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## Cost-effectiveness study of imipenem/cilastatin versus meropenem in intra-abdominal infections

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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.

### Health technology

The use of imipenem/cilastatin (I/C)(1.5g daily) versus meropenem (3.0g daily) in intra-abdominal infections.

### Type of intervention

Treatment.

### Economic study type

Cost-effectiveness analysis.

### Study population

The study population was 30,000 patients with IAI in Italy.

### Setting

The Study setting was hospital. The economic study was carried out in Italy.

### Dates to which data relate

Effectiveness and resource use data were collected from studies published between 1991 and 1997. Cost data were collected from sources published in 1996 and 1997. The price year was 1997.

### Source of effectiveness data

Effectiveness data were derived from a single study and from a review of the literature.

### Link between effectiveness and cost data

The costing was not undertaken on the same patient sample as that used in the effectiveness analysis. The costing was carried out retrospectively after the effectiveness results were known.

### Study sample

A total of 287 patients were enrolled. Patients were over 18 years old and with IAI (not life-threatening) extending beyond the organ wall and requiring surgical intervention within 24 hours from diagnosis. Exclusion criteria were the need for surgical intervention within 12 hours for traumatic bowel perforation or within 24 hours for perforation of gastroduodenal ulcers, or the administration of an antimicrobial treatment 48 hours before the pre-study evaluation. The trial had a planned enrollment of 100 patients in each treatment group. Power calculations to determine sample size were not reported.

### Study design

The study took the form of a randomised, parallel clinical trial, carried out at 20 surgical centres. Patients were followed up until discharge from the hospital.

### Analysis of effectiveness

It was not clear from the paper whether or not the analysis was based on intention to treat. Primary health outcomes were bacteriological outcome, length of antibiotic treatment, time to defervescence, and the incidence of adverse events. At analysis, groups were comparable in terms of gender, age, and APACHE II score.

### Effectiveness results

The effectiveness results were as follows:

No significant difference was noted in terms of bacteriological outcome (96% I/C, 98% meropenem,  $p=0.676$ ).

Ten of the 165 micro-organisms isolated from 101 patients in the I/C group were resistant to meropenem versus 1 of the 153 cultures isolated from 100 patients in the meropenem group that was found to be resistant to I/C, ( $p=0.02$ ).

There was no significant difference between the groups in clinical outcome (98% I/C versus 95% meropenem,  $p=0.439$ ).

The length of antibiotic treatment was shorter among patients in the I/C group than in the meropenem group (6.7 versus 7.2 days,  $p=0.019$ ).

Time to defervescence was shorter among patients in the I/C group than in the meropenem group (1.83 versus 2.46 days,  $p=0.019$ ).

The incidence of adverse events was low in both groups, but no statistically significant difference was found.

### Clinical conclusions

1.5 g/day of I/C was equivalent to 3 g/day meropenem in clinical and bacteriological outcome, as well as in incidence of side effects.

### Modelling

A decision tree was used to determine the cost-effectiveness of imipenem/cilastatin versus meropenem in intra-abdominal infections.

### Outcomes assessed in the review

The review assessed the number of patients with IAI, the risk of death, and the preparation time for I/C and meropenem.

### Study designs and other criteria for inclusion in the review

Not stated.

### Sources searched to identify primary studies

Not stated.

### Criteria used to ensure the validity of primary studies

Not stated.

### **Methods used to judge relevance and validity, and for extracting data**

Summary statistics from individual studies were used.

### **Number of primary studies included**

At least three additional studies were used in the review.

### **Methods of combining primary studies**

Primary studies were combined using the narrative method .

### **Investigation of differences between primary studies**

Not stated.

### **Results of the review**

A base estimate of 30,000 IAI patients was used. The risk of death was 12.2% for patients with inadequate antibiotic therapy and 5.6% among patients treated adequately. Ten percent of patients who died had previously been treated in the intensive care unit (ICU) for the entire time. The same preparation time was assumed for I/C and meropenem.

