

# Appendix E - Health Economics Extractions

## 11 **What is the utility and cost effectiveness of cardiac biomarkers in evaluation of individuals with acute chest pain of suspected cardiac origin?**

<b>No</b>	838	<b>Study Quality:</b>	The diagnostic value and cost-effectiveness of creatine kinase-MB, myoglobin and cardiac troponin-T for patients with chest pain in emergency department observation ward (Structured abstract)
<b>Author:</b>	Choi YF;Wong TW;Lau CC;		2004
<b>Relevance:</b>			
<b>Intervention:</b>			Standard clinical evaluation including serial ECG and troponin T determinations at presentation and again at 6 to 8 hours post presentation.
<b>Comparison:</b>			Standard clinical evaluation including serial ECG and CK-MB determinations at presentation and again at 6 to 8 hours post presentation.
<b>Population:</b>			480 patients presenting to a Hong Kong emergency department, all over age 30 years and had primary complaint of chest pain of suspected cardiac origin with onset within one week.
<b>Perspective:</b>			Not stated Exclusion criteria: Patients whose ECG suggested AMI or who had a clinical diagnosis of ACS or unstable angina or who had had an AMI or cardiac catheterisation within one month.
<b>Study type:</b>			Prospective study with cost benefit analysis
<b>Methods:</b>			Prospective study
<b>Health valuations:</b>			NOT APPLICABLE
<b>Cost components:</b>			Costs of cardiac biomarker tests, cost of false positive (estimated as cost of 2-day hospital admission), cost of AMI (estimated as cost of 6-day hospital admission)
<b>Currency:</b>			Hong Kong dollars (HK\$)
<b>Cost year:</b>			2002
<b>Time horizon:</b>			Patients were followed up for 6 months
<b>Discount rate:</b>			Not applicable

**Results-cost:** Costs of each strategy were measured as the cost of the cardiac biomarker tests.

Cost of TnT = HK\$25440  
 Cost of CK-MB = HK\$1259

**Results-effectiveness:** Effectiveness was measured as the cost of resources not used when unnecessary admission was avoided and when future AMIs were prevented through diagnosis with cardiac biomarker.

Effects of TnT = HK\$147900 (25 avoided hospital admissions) + HK\$53244 (3 prevented AMIs)  
 Effects of CK-MB = HK\$5916 (1 avoided hospital admission) + HK\$0 (0 prevented AMIs)

**Results-ICER:** As this was not a full economic evaluation, no incremental analysis was performed.

**Result-Uncertainty:** As this was not a full economic evaluation, no sensitivity analysis was undertaken.

**Source Funding:** Not stated

**Comments:** Results of the partial economic analysis showed that testing for TnT would yield a cost savings of an estimated HK\$171047 compared with testing for CK-MB. This was largely due to the superior sensitivity and specificity of TnT over CK-MB. Although the TnT test was about HK\$20 more expensive per unit, the savings generated by avoiding unnecessary hospital admissions (HK\$141984) and from correctly diagnosing significant coronary heart disease and thus avoiding future AMI (HK\$53244) made it a cost saving option. The study deemed myoglobin to be of no value due to its lack of specificity.

**No** 837 **Study Quality:** Cost effectiveness of diagnostic strategies for patients with acute, undifferentiated chest pain (Structured abstract)

**Author:** Goodacre S;Calvert N; 2003

**Relevance:**

**Intervention:** 3 enzyme testing strategies compared with a baseline strategy of discharging all patients without additional testing.

**Comparison:** Enzyme testing at presentation vs. Enzyme testing at presentation and again 6 hrs after onset of pain vs. 24 hr admission and then enzyme testing.

**Population:** Hypothetical cohort of 1000 patients presenting to hospital with acute undifferentiated chest pain and: no ECG changes diagnostic of AMI or UA; negligible risk of CHD based on clinical features/risk factors; no evidence of other serious abnormalities requiring hospital admission; no clinically obvious UA (defined as known CHD with prolonged or recurrent episodes of cardiac type chest pain).

**Perspective:**

**Study type:** CUA (QALYs)

**Methods:** DECISION ANALYSIS Model

**Health valuations:** 3-year survival data estimated using data from a multicentre chest pain study (Lee et al. 1992)

**Cost components:** Direct costs of running each strategy estimated by summing constituent elements: unit costs of admission, medical treatment of AMI and UA, cardiac enzyme tests, investigations of false positives and terminal care.

**Currency:** £

**Cost year:** 2000/01

**Time horizon:** Lifetime

**Discount rate:** 6% per annum for both costs and effects

**Results-cost:** Strategy 0 (discharge all patients without additional testing): 1,399,700 per 1,000 patients  
 Strategy 1 (enzyme testing at presentation): 1,499,600 per 1,000 patients  
 Strategy 2 (enzyme testing at presentation then observation until min 6 hrs and repeat enzyme testing): 1,597,100 per 1,000 patients  
 Strategy 4 (Admit to hospital for 24 hrs and then enzyme test): 1,796,100 per 1,000 patients

**Results-effectiveness:** Strategy 0: 8853.7 QALYs per 1000 patients  
 Strategy 1: 8859.4 QALYs per 1000 patients  
 Strategy 2: 8864.7 QALYs per 1000 patients  
 Strategy 4: 8870.2 QALYs per 1000 patients

**Results-ICER:** Strategy 1: £17,432/QALY  
 Strategy 2: £18,567/QALY  
 Strategy 4: £36,069/QALY

**Result-Uncertainty:** Results were insensitive to variation of prevalence of AMI or UA; utilities of AMI or UA; mortality estimates; treatment effect estimates; costs of treatment of AMI and UA; cost of terminal care; and cost of long term treatment of survivors.

Results were sensitive to variation in the cost of each strategy, the cost of ruling out false positives and the effect of false positive diagnosis on quality of life.

**Source Funding:** Public

**Comments:** The results show that a strategy of cardiac enzyme testing at presentation is likely to be cost-effective (£17,432/QALY) compared with a do-nothing strategy. A strategy of enzyme testing at presentation and again 6 hours after the onset of pain is also likely to be cost-effective (£18,567/QALY) compared with testing only at presentation. A strategy of testing after 24 hours of observation is unlikely to be considered cost-effective (£36,069/QALY). The analysis indicates that serial enzyme testing at presentation and again 6 hours after the onset of pain is a cost-effective strategy, and that strategies involving a long period of observation are unlikely to be.

Although the model is not sophisticated, it is one of only two UK studies looking at the economic impact of biomarkers. But,

because it does not compare specific enzyme tests, it does not give definitive information on the most cost-effective approach or whether any other approaches are more cost-effective.

