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Toronto Health Economics and Technology Assessment Collaborative

The Relative Cost-effectiveness of Five Non-invasive Cardiac Imaging Technologies for Diagnosing Coronary Artery Disease in Ontario

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Contents

Executive summary

Objectives
To determine the relative cost-effectiveness of five cardiac imaging technologies for the diagnosis of patients with suspected coronary artery disease (CAD) in two patient populations: out-patients presenting with stable chest pain with an intermediate risk of CAD following physical examination and a graded exercise test (stable outpatients); and patients presenting to emergency and subsequently admitted to hospital with an acute chest pain syndrome, low-intermediate risk of CAD, with a normal ECG and negative cardiac biomarker (acute inpatients).

The five cardiac imaging technologies are: stress echocardiography (stress ECHO); stress echocardiography with the use of contrast agent if necessary for interpretation (stress contrast ECHO); single photon emission computed tomography (SPECT); cardiac magnetic resonance imaging (cardiac MRI); and cardiac computed tomography (CT angiography).

Methods
The economic analysis consisted of three components: a systematic review of full economic evaluations of the relevant imaging technologies; a de novo cost-effectiveness analysis using a short term decision-analytic model; and a budget impact analysis from the perspective of the Ontario Ministry of Health and Long Term Care (MOHLTC).

The systematic review of existing full economic evaluations was based upon a systematic search of Medline and the National Health Service Economic Evaluation Database (NHSEED) from their inception up to October 2009. Only full economic evaluations describing both the costs and consequences of adopting one or more of the cardiac imaging technologies for the diagnosis of CAD were included in the systematic review. The primary outcome of interest was the incremental cost-effectiveness ratio (ICER) of each imaging technology in relation to another imaging technology of interest.

The de novo cost-effectiveness analysis was conducted using a short term decision analytic model to determine the cost-effectiveness of each of the non-invasive cardiac imaging tests in accurately diagnosing CAD in each of the two patient populations in Ontario. The perspective of the analysis was that of the MOHLTC. The primary outcome measure was accurate diagnosis of CAD resulting from non-invasive imaging. Resource use and costs were derived from Ontario data sources. A series of sensitivity analysis were conducted to determine the robustness of the results to alternative assumptions and to explore feasibility issues associated with the technologies in Ontario.

The budget impact analysis assessed the impact on the budget of the MOHLTC of replacing various proportions of each technology with an alternative technology (for example replacing 10% of SPECT tests with stress contrast ECHO, or 25% of stress ECHO tests with CT angiography).

Results
In the previous studies identified in the systematic review, CT angiography was often found to be cost-effective when compared to other technologies. SPECT and stress ECHO were also found to be cost-effective in several of the comparative studies examined, while cardiac MRI was not found to be cost-effective in any study.

In the base case cost-effectiveness analysis, for stable outpatients, CT angiography was found to be less costly and more effective than stress ECHO, SPECT and cardiac MRI, but not stress contrast ECHO. The ICER of CT angiography versus stress contrast ECHO was $1527 per accurate diagnosis. Stress contract ECHO therefore appears to be the most cost-effective non-invasive diagnostic test for stable outpatients at either WTP anchor. Stress contrast ECHO also appears to be the most cost-effective non-invasive diagnostic test for acute inpatients at either WTP anchor.

In sensitivity analyses, where the prevalence of CAD in the population under consideration was allowed to vary, CT angiography appeared cost-effective for stable outpatients at a higher prevalence of CAD or when stress contrast ECHO was unavailable. It also appeared cost-effective for acute inpatients at higher prevalence values when hospital wait times were equalized across technologies. If CT angiography was unavailable then stress contrast ECHO appeared cost-effective across all prevalence values for both populations. If neither CT angiography nor stress contrast ECHO were available then stress ECHO appeared cost-effective for stable outpatients, while SPECT appeared cost-effective for acute inpatients.

The budget impact analysis found that replacing 25% of stress ECHOs currently performed without the use of contrast with the strategy of stress ECHO testing with the use of contrast if necessary would cost the MOHLTC an estimated $831,482 over the next five years. Replacing the same number of tests with CT angiography would cost an estimated $13.1M over five years. Replacing 25% of SPECTs with stress contrast ECHO would save the MOHLTC an estimated $42.2M over five years, while replacing the same number of tests with CT angiography would save an estimated $28.8M over the same time frame. Replacing existing cardiac MRI tests with stress contrast ECHO or CT angiography would not have a large budget impact since cardiac MRI is not widely adopted as a diagnostic test for CAD.

