A randomized, prospective study measuring outcomes after antibiotic therapy intervention by a multidisciplinary consult team

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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
A timely consult with a multidisciplinary antimicrobial therapy team composed of pharmacists, a clinical microbiologist, and an infectious disease specialist, for hospitalised patients receiving intravenous antimicrobials. A number of methods were used to identify eligible patients: daily screening of culture and susceptibility reports and review of antibiotic orders, chart reviews of patients in the intensive care unit (ICU), review of aminoglycoside and vancomycin levels, drug profiles for all patients with serum creatinine levels above 1.8 mg/dl, and chart reviews of all patients receiving imipenem-cilastatin. Physicians received timely, detailed reviews of relevant microbiologic and clinical data with recommendations for possible optimal antibiotic choices, dosages, and rationales.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population was patients with documented or suspected infectious diseases who could benefit from the intervention. First- and second-phase eligibility criteria were applied. In the first 6 months of the study, the patients whose culture and susceptibility reports indicated significant bacterial resistance in vitro were included in the study. After this period, patients with the following characteristics were also included: inappropriate empiric therapy (antibiotic therapy not believed to cover anticipated organisms); incorrect dosing on the basis of renal function; redundant antibiotics; significant drug interactions, antibiotics that could cause substantial comorbidities with associated disease states (e.g. ascites, congestive heart failure, altered mental status, and malabsorption, and age over 80 years); an expensive regimen; and excessive duration of intravenous antibiotics. The following patients were excluded: those with dangerously inappropriate regimens who ethically could not be randomised to the control arm, those for whom a consultation from one of the coinvestigators had been requested, and those whose charts documented expected death or discharge within 48 hours of the review.

Setting
Hospital. The economic study was carried out in the USA.

Dates to which data relate
Effectiveness and resource use data corresponded to patients enrolled between 1 September 1994 and 10 March 1996. The price year was 1999.

Source of effectiveness data
The evidence for the final clinical outcomes was derived from a single study.
**Link between effectiveness and cost data**
Costing was prospectively undertaken on the same patient sample as that used in the effectiveness analysis.

**Study sample**
Power calculations were not used to determine the sample size. Out of 272 patients initially randomised, the final study sample consisted of 252 consecutive patients receiving suboptimal intravenous antibiotics identified by the clinical pharmacist. 127 were randomly assigned to the intervention group (mean (SD) age of 66 (19) years) and 125 to the control group (mean (SD) age of 69 (17) years). 20 randomised patients (9 control and 11 intervention) were excluded as they were considered not to be eligible for the analysis.

**Study design**
This was a randomised controlled study, carried out in a single centre. The duration of the follow-up was until discharge or in-hospital death. Loss to follow-up was not reported except for the 20 randomised patients (9 control, 11 intervention) who were excluded from the analysis. Eligible patients were blindly randomised to the intervention or control group. Patients were stratified by infectious disease category (IDC). Within IDC strata, randomisation was carried out in blocks of four (two to each study arm).

**Analysis of effectiveness**
The principle used in the analysis of effectiveness appears to have been treatment completers only. The primary end point of the study was length of stay after randomisation (LOS2). Other health outcomes were survival, types of intervention (simple versus complex consults, and empiric versus culture-specific therapy), and physician acceptance. The study groups were comparable in terms of severity of illness indicators, infection type, and time from admission to randomisation. Weibull regression was used to compare intervention and control group medians while controlling for baseline variables characterising severity of illness (age, ventilator dependency, mental status, infectious disease category, ambulatory status). Time-specific mortality rates were compared between arms, and differences were compared between various strata using Cox proportional hazards regression.

**Effectiveness results**
The median length of stay after randomisation for the control group was 9 days and for the intervention group was 5.7 days, (3.3 day difference, p=0.0001). Intervention LOS2 remained significantly lower overall after adjusting for the complexity of interventions, and was significantly lower for both complex (p=0.018) and simple interventions (p=0.001). After adjusting for the empiric status of interventions, intervention LOS2 remained significantly lower overall and also in both empiric and culture-driven consults, (p=0.008). Fifteen (12%) and eight patients (6.3%), respectively, died, although the time specific mortality risk was not significantly different when length of post-randomisation follow-up and time to death were taken into account. Complex and simple interventions or empiric status of the consults did not affect the difference in mortality rates between the groups. Physician acceptance of suggestions was 89%.