**No** 836 **Study Quality:** Systematic review and modelling of the investigation of acute and chronic chest pain presenting in primary care

**Author:** Mant J;McManus RJ;Oakes RL;Delaney BC;Barton PM;Deeks JJ;Hammersley L;Davies RC;Davies MK;Hobbs FR; 2004

**Relevance:**

**Intervention:** 4 testing and treatment strategies

**Comparison:** Compares testing for troponin T versus not testing for troponin T with and without pre-hospital telemetry ECG.

**Population:** Patients presenting in primary care with acute chest pain suspicious of ACS.

**Perspective:** NHS

**Study type:** CEA using Monte Carlo simulation model with outcomes measured as percent achieving 28-day survival

**Methods:** DECISION ANALYSIS (sens and spec of POCT indexed w time, values obtained from systematic review)

**Health valuations:** NOT APPLICABLE

**Cost components:** Ambulance call-out; telemetry ECG; Reteplase; Streptokinase; A&E died; A&E referred; A&E discharged; treatment of MI; TnT test

**Currency:** £

**Cost year:** 2000

**Time horizon:** 28 days

**Discount rate:** Not applicable

**Results-cost:** A&E ECG and POCT: £757 per patient  
A&E based on ECG: £916 per patient  
Pre-hosp thromb and A&E ECG only £1166 per patient  
Pre-hosp thromb and A&E ECG and POCT: £1209 per patient

**Results-effectiveness:** Percent achieving 28-day survival  
  
A&E ECG and POCT: 96.6%

A&E based on ECG: 96.4%  
Pre-hosp thromb and A&E ECG only 96.1%  
Pre-hosp thromb and A&E ECG and POCT: 97.3%

**Results-ICER:** Use of troponin T dominates non-use of troponin T with or without pre-hospital telemetry ECG.

**Result-Uncertainty:** Sensitivity analysis was performed allowing for first and second order uncertainty. Dominant results were robust to sensitivity analysis of varying the pain to needle time (15 minutes to 180 minutes to 3 hours) and cost of telemetry ECG (£50 - £400).

**Source Funding:** Public

**Comments:** A biomarkers analysis was elicited from the full Mant analysis, such that the incremental benefit of using a troponin T test could be isolated from other strategies modelled (e.g. pre-hospital telemetry ECG).

**No** 768 **Study Quality:** Impact of troponin T determinations on hospital resource utilization and costs in the evaluation of patients with suspected myocardial ischemia

**Author:** Zarich S;Bradley K;Seymour J;Ghali W;Traboulsi A;Mayall ID;Bernstein L; 2001

**Relevance:**

**Intervention:** Standard clinical evaluation including serial ECG and CK-MB determinations with the addition of serial troponin-T determinations measured at presentation, 3 and 12 hours post presentation (n=447).

**Comparison:** Standard clinical evaluation including serial ECG and CK-MB determinations only (n=409).

**Population:** 891 patients (aged over 18 years) presenting to the emergency department with chest pain symptoms suspicious for myocardial ischemia of >30 minutes duration that warranted an evaluation for myocardial infarction. 77% of the patients included presented with chest pain and 23% presented with no chest pain. A sub-group analysis of the chest pain patients is presented.

**Perspective:** THIRD-PAYER

**Study type:** RCT with analysis of resource impact

**Methods:** RCT

**Health valuations:** NOT APPLICABLE

**Cost components:** Total hospital charges (costs estimated at 60% of charges based on hospital accounting methods)

**Currency:** US\$

**Cost year:** Not stated

**Time horizon:**

**Discount rate:** Not applicable

**Results-cost:** In the sub-group analysis for patients presenting with chest pain, there was a strong trend toward reduced length of stay (1.4 vs 1.9 days; p=0.09) with a significant reduction in total hospital charges (\$6993 vs \$8753; p=0.05) in TnT compared with control patients.

In patients without ACS, fewer TnT group patients were admitted to hospital compared with controls (31% vs 25%; p=0.04) and there was a significant reduction in length of stay (1.2 vs 1.6 days; p=0.03) with a trend toward reduced total charges (\$4487 vs \$6187; p=0.17).

TnT determinations appeared particularly useful in patients with falsely elevated CK-MB values.

In patients with ACS both length of stay (3.7 vs 4.6 days; p=0.01) and total charges (\$15004 vs \$19202; p=0.02) were significantly reduced in TnT patients compared with controls. Significant reductions were also seen in telemetry or cardiac care unit length of stay (3.5 vs 4.6 days; p=0.03).

Patients examined in and discharged from the emergency department had an average stay of 10.5 hours at a charge of \$2047. Those admitted to telemetry were admitted for an average length of stay of 4.0 days at a charge of \$12636. Patients admitted to the cardiac care unit had an average length of stay of 7.0 days at a charge of \$31152. On average, total charges for TnT patients were \$1538 less than control patients (representing a potential \$923 cost saving). The estimated annual savings to the hospital based on this analysis were \$4 million in charges (\$2.4 million in costs). Savings are predominantly due to reduced length of stay in patients with and without ACS and to reduced admissions for patients without ACS in the TnT group.

**Results-effectiveness:** Cardiac events at 30 days occurred in 18 patients (3.1%) and did not differ between controls and interventions for whole cohort and subgroups.

**Results-ICER:** As this was not a true cost-effectiveness analysis, there was no incremental analysis undertaken.

**Result-Uncertainty:** Sensitivity analysis was not applicable to this study, therefore none was performed.

**Source Funding:** Roche Diagnostics

**Comments:** The study indicates that the utilisation of TnT in addition to CK-MB led to a 20-25% reduction in length of stay and total charges in high and low risk patients with and without ACS. The evidence indicates that the addition of TnT reduced admissions by 7-11% and that ACS patients were managed more efficiently with a lower length of stay, shorter telemetry or cardiac care unit stay and lower total charges (and costs) despite a similar number of hospital admissions.

The potential savings are substantial and may have been underestimated due to case mix in the TnT and control groups and as many as two-thirds of patients without ACS but with raised CK-MB and despite normal TnT were admitted to hospital (as emergency department physicians became more familiar with TnT determinations).

The use of TnT determinations in addition to CK-MB determinations is likely to be safe, effective and resource saving in the evaluation of high and low risk patients with suspected ACS/AMI presenting to an emergency department. Although the analysis was undertaken in North America, it is likely that these results are generalisable to an NHS A&E setting given the relatively low cost of TnT testing compared to the costs of admitting patients to hospital and cardiac care units.