Conclusion

New options for non-invasive cardiac diagnostic imaging (CT angiography, stress contrast ECHO) appear to have broadly similar sensitivity and specificity values in comparison to widely used current technologies (e.g. SPECT). CT angiography and stress contrast ECHO are consistently more economically attractive than competing technologies, and offer the potential for significant cost savings if they were used as replacement technologies for current, widely used tests. Clinical policy regarding implementation and wider use of these tests must also consider issues of radiation-related risk, long-term clinical and economic consequences of diagnostic imaging strategies (not considered here), the extent to which these tests may be used as complementary rather than replacement tests, and quality standards in the performance and interpretation of imaging technologies.

Study question

What is the relative cost-effectiveness of the following five non-invasive cardiac imaging technologies for the diagnosis of patients with suspected coronary artery disease (CAD): stress echocardiography (“stress ECHO”), stress echocardiography with the use of contrast agent only if necessary for interpretation (“stress contrast ECHO”), single photon emission computed tomography (“SPECT”), cardiac magnetic resonance imaging (“cardiac MRI”), and cardiac computed tomography (“CT angiography”)?

Systematic review of the economic literature

A systematic literature search was conducted in order to identify and retrieve studies evaluating the cost-effectiveness of selected cardiac imaging tests for the diagnosis of CAD.

Searched electronic databases were MEDLINE from 1950 until August 28, 2009, and the National Health Service Economic Evaluations Database (NHS EED) from its inception until August 20, 2009. In the case of the MEDLINE searches, a disease-specific search strategy was combined with a strategy designed to capture different types of economic evaluations; both of these strategies were combined with a cardiac imaging-specific set of terms to produce a balanced search that was highly sensitive but specific enough to be tractable. In the case of the NHS EED, searches were crafted that looked for the disease-specific articles referring to the technologies of interest only (the economic elements of the search were not required, since the database was designed to capture only articles referring to economic analysis). The complete database search strategy is described in the Appendix; a diagram summarizing the search results is given in Figure 1. Articles were restricted to English language and those published in full-text only.

Only full economic evaluations describing both the costs and consequences of adopting stress ECHO, SPECT, cardiac MRI, and/or CT angiography for the diagnosis of CAD were included in the systematic review. This included cost-benefit, cost-effectiveness and cost-utility analyses. No restrictions were placed on the types or forms of the selected technologies. For example, stress ECHO with either pharmacological or exercise stress, and either with or without the use of a contrast agent, were accepted and accounted for in the same stress ECHO diagnostic category. Similarly, multi-slice and multi-beam CT angiography were accounted for in the same category.

The included studies considered either inpatients or outpatients with known or suspected CAD at any pretest likelihood of underlying CAD. Studies which did not include at least one other selected cardiac imaging test as a comparator were automatically excluded. Studies published only as abstracts, letters or commentaries were excluded, as were duplicate publications or studies not reporting data.

Article selection was performed by independent pairs of researchers. Abstracts and titles found from the searched strategy were compiled in four reference databases and assessed for inclusion/exclusion. Pre-selected studies were read in full for final selection. If discrepancies arose from article selection between the reviewers then agreement was set by consensus. If consensus was not possible then a third reviewer was called to adjudicate the decision.

Target data for extraction included: study first author and year of publication; imaging tests compared; type of economic analysis; reported costs and outcomes; incremental cost-effectiveness ratio (ICER); currency; and patient characteristics (i.e. known or suspected CAD and risk of CAD). Data extraction was performed by one researcher and then validated by a second researcher.

Data analysis consisted of summarizing the reported cost-effectiveness of the selected cardiac imaging tests from all included studies.

Study results for each test were tabulated and summarized against all relevant comparators. The primary outcome of interest for the systematic review was the incremental cost-effectiveness ratio (ICER) of each imaging technology in relation to another technology of interest. ICER results were reported as described in the original study, or where necessary were calculated from the available data. As per the current approach for assessing cost-effectiveness, an ICER below Canadian Dollars (CAD) $50,000 per quality adjusted life-year (QALY) gained was considered to be cost-effective.

Search strategy results

A total of 883 non-duplicate citations were found from the two electronic databases after applying the literature search strategy. After an initial screen of titles and abstracts, 147 full-text articles were retrieved for further assessment.. Of those, 122 were rejected (Table 1). 25 articles were pre-included in the systematic review. Following the data extraction process, 13 studies were excluded.(1-12)[5-16] Table 1 outlines the reasons for excluding articles following pre-inclusion. A total of 12 studies were finally selected for analysis.(13-24)[17-28]

Characteristics of included studies

From the 12 studies included in the present systematic review, eight studies assessed the cost-effectiveness of two of the selected imaging tests,(16-19, 21, 23, 24)[20-23, 25, 27, 28] three evaluated three concomitant technologies,(13, 20, 22)[17, 24, 26] and one evaluated five technologies.(14)[18] Table 2 lists the comparison technologies and imaging tests from the included studies.