### **Measure of benefits used in the economic analysis**

The number of deaths avoided was used as the measure of benefit. Benefits were not discounted given the short time frame of the study (less than 1 year).

### **Direct costs**

Direct costs were not discounted given the short time frame of the study (less than 1 year). Quantities and costs were reported separately. Direct costs related to the costs of diagnostic procedures, drug acquisition and administration, management of drug adverse events and hospitalisation. The estimation of quantities and costs was based on actual data. Costs were collected from the National List for Ambulatory Care and the PIC list. The price year was 1997.

### **Statistical analysis of costs**

No statistical analysis was reported.

### **Indirect Costs**

Indirect costs were not included.

### **Currency**

Italian Lira (L) with L1,800 = US\$1.00.

### **Sensitivity analysis**

To take account of variability and assumptions in the data various sensitivity analyses were conducted on effectiveness estimates and costs. Ranges tested were derived from 95% confidence intervals (CIs) or reasonable estimates around the pint values used in the analysis.

### **Estimated benefits used in the economic analysis**

1.5% of patients would have received inadequate treatment if I/C were used as an empiric therapy in a real-world setting. Six percent of patients would have received inadequate treatment if meropenem were used as an empiric therapy in these patients. The number of deaths amounted to 1,710 with I/C and 1,807 with meropenem.

### **Cost results**

Total costs of I/C treatment in the INHS amounted to L106,874 million (L3.6 million/patient) versus L134,042 (L4.5 million/patient) of meropenem treatment.

Total costs of I/C treatment for a PIC amount to L110,500 million (L3.7 million/patient) versus L135,899 (L4.5 million/patient) of meropenem treatment.

### **Synthesis of costs and benefits**

The I/C option appears to be more effective and less costly than the meropenem option. I/C dominates meropenem treatment over a wide range of all variables.

### **Authors' conclusions**

The treatment of IAI with I/C is shown to be more effective (97 deaths avoided/year) and less costly than with meropenem (with a saving of L27,168 and L25,399 million/year for INHS and PIC, respectively).

### **CRD COMMENTARY - Selection of comparators**

A justification was given for the comparator used, namely that it represented currently available treatment. You, as a user of the database, should decide if these health technologies are relevant to your setting.

### **Validity of estimate of measure of effectiveness**

The analysis was based on a randomised controlled trial, which was appropriate for the study question and the study sample was representative of the study population. Patient groups were shown to be comparable at analysis. The analysis of effectiveness was handled credibly. Additional effectiveness estimates were derived from the literature, although the authors did not report the methods used to conduct the review. The validity of the results was enhanced by sensitivity analyses to account for variability in the estimates.

### **Validity of estimate of measure of benefit**

Estimation of benefits was obtained directly from the effectiveness analysis.

### **Validity of estimate of costs**

Good features of the cost analysis were that all relevant direct cost categories were included; quantities and costs were reported separately; and the price year was reported. Moreover, the validity of the cost analysis was enhanced by appropriate sensitivity analyses over plausible ranges. However, tariffs, which do not represent opportunity costs, were used to proxy prices. The authors noted that the perspectives of the INHS and a PIC did not reveal great differences because the analysis was based on tariffs and not on production costs.

### **Other issues**

The authors did make appropriate comparisons of their findings with those from other studies but did not address the issue of generalisability to other settings. The authors did not present their results selectively. The study considered IAI patients and this was reflected in the authors' conclusions. In terms of generalisability, the authors did not compare other treatment alternatives, such as combination regimens.

### **Implications of the study**

The treatment of IAI with I/C is shown to be more effective (97 deaths avoided/year) and less costly than with meropenem (with a saving of L27,168 and L25,399 million/year for INHS and PIC, respectively). These findings suggest the adoption of the intervention based on extended dominance over the comparator used.

### **Source of funding**

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