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 assessed was use of electron beam computed tomography (EBCT) combined with use of the Framingham Risk Index (FRI), as a screening strategy for the primary detection of patients at high risk for cardiovascular disease.

Type of intervention
Screening.

Economic study type
Cost-effectiveness analysis; cost-utility analysis.

Study population
The study population consisted of men and women aged 39 to 45 years old, without any symptoms of cardiovascular disease. Patients with known coronary heart disease or angina pectoris on the questionnaire by Rose were excluded.

Setting
The setting appears to have been secondary care; the economic study was conducted in the USA.

Dates to which data relate
Effectiveness evidence was derived from studies published between 1978-2000. Costs were based on literature published between 1995-2001. The price year was not stated.

Source of effectiveness data
The source of effectiveness data was a review of the literature and estimates based on opinion.

Modelling
An economic model was developed in the form of a decision tree, in order to estimate the additional costs and benefits resulting from a screening strategy that combined EBCT with FRI, in comparison to a strategy adopting FRI alone, for the detection of individuals "at risk" (as opposed to "low risk") of cardiovascular disease among a population without any symptoms. After initial screening with either of the two strategies assessed, a proportion of individuals found at risk were assumed to go on to further testing for obstructive coronary artery disease (stress test, cardiac catheterisation). A large proportion of individuals at risk were assumed to start on medication (such as statins, beta-blockers, aspirin and angiotensin-converting enzyme inhibitors); a small proportion of individuals at low risk were assumed to take medication, too. Finally, a proportion of patients were estimated to have an incidental finding at EBCT screening (e.g. osteophyte, hepatic lesion, pulmonary nodule), which might require further management. For every branch of the decision tree, associated costs, life expectancy and quality of life were assessed.
Outcomes assessed in the review
The outcomes assessed in the literature review were: the differential in life expectancy of a 42-year old individual between being at risk and being at low risk (based on life expectancy of untreated 42-year old patients being at risk or at low risk); the effectiveness of medications (used for primary prevention) in terms of reduction in cerebrovascular events; the decrement in quality of life of having been found at risk or being on medications, or both; the individual prognostic value of EBCT; the prevalence of individuals found "at risk" with each of the screening strategies assessed (EBCT plus FRI or FRI alone); the proportion of individuals at risk having an ischaemic evaluation; the proportion of individuals at risk and at low risk starting medications; and the frequency of incidentals at EBCT screening.

Study designs and other criteria for inclusion in the review
Most effectiveness data were based on a prospective cohort study; for more details the reader is referred to "other publications of related interest". No inclusion or exclusion criteria were listed for the rest of the studies included in the review.

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
Approximately 3 primary studies were included in the review.

Methods of combining primary studies
The results of individual primary studies were not combined.

Investigation of differences between primary studies
No investigation of differences between primary studies was discussed.

Results of the review
The differential in life expectancy of a 42-year old individual between being at risk and being at low risk was 5 years; left untreated, individuals at risk would live on average an additional 35 years (to age 77), whereas those at low risk would live an additional 40 years (to age 82).

Medication used for primary prevention was found to provide a 30% reduction in cerebrovascular events.

The utility of a year of life "at risk" or being on medication or both was 98% of utility of a year of life without the diagnosis.

The individual prognostic value of EBCT was 18%; the prevalence of individuals found at risk with EBCT plus FRI was estimated at 22.4%; with FRI alone this percentage was 7.2%.

Of those found at risk, 30% would have an ischaemic evaluation.
Individuals found at risk had a probability of 75% of starting on medication, while this probability was 10% for those found at low risk.

The frequency of incidentals at EBCT screening was found to be 8%.

Of these, 40% would be characterised as intermediate and 19% as major incidentals, often requiring invasive procedures.

**Methods used to derive estimates of effectiveness**
Some estimates of effectiveness were based on authors' assumptions, based on available literature.

**Estimates of effectiveness and key assumptions**
It was assumed that primary prevention for cardiovascular disease could improve life expectancy by 30%, based on the estimate of 30% reduction in cerebrovascular events by medications used for primary prevention. In addition, most of the values derived from the literature review were modified based on authors' further assumptions.

**Measure of benefits used in the economic analysis**
The outcome measures used in the economic analysis were the number of cases detected and the number of quality-adjusted life-years (QALYs) gained. QALY estimates were based on the assumption that, in terms of utility, the state of being "at risk" for cardiovascular disease was comparable with other asymptomatic disease states, for which utility values could be found in published literature.

**Direct costs**
Direct costs consisted of health service costs. These included cost of EBCT, cost of follow-up tests for individuals found at risk (stress test and, in case of a positive result, subsequent cardiac catheterisation), cost of medication, and cost of management of incidental findings. Costs associated with calculating a FRI were omitted from the analysis, since they were common to both screening strategies compared. Costs and quantities were not analysed separately. Costs were based on Medicare reimbursement rates when available, community averages of charges, literature published in 1995-2001, and further assumptions where charge data were not available. Total costs were derived using modelling. Discounting was not carried out, despite costs being estimated over lifetime. The price year was not stated.

