Cost-effectiveness analysis of oral N-acetylcysteine as a preventive treatment in 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
Oral N-acetylcysteine (NAC) as a preventive treatment against frequent exacerbations (AECBs) in chronic bronchitis.

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population consisted of patients with chronic bronchitis.

Setting
The study setting was hospital. The economic study was carried out in Switzerland.

Dates to which data relate
Effectiveness and resource use data were collected from studies published between 1976 and 1996. Cost data were collected from a 1998 source. The price year was 1998.

Source of effectiveness data
Effectiveness data were derived from a review of the literature.

Modelling
A decision analytic model was used to determine the cost-effectiveness of NAC.

Outcomes assessed in the review
The review assessed the effect of NAC on reducing AECBs, sick leave, hospitalisation, compliance, and the management of AECBs.

Study designs and other criteria for inclusion in the review
The review included prospective, double-blind, placebo-controlled trials.

Sources searched to identify primary studies
MEDLINE was searched, complemented with studies mentioned in references and cross-checked with the producer of NAC.

Criteria used to ensure the validity of primary studies
Not stated.

Methods used to judge relevance and validity, and for extracting data
Not stated.

Number of primary studies included
Nine trials and five other studies were included in the review.

Methods of combining primary studies
Meta-analysis was used to combine primary studies. Data were pooled by the means of Mantel-Haenszel-Peto's method.

Investigation of differences between primary studies
Not stated.

Results of the review
The results of the review were as follows:

The diagnostic procedure consisted of biological tests in 59%, X-rays in 65% and pulmonary function tests in 45% of patients.

Bronchodilators were used in 89% of AECBs, corticosteroids in 24% and others in 25%.

AECB rate was 25.5% for placebo versus 16.1% for NAC (difference: 9.4%; 95% CI: 5.8 - 12.9).

The number of AECBs per patient in a 6-month period was 0.97 (0.80 - 1.13) AECBs with NAC, and 1.53 (1.32 - 1.73) AECBs with placebo, (p<0.001).

The percentage of days sick per month was 5.3% (95% CI: 2.8 - 8.0) for placebo and 3.6% (95% CI: 1.4 - 5.8) for NAC.

Hospitalisation was 3.5% in the placebo group versus 1.2% in the NAC group, (p=0.054).

Study interruptions due to chest illness or bronchopneumonia were reported in 2.9% of patients in the placebo group and 2.2% in the NAC-treated group.

The death rates were 0.7 in the placebo group and 0.6% in the NAC-treated group.

The rate of satisfactory compliance was 80% in the NAC-treated population.

Measure of benefits used in the economic analysis
The number of AECBs prevented was used as the measure of benefits.

Direct costs
Direct costs were not discounted due to the short time horizon of the study (less than 1 year). Quantities and costs were
reported separately. Direct costs related to the costs of NAC treatment, the management of an AECB, and hospitalisations. The quantity/cost boundary adopted was that of the health service. The estimation of quantities and costs was based on actual data. Costs were collected from an insurance agency and a drug reference book. The price year was 1998.

**Statistical analysis of costs**
No statistical analysis was carried out.

**Indirect Costs**
Indirect costs were not discounted due to the short time horizon of the study (less than 1 year). Quantities and costs were reported separately. Indirect costs related to the costs of working days lost by the patient. The quantity/cost boundary adopted was that of society. The estimation of quantities and costs was based on actual data. The price year was 1998.

**Currency**
Swiss Francs (SFr).

**Sensitivity analysis**
Univariate and multivariate sensitivity analyses were performed on the number of AECBs, cost of medications, and percentage of hospitalisations.

**Estimated benefits used in the economic analysis**
NAC therapy would prevent approximately 0.6-0.7 AECBs for 6 months.

**Cost results**
A patient with chronic bronchitis treated with NAC generates direct costs of SFr 700 compared with SFr 869 in the placebo patient, or SFr 945 in the non-compliant patient.

Indirect costs were SFr 779 in the NAC patient and SFr 1,324 in the placebo patient.

Total costs were SFr 1,479 in the NAC patient and SFr 2,193 in the placebo patient.

**Synthesis of costs and benefits**
NAC therapy would reach cost neutrality if it prevented 0.3 AECBs per patient.

**Authors' conclusions**
Treating chronic bronchitis patients with NAC during the winter months is cost-effective both from the payer's and a social point of view.

**CRD COMMENTARY - Selection of comparators**
A justification was given for the comparator used, namely a placebo. You, as a user of the database, should decide if this health technology is relevant to your setting.

**Validity of estimate of measure of effectiveness**
It appears that a systematic review of the literature was undertaken, and the methodology and conduct of the review was
sound and well reported. Effectiveness estimates were combined using meta-analysis and appropriate techniques. The effectiveness results are, therefore, likely to have good validity, which was also enhanced due to the sensitivity analyses undertaken.

**Validity of estimate of measure of benefit**
The estimation of benefits was obtained directly and appropriately from the effectiveness analysis.

**Validity of estimate of costs**
Good features of the cost analysis were that all relevant direct and indirect cost categories were included, sensitivity analyses were conducted on costs, the price year was reported, and quantities and costs were reported separately. However, charges were used to proxy prices and this latter point tends to limit the generalisability of the cost results.

**Other issues**
This was a well conducted and thorough study. Examining the societal perspective, which is appropriate for this study population, also enhanced the analysis. 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 do not appear to have presented their results selectively. The study considered patients with chronic bronchitis and this was reflected in the authors' conclusions.

**Implications of the study**
The findings suggest that NAC represents a cost-effective therapy in chronic bronchitis for the reduction in the incidence and severity of acute exacerbations. The benefit is at least of a similar order of magnitude as other efficacious medications. Formal proof of this would require a very large prospective study.

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