**Clinical conclusions**
It is unlikely that factors other than the interventions were responsible for the improved outcomes, because the study was randomised and the severity-of-illness measures of the two groups were similar. The large therapeutic benefit observed was the result of patient selection, physician compliance, and the comprehensive, multidisciplinary nature of consultations.

**Measure of benefits used in the economic analysis**
No summary benefit measure was identified in the economic analysis, and only separate clinical outcomes were reported separately.
Direct costs
Costs were not discounted due to the short time frame of the cost analysis. Some quantities were reported separately from the costs and cost items were reported separately. Cost analysis covered the costs of antibiotics, laboratory, radiology, non-ICU stay, ICU stay, room and board, and costs of implementing the interdisciplinary approach (which were calculated based on team member salaries plus benefits and the amount of time each member spent providing consult services). The perspective adopted in the cost analysis was that of the hospital and the patient. Charge data were used to represent the costs to patients. A cost-to-charge ratio was used to convert charges into actual hospital costs. The source of charge data was patient billing information stored in the hospital's information system. The price year was 1999. The charges associated with other types of drugs or services such as physical and respiratory therapy, physicians' fees, and specific equipment and procedure were not included in the cost analysis in order to simplify the scope of cost measurements.

Statistical analysis of costs
Weibull regression was used to compare all intervention and control group median costs. Within that framework the ratio of the intervention group median to the control group median and the standard error of the ratio were estimated and used to generate 95% ratio confidence bounds.

Indirect Costs
Not included.

Currency
US dollars ($).

Sensitivity analysis
No sensitivity analysis was performed.

Estimated benefits used in the economic analysis
Not applicable.

Cost results
The Weibull median (SE) total cost was $9,153 ($761) in the intervention group versus $12,207 ($1,042) in the control group. Median patient charges for radiology, laboratory, pharmacy, and room were reduced by $4,404 per intervention, and median hospital costs were reduced by $2,642 per intervention.

Synthesis of costs and benefits
Costs and benefits were not combined since the intervention was the dominant strategy.

Authors' conclusions
A multidisciplinary antimicrobial therapy team can be a useful information source for physicians, can improve outcomes in hospitalised patients receiving intravenous antimicrobials, and can result in substantial cost savings.

CRD COMMENTARY - Selection of comparators
The choice of the comparator (the strategy of no intervention by the multidisciplinary team) allowed the active value of the treatment to be evaluated.
Validity of estimate of measure of effectiveness
The effectiveness results are likely to be internally valid given the randomised nature of the study design and the adjustments made for the effects of potential confounders. However, some of the study patients were excluded from the analysis after being randomised, and this may have introduced bias into the study. The study groups were found to be comparable in terms of severity of illness indicators, infection type, and time from admission to randomisation. The patient sample appears to have been representative of the study population (patients with a wide range of IDC). Physician education culminating in improved institutional antimicrobial therapy was noted as one of the benefits of the intervention which was not formally measured in the study.

Validity of estimate of measure of benefit
The authors did not derive a measure of health benefit. The study may therefore be regarded as a cost-consequences analysis.

Validity of estimate of costs
Some quantities were reported separately from the costs. Adequate details of the methods of cost estimation were given. Using a cost-to-charge ratio may strengthen the internal and external validity of the cost results. The effects of different procedures on indirect costs (productivity loss) were not addressed. Cost results may not be generalisable to other settings or countries. It was noted that the actual cost of adopting the multidisciplinary approach could be seen as zero by reallocating the available resources.

Other issues
The authors' conclusions appear to be justified given uncertainties in the data. The issue of generalisability to other settings or countries was not addressed although some comparisons were made with other studies. The degree to which the study sample was representative of the study population was not discussed.

Implications of the study
The high rate of acceptance by physicians of suggestions from the multidisciplinary team makes this approach one of the most attractive methods for improving antimicrobial therapy described so far. This study was not designed to show a mortality reduction; the total number of deaths was too small. Further study of the applied multidisciplinary team concept would be necessary for that.

Source of funding
None stated.

Bibliographic details

PubMedID
10600085

Indexing Status
Subject indexing assigned by NLM

MeSH
Aged; Anti-Bacterial Agents /economics /therapeutic use; Communicable Diseases /drug therapy /economics; Cost of Illness; Economics, Hospital; Humans; Infusions, Intravenous; Length of Stay; Patient Care Team; Prospective Studies; Survival Rate; Treatment Outcome