A health economic evaluation of aspirin in the primary prevention of cardiovascular disease in Japan

Tsutani K, Igarashi A, Fujikawa K, Evers T, Kabin M, Lamotte M, Annemans L

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 the use of low-dose aspirin (100 mg/day) as primary prevention in patients at increased risk of cardiovascular disease (CVD).

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised a hypothetical cohort of patients at increased risk of CVD, defined as a 1-year risk of coronary heart disease (CHD) of 1.5% (10-year risk of +/- 15%).

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

Dates to which data relate
The effectiveness data were derived from studies published between 1996 and 2003. No dates for resource use were explicitly reported. The price year was not reported but some costs were derived from sources published in 2002.

Source of effectiveness data
The clinical data used to populate the decision model were probabilities of events such as CHD (fatal and nonfatal) and stroke (fatal, nonfatal, haemorrhagic and ischaemic) associated with aspirin use in both primary and secondary prevention. The authors made assumptions about the annual risk of CHD and other events with no treatment.

Modelling
A Markov model was constructed to assess the health economic consequences of aspirin versus no aspirin therapy in patients at increased risk of CVD. The authors reported the structure of the model, the health states and the cycle length. In addition, a description of the transition pathways was provided. The model included all harms and benefits of the preventive strategy. Patients entered the model with no history of CVD and could receive either aspirin or no treatment. In the case of a nonfatal CVD event (myocardial infarction, stroke or systemic bleeding), all patients received aspirin as secondary prevention treatment. The time horizon of the model was 10 years.

Sources searched to identify primary studies
Clinical data on primary prevention with aspirin were derived from two published meta-analyses of five clinical trials. Data on secondary prevention with aspirin were retrieved from the CAPRIE trial (clopidogrel versus aspirin in patients at risk of ischaemic events).

**Methods used to judge relevance and validity, and for extracting data**

It was not stated whether the primary studies were identified selectively or through a systematic review of the literature. However, the choice of meta-analyses of clinical trials ensures a high internal validity of the clinical estimates.

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

The summary benefit measure used was the life-years (LYs). These were estimated using the decision model. An annual discount rate of 3% was applied to future benefits.

**Direct costs**

The analysis of costs was carried out from the perspective of the public health insurer. It included the costs associated with aspirin use and CVD events (including fatal and nonfatal stroke or myocardial infarction, gastrointestinal bleeding and follow-up of CVD events). The unit costs and the resource quantities were not presented separately, but the cost items were presented as macro-categories. The source of the resource use data was not explicitly reported. The costs came from Japanese sources such as the Ministry of Health, Labor and Welfare, as well as a survey of medical care activities in public health insurance and a patient survey. The price year was not explicitly reported. Discounting was relevant, as 10-year costs were evaluated, and an annual rate of 3% was used.

**Statistical analysis of costs**

The costs were treated deterministically.

**Indirect Costs**

The productivity costs were not included.

**Currency**

Japanese yen (JPY). The costs were converted in euros (EUR) at the rate EUR 1 = JPY 130.

**Sensitivity analysis**

The robustness of the cost-effectiveness results was tested in univariate sensitivity analyses. The model inputs varied were the annual risk of CHD, cost of stroke treatment, time horizon, gastrointestinal bleeding rate, stroke rate, cost of each event and discounting. The sources of the alternative values were not reported, but they appear to have been based on authors' assumptions.

**Estimated benefits used in the economic analysis**

Over a 10-year time horizon, 8.36 LYs were associated with aspirin and 8.33 LYs with no aspirin (difference 0.03).

**Cost results**

The 10-year total cost of care from the viewpoint of the public health insurer was JPY 634,000 (EUR 4,857) with no aspirin and JPY 518,000 (EUR 3,968) with aspirin. The difference was JPY 116,000 (EUR 889) (95% confidence interval: JPY 57,077 to JPY 175,151). Thus, the extra cost of aspirin was more than offset by a reduction in the costs associated with CVD events.
Synthesis of costs and benefits
An incremental analysis was performed in order to combine the costs and benefits of the alternative strategies. However, an incremental cost-effectiveness ratio was not calculated as aspirin was the dominant strategy, being more effective and less expensive than no aspirin.

The sensitivity analysis corroborated the base-case findings. Specifically, for any level of CHD risk higher than 0.20% (it was 1.5% in the base-case), aspirin was the dominant strategy. A similar conclusion was reached regardless of the variation in the cost of stroke or other model inputs. Cost-savings increased as the time horizon of the model increased.

Authors’ conclusions
Low-dose aspirin administered as primary prevention in patients at increased risk of cardiovascular disease (CVD) was effective and cost-saving from the perspective of the Japanese insurer. Savings were observed as early as in the first year of treatment.

CRD COMMENTARY - Selection of comparators
The selection of the comparator (i.e. no aspirin) was appropriate as it represented the conventional pattern of care in Japan. You should decide whether this is a valid comparator in your own setting.

Validity of estimate of measure of effectiveness
The clinical data used to populate the decision model were derived from high-quality sources. In effect, two meta-analyses of clinical trial and a randomised, clinical trial were selected. It was not stated whether these studies were identified selectively, but no details of a systematic review of the literature were provided. The authors did not provide any information on the primary studies. However, they did state that the primary studies (original clinical trials) were not homogeneous in terms of aspirin dose or CHD baseline risk.

Validity of estimate of measure of benefit
Survival, which was estimated using a modelling approach, represents an appropriate benefit measure. It can also be compared with the benefits of other health care interventions. The impact of the preventive strategy on quality of life was not investigated. Discounting was appropriately performed.

Validity of estimate of costs
The analysis of the costs was consistent with the perspective of the study. The costs were presented as macro-categories and a breakdown of the cost items was not given for each category. This may limit the possibility of replicating the analysis in other settings. The authors stated that the costs of co-administration, of anti-acids for example, were not considered. The sources of the costs were reported, but information on the sources of resource use was less clear. Statistical analyses of the costs were not carried out, but key cost items were varied in the sensitivity analysis. The price year was not reported, which will make deflation exercises in other time periods difficult.

Other issues
The authors did not make extensive comparisons of their results with those from other studies. They discussed the issue of generalisability of their findings and stated that a crucial point was the fact that clinical data referred to Caucasian patients, although the analysis was performed for Japanese individuals. However, it should be noted that the clinical impact of aspirin was modelled using relative risk estimates, which would appear to be more transferable across locations. In addition, an extensive sensitivity analysis showed that the model results were robust to variations in key clinical and economic parameters. Finally, as the authors acknowledged, the inclusion of the costs of co-administration products, such as antacids, might have reduced the cost-effectiveness of aspirin.

Implications of the study
The analysis supports international recommendations for primary CVD prevention from both clinical and economic
perspectives. The authors pointed out that some Japanese trials are ongoing and these will provide country-specific data more relevant to the authors' setting.

Source of funding
None stated.

Bibliographic details

PubMedID
17301509

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.


Indexing Status
Subject indexing assigned by NLM

MeSH
Adult; Aged; Aspirin /economics /therapeutic use; Cardiovascular Diseases /economics /mortality /prevention & control; Cost-Benefit Analysis; Dose-Response Relationship, Drug; Drug Administration Schedule; Drug Costs; Economics, Pharmaceutical /statistics & numerical data; Evaluation Studies as Topic; Female; Health Care Costs; Humans; Japan; Male; Markov Chains; Middle Aged; Primary Prevention /economics; Risk Assessment; Sensitivity and Specificity; Survival Analysis

AccessionNumber
22007000448

Date bibliographic record published
31/08/2007

Date abstract record published
31/08/2007