Cost-effectiveness of coronary artery disease screening in asymptomatic patients with type 2 diabetes and other atherogenic risk factors in Japan: factors influencing on international application of evidence-based guidelines


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 investigated four different screening strategies for coronary artery diseases (CAD) in asymptomatic patients with Type 2 diabetes. The strategies were exercise electrocardiography, exercise echocardiography, single-photon emission-tomography (SPECT) and no screening.

Type of intervention
Screening.

Economic study type
Cost-utility analysis.

Study population
The study population comprised a hypothetical cohort of asymptomatic Japanese men with Type 2 diabetes mellitus and two additional atherogenic risk factors (hypertension and smoking).

Setting
The study setting was outpatient secondary care. The economic analysis was carried out in Japan.

Dates to which data relate
The effectiveness data were derived from studies published between 1987 and 2004. The cost data were derived from sources published between 2000 and 2003. The price year was 2003.

Source of effectiveness data
The clinical and epidemiological data used in the evaluation included:

CAD prevalence,

the relative risk of CAD in patients with Type 2 diabetes;

the annual incidence of CAD,

the proportion of silent ischaemia in patients with myocardial infarction,

the mortality rates, and

the mortality risk reductions associated with coronary artery bypass grafting (CABG), percutaneous transluminal
coronary angioplasty (PTCA), aspirin and simvastatin.

The effectiveness data included the specificity and sensitivity of each of the four screening strategies.

Modelling
A Markov model with a lifetime horizon was developed. The model structure was based on that used to evaluate the cost-effectiveness of screening in the USA. Full details of the model are given in Hayashino et al, 2004, (see 'Other Publications of Related Interest' for bibliographic details). In this analysis, however, the data were based on Japanese settings.

Sources searched to identify primary studies
The clinical and epidemiological data were derived from a wide range of sources. Relative risks for the Japanese population were derived from the published literature. The prevalence of CAD was derived from routinely collected Japanese data. The transition probabilities were derived from Japanese data together with Framingham equations. The mortality rates were determined using all-cause mortality from Japanese life tables. Mortality risk ratios associated with CAD interventions were derived from the published literature. The authors also made a number of assumptions about the mortality risks associated with interventions aimed at treating CAD.

Methods used to judge relevance and validity, and for extracting data
The authors did not report the methods used to obtain published literature for the derivation of clinical and epidemiological data. In instances where the authors had to make assumptions about a particular parameter, these were normally informed by the published literature.

Measure of benefits used in the economic analysis
The measure of benefits used in was the quality-adjusted life-years (QALYs) gained. The utilities for symptomatic myocardial ischaemia and myocardial infarction were derived from 10 patients with uncomplicated diabetes. These patients were given hypothetical scenarios and then asked to value them using the time trade-off method. For all other alive health states, a value of 1 (perfect health) was given.

Direct costs
The direct costs included were those to the health care system. These were the costs of each of the screening options, the costs of treatment (PTCA, CABG and aspirin), the annual costs of symptomatic myocardial infarction, the costs of treating, acute myocardial treatment costs, and the annual costs of conventional diabetes care. Most of the costs were derived from medical charges based on the reimbursement schedule, with the authors reporting that the cost-to-charge ratio was close to one in CAD care. Data on therapeutic procedures for CAD and the cost of conventional diabetes care, on the other hand, were derived from the reimbursement data of a public teaching hospital. Discounting was relevant, as the costs could be incurred over the patient's lifetime, and was appropriately performed at an annual rate of 3%. The authors reported the average costs. All costs were adjusted to 2003 prices using the medical care component of the Consumer Price Index.

Statistical analysis of costs
The cost data were treated as point estimates (i.e. the data were deterministic).

Indirect Costs
The productivity costs included were those associated with the patients' time lost due to travel, waiting time and treatment time associated with office visits. Time lost due to treatment, waiting and travel was derived from a Japanese survey, conducted as part of a patient behavioural survey in 1999. Lost time was then valued using the average hourly earning of employed people. Discounting was relevant, as the costs could be incurred over the patient's lifetime, and
was appropriately performed at an annual rate of 3%. The authors reported the average costs. All costs were adjusted to 2003 prices using the medical care component of the Consumer Price Index.

Currency
Japanese yen (JPY). JPY were converted to US dollars ($) using the OECD Purchasing Power Parity rate in 2003 ($1.00 = JPY 130.3).

Sensitivity analysis
The authors performed a series of one-way sensitivity analyses on all the variables using the 95% confidence intervals around mean values or, when this was not possible, a range of plus or minus 30%. A two-way sensitivity analysis dealing with diagnostic performance was also conducted. The authors performed scenario analysis by varying the gender, age and atherogenic risk factors. They also varied the time interval of exercise echocardiography from only at initial stage to once every 3, 5 or 10 years.

