Cost-effectiveness evaluation of ertapenem versus piperacillin/tazobactam in the treatment of complicated intraabdominal infections accounting for antibiotic resistance

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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 investigated the cost-effectiveness of ertapenem versus the combination of piperacillin and tazobactam, for treating community-acquired intra-abdominal infections. The authors concluded that ertapenem was preferred as it produced superior health benefits at lower costs compared with piperacillin/tazobactam. The results were not fully and transparently reported and the authors’ conclusions might have limitations.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
The aim was to examine the costs and effects of the antibiotic agents ertapenem and the combination of piperacillin and tazobactam, for individuals with community-acquired, complicated, intra-abdominal infections.

Interventions
Ertapenem (1g per day) was compared with piperacillin/tazobactam (9g per day). If either treatment failed, the second-line treatment was a combination of imipenem and cilastatin.

Location/setting
Netherlands/in-patient care.

Methods
Analytical approach:
A mathematical model was used to estimate the sensitivity of bacteria to the antibiotic as a function of other relevant factors, such as the distribution of prescriptions (number treated), initial resistance, spontaneous rate of clearance, and rate of clearance with treatment. These data were then integrated into a decision tree to evaluate the cost-effectiveness of treatments at several time points (one, 15, 30, 45, and 60 months from treatment). The authors did not state the perspective.

Effectiveness data:
The clinical estimates included response, second-line antibiotic efficacy, antimicrobial resistance, and mortality. These data were primarily from a randomised controlled trial (Solomkin, et al. 2003, see ‘Other Publications of Related Interest’ below for bibliographic details). An alternative scenario was assessed that included *Escherichia coli* (*E. coli*) anti-microbial resistance, based on data from the European Study for Monitoring Antimicrobial Resistance Trends (SMART, Gallagher, et al. 2005, see ‘Other Publications of Related Interest’ below for bibliographic details). The primary clinical outcomes included treatment efficacy and life expectancy.

Monetary benefit and utility valuations:
The authors’ assumed that the disutility value, for the life-years expected when a patient survived an episode of intra-abdominal infection, was zero and this meant that discounted life-years were equal to discounted quality-adjusted life-years (QALYs).

Measure of benefit:
The measure of benefit was QALYs and they were discounted at 1.5% per year.
Cost data:
The types of resources, in the cost analysis, were the antibiotic agents (first-line and second-line), hospitalisation days, out-patient visits, and surgical intervention. The mean costs and ranges of values were presented for each of these four categories. The resource quantities were from three published studies (Solomkin, et al. 2003, Krobot, et al. 2004, and Davey, et al. 2001, see 'Other Publications of Related Interest' below for bibliographic details), and kostenhandleiding CVZ. The unit costs were from medicijnkosten.nl and kostenhandleiding CVZ, and the cost of surgical interventions was from Danish diagnosis-related group data (DBC). All costs were in Euros (EUR) and the price year was 2006. Values were adjusted for inflation and discounted at 4% per annum.

Analysis of uncertainty:
Two alternative scenarios were assessed, using E. coli resistance data from the SMART (Gallagher, et al. 2005) and different initial efficacy data. Parameter uncertainty was assessed in one-way sensitivity analyses of all the modelled values. Probabilistic sensitivity analyses were used to measure the uncertainty in all parameters simultaneously, with beta distributions for dose, treatment duration, and efficacy, and triangular distributions for costs. Cost-effectiveness acceptability curves were created to illustrate these results.

Results
In the base case, the initial efficacy for ertapenem was 0.867 at one month, changing to 0.68 at five years compared with 0.812 for piperacillin/tazobactam at one month and 0.558 at five years. The difference in discounted costs favoured ertapenem with an estimated cost saving of EUR 355 (95% CI 480 to 1,205) per patient at one month. At five years, this cost saving increased to EUR 672 (95% CI 232 to 1,617). Similarly, ertapenem compared with piperacillin/tazobactam produced incremental QALYs of 0.08 at one month and 0.17 (95% CI 0.07 to 0.30) at five years.

The results of the one-way sensitivity analyses did not change the conclusions of the base case. The probabilistic sensitivity analyses showed a 94% likelihood that the incremental cost per QALY for ertapenem relative to piperacillin/tazobactam would be lower than EUR 20,000 at one month and over a 99% likelihood at five years.

Authors' conclusions
The authors concluded that ertapenem was superior to piperacillin/tazobactam in the treatment of individuals with community-acquired, complicated, intra-abdominal infections in the Netherlands because it produced cost savings and higher QALYs.

CRD commentary
Interventions:
The two antibiotic treatments were clearly described and they were chosen because there was head-to-head trial evidence for them. Other agents were available, but were not considered due to the lack of head-to-head evidence.

Effectiveness/benefits:
The data on infection clearance rates and the extent of antimicrobial resistance were derived from one key randomised controlled trial (Solomkin, et al. 2003). The validity of the model depends on the quality of this evidence. The mathematical modelling seems to have been valid and was clearly reported. The clinical data were from trials, but the details of how these trials were selected were not given and no systematic review of the evidence was reported. This means that it is not possible to determine if the best available evidence was used. A full assessment of these trials was not possible, given the information presented, and each paper should be consulted to assess its internal validity.

Costs:
The authors did not specifically state the perspective, but the costs appear to have reflected a health provider's perspective. Adverse events and treatment switches were not analysed as the authors assumed that these occurred equally in each arm and that they were few and mild and would therefore not alter the results. This assumption seems reasonable. The costs of the types of resources were provided, but the details of the medical costs, such as the antibiotic unit costs and annual costs, were not reported. This may limit the generalisability of the results to other settings.

Analysis and results:
The decision-analytic model structure was illustrated and all the data were described well, along with their sources. The incremental QALYs were very favourable for ertapenem (and cost-effective), but the differences in costs and health benefits were very small and the results of the one-way sensitivity analysis were not reported. The 95% confidence intervals were also very wide and it is unclear whether the reported differences were economically or clinically important. It is difficult to determine what contributed most to the cost-savings for ertapenem.

Concluding remarks:
The methods were clear and transparent, but the results might have been selectively reported. It is difficult to fully assess the validity of the authors' conclusions.

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