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## What is the diagnostic utility MSCT coronary angiography in the diagnosis of patients with acute chest pain of suspected cardiac origin

<b>No</b>	1156	<b>Study Quality:</b>	Sixty-four-slice computed tomography of the coronary arteries: cost-effectiveness analysis of patients presenting to the emergency department with low-risk chest pain
<b>Author:</b>		Khare RK;Courtney DM;Powell ES;Venkatesh AK;Lee TA;	2008
<b>Relevance:</b>			
<b>Intervention:</b>		64 slice MDCTCA	
<b>Comparison:</b>		Stress Echocardiography, Stress ECG	
<b>Population:</b>		Patients presenting with low risk chest pain ( 2% to 10% risk) in an emergency department.	
<b>Perspective:</b>		US payer perspective	
<b>Study type:</b>		Cost-Utility analysis i.e. incremental cost per QALY	
<b>Methods:</b>		Decision analytic model	
<b>Health valuations:</b>		N/A. Used published estimates	
<b>Cost components:</b>		Cost of diagnostic tests, observation unity care, MI, death, coronary angiography, PCI, CABG, costs of missed CAD and MI.	
<b>Currency:</b>		US dollars	
<b>Cost year:</b>		2007	
<b>Time horizon:</b>		lifetime although only first 30 day costs included.	
<b>Discount rate:</b>		not used.	
<b>Results-cost:</b>		MDCT mean \$2,684 (SD range \$1,773 to \$4,418); Stress Echo = \$3,265 ( \$2,383 to \$4,836); Stress ECG = \$3,461 (\$2,533 to \$4,836).	

**Results-effectiveness:** MDCT mean 24.69 QALYs (SD range 24.54 to 24.76); Stress Echo = 24.63 ( 24.28 to 24.74); Stress ECG = 24.59 (24.21 to 24. 75).

**Results-ICER:** MDCT dominates stress Echo and stress ECG. I.e. more effective and less costly for all three levels of risk modelled ( 2%, 6% and 10%).

**Result-Uncertainty:** Probabilistic sensitivity analysis demonstrated that for the majority of Monte Carlo runs of the base case, the majority of plots are in the bottom right hand quadrant of the cost-effectiveness plane ( i.e. MDCT is dominant). Threshold sensitivity analysis indicate that in order for the cost saving result to become cost-neutral, prevalence of CAD would have to be greater than 70%, sensitivity of MDCT would have to drop to 65%, or there would have to be an MDCT indeterminate rate of 30%. In general the ICER remained below \$10,000 per QALY.

**Source Funding:** Agency for Healthcare Research and Quality

**Comments:** MDCT was cost-saving despite the exclusion of the ED work up costs from the analysis. The model results were robust to nearly all of the assumptions used in the model. Using a threshold willingness to pay of \$50,000 per QALY, MDCT would always be considered cost-effective in the scenarios modelled. Because 64 slice MDCT is a relatively new technology, there is relatively little evidence for test sensitivity and specificity although this was allowed for in the sensitivity analysis by examining quite wide ranges of uncertainty. Risk of radiation was not incorporated into the model. Any risk of renal failure from a double dye load for patients with a positive MDCT test who then require another immediate catheterization is also not incorporated into the model.

**No** 1161 **Study Quality:** Cost-effectiveness of coronary MDCT in the triage of patients with acute chest pain

**Author:** Ladapo JA;Hoffmann U;Bamberg F;Nagurney JT;Cutler DM;Weinstein MC;Gazelle GS; 2001

**Relevance:**

**Intervention:** 64-MDCTCA.

**Comparison:** Standard of Care (SOC) Algorithm based on biomarkers and randomly allocating patients to stress tests using SPECT, Echocardiography, or stress ECG.

**Population:** hypothetical cohort of 55 year old men and women (separately) with low risk acute chest pain, defined as negative initial troponins, normal or non-diagnostic ECG, and no history of heart disease.

**Perspective:** Stated as Societal perspective in the context of the US healthcare system but no evidence that patient costs or costs to the economy were included in the analysis.

**Study type:** Cost-Utility analysis i.e. Incremental costs per QALY.

**Methods:** A decision analytic model using various published sources for effectiveness/ test characteristics.

**Health valuations:** N/A used published estimates of health state valuations ( quality adjusted life expectancies)



**Cost components:** Emergency department visits and imaging/testing. Medical treatment for mild heart disease and hospital admissions and Treatment for moderate to severe heart disease.

**Currency:** US dollars.

**Cost year:** 2005

**Time horizon:** lifetime

**Discount rate:** 3% for both costs and QALYs

**Results-cost:** 64CTCA Men \$10,190; Women \$6,630;  
SoC Men \$9,990; Women \$7,010;

**Results-effectiveness:** 64CTCA Men 15.31 QALYs; Women 16.99 QALYs;  
SoC Men 15.27 QALYs; Women 19.98 QALYs;

**Results-ICER:** Men \$6,400 per incremental QALY  
Women 64CTCA is cost-saving and dominates SoC

**Result-Uncertainty:** Sensitivity analysis indicates that the ICER for men remains within generally acceptable levels of cost-effectiveness (e.g. reducing by 25% the ability of 64CT to correctly classify healthy patients increases the ICER to \$17,000). Women remain cost-saving of low cost-effectiveness. Using SPECT as the only stress test option results in 64CTCA dominating SoC for both man and women.

**Source Funding:** Walker Fund of the Harvard PhD programme in Health Policy

**Comments:** Only modest gains in QALYs because of the assumed low prevalence of ACS in the modelled population. Results were better for women because of the lower prevalence of ACS in 55 year old women compared to men. The authors indicate that the ICER for higher risk patients is uncertain and needs further investigation. They state that their results may not be generalisable to other countries due to demography and resource valuations, although their base case results are relatively stable under a variety of sensitivity analyses. The authors indicate that clinical trials evaluating this technology are underway and that the results "may ultimately illuminate a more efficient and cost-effective management approach to low risk patients with chest pain in an emergency department."

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## What is the diagnostic utility of calcium scoring for the evaluation of patients with stable chest pain of cardiac origin.