Estimated benefits used in the economic analysis
For men with hypertension who smoke, the QALYs gained for 55- and 60-year-olds, respectively, were:

- 13.2311 and 11.2402 QALYs with the strategy of no screening;
- 13.2889 and 11.3566 QALYs with exercise electrocardiography;
- 13.3038 and 11.3862 QALYs with exercise echocardiography; and
- 13.3042 and 11.3886 QALYs with exercise SPECT.

Cost results
For men with hypertension who smoke, the costs for 55- and 60-year-olds, respectively, were:

- $150,545 and $135,332 for the strategy of no screening;
- $154,086 and $138,986 for exercise electrocardiography;
- $154,989 and $139,917 for exercise echocardiography; and
- $155,770 and $140,699 for exercise SPECT.

Synthesis of costs and benefits
The costs and benefits were combined using an incremental cost-utility ratio (i.e. the additional cost per QALY gained).

Compared with no screening, exercise electrocardiography was found to be dominant (both more effective and less costly) for 55-year-old men.

For 60-year-old men, the incremental cost-utility ratio was $31,400 per QALY gained.

When exercise echocardiography was compared with exercise electrocardiography, the incremental cost-utility ratio was $61,100 per QALY gained for 55-year-old men and $31,500 per QALY gained for 60-year-old men.

When exercise SPECT was compared with exercise echocardiography, the incremental cost-utility ratio was $195,000 per QALY gained for 55-year-old men and $326,000 per QALY gained for 60-year-old men.

The results of the sensitivity analysis showed variation according to age, gender, the combination of additional...
atherogenic risk factors, and the frequency of exercise echocardiography screening. Changes in the costs of CABG and also risk reductions in mortality due to CAD treatment had less impact on the results.

Authors’ conclusions
US guidelines recommending screening for coronary artery disease (CAD) in asymptomatic diabetic patients with atherogenic risk factors could also be applied to Japanese patients.

CRD COMMENTARY - Selection of comparators
A justification was given for assessing the four screening options used in this study. They represented the strategies assessed in American College of Cardiology/American Diabetes Association guidelines. You should decide if these screening strategies represent current practice in your own setting.

Validity of estimate of measure of effectiveness
The parameters used in the model were derived from published literature, routinely collected Japanese data, and the authors’ assumptions. The authors did not report if data from different studies were combined, and no methods were described. The authors did not report how the included studies were identified, nor did they report any of the methods used in their review of the literature (i.e. whether it was systematic, the databases searched, and inclusion criteria). Overall, it was not possible to ascertain the validity of the estimates derived.

Validity of estimate of measure of benefit
The estimation of health benefit (QALYs) was derived using a Markov model. The QALYs gained were appropriately discounted. Utility values were derived from a sample of 10 patients using time trade-off exercises. The authors only valued two of the many health states in the model, with all other "alive" health states being assigned a utility of 1, which might not be representative of the actual quality of life attained in these health states.

Validity of estimate of costs
The analysis of the costs was performed from a societal perspective. All the relevant categories of costs appear to have been included in the analysis. However, the authors did omit some relevant costs such as the mortality and morbidity costs associated with CAD. These omissions would appear to bias against the screening options, as they were found to generate more QALYs than the no screening option.

The costs were derived from hospital reimbursement data and charges were used. Generally, charges do not capture the true costs of the intervention and treatment, and they are therefore not recommended for use when a societal perspective is adopted. However, the authors reported that, in the case of CAD in Japan, the costs and charges were virtually identical. Since the costs could be incurred over the lifetime of the patient, future costs were appropriately discounted.

The authors performed a series of one-way sensitivity analyses, but only reported the effects of these analyses on exercise echocardiography and electrocardiography. Further, no results of the two-way sensitivity analyses were reported. The price year was reported, which will ease future inflation exercises.

Other issues
The authors compared their findings with those obtained in US guidelines and found that the recommendations were similar. The issue of generalisability to other settings (i.e. the USA) was addressed by comparing the cost-effectiveness of screening for CAD in Japan with the USA using the same model, but with Japanese-specific data. The authors do not appear to have presented their results selectively and their conclusions reflected the scope of the analysis. The authors reported a number of further limitations to their study. First, some of the clinical data was derived from studies published over the last 10 years. Second, the Framingham cohort contained few patients with diabetes, thus some of the data might not be applicable to patients with diabetes.

Implications of the study
The authors report that the actual population that could benefit from the screening strategies depends on the patient’s
characteristics and the diagnostic performance of the screening tests.

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**Other publications of related interest**
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**Indexing Status**
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