Cost-effectiveness of amiodarone for prophylaxis of atrial fibrillation in coronary artery bypass surgery

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
Amiodarone for prophylaxis of atrial fibrillation in coronary artery bypass surgery.

Type of intervention
Secondary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients undergoing CABG.

Setting
The setting was hospital; the economic analysis was carried out in the USA.

Dates to which data relate
Effectiveness and resource use data were collected from studies published between 1972 and 1997 and a review of data collected at the authors' institution from January 1997 until March 1998. Cost data were taken from the authors' institution. The price year was 1998.

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

Modelling
A decision analytic model was used to synthesise data from various sources to determine the cost-effectiveness of amiodarone prophylaxis versus no prophylaxis.

Outcomes assessed in the review
The review assessed the probability of AF, probability of electrical cardioversion being needed, probability of spontaneous conversion, probability of successful cardioversion with drugs, and probability of successful electrical cardioversion.

Study designs and other criteria for inclusion in the review
Effectiveness data were collected from published studies and a review of data collected at the authors' institution. For
length of stay data, only studies that began recruiting patients after 1994 were included in order more accurately to reflect current practice.

Sources searched to identify primary studies
Not stated.

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
Ten primary studies were included in the review.

Methods of combining primary studies
Not stated.

Investigation of differences between primary studies
Not stated.

Results of the review
All of the following results are for the base case:

The probabilities of AF with amiodarone was 0.255, and without prophylaxis 0.312.

The probability of electrical cardioversion being needed in AF was 0.130.

The probability of spontaneous conversion from AF was 0.330.

The probability of successful cardioversion with sotalol was 0.850.

The probability of successful electrical cardioversion was 0.850.

The probability of successful cardioversion with ibutilide was 0.570.

Based on institutional evidence, digoxin was the most frequently used agent to treat AF.

Methods used to derive estimates of effectiveness
Additional effectiveness estimates were based on authors’ assumptions.

Estimates of effectiveness and key assumptions
All post-operative CABG patients were assumed to be admitted to the intensive care unit (ICU) and to require at least one day of observation there. They were then transferred to the cardiac step-down unit (SDU). AF was assumed to have developed on post-operative day 2. An initial intravenous loading dose of digoxin followed by 0.25mg of digoxin per day orally until discharge was assumed. It was assumed that patients who developed AF were treated with anticoagulants if AF did not spontaneously convert to sinus rhythm within 48 hours. For patients who required
Anticoagulation, i.v. heparin was assumed to be given for two days, starting four days post-operatively. All patients receiving heparin were assumed to require two activated partial thromboplastin time tests per day. Eight days of warfarin therapy was used. Of the drugs used for chemical cardioversion in the treatment of AF, sotalol hydrochloride was used most frequently. An oral dosage of 80mg twice daily to a maximum of 80mg three times daily was assumed.

**Measure of benefits used in the economic analysis**
The number of AF events avoided was used as the measure of benefits.

**Direct costs**
Direct costs were not discounted (time horizon less than one year). Quantities were reported separately only for length of stay. No prices were given. Direct costs were costs of hospitalisation, cardioversion costs, electrocardiogram costs, drug costs, nursing administration charges, and pharmacy i.v. admixture charges. The quantity/cost boundary adopted was that of the hospital. Costs and quantities were obtained from the authors’ institution. Drug costs were obtained from CardinalCHOICE software. Charges were converted into costs by using the hospital-derived cost-to-charge ratio. The price year was 1998. Length of stay in the cardiac SDU was 5.7 days with AF, and 3.7 days without AF. Length of stay in the ICU was 4.32 days with AF and 3.02 days without AF. Physician costs were excluded as the physicians were not employed by the hospital.

**Statistical analysis of costs**
No statistical analysis of costs was reported.

**Indirect Costs**
Indirect costs were not included.

**Currency**
US dollars ($).

**Sensitivity analysis**
A Monte Carlo simulation with 1,000 trials was conducted on the following variables: AF frequency, rate of spontaneous cardioversion, efficacy of cardioversion, length of stay, and drug costs. Probability distributions were not summarised. Additional one-way sensitivity analyses were carried out.