**No 1015 Study Quality:** Coronary calcification by electron beam computed tomography and obstructive coronary artery disease: a model for costs and effectiveness of diagnosis as compared with conventional cardiac testing methods

**Author:** Rumberger JA;Behrenbeck T;Breen JF;Sheedy PF; 1999

**Relevance:**

**Intervention:** Electron beam computed tomography with calcium scoring - 4 different Agatston calcium score thresholds (>0; =37; =80; =168) were used to define positive diagnosis

**Comparison:** Stress ECG, stress thallium scintigraphy, stress echo and coronary angiography

**Population:** Hypothetical cohort of 100 patients for each CAD prevalence's tested (10%, 20%, 50%, 70% and 100%).

**Perspective:** THIRD PAYER

**Study type:** CEA (average cost per correct diagnosis of CAD)

**Methods:** DECISION ANALYSIS

**Health valuations:** NOT APPLICABLE

**Cost components:** Total direct costs: cost of test performed and cost of complications (death, ventricular fibrillation, myocardial infarction, cerebral infarction and vascular surgical repair)

**Currency:** US\$

**Cost year:** Not stated

**Time horizon:** Not applicable

**Discount rate:** Not applicable

**Results-cost:** Total costs for the entire 100 patient cohort at each CAD prevalence:

10% CAD Prevalence:  
 EBCT (=168) = \$105112  
 EBCT (=80) = \$126400  
 EBCT (=37) = \$151236  
 ETT = \$166019  
 Echo = \$191295  
 Thallium = \$241083  
 EBCT (>0) = \$247030  
 CA = \$354000

20% CAD Prevalence:  
 EBCT (=168) = \$126392  
 EBCT (=80) = \$151232  
 EBCT (=37) = \$171864

ETT = \$180210  
Echo = \$216121  
EBCT (>0) = \$261212  
Thallium = \$265914  
CA = \$354000

50% CAD Prevalence:  
EBCT (=168) = \$186696  
EBCT (=80) = \$222180  
ETT = \$222804  
EBCT (=37) = \$243450  
Echo = \$283542  
EBCT (>0) = \$303792  
Thallium = \$333315  
CA = \$354000

70% CAD Prevalence:  
EBCT (=168) = \$229350  
ETT = \$247605  
EBCT (=80) = \$268273  
EBCT (=37) = \$289548  
Echo = \$329640  
EBCT (>0) = \$332119  
CA = \$354000  
Thallium = \$377748

100% CAD Prevalence:  
ETT = \$290175  
EBCT (=168) = \$293112  
EBCT (=80) = \$335664  
CA = \$354000  
EBCT (=37) = \$356940  
EBCT (>0) = \$374680  
Echo = \$397035  
Thallium = \$446810

**Results-effectiveness:** Effectiveness was measured as the number of patients out of 100 correctly diagnosed as having obstructive CAD.

10% CAD Prevalence:  
EBCT (=168) = 7 True Positive (TP) and 3 False Negative (FN)  
EBCT (=80) = 8 TP and 2 FN  
EBCT (=37) = 9 TP and 1 FN  
ETT = 7 TP and 3 FN  
Echo = 9 TP and 1 FN  
Thallium = 9 TP and 1 FN  
EBCT (>0) = 10 TP and 0 FN

CA = 10 TP and 0 FN

20% CAD Prevalence:

EBCT (=168) = 14 TP and 6 FN

EBCT (=80) = 17 TP and 3 FN

EBCT (=37) = 18 TP and 2 FN

ETT = 15 TP and 5 FN

Echo = 17 TP and 3 FN

EBCT (>0) = 19 TP and 1 FN

Thallium = 18 TP and 2 FN

CA = 20 TP and 0 FN

50% CAD Prevalence:

EBCT (=168) = 36 TP and 14 FN

EBCT (=80) = 42 TP and 8 FN

ETT = 36 TP and 14 FN

EBCT (=37) = 45 TP and 5 FN

Echo = 43 TP and 7 FN

EBCT (>0) = 48 TP and 2 FN

Thallium = 45 TP and 5 FN

CA = 50 TP and 0 FN

70% CAD Prevalence:

EBCT (=168) = 50 TP and 20 FN

ETT = 51 TP and 19 FN

EBCT (=80) = 59 TP and 11 FN

EBCT (=37) = 63 TP and 7 FN

Echo = 60 TP and 10 FN

EBCT (>0) = 67 TP and 3 FN

CA = 70 TP and 0 FN

Thallium = 63 TP and 7 FN

100% CAD Prevalence:

ETT = 73 TP and 27 FN

EBCT (=168) = 72 TP and 28 FN

EBCT (=80) = 84 TP and 16 FN

CA = 100 TP and 0 FN

EBCT (=37) = 90 TP and 10 FN

EBCT (>0) = 95 TP and 5 FN

Echo = 85 TP and 15 FN

Thallium = 91 TP and 9 FN

**Results-ICER:**

The authors presented only average cost-effectiveness of the strategies. However, the presentation of their results allowed for an incremental cost-effectiveness analysis to be performed. ICERs for each strategy compared to the next best strategy are presented here. ICERs are presented as the cost (\$) per additional correct CAD diagnosis:

10% CAD Prevalence:

EBCT (=168) =  
EBCT (=80) = \$21288  
EBCT (=37) = \$24836  
ETT = dominated  
Echo = dominated  
Thallium = dominated  
EBCT (>0) = \$95794  
CA = dominated

20% CAD Prevalence:

EBCT (=168) = extendedly dominated  
EBCT (=80) = \$8280  
EBCT (=37) = \$20632  
ETT = dominated  
Echo = dominated  
EBCT (>0) = \$89348  
Thallium = dominated  
CA = \$92788

50% CAD Prevalence:

EBCT (=168) = \$5186  
EBCT (=80) = \$5914  
ETT = dominated  
EBCT (=37) = \$7090  
Echo = dominated  
EBCT (>0) = \$20114  
Thallium = dominated  
CA = \$25104

70% CAD Prevalence:

EBCT (=168) = extendedly dominated  
ETT = extendedly dominated  
EBCT (=80) = \$2584  
EBCT (=37) = \$5319  
Echo = dominated  
EBCT (>0) = extendedly dominated  
CA = \$7290  
Thallium = dominated

100% CAD Prevalence:

ETT = extendedly dominated  
EBCT (=168) = dominated  
EBCT (=80) = extendedly dominated  
CA = \$1146  
EBCT (=37) = dominated

EBCT (>0) = dominated  
Echo = dominated  
Thallium = dominated

**Result-Uncertainty:** No sensitivity analysis was undertaken.

**Source Funding:** Mayo Clinic and Foundation

**Comments:** The incremental analysis performed on the published findings shows that using EBCT using any calcium score threshold (>0; =37; =80; =168) is cost saving compared with stress echo and stress thallium testing. At low to moderate disease prevalence (10% to 20%), EBCT using thresholds of =37, =80 or =168 are cost saving compared with ETT. Without an explicit cost-effectiveness threshold, it is difficult to determine which is the most cost-effective strategy at 50% CAD prevalence. It is clear that EBCT strategies with higher calcium thresholds are less expensive than an EBCT strategy with a >0 calcium score threshold. However, the lower sensitivity of higher calcium score thresholds means that many true positives are misdiagnosed as negatives. At high CAD prevalence, (70% and 100%), direct to coronary angiography is likely to be the most cost-effective strategy.

