An Economic Model to Compare the Different Empiric and First/Second Line Treatment Regimens for Suspected Methicillin-Resistant Staphylococcus Aureus Nosocomial Pneumonia

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Background
- Nosocomial pneumonia (NP) has been reported to be the second most frequent hospital-acquired infection in the United States [1].
- Methicillin-resistant Staphylococcus aureus (MRSA) is responsible for a large number of cases of healthcare-associated pneumonia, hospital-acquired pneumonia, and ventilator-associated pneumonia [2, 3].
- Appropriate and timely empiric treatment is important for MRSA-related infections. Inadequate empiric treatment is associated with increased mortality and longer hospital stay [4, 5].

Objective
- The purpose of this analysis was to compare the economic impact of initial empiric linezolid (Emp-LIN) vs. vancomycin (Emp-VAN) vs. no empiric MRSA coverage (NE-MRSA) before culture-confirmed treatment, for suspected MRSA NP. After MRSA confirmation, the model predicts how patients may be switched to linezolid or vancomycin and vice versa. In the base-case, empiric linezolid was switched to vancomycin and vice versa). In the sensitivity analysis, the model was based on clinical and resource use data from a recently published clinical trial comparing empiric linezolid and vancomycin in MRSA NP [6] (Table 1).

Methods
- A 4-week decision model was developed to capture empiric, 1st and 2nd line therapy (Figure 1).
- A total payer perspective was considered in the base case analysis, which was comprehensive and comprised all inpatient and outpatient health care costs (antibiotic and medical).
- Patients enrolled the model when diagnosed with an episode of suspected gram+ NP, and could receive treatment with empiric linezolid, vancomycin, or no empiric MRSA coverage (Figure 1a).
- Patients with negative culture for MRSA (i.e., methicillin-susceptible Staphylococcus aureus [MSSA]) got assigned aggregated costs and outcomes for MSSA treatment.
- Patients with positive culture entered the confirmed MRSA treatment phase (Figure 1b). The proportion of patients with confirmed MRSA infection can vary in the model (base-case value was 30%).
- Possible treatment outcomes associated with therapy after MRSA confirmation were: 1) treatment success; 2) failure due to lack of efficacy among survivors; 3) drug discontinuation due to AEs; or 4) failure due to death

Results
- The model was primarily based on clinical and resource use data from a recently published clinical trial comparing linezolid and vancomycin in MRSA NP [6] (Table 1).
- After any failure of first-line treatment or discontinuation due to AEs, patients were switched to second-line treatment (e.g., patients who failed first-line treatment with linezolid switched to vancomycin and vice versa). In the base-case, this switch was assumed to be after 7 days of first-line treatment, with second-line treatment duration of 10 days. The model did not include a third-line treatment.
- The model made several assumptions, and a few key ones are listed below:
  - Patients with MSSA were assumed to have efficacy proportions, LY, QALY and similar to the MSSA cohort. Hence, the model used the same linezolid and vancomycin values for the MSSA cohort. This assumption does not affect the model results’ conclusions across treatment arms, since it is applied uniformly to all treatment arms, and does not introduce any bias.
  - In the absence of published data for second-line treatment, the clinical inputs for second-line treatment were the same as for first-line treatment (7).

Table 1. Model input clinical and resource use data

Table 2. Unit cost data

Sensitivity Analyses
- A univariate (one-way) sensitivity analyses was conducted to assess the impact of model uncertainties and robustness of our analysis. Key model parameters were individually varied within the pre-defined sensitivity ranges, and ICERs were recorded. A published source was used for ranges whenever possible. In absence of strong published data, an arbitrary range was used (such as ±4 to 8 for length of stay or ±10% for costs).
- A probabilistic sensitivity analysis (PSA) was also performed, wherein all parameters were varied simultaneously within their range using 10,000 second order Monte Carlo simulations. Gamma distribution was specified for costs to account for all sources of uncertainty.

Table 3. Base case results

Conclusion
- In conclusion, this US health economic model showed that in a hospital setting with 30% MRSA rate, early treatment with Emp-LIN can be a cost-effective alternative compared to Emp-VAN and NE-MRSA at reasonable WTP threshold.
- Hence, initiating empiric treatment with linezolid should be considered a preferred treatment choice, especially at hospitals with high MRSA rate.
- Cost-effectiveness of linezolid was primarily driven by its higher clinical response rate.
- Future analyses should use other country costs/resource use data to test result generalizability.

References

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