Economic evaluation of an asthma therapy: effect of salmeterol on loss of labor productivity in Japan
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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 examined salmeterol combined with inhaled corticosteroids (ICS) and long-acting beta2-agonists, administered in compliance with the Global Initiative for Asthma (GINA) guidelines. The comparator was treatment prior to salmeterol introduction. This was a combination of ICS, leukotriene modifiers, inhaled short-acting beta2 stimulants, and/or sustained theophylline.

Type of intervention
Treatment.

Economic study type
Cost-benefit analysis.

Study population
The study population comprised asthma patients who had consulted the authors' clinic in 2002. The inclusion criteria specified that the patients had to be aged 15 or under, have a diagnosis of Step 3 (moderate) to 4 (severe) bronchial asthma, and have no serious co-morbidities. A further inclusion criterion was that the patients had to be receiving combination therapy of ICS, leukotriene modifiers, inhaled short-acting beta2 stimulants, and/or sustained theophylline. The patients were required to have been receiving stable doses of asthma medication other than ICS prior to the introduction of salmeterol. The results were extrapolated to the Japanese population.

Setting
The setting was primary care. The economic study was carried out in Kyoto, Japan.

Dates to which data relate
The effectiveness data and income values used to estimate productivity losses were derived from 2002 data.

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 total asthmatic Japanese population in 2002.

Study sample
Power calculations were not reported as being used to determine the sample size. Of the 270 patients randomly selected from the 1,080 patients attending the clinic in 2002, and who met the inclusion criteria, 54 patients agreed to participate.
in the study. Of these, 33 were paid labours and 21 were unpaid ones. In the paid group, 18 participants (54.5%) were females and the mean age was 55.6 years. In the unpaid group, 16 participants (76.2%) were females and the mean age was 67.4 years. Of the 33 patients in paid labour, 4 (12.1%) had Step 2 disease, 24 (72.7%) had Step 3 disease and 5 (15.2%) had Step 4 disease. Of the 21 patients in unpaid labour, 2 (9.5%) had Step 2 disease, 18 (85.7%) had Step 3 disease, and 1 (4.8%) had Step 4 disease. The study sample was appropriate for the clinical study question since the patients received appropriate medications prior to and after the introduction of salmeterol.

Study design
The study was a single-centre, historical case series study (before-and-after study). The length of follow-up after the introduction of salmeterol was 1 year. The outcomes in the year prior to the introduction of salmeterol were also assessed. No loss to follow-up was reported.

Analysis of effectiveness
All of the patients included in the observational study were accounted for in the analysis. The primary health outcomes used were the numbers of symptom-free days (SFDs) and symptom-free nights (SFNs). A secondary outcome was the number of unscheduled visits. Data were collected retrospectively from medical records and asthma diaries. The study and comparator groups were the same patient sample following and prior to salmeterol introduction. No statistical comparison of the characteristics of the study and comparator groups was performed.

Effectiveness results
Following the introduction of salmeterol, the number of SFDs was increased by 120.7 days per year in paid patients (95% confidence interval, CI: 83.2 - 158.2; p<0.001) and by 159.2 days per year in unpaid patients (95% CI: 99.4 - 218.9; p<0.001).

The number of SFNs was increased by 42.5 nights per year in paid patients (95% CI: 17.5 - 102.3; p<0.001) and by 84.3 nights per year in unpaid patients (95% CI: 24.2 - 144.4; p<0.001).

The number of unscheduled clinic visits requiring a drip infusion of either corticosteroids or aminophylline was reduced by 6.2 days (95% CI: 2.9 - 9.5; p<0.001) in paid patients.

The reduction in unscheduled clinic visits by 3.8 days in unpaid patients was not statistically significant (95% CI: -10.9 - 3.3).

Clinical conclusions
The authors concluded that the improvement of clinical symptoms occurred in association with the introduction of salmeterol.

Measure of benefits used in the economic analysis
The measure of benefit used was the savings due to productivity gains. Productivity gains were valued assuming that severe, moderate and mild attacks, stridor, and absence of attacks in the asthma diary corresponded to productivity losses of 100%, 75%, 50%, 25%, and 0%, respectively. The reader is referred to the 'Indirect costs' section for further details on the method used to assess productivity gains and losses.

Direct costs
The direct costs were not included in the economic analysis.

Statistical analysis of costs
The non-parametric Wilcoxon's signed rank test was used to compare productivity losses before and after the introduction of salmeterol.
introduction of salmeterol in the study population. This non-parametric test was used since the null hypothesis, that the distribution of productivity losses before and after the introduction of salmeterol would show equal variation, was rejected at the 5% significance level using an F-test.

**Indirect Costs**

The economic analysis was based on productivity costs. The quantities (productive days) and the costs were analysed separately. A societal cost boundary was adopted. Discounting was not carried out since the timeframe of the analysis was 1 year. Productivity losses were estimated via the human capital approach in the year before and the year after the introduction of salmeterol. Productivity losses were based on the proportions of asthma attacks according to severity in the clinical study, the authors’ assumed productivity loss for each severity of attack, and published mean incomes.