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## What is the diagnostic utility of non-invasive and invasive tests for the evaluation of patients with stable chest pain of suspected cardiac origin.

**No** 879 **Study Quality:** Systematic review of the clinical effectiveness and cost-effectiveness of 64-slice or higher computed tomography angiography as an alternative to invasive coronary angiography in the investigation of coronary artery disease

**Author:** Mowatt G;Cummins E;Vaugh N;Walker S;Cook J;Jia X;Hillis GS;Fraser C; 2008

**Relevance:**

**Intervention:** 64-slice MDCT ( multidetector computed tomography)

**Comparison:** ETT (exercise tolerance test), MPS (myocardial perfusion scintigraphy) and invasive CA (coronary angiography)

**Population:** A hypothetical cohort of male patients coming through from resting ECG. In the first analysis, a short-term diagnostic model, patient age was not reported, although the earlier model on which it is based assumes a starting age of 60 years (Mowatt 2008).

**Perspective:** In the long-term model the cohort age is 50.

The prevalence of CAD in the population is a modelled variable ranging from 10% to 70%. The cost- effectiveness of the different diagnostic strategies are estimated with CAD prevalence of 10%, 30%, 50% and 70%.

**Study type:** CUA



Strategy 3 cost per QALY = £585

**Result-Uncertainty:** In the short term diagnostic model, base case CAD prevalence is 10% but is allowed to vary from 10% to 70%. Cost per true positive for each strategy at 70% CAD prevalence is as follows: Strategy 1= £724, strategy 2= £533 and strategy 3= £400.

Cost of CA is uncertain and in base case was £320 although another cost for CA is estimated at £1556. A mid point estimate of £900 was used in sensitivity analysis. This has an effect on strategies where CT replaces CA. To render CT strategies more expensive than CA (CAD prevalence 10%) the additional cost of a false positive would have to be around £7000. For CAD prevalence of 70% cost range would have to be £20,000 to £30,000.

In the longer-term model higher costs for CA increases the anticipated savings from using strategy 3 to around £300 per patient.

Sensitivity analysis used lower values for sensitivity(97% vs. 99% in the base case) and specificity(83% vs. 89% in the base case) for 64-slice CT. This causes CT to perform slightly worse when set against those strategies where patients go straight to CA. For the short term diagnostic model these lower values produced the following results:

Strategy 1 cost per true positive = £3,009

Strategy 2 cost per true positive = £3,034

Strategy 3 cost per true positive = £2,377

In the longer term model these lower values for sensitivity and specificity of 64-slice CT leads to a lower aggregate QALY. But given the tightness of the confidence intervals for sensitivity and specificity bounds, the impact of this is limited.

**Source Funding:** UK NHS Health Technology Assessment programme.

**Comments:** The report concludes that the high sensitivity and negative predictive value of 64-slice CT suggest scope for avoiding unnecessary CAs in those referred for investigation but who do not have CAD. Given the small risk of death associated with CA, CT might also confer a small immediate survival advantage. Avoidance of CAs may result in cost savings even if positive results mean confirmation by CA. Also, of note is the suggestion that if CT were available immediately in a emergency department setting it may reduce the need to admit patients. The resulting cost savings have not been included in this analysis.

**No** 878 **Study Quality:** Cost-effectiveness of functional cardiac testing in the diagnosis and management of coronary artery disease: a randomised controlled trial. The CECaT trial. [Review] [207 refs]

**Author:** Sharples L;Hughes V;Crean A;Dyer M;Buxton M;Goldsmith K;Stone D; 2007

**Relevance:**

**Intervention:** Coronary angiography

**Comparison:** SPECT, stress echo, stress MRI

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<b>Population:</b>	Patients referred for non-urgent coronary angiography
<b>Perspective:</b>	<p>NHS and PSS inclusion criteria: Established or suspected chronic stable angina referred for angiography and an ETT result which merited referral for angiography</p> <p>NOTE: Because these are patients who have already undergone an ETT and have been referred for angiography, the prevalence of/pre-test likelihood for CAD within this population is likely to be high.</p>
<b>Study type:</b>	CUA (QALYs)
<b>Methods:</b>	Economic evaluation conducted alongside RCT
<b>Health valuations:</b>	Face-to-face interviews using the Seattle Angina Questionnaire, Short Form-36 and EQ5D
<b>Cost components:</b>	Diagnostic tests, revascularisation procedures, admissions, cardiac-related tests (e.g. echo, ETT, CT scan, blood pressure monitoring), outpatient and GP visits, medications (e.g. statins, beta-blockers, nitrates, etc).
<b>Currency:</b>	£
<b>Cost year:</b>	2005-06
<b>Time horizon:</b>	18 months
<b>Discount rate:</b>	3.5% per annum
<b>Results-cost:</b>	<p>Mean cost per patient per strategy:</p> <p>Angiography: £3,630 (95%CI: 3,196 to 4,154)</p> <p>SPECT: £4,045 (95%CI: 3,494 to 4,590)</p> <p>Stress MRI: £4,056 (95%CI: 3,575 to 4,550)</p> <p>Stress echo: £ 4,452 (95%CI: 3,817 to 5,223)</p> <p>Cost comparison:</p> <p>SPECT cf angiography: £415 (95%CI: -310 to 1,084)</p> <p>Stress MRI cf angiography: £426 (95%CI: -247 to 1,088)</p> <p>Stress echo cf angiography: £821 (95%CI: 10 to 1,715)</p> <p>There is substantial probability around values of zero difference in costs giving little evidence of higher costs associated with functional testing. Extra costs for patients in these groups were largely due to patients who underwent confirmatory angiography following positive test results. The significant difference between stress echo and angiography was caused mainly by a greater number of hospital admissions as a result of adverse events (one patient in particular who had 7 admissions for chest pain plus both PCI and CABG surgery).</p>
<b>Results-effectiveness:</b>	<p>Mean effect per patient per strategy:</p> <p>Angiography: 1.13 QALYs (95%CI: 1.08 to 1.17)</p> <p>SPECT: 1.17 QALYs (95%CI: 1.13 to 1.20)</p>

Stress MRI: 1.14 QALYs (95%CI: 1.10 to 1.18)  
Stress echo: 1.17 QALYs (95%CI: 1.13 to 1.20)

QALY comparison:  
SPECT cf angiography: 0.0362 (95%CI: -0.092 to 0.080)  
Stress MRI cf angiography: 0.00956 (95%CI: -0.055 to 0.074)  
Stress echo cf angiography: 0.0371 (95%CI: -0.024 to 0.095)

Results of the QALY estimates did not show any statistically significant differences between the groups. There was little difference in overall quality-adjusted survival between groups, nor significant differences in EQ-5D utilities up to 18-months post-randomisation.

