A cost-effectiveness analysis of aspirin versus oral anticoagulants after acute myocardial infarction in Italy: equivalence of costs as a possible case for oral anticoagulants

Gianetti J, Gensini G, De Caterina R

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
Aspirin (antiplatelet) and warfarin (anticoagulant) for the prevention of coronary artery disease after acute myocardial infarction (MI).

Type of intervention
Secondary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients having had an acute myocardial infarction.

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

Dates to which data relate
The effectiveness and resource use data were taken from sources published between 1994 and 1995. Prices were reported in ECUs, having been converted from Italian Lira. The price year was not stated.

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

Outcomes assessed in the review
For patients receiving warfarin or aspirin, the number of events during 36 months follow-up, and the percentage odds reduction and hazard ratio relative to placebo, were assessed for each type of vascular event. The vascular events included in the review were recurrent myocardial infarction, unstable angina pectoris, percutaneous transluminal coronary angioplasty (PTCA), coronary artery bypass graft surgery (CABG), coronary angiography, major bleeding, cerebrovascular events, and AV thromboembolism. The aspirin-warfarin efficacy ratio for all cardiovascular events was also assessed (this is the ratio of the odds reductions relative to placebo).

Study designs and other criteria for inclusion in the review
The study designs included in the review were a large placebo-controlled trial (warfarin) and a meta-analysis of clinical trials performed in the late infarction period (aspirin). The results of the warfarin trial were elaborated in a cost-effectiveness analysis, which was also included in the review. No inclusion or exclusion criteria were reported.
Sources searched to identify primary studies
The primary studies included were previously used in a North American study; the present study attempts to recalculate the cost results for application to a European setting.

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

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

Number of primary studies included
Three primary studies were included in the review.

Methods of combining primary studies
Each primary study provided results for each therapy; hence study results did not need to be combined.

Investigation of differences between primary studies
Not reported.

Results of the review
The event rates during a 36-month follow up were:

- recurrent myocardial infarction, warfarin 6.70% versus aspirin 9.78%;
- unstable angina pectoris, warfarin 12.70% versus aspirin 13.32%;
- PTCA, warfarin 4.18% versus aspirin 4.95%;
- CABG, warfarin 7.52% versus aspirin 8.20%;
- coronary angiography, warfarin 20.00% versus aspirin 22.10%;
- major bleeding, warfarin 3.00% versus aspirin 2.61%;
- cerebrovascular events, warfarin 2.20% versus aspirin 2.25%; and
- AV thromboembolism, warfarin 0.88% versus aspirin 1.10%.

The aspirin-warfarin efficacy ratio for all cardiovascular events was 0.68.

Measure of benefits used in the economic analysis
The measure of benefits used were the differential incidence of vascular events, between the two therapies.

Direct costs
Direct costs included in the analysis were the costs of drugs, International Normalised Ratio (INR) testing (warfarin only), medical follow-up (warfarin only), and treatment of vascular events. Quantities and costs were not analysed separately. The boundary of the Italian National Health System was adopted. Treatment costs are estimated as the mean
total cost, or the mean per-day cost multiplied by the mean length of stay (in days), for hospitalisations with a Diagnosis Related Group (DRG) code corresponding to that vascular event. These data were published in 1994. Costs of drugs, INR testing and follow-up were converted from the US study. Discounting would have been relevant but was not performed. The price year does not appear to have been common over all elements of cost.

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

**Indirect Costs**
No indirect costs were included in the analysis.

**Currency**
Costs were expressed in ECU, and were converted from Italian Lira (L) at an exchange rate of ECU1.00 = L1,923.02. Total costs are also expressed in US dollars ($), where a conversion rate of $1.00 = L1,513.95 was used.

**Sensitivity analysis**
A two-way sensitivity analysis on the aspirin/warfarin efficacy ratio (range: 0 - 1) and total cumulative cost (range: -5% to +5%) was carried out.

**Estimated benefits used in the economic analysis**
See effectiveness results above. These rates of cardiovascular events were applied to a hypothetical cohort of 1,000 patients, though the results were not reported. The follow-up period was 36 months. Side effects were accounted for in the rate of certain vascular events (e.g. major bleeding).