Five studies were cost-effectiveness analysis, where the most observed outcome was cost per correct/successful CAD diagnose.(13, 14, 21, 23, 24)[17, 18, 25, 27, 28] The other seven studies were cost-utility analysis using cost per QALYs as their primary outcome.(15-20, 22)[19-24, 26] The time-horizon used across the included studies ranged from 30 days to lifetime, where five studies used 25 years of more of follow-up.(15-17, 19, 23)[19-21, 23, 27] The remaining studies used 18 months,(22)[26] 3 months,(24)[28] and 30 days of analytical time horizon.(18)[22] Four studies did not report the time-horizon used in their analysis.(13, 14, 20, 21)[17, 18, 24, 25]

All included studies evaluated at least one form of ECHO against one of the other remaining selected imaging test.(13-24)[17-28] The cost-effectiveness of SPECT was assessed in nine studies.(13, 15-17, 19, 20, 22, 24)[17, 19-21, 23, 24, 26-28] Three studies assessed CT angiography in comparison to stress ECHO or MRI.(14, 18, 21)[18, 22, 25] MRI was compared to each of the three other selected imaging tests in two studies.(14, 22)[18, 26] No full economic analysis between CT angio and SPECT was found in the published literature.

Literature results

Table 7 shows a summary of the cost-effectiveness strategies for the different cardiac imaging modalities evaluated in the literature.

CT angiography was found to be cost-effective or cost-saving in all 4 comparisons for that technology. Stress ECHO was cost-effective in 8 of the 13 comparisons in which it was evaluated, and SPECT was cost-effective in 3 of the 9 comparisons. Cardiac MRI was not cost-effective or cost-saving in any of these 4 comparisons.

Stress ECHO

The cost-effectiveness of stress ECHO was assessed against three selected cardiac imaging tests: SPECT, CT angiography and cardiac MRI. Table 3 summarizes the cost-effectiveness comparisons of stress ECHO versus SPECT and cardiac MRI.

Nine comparisons were made against SPECT. In three of them stress ECHO was considered dominant (i.e., lower cost, better outcome)(13, 16, 17)[17, 20, 21]. In one comparison, stress ECHO resulted in the same QALY gain as SPECT but at a higher cost, and so was not considered cost-effective.(22)[26]. In three other comparisons, the base case ICER reported for stress ECHO versus SPECT was above the $50,000 per QALY threshold.(15, 19, 23)[19, 23, 27] However, in all three analysis stress ECHO showed lower costs and worse outcomes, and was therefore still accepted as cost-effective. Another analysis of stress ECHO versus SPECT estimated an ICER of CDN $5,029 per correct CAD diagnosis, however stress ECHO was the alternative with lower costs and worst outcome.(24)[28] The final comparison did not report an ICER for the analysis, however it was stated that stress ECHO was cost-effective only when the probability of CAD was lower or equal to 20%.(20)[24]

When compared to CT angiography, ECHO was not considered cost-effective in all three analyses.(14, 18, 21)[18, 22, 25] In one of the comparisons, stress ECHO was dominated (i.e., higher cost, worst outcome).(18)[22] The remaining studies evaluated the cost per correct/successful diagnosis, but these did not report an ICER value of stress ECHO versus CT angiography. Both studies reported that under pre-test likelihood or prevalence of CAD greater than 60%, CT angiography was the cost-effective strategy.(14, 21)[18, 25]

Two economic evaluations compared stress ECHO to cardiac MRI.(14, 22)[18, 26] In one analysis, stress ECHO was found cost-effective over MRI with a reported base-case ICER per QALY of GBP £13,200.(22)[26] The remaining study did not report an ICER, however it was addressed that both stress ECHO and MRI were not considered cost-effective when compared to CT angiography.(14)[18]

SPECT

SPECT imaging for the diagnosis of CAD was compared against stress ECHO and cardiac MRI imaging modalities. Table 4 summarizes the cost-effectiveness comparisons of SPECT versus stress ECHO and cardiac MRI.