All data were from 2002. For paid patients, loss of productivity was expressed in yen. The mean income of paid patients was calculated according to their gender and occupation, and was based on the 2002 wages of full-time and part-time employees of the manufacturing, construction and mining industries. For unpaid patients, loss of productivity was expressed in days. Then, the authors assumed that the mean income for paid patients also applied to unpaid patients. The results for the study population were extrapolated to the wider Japanese population. This was based on 2002 data from published labour and asthma patient surveys. For example, the numbers of paid and unpaid workers in the Japanese asthmatic population, the published proportion of Step 3 and step 4 asthmatics in that population (39.4%), and the productivity gains estimated from the study population.

**Currency**

Japanese yen (Y).

**Sensitivity analysis**

A one-way sensitivity analysis was carried out to examine the generalisability of the results, by excluding data for patients with Step 2 asthma.

**Estimated benefits used in the economic analysis**

In paid patients, there was a saving of Y 782,810 (95% CI: 569,300 - 999,300) from reduced loss of productivity in the year after the introduction of salmeterol compared with the year prior.

In unpaid patients, there was a reduction of about 61.3 days (95% CI: 41.2 - 81.3) after the introduction of salmeterol compared with the year prior. This productivity gain represented a saving of Y 756,414 (CI not reported). The side effects of treatment were not considered.

**Cost results**

In paid patients, the total productivity loss was Y 1,744,900 in the year prior to the introduction of salmeterol and Y 962,090 in the year following its introduction.

These data were not reported for unpaid patients.

**Synthesis of costs and benefits**

When the results were extrapolated to the Japanese population, it was estimated that the introduction of salmeterol resulted in productivity gains of Y 105.4 billion in the paid group and Y 64.5 billion in the unpaid group. The results were not influenced by the exclusion of Step 2 patients in the sensitivity analysis.

**Authors’ conclusions**

The introduction of salmeterol to the range of treatments currently available for asthma in Japan has had a beneficial
impact on clinical symptoms and has reduced productivity losses due to asthma.

**CRD COMMENTARY - Selection of comparators**
A justification was given for the choice of the comparator used. Combination therapy was the recommended treatment prior to the introduction of salmeterol. You should decide if this is a widely used treatment in your own setting.

**Validity of estimate of measure of effectiveness**
The analysis was based on a before-and-after study. The authors acknowledged that data from this type of study might not be as robust as data obtained from randomised controlled trials. The patient groups were not shown to be comparable at analysis. The same patients were used in the study group (year after salmeterol introduction) and comparator group (year before salmeterol introduction). However, changes over time (e.g. patient age and severity of asthma) might have influenced the results. The study sample was representative of the study population. Although the methods for estimating the numbers of SFDs and SFNs were reported, the methods and results for the proportions of asthma attacks by severity were not reported.

**Validity of estimate of measure of benefit**
The estimation of benefits was modelled. The authors assumed a specific reduction in productivity for each severity of asthma attack. However, these assumptions were not justified. Productive days were valued using appropriate mean income values.

**Validity of estimate of costs**
The economic analysis adopted a societal perspective since it included productivity losses to the general economy. However, as the authors acknowledged, the direct costs of asthma medication and treatment of asthma attacks (including hospitalisation) were not included in the economic analysis. The authors referred to a paper where these costs are detailed for the study population (Miyagawa et al. 2003, see ‘Other Publications of Related Interest’ below for bibliographic details).

In estimating the productivity losses for unpaid patients, the authors’ assumption that the mean income of unpaid patients is equivalent to the mean income of paid patients was not validated. Although SFDs, SFNs and total productivity losses were reported separately, the proportions of patients experiencing each severity of asthma attack were not reported. A statistical analysis was performed for SFDs and SFNs, but no statistical analysis was reported for the incidence rates of asthma attacks used to estimate productivity loss. A sensitivity analysis of mean income was not performed. Productivity losses were reported as 2002 values, thus aiding future reflation exercises. Discounting was not applied, which was appropriate given the short time horizon of the cost analysis.

**Other issues**
The authors compared their results with those of a US study that concluded that salmeterol was cost-effective, based on its ability to reduce the direct costs of hospitalisation. However, the two studies were not comparable since the authors’ study omitted the direct costs. The issue of generalisability to other settings was addressed. The results of the study were extrapolated to the general population and were also shown to be similar when Step 2 patients were assumed to not receive salmeterol. However, the study only estimated the productivity gain in the year after salmeterol introduction and the results might not be generalisable to longer time periods. The authors do not appear to have presented their results selectively. The study only assessed benefits and costs as symptom-free periods and productivity gains or losses, and this was reflected in the authors’ conclusions.

The authors reported a number of further limitations to their study. For example, the exclusion of mortality costs (productivity losses due to fatal asthma attacks), health-related quality of life, and friction costs, which might have biased the estimated productivity gains with salmeterol in either direction.
Implications of the study
The authors suggested that the introduction of salmeterol for the treatment of asthma in Japan would be beneficial for patients, medical institutions and the general economy. The authors did not make any recommendations or suggestions for further work following their study.

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Other publications of related interest

Indexing Status
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MeSH
Adrenal Cortex Hormones /administration & dosage /therapeutic use; Aged; Albuterol /administration & dosage /therapeutic use; Asthma /prevention & control /drug therapy; Cost-Benefit Analysis; Costs and Cost Analysis; Japan; Occupational Health; Retrospective Studies; Sensitivity and Specificity; Treatment Outcome

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