**Estimated benefits used in the economic analysis**
Benefits were not reported separately.

**Cost results**
Costs were not reported separately.

**Synthesis of costs and benefits**
In the base case, the cost per AF event avoided was $15,750 with amiodarone prophylaxis and $17,426 with usual care.

In the scenario with ibutilide, the cost per AF event avoided was $15,801 with amiodarone prophylaxis and $17,705 with usual care.

In the scenario with diltiazem, the cost per AF event avoided was $16,139 with amiodarone prophylaxis and $17,835 with usual care.
In the scenario with adverse events, the cost per AF event avoided was $15,883 with amiodarone prophylaxis and $17,427 with usual care.

For patients treated with amiodarone who did not develop AF, the drug was stated to be no longer cost-effective once the cost of hospitalisation in the ICU or the SDU increased by $1,000-2,000 (depending on whether treatment took place in the ICU or SDU).

If the frequency of AF with amiodarone increased from 25.5% to 30.9% or fell from 31.2% to 25.9% in the control group, amiodarone was no longer cost-effective.

**Authors’ conclusions**
Prophylaxis of AF with amiodarone in CABG patients was more cost-effective than usual care in the short term and from the hospital perspective. The results were sensitive to changes in the cost of hospitalisation of patients who did not develop AF and to the efficacy of amiodarone.

**CRD COMMENTARY - Selection of comparators**
A justification was given for the comparator used, namely that it represented usual care. You, as a user of the database, should decide if these health technologies are relevant to your setting.

**Validity of estimate of measure of effectiveness**
The authors undertook a literature review to derive effectiveness estimates, which seemed appropriate, although they did not state that a systematic review of the literature had been undertaken. Additional effectiveness estimates were, appropriately, based on authors’ assumptions. The validity of the results was enhanced by sensitivity analyses to account for variability in the estimates.

**Validity of estimate of measure of benefit**
The estimation of benefits was obtained directly from the effectiveness analysis, although benefits were not reported separately. Also, the use of AF events avoided as the measure of benefit does not permit comparison with other technologies, and some measure which accounted for quality of life or individual preferences could have avoided this (for example through the use of quality-adjusted life years).

**Validity of estimate of costs**
Good features of the cost analysis were that many relevant direct cost categories were included; the validity of cost results was enhanced by appropriate sensitivity analyses; length of stay was reported separately, which enhances the generalisability of the results; the price year was reported, which would make reflation exercises in other settings possible; and charges were converted to costs, although no formula was given. However, a flaw in the presentation of the results was the use of average cost-effectiveness ratios rather than the more technically correct incremental ratios. Without the benefit results, and with only these ratios, it would not be possible to tell whether the intervention group derived increased or decreased benefit (AF avoided). This knowledge would be critical to any decision with regard to the adoption of the technology. A lower average would mean that, either there were reduced benefits and proportionately greater reduced cost, or increased cost with proportionately higher benefit. In the latter case consideration of whether it would be worth paying the extra amount to attain the greater benefit would be required. In the former case one would want to consider whether the cost saving was worth the reduction in benefit. This requires a comparison with other technologies and knowledge of the budget constraint.

**Other issues**
The authors did make appropriate comparisons of their findings with those from other studies and the issue of generalisability to other settings was addressed. It is unfortunate that the benefits results were not given. The study simulated CABG patients and this was reflected in the authors’ conclusions, although no other population characteristics...
were given (e.g., age).

The authors identified the following limitations of the study:

the cost of adverse drug reactions post-discharge was not considered;

hospital costs were specific to the authors’ institution and may not reflect costs at other centres;

costs of routine laboratory tests, drugs, and respiratory services were assumed to be equivalent between the two groups, although patients with AF may have higher total costs than patients who do not develop AF;

because the time frame of the study was limited to the initial hospitalisation, costs avoided as a result of the prevention of stroke and the number of life years saved were not considered.

**Implications of the study**

The authors claimed that prophylaxis of AF with amiodarone in CABG patients was more cost-effective than usual care in the short term from the hospital perspective, and that the results were sensitive to changes in the cost of hospitalisation of patients who did not develop AF and the efficacy of amiodarone. These conclusions are clearly flawed in the light of the criticism regarding the cost-effectiveness calculation.

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