An economic and outcomes assessment of first-line monotherapy in the treatment of community-acquired pneumonia within managed care

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
Four first-line monotherapy options for the treatment of community-acquired pneumonia (CAP) were examined. The options were erythromycin (ERY), azithromycin (AZI), clarithromycin (CLA) and levofloxacin (LEV).

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised individuals aged 18 years or older with a positive diagnosis for CAP. Patients with a positive diagnosis for human immunodeficiency virus were excluded.

Setting
The setting was a hospital. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness and resource use data were gathered from January 1995 to April 2002. The price year was not reported.

Source of effectiveness data
The effectiveness evidence was derived from a single study.

Link between effectiveness and cost data
The costing was carried out retrospectively on the same sample of patients as that used in the clinical study.

Study sample
Power calculations for the clinical outcomes were not performed, but a large sample of patients was used. The patients were identified from a retrospective analysis of the database of the MCO, which covered approximately three million lives. The inclusion criteria were:

- individuals aged 18 years or older;
- positive diagnosis for CAP based on the ICD-9-CM codes 481-483.8 and 484.8-486 relating to specified or non
specified bacterial pneumonia;

initial monotherapy with ERY, AZI, CLA or LEV on the first ambulatory presentation with CAP;

no interruption in eligibility in the claims database for the 6 months prior to CAP diagnoses and 6 months after CAP diagnoses;

no other antimicrobial 2 weeks preceding the first diagnoses of CAP;

no inpatient care for a CAP diagnosis for 6 months prior to diagnosis; and

no hospital admission within 2 days after an ambulatory diagnosis of CAP.

Overall, a sample of 1,952 patients was identified. There were 228 patients (47.8% men) in the ERY group, 910 (41.1% men) in the AZI group, 532 (44.6% men) in the CLA group and 282 (45.8% men) in the ERY group. The mean age of the patients was 44.4 (+/- 14.2) years in the ERY group, 45.4 (+/- 13.9) years in the AZI group, 45.9 (+/- 13.4) years in the CLA group and 51.0 (+/- 14.2) years in the ERY group.

**Study design**

This was a retrospective cohort study that was carried out in several medical centres. The length of follow-up was 6 months after first CAP hospital admission. However, data related to the 6 months prior to CAP diagnosis were also considered. Thus, data for one year were gathered. No patient was lost to follow-up as only patients with complete data were included.

**Analysis of effectiveness**

All of the patients included in the initial study sample were accounted for in the analysis of effectiveness. The primary outcome measure was success rate, which was defined as both no hospitalisation subsequent to CAP and no second antibiotic added. At baseline, the study groups were significantly different in terms of age, the proportion of patients older than 50 years, the proportion of patients with one or more co-morbid conditions, co-morbidities of pulmonary and heart disease, second antibiotic added, and treatment success. A logistic regression was conducted using treatment success as a dependent variable. The independent variables were pre-treatment costs, initial treatment group, age, gender, co-morbidities and chronic disease score (CDS).

**Effectiveness results**

For the whole sample, treatment success rates were very high across all treatment groups (95.8%), the use of second antibiotics was infrequent (2.3%), and hospitalisation rates were low (2.0%).

The success rate without controlling for the patients' characteristics was 96.5% with ERY, 94.6% with AZI, 97.9% with CLA and 95% with LEV.

The regression analysis found statistically significant associations between treatment success with CDS, (p<0.001), gender, (p=0.027), and active cancer co-morbidity, (p=0.033).

No statistically significant differences in treatment success between ERY, AZI or CLA compared with LEV were observed.

**Clinical conclusions**

The effectiveness analysis showed no significant differences in terms of success rates among treatment options.

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

Since there was no statistically significant difference in success rate between the groups, no summary benefit measure
was used. In effect, a cost-minimisation analysis was performed.

**Direct costs**

The economic analysis was performed from the perspective of the MCO. Thus, only direct medical costs were included in the analysis. These were estimated from the longitudinal patient-level dataset with combined medical and pharmaceutical claims. The health services considered in the economic evaluation were resources used to treat CAP on an outpatient, inpatient and emergency department basis. In particular, provider and visit costs, medication costs, laboratory costs, and other costs incurred based upon the place of service were included. The unit costs were not presented separately from the quantities of resources used because the costs were reported using macro-categories. The price year was not reported. Discounting was not relevant since the costs were estimated for a 1-year timeframe.

**Statistical analysis of costs**

The costs were presented as median values, owing to their skewed distribution. Non-parametric analyses were carried out to test the statistical significance of differences in the total costs. Power calculations were carried out to detect statistically significant differences in the costs on the basis of prior analyses, and a minimum sample of 1,100 patients was required. A general linear regression was used to assess the difference between the treatment groups, with total costs as the dependent variable and the same independent variables as those used in the regression analysis for success rate.

**Indirect Costs**

The indirect costs were not included in the economic evaluation.

**Currency**

US dollars ($).