**Cost results**
The total cost of therapy per patient/year, was ECU277.56 (warfarin) and ECU62.53 (aspirin).

The cost of morbidity per patient per year, using DRG mean total costs, was ECU1,873.32 (warfarin) and ECU2,125.4 (aspirin).

The cost of morbidity per patient per year, using the product of DRG mean cost per day and mean length of stay, was ECU1,848.06 (warfarin) and ECU2,074.01 (aspirin).

**Synthesis of costs and benefits**
Benefits and costs were combined by calculating the total cost per patient per year of aspirin and warfarin, and accounting for the costs of therapy and treatment of vascular events. No incremental analysis was performed: results were reported separately for each therapy.

The total cost per patient per year, using DRG mean total costs, was ECU2,150.8 or $2,731.4 (warfarin), and ECU2,187.9 or $2,778.9 (aspirin).

The total cost per patient per year, using the product of DRG mean cost per day and mean length of stay, was ECU2,125.2 or $2,699.0 (warfarin), and ECU2,136.6 or $2,713.9 (aspirin).

Results were sensitive to variations in the aspirin-warfarin efficacy ratio. Warfarin is no longer the cost-effective strategy in Italy once an efficacy ratio of approximately 0.72 is reached.
Authors' conclusions
Warfarin is likely to be no less cost-effective than aspirin, in the management of post-MI patients, in a few European countries.

CRD COMMENTARY - Selection of comparators
A justification was given for the comparator used; namely that aspirin represents common medical practice in European countries. You, as a user of the database, should decide if this is a widely used health technology in your own setting.

Validity of estimate of measure of effectiveness
The authors did not state that a systematic review of the literature had been undertaken. Effectiveness estimates were combined using narrative methods. The incidence of vascular events was taken from a large trial of warfarin and a meta-analysis of aspirin trials. Although the total sample sizes were not reported, the authors implied that the results would be more precise than those obtained in the direct comparisons of warfarin and aspirin on small sample sizes.

Validity of estimate of measure of benefit
The measure of benefit was implied to be the differential rate of vascular events under aspirin and warfarin. Numbers of events among the hypothetical cohort were modelled by applying incidence rates obtained from the primary studies. The analysis was therefore categorised as a cost-effectiveness analysis.

Validity of estimate of costs
All categories of cost relevant to the perspective adopted were included in the analysis. Since treatment costs were based on DRG prices it was assumed that they covered all cost items incurred by the hospital. Costs incurred by the wider health service were included in the costs of drugs, laboratory monitoring and medical follow-up. Costs and quantities were not reported separately. No sensitivity analysis of quantities or prices was conducted. Since the cost estimates were derived from previous studies and national averages, an arbitrary variation of 5% around total treatment cost was used in the sensitivity analysis. However, the authors did not provide a justification for why the figure of 5% was chosen. Treatment costs were estimated for two DRG pricing schemes: the mean price and the daily price multiplied by mean length of stay. Results were similar under both methods. The authors reported results in Italian Lira, US Dollars, ECU and Netherlands Guilders, using appropriate currency conversions. DRG prices relate to 1994. It is unclear whether costs obtained from previous studies have been inflated to the current price year.

Other issues
The authors made appropriate comparisons of their findings with those from other studies. The issue of generalisability to other European countries (specifically, the Netherlands) was addressed, by providing a comparison of hospitalisation and follow-up costs. The authors did not present their results selectively. The study modelled results for patients having had acute MI, and this was reflected in the authors' conclusions. The authors reported a number of limitations to their study. Firstly, the aspirin-warfarin efficacy ratio was based on indirect comparisons (i.e. each drug being compared with placebo, and the results combined) and may not reflect true relative efficacy. Secondly, DRG prices under which treatment costs were estimated were based on regional reimbursements, which may not reflect real costs, and a coding system that simplified the disease process. Finally, the true variability (confidence limits) of cost items was not accounted for, and only an arbitrary value of 5% was imposed.

Implications of the study
A large, direct comparison study of morbidity following aspirin or warfarin is required to estimate better the aspirin-warfarin efficacy ratio. In its absence, the result of this study, that warfarin is likely to be at least as cheap and cost-effective as aspirin, may potentially be able to influence therapeutic policies in Europe.

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**Other publications of related interest**


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