Equal effectiveness of older traditional antibiotics and newer broad-spectrum antibiotics in treating patients with acute exacerbations of chronic bronchitis

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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 study compared the effectiveness and costs of different antibiotic therapies for the treatment of acute exacerbations of chronic bronchitis (AECB). Antibiotics were categorised as either first- or second-line agents. First-line agents were considered to be the older traditional antibiotics (amoxicillin, cephalexin, doxycycline, erythromycin and sulfamethoxazole-trimethoprim). Second-line agents were considered to be newer broad-spectrum antibiotics (amoxicillin-clavulanate, azithromycin, cefuroxime, clarithromycin, levofloxacin and ofloxacin). The first-line antibiotics were further divided into two groups according to their effectiveness against organisms most commonly associated with respiratory tract infections. Those with partial coverage were amoxicillin, cephalexin and erythromycin, while those with full coverage were doxycycline and sulfamethoxazole-trimethoprim. Three groups were compared.

In group 1 patients with AECB were treated with first-line antibiotics having partial coverage against organisms associated with AECB.

In group 2 patients with AECB were treated with first-line antibiotics with full coverage against organisms associated with AECB.

In group 3 patients with AECB were treated with newer broad-spectrum antibiotics.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients who had a clinical diagnosis of chronic obstructive pulmonary disease (COPD) and who received outpatient antibiotic therapy. Patients were excluded from the study if they had no documented COPD, received an antibiotic that was not used for an AECB, or received antibiotic therapy for an AECB while hospitalised. They were also excluded if they had a standing prescription for self-administered antibiotics, had no pulmonary function tests within the past 3 years, or had an AECB within 3 months before their first visit. Other criteria for exclusion were radiographic evidence of pneumonia, documented acquired immunodeficiency syndrome, New York Heart Association Class IV heart failure, clinical or laboratory data suggestive of atypical pathogens, tuberculosis, Pneumocystis carinii pneumonia, active lung cancer, lymphoma, leukaemia, ongoing dialysis, or a lack of documentation of antibiotic use in the medical records. Patients were identified from the medical centres’ pharmacy database.

Setting
The setting was secondary care. The economic study was conducted in Pittsburgh USA.
Dates to which data relate
The effectiveness data related to the period between January 1999 and December 1999. The price year was not reported.

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

Link between effectiveness and cost data
The costing was undertaken retrospectively on the same population sample as that used in the effectiveness study.

Study sample
Potential patients were identified from the pharmacy database and their medical records, and pulmonary function laboratory results were reviewed. No power calculations were performed to determine the sample size. The authors acknowledged that the small sample size was a limitation of their study.

A total of 121 patients were included in the study. They had 170 documented AECB episodes. Of these, 48 were treated with first-line antibiotics that have partial coverage, 87 were treated with first-line antibiotics that have full coverage, and 35 were treated with second-line antibiotics.

Of the 602 patients initially screened, 431 were excluded. The majority of exclusions resulted from no documentation of antibiotic use in medical records (101) or no documentation of COPD (99). All of the patients included in the study were male. The mean age of the patients was 65.14 (+/- 9.06) years and 77% were white. The authors presented demographic and clinical characteristics for each antibiotic group.

Study design
The study was a retrospective cohort study that was carried out in a single centre. The duration of follow-up was 12 months from the time of the patient's initial AECB.

Analysis of effectiveness
The primary outcome was the treatment failure rate. This was defined as the number of episodes that failed to respond to antibiotic therapy within 2 weeks of the AECB. Other outcomes were the need for hospitalisation within 2 weeks of initial outpatient treatment, and the time between episodes of AECB. The groups were comparable in terms of age, gender, ethnicity, whether current or former smoker, and clinical characteristics such as the severity of COPD and co-morbidities.

Effectiveness results
There were no significant differences among the three antibiotic groups in failure rate, hospitalisation rate, or time until subsequent AECB.

The failure rate was 10.3% for those treated with first-line antibiotics and 8.6% for those treated with second line antibiotics. The difference was not statistically significant, (p=0.84). The failure rate for those treated with first-line antibiotics was 18.8% for antibiotics with partial coverage and 5.7% for those with full coverage. There was no significant difference, (p=0.13).

The hospitalisation rate was 5.2% among those treated with first-line antibiotics and 2.9% among those with second-line antibiotics. This difference was not statistically significant. Among those hospitalised after initial treatment with first-line antibiotics, 5 were initially treated with antibiotics with partial coverage (10.4% hospital rate) and 2 were treated with antibiotics with full coverage (2.3% hospitalisation rate). There was no significant difference between hospitalisation rates, (p=0.14).
A subsequent AECB occurred, on average, 33.4 (+/- 19.3) weeks after treatment with first-line antibiotics, 36.4 (+/- 19.3) weeks for antibiotics with partial coverage and 33.1 (+/- 19.8) weeks for those with full coverage. Among those treated with second-line antibiotics the next AECB occurred, on average, 32.9 (+/- 19.6) weeks later. There was no significant difference in time to the next AECB between first- and second-line antibiotics, (p=0.73), or among the three groups when analysed separately, (p=0.44).

