Cost-effectiveness analysis of linezolid, daptomycin, and vancomycin in methicillin-resistant 
Staphylococcus aureus: complicated skin and skin structure infection using Bayesian 
methods for evidence synthesis 
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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 evaluated the cost-effectiveness of linezolid, daptomycin, and vancomycin, for methicillin-resistant Staphylococcus aureus (MRSA) complicated skin and skin structure infections. The authors concluded that linezolid and daptomycin were less costly and more effective than vancomycin, and that linezolid was less costly and more effective than daptomycin. The synthesis methods were clearly reported and generally sound. The omission of relevant comparators, and the uncertainty in the resource use, make firm conclusions difficult.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
This study evaluated the cost-effectiveness of linezolid, daptomycin, or vancomycin, for methicillin-resistant Staphylococcus aureus (MRSA) complicated skin and skin structure infection.

Interventions
The three treatment strategies each started with a different antibiotic, and changes or switches were made, if necessary. The three initial treatments were vancomycin 1g every 12 hours; linezolid 600mg every 12 hours; and daptomycin 4mg per kg per day.

Location/setting
USA/primary and secondary care.

Methods
Analytical approach:
A Bayesian, indirect treatment comparison, meta-analysis was used to inform a decision-tree model. The authors stated that the perspective was that of the US health care payer.

Effectiveness data:
The clinical effectiveness and safety data were from an indirect treatment comparison meta-analysis that synthesised nine comparative effectiveness studies, found by a systematic review. The primary effectiveness measure was the probability of treatment success, which was defined as the clinical resolution of the signs and symptoms of MRSA. A random-effects meta-analysis was used to incorporate between-study heterogeneity, in the relative treatment effects. The adverse event rates were from Bayesian indirect treatment meta-analysis. Assumptions were made for the drugs that were switched to if a patient was found to be MRSA negative, if a patient had an adverse reaction, or if treatment failed. Treatment after any of these events was assumed to be 100% effective.

Monetary benefit and utility valuations:
Not relevant.

Measure of benefit:
The benefit was measured by treatment success. The authors stated that they applied no discounting because of the short time frame of the study.
Cost data:
The total direct costs of the intervention included study medications, laboratory analysis, microbiology, and a night in hospital. The drug costs were from the Drug Red Book. Resource use was based on data from the Decision Support System database of the US Department of Veterans Affairs. All costs were in 2009 US $. Where necessary, adjustments were made using the medical component of the Consumer Price Index.

Analysis of uncertainty:
The authors performed four scenario analyses, several univariate analyses, and a probabilistic sensitivity analysis. All univariate analyses compared linezolid with daptomycin. Probabilistic sensitivity analysis was performed by applying probabilistic distributions to the parameters in the model and sampling from these 10,000 times. Gamma distributions were used for the unit costs, with triangle distributions for the resource use. The results of the pair-wise comparisons were plotted on cost-effectiveness planes and cost-effectiveness acceptability curves.

Results
The total direct costs were $18,057 for linezolid, $20,698 for daptomycin, and $23,671 for vancomycin. The estimated probability of treatment success was 0.480 for linezolid, 0.469 for daptomycin, and 0.449 for vancomycin.

Linezolid and daptomycin were less costly and more effective (dominant), compared with vancomycin. Compared with daptomycin, linezolid was dominant.

In the one-way sensitivity analyses, comparing linezolid with daptomycin, the incremental cost-effectiveness ratio was sensitive to three model parameters related to the duration of treatment with daptomycin and linezolid. The scenario analyses and probabilistic sensitivity analysis did not alter the initial conclusions.

Authors’ conclusions
The authors concluded that linezolid and daptomycin were less costly and more effective than vancomycin, and that linezolid was less costly and more effective than daptomycin.

CRD commentary
Interventions:
The interventions were clearly explained. The authors reported that several other drugs had evidence for use for MRSA complicated skin infections, but only one (tigecycline) was included as an option, and only after the failure of initial treatment. Two of the excluded drugs were treatments approved by the US Food and Drug Administration. The authors indicated that vancomycin was the standard treatment.

Effectiveness/benefits:
The reporting of the effectiveness and benefits was generally good. The inclusion criteria for the systematic review were clearly described, and sufficiently broad, but only one database was searched, and no efforts were reported to find unpublished studies, so some evidence may have been missed. In the studies used in the meta-analysis, the average age of treatment was lower for patients receiving daptomycin, than for patients receiving linezolid. It is unclear what effect this could have on the results, and no efforts were made to adjust for any such baseline differences. The only baseline characteristics that were reported were the mean age of the participants, and the proportions of patients who were MRSA positive and negative.

Costs:
It appears that the relevant cost categories were included, and the reported unit costs appear to have been relevant to the analytic perspective and setting. The costs were generally well reported, including the adjustment methods, and they appear to have been from reasonable sources.

Analysis and results:
The modelling and results were mostly transparent, but most of the assumptions were made with minimal justification and they were not tested in the sensitivity analyses. No adjustments were made for differences in the initial characteristics between groups. Meta-regression, or subgroup analyses could have provided valuable insights into the drivers of effectiveness. The sensitivity analyses indicated that resource use was a key driver for the model. Uncertainty in the resource use was estimated using triangular distributions, which are not accurate representations, as they are
defined by three points: the mode, minimum, and maximum; none of which relate to uncertainty. It is not clear how robust the resource use parameters were to uncertainty.

**Concluding remarks:**
The synthesis methods were clearly reported and generally sound. The omission of relevant comparators, and the uncertainty in the resource use, make firm conclusions difficult.

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