Cost-effectiveness analysis of linezolid vs vancomycin in treating methicillin-resistant Staphylococcus aureus complicated skin and soft tissue infections using a decision analytic model

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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.

CRD summary
This study examined the cost-effectiveness of four strategies, using vancomycin and linezolid, for the treatment of complicated skin and soft tissue infections of methicillin-resistant Staphylococcus aureus. The authors concluded that linezolid was the most cost-effective strategy for payers with a high willingness to pay for cured patients, but vancomycin strategies that took advantage of early discharge were cost-effective. The study was well conducted and the authors' conclusions appear to be valid.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
This study examined the cost-effectiveness of four strategies, using vancomycin, linezolid, or both, for the treatment of complicated skin and soft tissue infections of methicillin-resistant Staphylococcus aureus (MRSA).

Interventions
The four strategies were: intravenous linezolid, followed by oral linezolid; intravenous vancomycin for the entire course of therapy as an in-patient; intravenous vancomycin for five days, followed by oral linezolid upon discharge; and intravenous vancomycin for five days, followed by home intravenous vancomycin.

Linezolid was given at a dose of 600mg every 12 hours intravenously or orally and vancomycin was given at 1g every 12 hours intravenously.

Location/setting
USA/out-patient.

Methods
Analytical approach:
The analysis was based on a decision analytic model. The time horizon was not explicitly stated. The authors stated that the analysis was carried out from the perspective of the health care system.

Effectiveness data:
A search of the PubMed database was undertaken to identify the relevant randomised controlled trials (RCTs). References from each trial report were also searched. The inclusion criteria and key search criteria were reported and weighted means and standard deviations were calculated for each clinical input. The key clinical endpoint was the rate of response to therapy.

Monetary benefit and utility valuations:
Not included.

Measure of benefit:
The summary benefit measure was the cure rate, which was defined as the probability that patients, who had a MRSA-
positive culture, would respond to the initial drug and would not experience any relapse after treatment.

Cost data:
The economic analysis included study medications, laboratory analysis, microbiology, and hospital stay. Drug costs were based on average wholesale prices, while other costs and resource quantities came from the national Veterans' Affairs database. All costs were in US dollars ($) and the price year was not explicitly reported.

Analysis of uncertainty:
A deterministic one-way sensitivity analysis was undertaken on all the model inputs and was illustrated in a tornado diagram. A second-order Monte Carlo simulation was carried out using pre-determined probability distributions for the model inputs. The average outcomes and 95% confidence intervals were generated, together with cost-effectiveness acceptability curves, for various willingness-to-pay thresholds.

Results
The expected costs were $9,749.17 with vancomycin at home, $10,017.29 with vancomycin then linezolid, $16,686.43 with vancomycin in hospital, and $10,975.19 with linezolid at home. The benefits were 0.3633 with vancomycin at home, 0.3626 with vancomycin then linezolid, 0.3633 with vancomycin in hospital, and 0.4926 with linezolid at home.

The incremental analysis showed that vancomycin at home dominated vancomycin then linezolid, which means it was more effective and less expensive. Linezolid at home dominated vancomycin in hospital. The incremental cost per patient successfully treated with linezolid at home was $9,488.19 over vancomycin at home and $7,370.61 over vancomycin then linezolid.

The most influential model inputs were the duration of in-patient stay for linezolid patients and for vancomycin at home patients. Changes in the other inputs favoured vancomycin at home over linezolid at home, in incremental costs.

The key results of the probabilistic analysis were that: linezolid at home dominated vancomycin in hospital in most scenarios; it was more cost-effective than vancomycin then linezolid in only 33% of simulations and than vancomycin at home in 30% of simulations; and vancomycin at home was more cost-effective than vancomycin then linezolid in 74% of simulations.

Authors' conclusions
The authors concluded that intravenous then oral linezolid was the most cost-effective strategy for payers with a high willingness to pay for cured patients, but the vancomycin strategies that took advantage of early discharge were also cost-effective.

CRD commentary
Interventions:
The selection of the comparators was appropriate as they were relevant therapies for the patient population. A clear description of all strategies was provided.

Effectiveness/benefits:
The approach used to identify the clinical inputs was appropriate as the literature review included all relevant sources of data. The authors provided the key details of the methods and conduct of the review. The selection of RCTs enhanced the validity of the clinical data and the pooling methods were reported. In general, the clinical analysis appears to have been well carried out. The benefit measure was disease-specific and might not have been appropriate for capturing the global impact of the treatments on patients' health. It is also not comparable with the benefits of other health care interventions and the threshold for the willingness-to-pay for a cured patient was not determined.

Costs:
The economic analysis was consistent with the perspective of the payer in terms of the types of costs and the sources of data. Most of the unit costs and quantities of resources (especially for drug consumption) were presented, which enhances the transparency of the economic analysis. The price year was not explicitly reported, but it appears, from the sources of unit costs, to have been 2008.
Analysis and results:
The results were clearly presented and both average and incremental cost-effectiveness ratios were calculated. The authors did not mention that because the vancomycin then linezolid option was dominated by vancomycin at home, the relevant incremental cost-effectiveness ratio was the $9,488 for linezolid versus vancomycin at home. The issue of uncertainty was well investigated using various approaches, and the findings were satisfactorily presented and discussed. Details of the decision model were appropriately reported. The main limitation of the analysis was the fact that, as no willingness-to-pay threshold for a cured patient was available, it is hard to assess which treatment should be considered to be the most cost-effective. The authors stated that some assumptions were made, such as the exclusion of adverse events, but these should not have had a strong impact on the results.

Concluding remarks:
The study was well conducted and the authors' conclusions appear to be valid.

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