SPECT was compared to stress ECHO in nine economic evaluations. SPECT was dominated (i.e., higher cost, worst outcome) in three comparisons.(13, 16, 17)[17, 20, 21] In one study, SPECT over stress ECHO reported an ICER per correct CAD diagnosis of CDN $5,029,(24)[28] and in another economic evaluation, SPECT reported to be cost-saving against stress ECHO.(22)[26] In three other comparisons, the base-case ICER per QALY reported for SPECT in comparison to stress ECHO was above the $50,000 per QALY threshold.(15, 19, 23)[19, 23, 27] Although, the last study did not report an ICER, it reported that SPECT was cost-effective when the probability of CAD was greater than or equal to 30%.(20)[24]

One study compared the incremental cost-effectiveness of SPECT versus cardiac MRI. It was reported that in the base-case analysis, SPECT was dominant over cardiac MRI for producing lower costs and greater number of QALYs.(22)[26]

CT angiography

CT angiography for the diagnosis of CAD was compared against stress ECHO and cardiac MRI imaging modalities. Table 5 summarizes the cost-effectiveness comparisons of CT angiography versus stress ECHO and cardiac MRI.

CT angiography was compared to cardiac MRI and stress ECHO in three published economic evaluations.(14, 18, 21)[18, 22, 25] Only one study reported an ICER value, in which CT angiography was found to dominate (i.e., lower cost, better outcome) stress ECHO.(18)[22] In the remaining studies, ICERs were not used;however the study authors stated that CT angiography was considered cost-effective in comparison to stress ECHO(14, 21)[18, 25] and cardiac MRI(14)[18] when the pre-test likelihood or prevalence of CAD was greater than or equal to 60%.

Cardiac MRI

Cardiac MRI for the diagnosis of CAD was compared against CT angiography, SPECT and stress ECHO imaging modalities. Table 6 summarizes the cost-effectiveness comparisons of CT angiography versus CT angiography, SPECT and stress ECHO.

Two studies evaluated the cost-effectiveness of cardiac MRI versus CT angiography, SPECT, or stress ECHO.(14, 22)[18, 26] In one analysis, cardiac MRI was the alternative with lower costs and worst outcome, thus it was considered not cost-effective at an ICER per QALY of GBP £13,200 and against stress ECHO.(22)[26]

Discussion

The present research summarized the cost-effectiveness results of published economic evaluations of four cardiac imaging technologies for the diagnosis of inpatients or outpatients with known or suspected CAD, and at any risk level of undergoing or developing CAD. A total of 12 studies were identified and a summary of cost-effectiveness findings are described in Table 7. Overall, of the selected strategies, stress ECHO was the most frequently evaluated, followed by SPECT, and CT angiography and cardiac MRI. CT angiography was considered the most cost-effective strategy in all comparisons. However, this conclusion was restricted to specific situations such as in the presence of high likelihood or prevalence of CAD or versus stress ECHO and cardiac MRI. Under base-case (average) situations, stress ECHO was reported to be relatively cost-effective, especially when compared to SPECT and cardiac MRI, but not CT angiography. SPECT follows with few positive cost-effectiveness results, and cardiac MRI did not achieve any cost-effectiveness over the other remaining strategies.

According to the published economic data from the literature, CT angiography is often found to be cost-effective when compared to other technologies. SPECT and stress ECHO were also found to be cost-effective in several of the comparative studies examined, while cardiac MRI was not cost-effective in any study. Limitations to these conclusions apply, such as the analyses found in the literature evaluated other forms of the selected cardiac imaging tests which might change the proposed relative cost-effectiveness.

Given the results observed and reported in this review, it is worth discussing that the use of ICERs for comparing the cost-effectiveness of cardiac imaging technologies was not widely used across the reviewed studies. In some cases, the study authors reported simple ratios of costs and health effects, rather than incremental costs and health effects.. In two situations this ratio was wrongly interpreted as implying improved cost-effectiveness.(14, 21)[18, 25] Traditionally, comparing *incremental* costs and *incremental* health effects is is the preferred method of analysis.

Additionally, it was observed that many of the studies described here did not use a threshold (under a certain willingness to pay value) for defining cost-effective cardiac imaging strategies. Especially in the case of studies evaluating cost per successful or correct CAD diagnosis, instead of QALYs. For example, in the study of Tardif et al.,(24)[28] it was not possible to define whether in the comparison of stress ECHO versus SPECT, which of these strategies was considered cost-effective since no willingness to pay was defined for an incremental successful or correct CAD diagnosis. In the case of evaluations reporting the use of QALY, then it was assumed that a $50,000 per QALY would be acceptable and considered the cost-effectiveness limit. However, it is worth mentioning that not all jurisdictions use the same willingness to pay threshold, and the results summarized in the present systematic review must be adjusted accordingly.

