Cost-effectiveness analysis of early treatment with lisinopril for patients with acute myocardial infarction: results from the GISSI-3 Trial
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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 technology examined in the study was lisinopril, an angiotensin-converting enzyme (ACE) inhibitor, for the early (within 24 hours) treatment of acute myocardial infarction (MI).

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with advanced MI and admitted to the Intensive Care Unit (ICU).

Setting
The setting was hospital. The economic study was carried out at the Dipartimento di Ricerca Cardiovascolare, Istituto di Ricerche Farmacologiche Mario Negri, Milano, Italy.

Dates to which data relate
The dates during which the effectiveness evidence and resource use data were gathered were not indicated. The price year was 1993.

Source of effectiveness data
The effectiveness evidence was derived from a single study. The study was first published elsewhere and few details of the analysis were reported in the present study.

Link between effectiveness and cost data
The costing was undertaken prospectively on the same patient sample as that used in the effectiveness analysis.

Study sample
Power calculations were not performed (however the sample size was very high). The overall study sample of patients admitted to the ICU after MI, comprised 19,394 subjects who were allocated to the lisinopril and placebo groups. Several subgroups of patients were also considered on the basis of age, type of MI, etc.

Study design
The study was a randomised controlled trial, carried out by the Italian Group for the Study of Survival after Infarction (GISSI-3). Details about the randomisation and blinding of assessment and the number of centres in which the study was carried out were reported in a different paper. Patients were treated with lisinopril or placebo for 6 weeks after randomisation and were then followed for 6 months. Overall loss to follow-up was 2.6% after 6 weeks: 247 patients in the lisinopril group and 252 patients in the placebo group. There was no difference with respect to baseline characteristics in the loss to follow-up in the two groups.

**Analysis of effectiveness**

The basis of the analysis of effectiveness was not stated. The primary health outcome used in the analysis was the death rate after 6 weeks. Secondary health outcomes were the number of deaths within the first week, cardiac insufficiency, re-infarction, post-infarct angina, cardiac shock, persistent hypotension, renal disorder, ventricular fibrillation, advanced atrioventricular block, and length of hospital stay. The comparability of groups at baseline was not reported.

**Effectiveness results**

The number of deaths after six weeks was 619 (6.4%) in the lisinopril group and 693 (7.2%) in the control group.

The number of deaths in the first week was 374 (3.9%) in the lisinopril group and 437 (4.5%) in the control group.

In the lisinopril group the number of patients with cardiac insufficiency was 462 (4.9%), re-infarction 303 (3.2%), and post-infarct angina 1,985 (21%). In the control group the number of patients with cardiac insufficiency was 454 (4.8%), re-infarction 292 (3.1%), and post-infarct angina 1,909 (20.2%).

In the lisinopril group the number of patients with cardiac shock was 234 (2.5%), persistent hypotension 852 (9%), renal disorder 226 (2.4%), ventricular fibrillation 232 (2.5%), and advanced atrioventricular block 503 (5.3%). In the control group the number of patients with cardiac shock was 208 (2.2%), persistent hypotension 351 (3.7%), renal disorder 106 (1.1%), ventricular fibrillation 251 (2.7%), and advanced atrioventricular block 445 (4.7%)

Length of hospital stay was not significantly different: 15.1 days (+/- 6.7 days) in the lisinopril group and 14.9 days (+/- 6.8 days) in the control group.

Death rates both within the first weeks and after 6 weeks were significantly lower in the lisinopril group than in the control group.

Cases of persistent hypotension and renal disorder were significantly more numerous in the lisinopril group.

The other outcomes were not significantly different.

**Clinical conclusions**

Lisinopril was considered more effective than placebo because it was associated with fewer deaths in the 6 weeks of treatment.

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

The benefit measure used in the economic analysis was the number of extra lives saved with lisinopril over placebo after 6 weeks of treatment. It was obtained directly from the effectiveness analysis.

**Direct costs**

Discounting was not carried out as the time horizon of the study was six months. Quantities and unit costs were reported separately. The cost/resource boundary adopted was that of the Italian SSN. The costs comprised medical procedures, concomitant drug therapies, and lisinopril. Costs of medical procedures were then excluded because the resources used in the two groups were not significantly different. The estimation of costs was based on actual data, derived from the DRG Italian reimbursement system. The period of collection of quantities of resources was not reported. The price year
was 1993.

Statistical analysis of costs
Statistical analyses of costs were carried out to test for statistical significance of the results.

Indirect Costs
Indirect costs were not included.

Currency
Italian lira (L). Lira were converted into US dollars ($) at the 1993 exchange rate: $1 = L1,570.

Sensitivity analysis
One-way sensitivity analyses were conducted to assess the impact of variations of mortality rates and costs on the results of the study.

Estimated benefits used in the economic analysis
74 extra lives were saved with lisinopril compared to placebo after 6-weeks of treatment.

Cost results
The costs of concomitant drug therapies amounted to $32,677 in the lisinopril group and $62,472 in the control group. The extra costs of lisinopril were $189,013. Total cost were $221,690 in the lisinopril group and $67,472 in the control group and the difference was statistically significant.

Synthesis of costs and benefits
Costs and benefits were combined by performing an incremental cost-effectiveness analysis. The incremental cost of lisinopril over placebo was $2,080 per life saved. The sensitivity analyses indicated that even in the worst scenario (high costs of lisinopril and very low number of lives saved) the cost-effectiveness of lisinopril never fell below the commonly used threshold of $50,000 per life-year saved. Subgroup analyses suggested that high-risk patients, such as those with previous MI or older than 70 years, benefited more from the treatment.

Authors' conclusions
The authors concluded that lisinopril was cost-effective in a general population of patients with advanced MI and compared favourably with other commonly used therapies in the health care sector.

CRD COMMENTARY - Selection of comparators
The reason for the selection of the comparator was clear. Placebo was chosen because the objective of the study was to assess the active value of lisinopril. You, as a user of this database, should assess whether the comparator represents current practice in your own setting.

Validity of estimate of measure of effectiveness
The internal validity of the study was likely to be high, due both to the randomised design and the large sample size. However, only a few details of the analysis were reported in the study; full details were published in other papers.

Validity of estimate of measure of benefit
The selection of the benefit measure was justified by the authors as being the most appropriate measure for the specific disease.

Validities of estimate of costs

The estimation of costs was based on actual data, which appears to have been specific to the Italian setting. However, extensive sensitivity analyses were carried out and costs and quantities were reported separately. Therefore the external validity of the study is likely to be high. The authors made appropriate currency conversions.

Other issues

The generalisability of the study results to other settings is quite high. The authors made several interesting comparisons of their findings with other studies reporting different technologies for the same intervention. The authors recognised that the time horizon of the analysis was limited, but it appears to have been appropriate to the study objective.

Implications of the study

The implication of the study is that lisinopril should be routinely adopted for the treatment of patients with acute MI.

Source of funding

None stated.

Bibliographic details


Other publications of related interest


Indexing Status

Subject indexing assigned by NLM

MeSH

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