**Sensitivity analysis**

No sensitivity analyses were performed.

**Estimated benefits used in the economic analysis**

See the 'Effectiveness Results' section.

**Cost results**

The total median costs without controlling for the patients’ characteristics or risk factors were $68 (mean 105; range: 0 - 1,329) with ERY, $102 (mean 215; range: 0 - 13,499) with AZI, $132 (mean 373; range: 0 - 72,159) with CLA and $162 (mean 480; range: 0 - 10,561) with LEV. Differences between the groups were statistically significant, (p<0.001).

The regression analysis showed that significant predictors of total costs were pre-treatment costs, (p<0.001), age, (p=0.011) and treatment groups.

ERY, (p<0.001), AZI, (p<0.001) and CLA, (p=0.015) were associated with significantly lower total treatment costs in comparison with LEV. In particular, ERY was associated with total costs that were 92.7% lower than for LEV. The costs were 48.7% lower with AZI and 21.3% lower with CLA.

Several sub-group analyses were carried out.

A sub-group analysis was carried out among patients aged older than 50 years, patients with coexisting illnesses, and patients with a CDS of at least 2.5. The results of the regression analysis showed that the predictors of the total costs were:
pre-treatment costs, ERY and AZI in patients over 50 years of age (n=712);
pre-treatment costs, CDS, ERY and AZI in patients with one or more co-morbid conditions (n=816); and
pre-treatment costs, age, CDS, ERY and AZI in patients with a CDS of at least 2.5 (n=759).

When ERY was excluded from the comparison in patients with a CDS of at least 2.5, the predictors of the total costs were pre-treatment costs, CDS, age and AZI.

When ERY was excluded from the comparison, the predictors of the total costs were pre-treatment costs, age, AZI and CLA.

**Synthesis of costs and benefits**

A synthesis of the costs and benefits was not relevant because a cost-minimisation analysis was carried out.

**Authors' conclusions**

All monotherapy options for community-acquired pneumonia (CAP) were equally effective in terms of success rate. However, significantly lower costs were observed with erythromycin (ERY), azithromycin (AZI) and clarithromycin (CLA) in comparison with levofloxacin (LEV). Among only newer antibiotics, both AZI and CLA were associated with lower total costs than LEV and CLA. Also among newer agents, in the sub-group of patients with a chronic disease score (CDS) above the sample's mean, AZI was associated with lower costs in comparison with LEV.

**CRD COMMENTARY - Selection of comparators**

The rationale for the choice of the comparators was clear. The four treatments under examination were extensively used, either as single-agent or combination therapy, for the treatment of CAP in adults. LEV was considered as the basic comparator, but no justification was provided for this choice. The authors stated that other therapeutic approaches for CAP or other antimicrobial agents were not considered. You should decide whether they are valid comparators in your own setting.

**Validity of estimate of measure of effectiveness**

The effectiveness data came from a retrospective review of the database of the MCO. The use of administrative data has several drawbacks, such as the limited clinical information available for each patient, the potential impact of selection bias and confounding factors, the retrospective nature and the risk of misdiagnosis of CAP. However, such limitations should be weighted against the main advantage, the large number of patient-level data available. The study groups were not well matched at baseline, thus a regression analysis was required to account for possible selection bias and to assess the impact of treatment options, patients' characteristics, and risk factors. The length of follow-up appears to have been appropriate. A large sample of patients was used, although power calculations were performed only for the cost outcomes.

**Validity of estimate of measure of benefit**

No summary benefit measure was used in the analysis because a cost-minimisation analysis was conducted. Please refer to the comments in the 'Validity of estimate of measure of effectiveness' field (above).

**Validity of estimate of costs**

Only direct medical costs were included in the economic evaluation because the perspective of an MCO was adopted. Since the costs came from claims records, only macro-categories of costs were reported, and a detailed breakdown of the items was not provided. Statistical analyses of the costs were performed because of the non-normal distribution of the data. Further, several sub-group analyses were performed. However, the cost estimates were specific to the study setting and no sensitivity analyses were carried out. The period during which the costs were gathered was reported, but
the price year was not given, which limits the possibility of performing reflation exercises. A limitation of the analysis was the fact that it was not possible to distinguish between the types of hospital service available (intensive care versus other inpatient locations).

Other issues
The authors compared their findings with those from a published study that showed different cost results. However, the authors stated that several factors might have impacted on the cost of care. In terms of the external validity of the analysis, the authors noted that their findings might not be generalisable to other health systems with different cost structures and patient populations. Sensitivity analyses were not performed, which further limits the external validity of the study.

Implications of the study
The study results suggested that ERY, AZI and CLA are associated with lower costs than LEV, thus health plans should consider whether the findings of the current study are applicable to their patient populations. The authors noted that future research should assess resistance, patient adherence, dosing or treatment duration, and physical or laboratory findings. Further, prospective studies should be performed to compare the costs and outcomes among all first-line treatment options for CAP.

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