Clinical and economic considerations in the treatment of acute exacerbations of chronic bronchitis

Destache C J, Dewan N, O'Donohue W J, Campbell J C, Angelillo V A

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
Antibiotic therapy in the treatment of acute exacerbation of chronic bronchitis (AECB) in patients with a diagnosis of chronic obstructive pulmonary disease (COPD) and chronic bronchitis episodes. The empirical antibiotic treatments selected were classified as first-line agents including amoxycillin, co-trimoxazole, tetracyclines, and erythromycin; second-line agents including cephradine, cefuroxime, cefaclor, and cefprozil; and third-line agents consisting of co-amoxiclav, azithromycin, and ciprofloxacin.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Patients (aged over 36 years) with a diagnosis of COPD and chronic bronchitis episodes, and signs or symptoms of acute exacerbation.

Setting
Secondary care. The economic study was carried out in the USA.

Dates to which data relate
Effectiveness and resource use data corresponded to patients treated between January 1990 and January 1994. The price year was 1994.

Source of effectiveness data
Effectiveness data were derived from a single study.

Link between effectiveness and cost data
Costing was retrospectively performed on the same patient sample as that used in the effectiveness analysis.

Study sample
Power calculations were not used to determine the sample size. The study sample consisted of 60 patients with a mean (SD) age of 58.3 (31.1) years, who met the inclusion/exclusion criteria (selected from a total of 285 patient medical records), and who had 224 documented episodes of AECB. The first-line group comprised of the medical records of 100 AECB episodes (amoxycillin (n=44), co-trimoxazole (n=45), tetracyclines (n=3), and erythromycin (n=8)); the
second-line group had 67 AECB episodes (cephradine (n=3), cefuroxime (n=23), cefaclor (n=39), and cefprozil (n=2)); and the third-line group consisted of 57 AECB episodes (co-amoxiclav (n=15), azithromycin (n=22), and ciprofloxacin (n=20)).

**Study design**
This was a retrospective cohort study, carried out in a single centre. The duration of the follow-up in terms of mean (SD) time until next AECB treatment ranged from 17.1 (22) weeks to 34.3 (35.5) weeks. Loss to follow-up was not reported. The consensus of resident pulmonologists was the main reference source for the classification of the antimicrobial agents.

**Analysis of effectiveness**
The principle (intention to treat or treatment completers only) used in the analysis of effectiveness was not explicitly specified. The clinical outcome measures were failure rate within 14 days of initiation of antimicrobial therapy, the number of cases hospitalised within 2 weeks for failed patients, the duration of antibiotic therapy, and the time until the next AECB treatment. The antibiotic groups were reported to be comparable in terms of vital signs, pulmonary function tests, and spirometry. Severity of disease, as measured by pulmonary function tests (PFTs) or spirometry, was treated as the covariate in the analysis of variance (ANOVA).

**Effectiveness results**
The effectiveness results were as follows:

Failure rate within 14 days of initiation of antimicrobial therapy for the whole study sample was 15.2% (34 of 224). This was broken down into 19% (19 of 100) for the first-line agents, 16.4% (11 of 67) for the second-line agents, and 7% (4 of 57) for the third-line agents (p<0.05 for the difference between first-line and third-line agents).

The total hospitalisation rate within 2 weeks for failed patients was 76% (26 of 34). This was broken down into 18 cases receiving first-line agents (18% in terms of the first-line group's sample size), 5 cases in the second-line group (7% in terms of the second-line group's sample size), and 3 cases receiving third-line agents (5% in terms of the third-line group's sample size) (p<0.02 for the difference between first-line and third-line agents and p<0.054 for the difference between second-line and third-line agents).

The first-line group had a mean (SD) duration of antibiotic therapy of 8.9 (3.3) days of therapy versus 8.3 (2.3) days in the second-line group, and 7.5 (2.5) days in the third-line group (p<0.02 for the difference among the three groups).

The corresponding values in terms of time until the next AECB treatment were 17.1 (22) weeks in the first-line group, 22.7 (30) weeks in the second-line group, and 34.3 (35.5) weeks, in the third-line group (p<0.005 for the difference among the three groups).

**Clinical conclusions**
The use of second- or third-line antibiotics in the outpatient setting could decrease the number of hospitalisations and the degenerative disease process.

**Measure of benefits used in the economic analysis**
No summary benefit measure was identified in the economic study, and only separate clinical outcomes were reported.

**Direct costs**
Costs were not discounted, although they appear to have been incurred over a 4-year period. Quantities were reported separately from the costs in terms of days of therapy, and the number of office visits. Cost items were partially reported separately. The cost analysis covered the costs of laboratory work, radiology, physician office visits, and prescriptions.
for each episode. The perspective adopted in the cost analysis was not explicitly specified. The source of cost data was a hospital financial office. Charges were used to represent the true costs. The average consumer price index was used to adjust the costs to the financial year adopted for the study. The date of the price data was 1994. The cost of an outpatient procedure (such as bronchoscopy) was not taken into account in the cost analysis.

**Statistical analysis of costs**
One-way ANOVA was used to compare the study groups in terms of pharmacy and hospitalisation costs.

**Indirect Costs**
Not considered.

**Currency**
US dollars ($).

**Sensitivity analysis**
Not conducted.

**Estimated benefits used in the economic analysis**
Not applicable.

**Cost results**
The first-line group had an average (SD) total charge of $942 ($2,173), versus $563 ($2,296) for the second-line group and $542 ($1,946) for the third-line group.

**Synthesis of costs and benefits**
Costs and benefits were not combined since the use of the third-line agents was the dominant strategy.

**Authors' conclusions**
The use of third-line antimicrobials, co-amoxiclav, ciprofloxacin or azithromycin, significantly reduced the failure rate and need for hospitalisation, prolonged the time between AECB episodes, and showed a lower total cost for the management of AECB.

**CRD COMMENTARY - Selection of comparators**
No specific alternative was chosen as the comparator. The three groups of antibiotics represented the common practice in the authors' setting.

**Validity of estimate of measure of benefit**
The internal validity of the effectiveness results cannot be guaranteed due to the biases inherent in the retrospective observational study design and the small sample size. The study may be regarded as a cost-consequences analysis.

**Validity of estimate of costs**
Quantities of resource use were partially reported separately from the costs. Adequate details of methods of cost estimation were given. Charge data were used as opposed to true costs. Discounting was not applied although it would appear to have been appropriate. Only hospital costs were included in the analysis and outpatient procedures were
omitted since, as the authors reported, it was not possible to gather the relevant information. Also, costs to patients and others in society could have been considered. The cost data may not be generalisable to other settings or countries, as pointed out by the authors.

**Other issues**
In view of the lack of a prospective study design, sensitivity analysis, and the inherent limitations of the cost estimates, the results should be treated with some caution. The issue of generalisability to other settings or countries was not fully addressed, although appropriate comparisons were made with other studies.

**Implications of the study**
Prospective studies are needed to confirm these findings.

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**Other publications of related interest**

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