**Results-ICER:** Cost (£) per QALY gained:

SPECT cf angiography: 11,463/QALY (95%CI: -99,480 to 120,130)  
Stress MRI cf angiography: 44,573/QALY (95%CI: -80,543 to 282,058)  
Stress echo cf angiography: 22,157/QALY (95%CI: -253,083 to 213,286)

A strategy of going to angiography is less expensive but only marginally less effective than SPECT, stress MRI and stress echo. Although non-invasive tests are slightly more effective, the benefit is so near to zero in all three cases that the ICERs are unstable. CIs around the ICERs are so wide that they are effectively uninformative.

**Result-Uncertainty:** Various one-way sensitivity analyses together demonstrate that the rank order of costs and QALYs and the magnitude of differences between options are sensitive to reasonable alternative methods of estimation. However, in no case do the 18-month costs of the 3 non-invasive alternatives fall below those of angiography, and the alternative estimation of QALYs (using SF-6D) makes all three alternatives less effective (in QALY terms) than angiography.

Assumptions tested in sensitivity analysis:  
Use of SF-6D utility measure in place of EQ-5D  
Unit costs of diagnostic strategies  
Potential cost savings if negative functional tests were not followed by confirmatory angiography  
Removing outliers  
Sub-group analysis by type of referring clinical (interventional vs non-interventional cardiologists)

**Source Funding:** NA

**Comments:** In terms of cost-effectiveness, all three non-invasive strategies were slightly more expensive than angiography and with similar QALYs. Overall results suggest that functional testing may have a valuable place in the diagnostic pathway for the assessment of chest pain in an outpatient population because of 'process' advantages to patients, clinicians and hospitals. All three tests can avoid invasive diagnostic tests in a significant proportion of patients.

**No** 823 **Study Quality:** Cost effectiveness of coronary angiography and calcium scoring using CT and stress MRI for diagnosis of coronary artery disease

**Author:** Dewey M;Hamm B; 2007

**Relevance:**

**Intervention:** ETT, stress echo, coronary angiography

**Comparison:** CT angiography, EBT, stress MRI

**Population:** Hypothetical cohort of patients with different pre-test likelihoods for CAD.

**Perspective:** partial SOCIETAL

**Study type:** CEA (outcome measure: average cost per correctly identified patient with CAD)

**Methods:** DECISION ANALYSIS (effectiveness data taken from published meta-analyses)

**Health valuations:** NOT APPLICABLE

**Cost components:** Direct costs (reimbursement rates for the test) and indirect costs (costs of subsequent tests, complications, additional tests and false negative diagnosis)

**Currency:** EURO

**Cost year:** not stated

**Time horizon:** For patients receiving a false negative diagnosis, the model includes follow-up for AMI over 10 years.

**Discount rate:** 5% per annum

**Results-cost:** Results were presented in graphical form, and thus providing specific numerical data is difficult. However, from the graphs, results indicate that the cost per correctly diagnosed CAD patient decreased hyperbolically with increasing pre-test likelihood in all diagnostic tests.

**Results-effectiveness:** Results were presented in graphical form, and thus providing specific numerical data is difficult. However, from the graphs, results show that coronary angiography (the gold standard) was 100% accurate and its advantage over other diagnostic tests increased with pre-test likelihood for CAD. CT angiography was second most accurate, followed by EBT, stress MRI and stress echo.

**Results-ICER:** The authors presented their results only in terms of average cost-effectiveness and did so only in graphical form. In order to perform an incremental analysis based on the published findings, the results were estimated from the graphs. Although the figures are estimated, some strategies were clearly dominated. Estimated results of the incremental analysis are given below as the cost per additional correct CAD diagnosis.

10% CAD prevalence:  
MSCT =  
CA = €86600

20% CAD prevalence:  
MSCT =  
CA = €35000

30% CAD prevalence:  
MSCT =  
CA = €20100

40% CAD prevalence:  
MSCT =  
CA = €10700

50% CAD prevalence:  
MSCT =  
CA = €3300

Exercise stress testing was ruled out through extended dominance at 10-40% CAD prevalence and was dominated at 50-100%. Stress echo, stress MRI and EBCT were dominated at all CAD prevalence. MSCT was the least cost non-dominated or extendedly dominated strategy from 10-50% CAD prevalence. MSCT was ruled out through extended dominance at 60-70% and was dominated at 80-100%. At 60-70%, coronary angiography was the least cost non-dominated or extendedly dominated strategy, and from 80-100% it is the least cost strategy.

**Result-Uncertainty:** At a maximally increased and decreased accuracy within the 95% CI, CT angiography remained the most effective and least costly strategy up to 60% and 50% pre-test likelihoods respectively.

If diagnostic accuracy of CT angiography was reduced maximally (within in 95% CI) and increased maximally for EBT, CT angiography remained more effective than EBT.

Neither increasing nor decreasing the complication rates of coronary angiography changed the ranking of diagnostic tests: coronary angiography had the lowest average cost per correctly identified CAD patient for pre-test likelihoods of  $\geq 50\%$ . At higher and lower complication-related costs (€15,000 and €5,000), CT angiography remained most effective and least costly up to pre-test likelihoods of 60% and 70%.

An increase (€750) and decrease (€500) of the reimbursement for coronary angiography meant that invasive coronary angiography was more effective and less expensive than CT angiography for pre-test likelihoods from 80% and 50% on, respectively.

Up to a reimbursement rate of €260, CT angiography was the non-invasive diagnostic test with the lowest average cost per correctly identified CAD patient at all pre-test likelihoods.

**Source Funding:** Not reported

**Comments:** The study offers a straightforward analysis of cost for diagnostic accuracy of each test, without looking at the prognostic value any of the technologies might add. The incremental analysis performed is based on estimates derived from the graphical presentation of results. Despite rough estimation, some strategies were clearly dominated.

**No** 801 **Study Quality:** Systematic review of the effectiveness and cost-effectiveness, and economic evaluation, of myocardial perfusion scintigraphy for the diagnosis and management of angina and myocardial infarction

**Author:** Mowatt G;Vale L;Brazzelli M;Hernandez R;Murray A;Scott N;Fraser- C;McKenzie L;Gemmell H;Hillis G;Metcalfe M; 2004

**Relevance:**

**Intervention:** SPECT MPS (single photon emission computed tomography myocardial perfusion scintigraphy)

**Comparison:** Stress ECG (electrocardiography) and CA (coronary angiography)

**Population:** Hypothetical cohort of male patients aged 60 years. A subgroup analysis was conducted for a hypothetical cohort of women aged 60 years.