**Statistical analysis of costs**
Costs were treated in a deterministic way; no statistical analysis of costs was undertaken.

**Indirect Costs**
Indirect costs were not included in the analysis.

**Currency**
US dollars ($).

**Sensitivity analysis**
A sensitivity analysis was carried out to test the robustness of the results under a range of input values. One- and two-way sensitivity analyses were undertaken. The ranges of values used were based on published literature and further assumptions.

**Estimated benefits used in the economic analysis**
Total or incremental benefits resulting from adopting each of the screening strategies assessed were not reported. Benefits expressed in the form of QALYs were estimated over the lifetime of individuals screened. However, they were not discounted. Side effects of screening (both physical and psychological harm) were not taken into account in the economic analysis.

Cost results
Total and incremental costs associated with each of the screening strategies compared were not reported. Costs were estimated over the lifetime of individuals screened, but no discounting process was applied. Costs of physical harm from the initial test and from evaluation of abnormal tests were not considered in the economic analysis; however, costs associated with incidental abnormalities detected at screening were taken into account.

Synthesis of costs and benefits
Costs and benefits were combined in the form of Incremental Cost-Effectiveness Ratios (ICERs). Two ICERs were estimated: cost per additional case (individual at risk) detected, and also cost per additional QALY saved, by applying EBCT plus FRI versus FRI alone.

The cost per additional case detected was $9,789 in the base-case scenario. This cost was most sensitive to the cost of EBCT itself and the cost of medication; substantial changes in the values of these parameters (even 100%) resulted in a range of ICERs between $5,276 and $16,565. The cost per case detected was not sensitive to any other variables.

The cost per additional QALY saved was equal to $86,752 in the base-case scenario. This cost was most sensitive to the efficacy of primary prevention and the utility placed on a year of life taking medications. By decreasing the efficacy of primary prevention to 25%, combination of EBCT plus FRI became dominated by FRI alone. If primary prevention had an efficacy equal to 35%, then the ICER would fall at $36,076 per QALY. As the utility of a year of life at risk rose higher than the base-case (98%) to 98.3% of a year of life without the diagnosis, then the ICER fell at $50,866 per QALY. If this value became lower than 97.6%, then FRI alone dominated combination of EBCT plus FRI.

Increasing the independent prognostic value of EBCT decreased the ICER only modestly: even if EBCT could identify an additional 50% of individuals at risk, the ICER would still be high, equalling $60,000 per QALY. If EBCT could identify only an additional 10% of individuals at risk, then the ICER would rise to $118,000 per QALY.

The cost of medications and of EBCT both influenced the cost-effectiveness of incorporating EBCT into risk assessment, although the ICER remained greater than $45,000 per QALY, even with very low prices. The remaining variables had relatively little influence on the relative cost-effectiveness between combination of EBCT plus FRI versus FRI alone.

Authors’ conclusions
The use of EBCT to improve cardiovascular risk prediction in a young population with no cardiac symptoms who were at low absolute risk was expensive and not cost-effective by conventional standards. If the utility of being "at risk" was comparable to other asymptomatic disease states, EBCT might have a detrimental effect on screening populations.

CRD COMMENTARY - Selection of comparators
No explicit justification was provided for the selection of the comparator (FRI), but it probably represented a simple, cheap and effective screening method for identification of individuals at risk for cardiovascular disease. You should consider whether the comparator reflects 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 not combined. The majority of effectiveness data were based on a prospective cohort study.
Validity of estimate of measure of benefit
The estimation of benefits was modelled. The model used, in the form of a decision tree, was appropriate for this purpose. Benefits were not discounted, although they were estimated over the lifetime of the study population.

Validity of estimate of costs
The perspective of the study was not stated, but seemed to be that of a third-party payer. All categories of cost relevant to this perspective were included in the analysis. The cost of FRI was omitted from the analysis, because it was common to both therapies; therefore its omission is unlikely to have affected the results. Costs and quantities were not reported separately, and this hinders the generalisability of the results. A sensitivity analysis of costs was undertaken, using a wide range of cost values, based on published literature and authors' further assumptions. In most cases, charges were used to proxy prices, but this was consistent with the perspective of a third-party payer. Although costs were incurred over a lifetime, discounting was not undertaken. The date to which prices referred was not reported, and this limits the reproducibility of the results.

Other issues
The authors did not compare their findings to those of other studies. The issue of the generalisability of results to other settings was not discussed; however, the authors addressed the issue of generalisability to other populations. Results were not presented in a disaggregated form (benefits and costs were not reported separately). The authors reported a number of limitations to their study, such as the difficulty in interpreting the results (i.e. when expressed as cost per case detected), the substantial uncertainty about the true value of several variables, and the lack of discounting process in estimation of future costs and benefits. The authors performed their analysis based on data from a young, low risk population, and this was reflected in their conclusions.

Implications of the study
The authors suggested that, based on the study results, EBCT screening should not be recommended for populations at low risk for coronary artery disease. Its use should be limited to situations in which clinicians can identify a clear benefit.

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Other publications of related interest