate of effectiveness. However, extensive sensitivity analysis around the estimate of effectiveness was carried out.

Validity of estimate of measure of benefit
The estimate of benefit was obtained directly from the effectiveness analysis using modelling. The reader is therefore referred to the comments in the 'Validity of estimate of measure of effectiveness' field (above).

Validity of estimate of costs
The perspective of the analysis was not explicitly stated. However, it appears to have been that of the hospital, in which case all the relevant costs have been included. The costs and the quantities were not reported separately, which will limit the generalisability and transferability of the authors' conclusions. The costs were obtained from billed charges, which the authors acknowledged do not necessarily reflect true costs, therefore the costs were subject to extensive sensitivity analysis.

Other issues
The authors did not compare their findings with those from other studies, although they did acknowledge that few studies have examined the cost-effectiveness of different pharmacologic approaches to the treatment of NP caused by MRSA. The issue of generalisability to other settings was not addressed. The authors do not appear to have presented their results selectively. The study was concerned with hospital-acquired MRSA pneumonia and this was reflected in the authors’ conclusions. The authors acknowledged a number of limitations to their study. For example, the absence of a specific ICD-9-CM diagnosis code for NP, and the limitation of the analysis to hospital inpatient treatment charges only.

Implications of the study
The authors concluded that linezolid is a cost-effective alternative to vancomycin for the treatment of NP caused by MRSA. They did not make explicit recommendations for changes in policy or practice.

Source of funding
Funded by Pfizer Inc., New York.

Bibliographic details

PubMedID
16982296
Other publications of related interest
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Indexing Status
Subject indexing assigned by NLM

MeSH
Acetamides /therapeutic use; Adult; Aged; Anti-Bacterial Agents /therapeutic use; Cost-Benefit Analysis; Cross Infection /drug therapy; Female; Health Care Costs; Humans; Linezolid; Male; Methicillin Resistance; Middle Aged; Oxazolidinones /therapeutic use; Pneumonia, Staphylococcal /drug therapy; Randomized Controlled Trials as Topic; Staphylococcus aureus /drug effects; Vancomycin /therapeutic use

AccessionNumber
22006008338

Date bibliographic record published
28/02/2007

Date abstract record published
28/02/2007