**Perspective:** NHS

**Study type:** CUA

**Methods:** DECISION ANALYSIS

**Health valuations:** NOT APPLICABLE

**Cost components:** The decision tree model which considered a clinical decision problem included costs of the three interventions: ECG, CA and SPECT MPS. The Markov model estimated costs over the cohort's lifetime: med mgt, myocardial infarction and revascularisation.

**Currency:** £

**Cost year:** 2001/02

**Time horizon:** The decision tree model (DTM) was "static" but in reality the decision may have taken weeks or even months. The time horizon for the Markov model was 25 years.

**Discount rate:** No discount rate used in the DTM. Markov model used a rate of 6% for costs and 1.5% for benefits.

**Results-cost:** The model included 4 diagnostic strategies. For the base case of 10.5% prevalence of CAD, the average diagnostic cost as well as the diagnostic + treatment cost combined were respectively:  
Strategy 1 = ECG-SPECT-CA £603 and £5190

Strategy 2 = ECG-CA £799 and £5395  
 Strategy 3 = SPECT-CA £921 and £5529  
 Strategy 4 = CA £1310 and £5929

**Results-effectiveness:** In the base case (10.5% CAD prevalence) the percent of true positives (TP) diagnosed and the % of accurate diagnoses respectively, are:

Strategy 1 = ECG-SPECT-CA 6.39 and 95.85  
 Strategy 2 = ECG-CA 7.56 and 96.99  
 Strategy 3 = SPECT-CA 8.86 and 98.30  
 Strategy 4 = CA 10.48 and 99.85

The numbers of QALYs for each of the 4 strategies are respectively: 12.473, 12.481, 12.497 and 12.506

**Results-ICER:** For the four strategies (10.5% CAD prevalence) incremental cost-effectiveness results (£) are as follows for per TP diagnosed, per accurate diagnosis and per QALY, respectively.

	TP	Acc diag	QALY
ECG-SPECT-CA			
ECG-CA	16761	17267	23468
SPECT-CA	9339	9295	8723
CA	23956	24998	42225

**Result-Uncertainty:** Sensitivity analysis (SA)

1. SPECT is able to identify 50% (vs. 0% in base case) of positive patients who can be satisfactorily managed medically. Result is improved CE for SPECT strategies. Incremental cost per QALY is reduced compared to base case:

	SA1	Base case
Strategy 1 = ECG-SPECT-CA		
Strategy 2 = ECG-CA	17928	23648
Strategy 3 = SPECT-CA	6495	8723
Strategy 4 = CA	16558	42225

2. Higher rate of indeterminacy for stress ECG (30 vs. 18%) and lower rate of indeterminacy for SPECT (2 vs. 9%). Result is improved CE for SPECT strategies. Incremental cost per QALYs as follows:

	SA2	Base case
Strategy 1 = ECG-SPECT-CA		
Strategy 2 = ECG-CA	Dominated by SPECT-CA	23648
Strategy 3 = SPECT-CA	11422 (relative to strategy 1)	8723 (relative to strategy 1=£14,123)
Strategy 4 = CA	41404	42225

3. Cost of stress ECG varied from £25 to £225, angiogram from £895 to £1724 and SPECT from £128 to £340. Result is no change in rank order of strategies from base case.

4. Changing the time horizon from 25 years. Result is that as the time horizon reduces, the incremental cost per QALY increases as the costs of initial diagnosis and treatment are not offset by survival and QoL gains. Results shown in graph form.

5. Changing the time it takes false negative to be correctly diagnosed. In base case all survivors are correctly diagnosed by

year 10. SA changed this to 2 years and 5 years and never. Result is that it improves the CE of non-invasive strategies compared with CA. Incremental cost per QALY for 5 years compared to base case is as follows:

	SA5	Base case
Strategy 1 = ECG-SPECT-CA		
Strategy 2 = ECG-CA	16931	23648
Strategy 3 = SPECT-CA	7644	8723
Strategy 4 = CA	28868	42225

6. Other sensitivity analysis results CA assumed to give perfect information. If that is not the case then the relative CE of a non-invasive strategy would improve.

Risk of MI for all risk states were allowed to increase. There was no difference in the order of the strategies compared to the base case.

Discount rate for costs and benefits was set at 0% for both and 6% for both. There was one change in the order of the strategies compared to base case. For low values of cost for SPECT and zero discount rates SPECT-CA dominates the stress ECG-CA strategy.

QALY value were allowed to vary due to mortality risk reduction after revascularisation. No changes were observed in the order of strategies compared to base case.

**Source Funding:** Public

**Comments:** Subgroup analysis was conducted for women aged 60, using sensitivities and specificities for that group and a lower prevalence rate of CAD, different MI rates and mortality rates for women aged 60. Strategy 1 was less costly whereas stress ECG-CA and CA were dominated by the SPECT-CA strategy (less costly and slightly more effective in the second case).

The model suggests that for low levels of prevalence it is possible that the incremental cost per unit of output (TPs diagnosed, accurate diagnosis, QALY) for the move from stress ECG-SPECT-CA and from stress ECG-CA to SPECT-CA might be considered worthwhile. At high risk of prevalence (e.g. 85% risk of CAD) the stress ECG-SPECTCA strategy is dominated by the stress ECG-CA strategy.

**No** 790 **Study Quality:** The value of myocardial perfusion scintigraphy in the diagnosis and management of angina and myocardial infarction: a probabilistic economic analysis

**Author:** Hernandez R;Vale L; 2007

**Relevance:**

**Intervention:** MPS SPECT, alone or in combination with other non-invasive tests; stress echocardiography was evaluated in a sensitivity analysis

**Comparison:** ETT (exercise tolerance test), invasive CA (coronary angiography)

**Population:** Hypothetical cohort of patients aged 60 years. Prevalence of CAD in the population is a modelled variable ranging from 10.5% to 85%. The cost-effectiveness of the different diagnostic strategies are estimated with CAD prevalence of 10.5%, 30%, 50% and 85%.

**Perspective:** NHS, 50% and 85%.

**Study type:** CUA with deterministic and probabilistic results

**Methods:** Cost and effectiveness data obtained from literature - specifically Mowatt et al. 2004

**Health valuations:** NA

**Cost components:** Short term diagnostic model includes costs of diagnostic tests. Longer term model includes additional costs of treating CAD (medical management, MI event management, revascularisation).

