Cost-effectiveness and healthcare budget impact in Italy of inhaled corticosteroids and bronchodilators for severe and very severe COPD patients

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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 health technologies examined were the use of combined inhaled corticosteroids and long-acting bronchodilators as strategies for the treatment of severe and very severe patients with chronic obstructive pulmonary disease (COPD), in agreement with the Global Initiative for Chronic Lung Disease (GOLD) recommendations. These included:

- combined salmeterol/fluticasone (SF), 50/500 μg twice daily (b.i.d.) in GOLD Stages III and IV patients in addition to the standard therapy already in use;
- combined formoterol/budesonide (FB), 160/4.5 μg b.i.d. in GOLD Stages III and IV patients in addition to the standard therapy already in use.

The comparators were:
- fluticasone, 500 μg b.i.d. in GOLD Stages III and IV patients in addition to the standard therapy already in use;
- salmeterol, 50 μg b.i.d. in GOLD Stages III and IV patients in addition to the standard therapy already in use;
- standard practice.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis

Study population
The study population comprised a hypothetical cohort defined to be representative of the whole Italian population with COPD.

Setting
The study setting was inpatient and outpatient care. The economic study was carried out in Italy.

Dates to which data relate
The effectiveness data were derived from studies published between 1976 and 2004. The dates to which the resource use data referred were 2003 and 2005. The price year was not reported.

Modelling
A Markov model with a lifetime horizon was developed, and a simplified graphical representation of the model was provided. Other details of the model, such as cycle length and health states, were also given. The transitional probabilities were not reported, but readers were referred to published literature.

Study designs and other criteria for inclusion in the review
The main clinical data used to populate the model included:
the prevalence of respiratory symptoms and COPD among the Italian population;
the probabilities of transitions among health states;
the treatment efficacy for each strategy;
the average forced expiratory volume in 1 second per patient per year value; and
the average exacerbation per patient per year.

**Sources searched to identify primary studies**
The treatment efficacy data for each strategy were derived from two international randomised controlled trials. Other clinical data were derived from published literature.

**Methods used to derive estimates of effectiveness**
The authors did not report their search methods or the inclusion criteria used to identify relevant studies.

**Measure of benefits used in the economic analysis**
The authors did not derive a summary measure of benefit. The primary model outcomes were the annual average number of exacerbations avoided, and the number of symptom-free days (SFDs) per patient. Although relevant, discounting of the health benefits does not appear to have been conducted.

**Direct costs**
The direct costs of the health care payer included the costs of hospitalisation, medical visits and examinations, pharmaceutical treatments, oxygen therapy, lung ventilation and rehabilitation therapy. The cost data for each disease stage were derived from two published studies (Dal Negro et al. 2003, and Lucioni et al. 2005, see ‘Other Publications of Related Interest’ below for bibliographic details). No discounting or price year was reported.

**Statistical analysis of costs**
No statistical analysis of the resource use or cost data was undertaken. The costs and quantities appear to have been treated deterministically.

**Indirect Costs**
Initially, productivity costs were included in the analysis. However, as their significance was narrow compared with that of the direct costs, the authors dropped the societal perspective, i.e., the economic analysis was performed only from the perspective of the National Health Service.

**Currency**
Euros (EUR).

**Sensitivity analysis**
One-way sensitivity analyses were performed on the main model parameters in order to evaluate the robustness of the model. The ranges used were not reported.

**Estimated benefits used in the economic analysis**
The following average lifetime health benefits were estimated:

- for the control group, 12.04 exacerbations and 0 SFDs;
- for the salmeterol alone group, 10.07 exacerbations and 55 SFDs;
- for the fluticasone alone group, 10.14 exacerbations and 37 SFDs;
- for the SF group, 9.09 exacerbations and 257 SFDs; and
for the FB group, 9.66 exacerbations and 220 SFDs.

Cost results
The following average lifetime direct costs were identified:

for the control group, EUR 34,632.09;
for the salmeterol alone group, EUR 33,369.28;
for the fluticasone alone group, EUR 34,754.38;
for the SF group, EUR 34,037.71; and
for the FB group, EUR 33,944.51.

The following average lifetime direct and indirect costs were identified (although indirect costs were not used in the cost-effectiveness analysis):

for the control group, EUR 35,347.83;
for the salmeterol alone group, EUR 33,989;
for the fluticasone alone group, EUR 35,377.93;
for the SF group, EUR 34,609.54; and
for the FB group, EUR 34,544.25.

Synthesis of costs and benefits
Incremental cost-effectiveness ratios (ICERs) were calculated in order to combine the costs and benefits (one exacerbation avoided or an SFD) of the alternative strategies.