Clinical conclusions
The authors found no difference in efficacy between older traditional antibiotics and newer broad-spectrum antibiotics. Although not statistically significant, a trend towards greater failure rates and the need for hospitalisation was evident among first-line antibiotics that had partial coverage.

Measure of benefits used in the economic analysis
No summary measure of benefit was used in the analysis. In effect, a cost-consequences analysis was performed.

Direct costs
Discounting was not undertaken, but this was appropriate given the short time-frame of the study. The resource quantities and the costs were reported separately. The quantity/cost boundary adopted was that of the hospital where the study was set. The direct costs included pharmacy costs, cost for physician or emergency room visits, laboratory and radiology costs, and the average hospitalisation cost. Inpatient costs were based on the institution's average cost for an AECB hospitalisation. Outpatient costs were determined by summing all the costs of all laboratory work, radiology, physician or emergency care visits, and pharmacy costs for each episode. The pharmacy costs included the drug acquisition cost and the pharmacy dispensing fee. The resource quantities were derived from patient medical records collected for 12 months from the time of the initial AECB. The study reported the average pharmacy costs and the average total costs. No price year was stated.

Statistical analysis of costs
The costs were treated stochastically, with mean costs and confidence intervals being presented. Statistical tests of significance were performed to compare the average cost of treatment across the groups. The authors noted that the small sample size was a limitation of the study.

Indirect Costs
The indirect costs were not included in the analysis.

Currency
US dollars ($).

Sensitivity analysis
No sensitivity analysis was undertaken.

Estimated benefits used in the economic analysis
Due to the cost-consequences approach, the reader is referred to the 'Effectiveness Results' section.

Cost results
Over 12 months, the average pharmacy costs were $3.18 (+/- 0.64) for first-line antibiotics with partial coverage, $3.00 (+/- 0.48) for first-line antibiotics with full coverage, and $36.70 (+/- 16.29) for second-line antibiotics. The difference between first- and second-line antibiotics was significant, (p<0.001).
Overall, first-line antibiotics with full coverage had the lowest average total cost at $227.75 (+/- 1,422.21). First-line antibiotics with partial coverage had an average cost of $1,024.14 (+/- 2,947.73) and second-line antibiotics had an average total cost of $328.21 (+/- 615.59). The difference between first- and second-line antibiotics was not significant, (p=0.58). When all three groups were analysed there was no significant difference, (p=0.22).

**Synthesis of costs and benefits**
The study was, in effect, a cost-consequences analysis. Therefore, the costs and benefits were not combined.

**Authors’ conclusions**
There was no difference in outcome between older traditional antibiotics with adequate coverage against organisms associated with acute exacerbations of chronic bronchitis (AECB) and newer-broad spectrum antibiotics. The findings of the study supported the concept that the use of antibiotics with only partial coverage against organisms associated with AECB may be associated with poorer outcomes and, ultimately, higher overall costs.

**CRD COMMENTARY - Selection of comparators**
The comparator was chosen to reflect current practice in the authors’ setting. The reader should consider whether this comparator reflects current practice in their own setting.

**Validity of estimate of measure of effectiveness**
The study was based on a retrospective cohort analysis. This design is open to the impact of bias and confounding factors. In addition, the cohort was highly selective of the study population, as only patients with records with sufficient documentation could be included. The authors acknowledged that the small sample size also represented a weakness of the study. The internal validity of the analysis was limited because power calculations were not performed and the power of the study is likely to have been low. The authors also noted the limitation of basing the estimates of effectiveness on documented evidence, since the clinical data were not collected in a uniform manner. The patient groups were shown to be comparable at baseline analysis in terms of clinical characteristics, although the authors acknowledged that there might have been other unmeasured factors that may have been different across treatment groups (e.g. prescribing clinicians or speciality type). The analysis, however, was handled credibly although no analysis of potential biases or confounding factors was undertaken.

**Validity of estimate of measure of benefit**
The authors did not derive a summary measure of health benefit and the study was, in effect, a cost-consequences analysis. Therefore, the comments in the "Validity of measure of estimate of effectiveness" field (above) apply. The lack of a generic benefit measure means that the results cannot be compared with those from studies of other health technologies.

**Validity of estimate of costs**
The authors limited their analysis to direct costs. The perspective adopted in the economic analysis was that of the hospital. As such, all the categories of cost relevant to the hospital perspective, as well as all the relevant costs for each category, were included in the analysis. The costs and the quantities were reported separately. A statistical analysis of the prices was not conducted. The date to which the costs referred was not reported and this hinders reflation exercises. Discounting was not carried out, which was appropriate given the short follow-up period.

**Other issues**
The authors made appropriate comparisons of their results with those of other studies. However, the issue of generalisability to other settings was not addressed. The authors do not appear to have presented their results selectively, although it should be noted that the study included only male patients but the conclusions were generalised across all patients.
Implications of the study
The authors acknowledged the limitations of their study. They stated that an "appropriately powered, prospective, clinical trial" is required to investigate the efficacy and costs of various antibiotics for the treatment of AECB.

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