**Currency:** UK pounds sterling

**Cost year:** 2001/2002

**Time horizon:** Short term diagnostic model did not specify time horizon. Longer term model has 25 year time horizon.

**Discount rate:** NA to short term diagnostic model. Longer term model used 6% for costs and 1.5% for outcomes.

**Results-cost:**

Deterministic results of base case at 10.5% CAD prevalence (95% CI from probabilistic SA):  
 ETT-SPECT-CA = £5192 (£4906 - £5473)  
 ETT-CA = £5396 (£5081 - £5722)  
 SPECT-CA = £5529 (£5183 - £5821)  
 CA = £5929 (£5505 - £6345)

Deterministic results of at 30% CAD prevalence (95% CI from probabilistic SA):  
 ETT-SPECT-CA = £5787 (£5506 - £6070)  
 ETT-CA = £5958 (£5647 - £6297)  
 SPECT-CA = £6155 (£5793 - £6471)  
 CA = £6484 (£6052 - £6926)

Deterministic results of at 50% CAD prevalence (95% CI from probabilistic SA):  
 ETT-SPECT-CA = £6397 (£6068 - £6709)  
 ETT-CA = £6535 (£6167 - £6906)  
 SPECT-CA = £6797 (£6356 - £7198)  
 CA = £7053 (£6539 - £7551)

Deterministic results of at 85% CAD prevalence (95% CI from probabilistic SA):  
 ETT-SPECT-CA = £7464 (£7002 - £7917)  
 ETT-CA = £7543 (£7034 - £8060)  
 SPECT-CA = £7921 (£7306 - £8469)



CA = £8049 (£7364 - £8726)

**Results-effectiveness:** Deterministic results of base case at 10.5% CAD prevalence (95% CI from probabilistic SA):

ETT-SPECT-CA = 12.510 QALYs (11.902-13.501)

ETT-CA = 12.518 QALYs (11.907 - 13.066)

SPECT-CA = 12.532 QALYs (11.930 - 13.084)

CA = 12.541 QALYs (11.926 - 13.089)

Deterministic results of at 30% CAD prevalence (95% CI from probabilistic SA):

ETT-SPECT-CA = 11.727 QALYs (11.235 - 12.173)

ETT-CA = 11.759 QALYs (11.270 - 13.215)

SPECT-CA = 11.798 QALYs (11.310 - 12.264)

CA = 11.840 (11.330 - 12.311)

Deterministic results of at 50% CAD prevalence (95% CI from probabilistic SA):

ETT-SPECT-CA = 10.924 (10.524 - 11.294)

ETT-CA = 10.979 (10.578 - 11.367)

SPECT-CA = 11.045 (10.631 - 11.455)

CA = 11.121 (10.668 - 11.551)

Deterministic results of at 85% CAD prevalence (95% CI from probabilistic SA):

ETT-SPECT-CA = 9.518 (9.146 - 9.862)

ETT-CA = 9.616 (9.219 - 9.994)

SPECT-CA = 9.726 (9.284 - 10.147)

CA = 9.862 (9.330 - 10.337)

**Results-ICER:**

Incremental cost-effectiveness results are as follows for cost per QALY:

	ICER
10.5% CAD Prevalence:	
ETT-SPECT-CA	
ETT-CA	26249
SPECT-CA	9261
CA	48576
30% CAD Prevalence	
ETT-SPECT-CA	
ETT-CA	5454
SPECT-CA	4997
CA	7893
50% CAD Prevalence	
ETT-SPECT-CA	
ETT-CA	2473
SPECT-CA	4032
CA	3372

85% CAD Prevalence	
ETT-SPECT-CA	
ETT-CA	803
SPECT-CA	3428
CA	948

**Result-Uncertainty:** Authors presented the results of the probabilistic sensitivity analysis in a series of cost-effectiveness acceptability curves for each level of CAD prevalence modelled. In the base case (10.5% CAD prevalence), ETT-CA is highly unlikely to be optimal. If willingness to pay is £8000 per QALY, the strategy with a higher probability of being optimal is ETT-SPECT-CA. At £9000 per QALY, ETT-SPECT-CA and SPECT-CA strategies have a similar probability of being optimal. At a ceiling ratio of £20000 per QALY, SPECT-CA has a 90% likelihood of being considered the more cost-effective option, but beyond this value, the likelihood falls such that at a WTP over £75000 per QALY, CA is the strategy most likely to be optimal.

At 30% CAD prevalence, strategies that involve SPECT seem to be optimal for a WTP of up to £20000, with CA being the optimal strategy for higher WTP values. For higher levels of CAD prevalence and for thresholds greater than £10000 per QALY, CA is the optimal decision.

The diagnostic accuracy of SPECT was taken to both optimistic and pessimistic extremes, and as expected, when less favourable SPECT figures were used (i.e. lower sensitivity and specificity), the SPECT-CA strategy did not appear on the CEAC frontier of optimal strategies at any level of CAD prevalence. However, in this scenario ETT-SPECT-CA appear optimal at 10.5% CAD prevalence when the WTP threshold is £5000. Using more favourable SPECT parameter values produced similar results to the base case. The authors point out that even for the most optimistic scenario, when CAD prevalence is greater than 60% and the WTP threshold is more than £16000, the CA strategy appears to be optimal.

When the time horizon for the longer term model was reduced, the incremental cost per QALY increases. This is because the costs of initial diagnosis and treatment are not offset by survival and quality-of-life gains.

Increasing the likelihood that misdiagnoses will be rectified reduces the penalty associated with making a false-negative diagnosis (i.e. it improves the cost-effectiveness of non-invasive strategies compared with CA).

Using higher values for ETT indeterminacy and lower values for SPECT indeterminacy, it was found that SPECT strategies were more likely to be considered cost-effective.

Results were relatively insensitive to changes in cost and to changes in the sensitivity and specificity of CA (reduced to 99% CI (98.995 to 99.005)).

When subgroup analysis was restricted to women, results were slightly more favourable to SPECT-based strategies.

When stress echo were added to the model, they were shown to be potentially cost-effective options. At 10.5% CAD prevalence, ECHO-SPECT-CA dominated both ETT-SPECT-CA and ETT-SPECT strategies, whereas ECHO-CA dominated both ETT-CA and SPECT-CA strategies.

At low levels of CAD prevalence, up to 1%, ETT-SPECT-CA strategy dominated all others. For prevalence between 1% and 4%, SPECT-based strategies dominated non-SPECT-based strategies. At 5% CAD prevalence, SPECT-CA strategy dominated CA only strategy.

**Source Funding:** UK Department of Health on a grant administered by NCCHTA

**Comments:** Results of the probabilistic analysis show that ETT-CA is unlikely to ever be the optimal strategy. SPECT-CA looks optimal below 30% CAD prevalence, and CA only looks optimal above 30% CAD prevalence. Stress echocardiography has a possible role, although the test data used came from an ad hoc review and included indirect comparator analysis. Thus the results of the analysis which included stress echo should be interpreted with some caution.