The authors reported that all treatment strategies were dominant (more effective and less costly) when compared with current practice, the exception being salmeterol alone, which was more costly. SF and FB were the most effective strategies, but more costly than salmeterol. Consequently, the authors computed the ICERs of SF and FB with respect to salmeterol (the less expensive strategy). In fact, it appears that the authors misidentified the dominant strategies in their analysis. For this reason, the reader is referred to the ‘Critical commentary – Other issues’ field for further details.

The sensitivity analyses showed that the results were sensitive to changes in the initial number of exacerbations, the treatment efficacy, hospitalisation costs and the pharmaceutical costs.

Authors’ conclusions
The authors concluded that, compared with current practice, the recommended use of inhaled corticosteroid and long-acting bronchodilators for severe and very severe COPD patients in addition to usual treatment may result in increased health benefits, without increasing health care costs.

CRD COMMENTARY - Selection of comparators
This study compared two regimens of combined inhaled corticosteroids and bronchodilators with a single inhaled corticosteroid, single long-acting bronchodilator and current practice. Unlike all the intervention strategies, current practice was not described. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The model parameters were taken from published sources. Data on the efficacy of the treatment options were taken from randomised controlled trials; therefore, estimates from these studies would appear to have a high degree of
internal validity. On the other hand, the authors did not report their search methods or any inclusion criteria, and this limits the possibility of evaluating the validity of the primary studies used.

**Validity of estimate of measure of benefit**
The estimations of health benefits (the annual average exacerbation number and percentage of SFDs per patient) were derived appropriately from the model. However, these outcome measures may hinder comparisons of the results with the benefits of other health care interventions as they do not capture all possible outcomes. The use of a generic quality-of-life (quality-adjusted life-year) measure would have been more appropriate. Although the time horizon of the analysis was lifetime, discounting was not performed.

**Validity of estimate of costs**
The analysis of the costs was consistent with the perspective adopted (Italian National Health Service) and all appropriate costs appear to have been included. The costs associated with each health state were reported in the paper, but no detailed breakdown of the unit costs and resource use was given. Future costs do not appear to have been discounted and no price year was reported, which will prevent future reflation exercises. The impact of uncertainty appears to have been addressed in the sensitivity analysis although no results were reported.

**Other issues**
As already highlighted, it appears that the authors misidentified the dominant strategies in their analysis. In fact, they have reported that generally all strategies appeared to be dominant with respect to the control, salmeterol being the exception. However, when comparing the five alternatives (for both health benefits), standard practice and fluticasone are simply dominated and for that reason they should have been eliminated from the analysis, leaving salmeterol, FB and SF as the relevant strategies.

With regard to the number of exacerbations, FB is ruled out by extended dominance relative to salmeterol and SF. The final choice is thus between salmeterol and SF. This is according to the authors’ analysis. The ICER computed was EUR 679.55/exacerbation per patient.

With regard to the number of SFDs per patient, salmeterol and FB are ruled out by extended dominance relative to SF, SF being the eventual cost-effective strategy. The ICER of SF relative to the immediately less expensive and less effective option was not computed.

The authors compared their findings with those from other similar studies and, in general, found apparent agreement. The authors acknowledged the limitations inherent to the use of decision analytical modelling. The issue of generalisability to other settings was not addressed.

**Implications of the study**
The authors suggest that it would be possible to improve the health status of severe and very severe COPD patients without further increasing social costs by following GOLD guidelines.

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Funded by GlaxoSmithKline Italia.

**Bibliographic details**

**PubMedID**
18044689

**Other publications of related interest**
Because readers are likely to encounter and assess individual publications, NHS EED abstracts reflect the original publication as it is written, as a stand-alone paper. Where NHS EED abstractors are able to identify positively that a
publication is significantly linked to or informed by other publications, these will be referenced in the text of the abstract and their bibliographic details recorded here for information.

Dal Negro RW, Rossi A, Cerveri I. The burden of COPD in Italy: results from the Confronting COPD survey. Respir Med 2003;97 Suppl C:S43-S50.


**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Administration, Inhalation; Adrenal Cortex Hormones /administration & dosage /economics /therapeutic use; Albuterol /analsogs & derivatives /economics /therapeutic use; Androstadienes /economics /therapeutic use; Bronchodilator Agents /administration & dosage /economics /therapeutic use; Budesonide /economics /therapeutic use; Budgets; Computer Simulation; Cost-Benefit Analysis; Drug Combinations; Drug Costs; Drug Therapy, Combination; Ethanolamines /economics /therapeutic use; Fluticasone Propionate, Salmeterol Xinafoate Drug Combination; Formoterol Fumarate; Guideline Adherence; Health Care Costs; Health Care Rationing /economics; Humans; Italy; Markov Chains; Models, Economic; Practice Guidelines as Topic; Pulmonary Disease, Chronic Obstructive /drug therapy; Quality of Life; Severity of Illness Index; Treatment Outcome

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