Moreover, two studies reported the used of short time-horizons (less than three months),(18, 24)[22, 28] which were conducted primarily for determining the cost-effectiveness of accurate diagnosis of CAD. However, short follow-up periods might not reflect downstream economic consequences of false positive diagnosis, thus assessing only immediate costs of imaging tests (i.e., detection of true CAD positives). Therefore, the inherent limitation of short-term analysis lies in the fact that it cannot fully evaluate the cost-effectiveness of imaging technologies especially with respect to economic consequences resulting from an incorrect diagnosis.

Limitations

An important limitation of this and other systematic reviews lies in the potential problems with identifying studies that are relevant but might have not been captured with the applied search strategy. By browsing the two scientific databases included in the literature search strategy it was assumed that all available and published economic evaluations of the selected cardiac imaging tests would be identified and included in the review. Furthermore, the presence of publication bias (i.e., studies of strategies with null or negative cost-effectiveness not published) favouring a particular technology cannot be ruled out. However, the extent of both selection and publication bias in the present study is unknown.

Due to the diversity of the published studies it was not possible to carry out a quantitative summary of the results. For example, it was not possible to conduct a meta-analysis of the ICERs reported in each study due to – among other things – a difference in the outcome measures reported.

Another limitation is the lack of assessment of the cost-effectiveness of other relevant non-invasive cardiac imaging strategies such as Positron Emission Imaging (PET) or electrocardiogram (ECG). Additionally, the present research did not include the comparison of non-invasive tests with invasive cardiac tests, such as coronary angiography (CA) considered the gold-standard for the diagnosis of CAD in many aspects (i.e., test sensitivity and specificity). The study by Sharples et al.,(22)[26] reviewed the economic literature of non-invasive versus invasive diagnostic techniques and concluded that CA was cost-effective in patients with higher prevalence of CAD (greater than 60%), followed by stress ECHO and SPECT in comparison to ECG. No results were reported for cardiac MRI or CT angiography.

Finally, it was not possible to stratify the selected cardiac imaging strategies by sub-categories of special characteristics. For example, stress ECHO was constantly reported from the reviewed studies as a combination of exercise and pharmacological stress inductions. It is possible that the two forms of stress ECHO might have different sensitivity and specificity for detecting true positives and negative cases of CAD, respectively, thus influencing in their cost-effectiveness of CAD diagnosis. The same is true for the other technologies as well, such as SPECT, CT angiography, and cardiac MRI. Therefore, the analysis of other forms of the selected cardiac imaging tests might change the proposed relative cost-effectiveness ranking.

Conclusion of systematic review

Overall, CT angiography is often found to be cost-effective when compared to other technologies. SPECT and stress ECHO were also found to be cost-effective in several of the comparative studies examined, while cardiac MRI was not cost-effective in any study. Limitations to these conclusions apply, such as the analyses found in the literature evaluated other forms of the selected cardiac imaging tests which might change the proposed relative cost-effectiveness.

Cost-effectiveness analysis

Methods

A cost-effectiveness analysis was carried out using a *de novo* decision-analytic model to assess the relative cost-effectiveness of each of the five non-invasive cardiac imaging technologies. Two patient populations were considered:

1) Outpatients presenting with stable chest pain with an intermediate risk of CAD following physical examination and a graded exercise test ("stable outpatients"); and

2) Patients presenting to emergency and subsequently admitted to hospital with an acute chest pain syndrome, low-intermediate risk of CAD, with a normal ECG and negative cardiac biomarker ("acute inpatients").

The model adopted a short time horizon, with all events following diagnosis with a non-invasive test specifically excluded. Estimates of diagnostic test characteristics (sensitivity and specificity) were obtained from a systematic evidence review conducted by the Medical Advisory Secretariat (MAS) of the Ontario MOHLTC. Cost estimates were obtained from the Ontario Health Insurance Plan (OHIP) database and the Ontario Case Costing Initiative (OCCI) database.(25, 26)[32, 33] The remaining parameters were derived from estimates given by content experts in cardiology and cardiac imaging drawn from an Expert Advisory Panel convened by MAS. The perspective of the analysis was that of the Ontario Ministry of Health and Long-term Care (MOHLTC).

Model structure

Figure 2 provides a simplified illustration of the decision-analytic model structure. The square node represents the 'decision node' – to the right of this node are five branches which represent the cardiac imaging tests under consideration. Moving left to right, the next node is a circular node which represents a 'chance node'. The probabilities assigned to the branches emanating from this chance node represent the underlying prevalence of CAD in the patient population under consideration. The next chance node to the right represents the proportion of patients who will receive pharmacologic stress or exercise stress. Subsequently to the right, another chance node represents the probability that a cardiac test result will be uninterpretable. The model assumed that patients with an uninterpretable test result would undergo a second, different cardiac imaging test. The choice of second test was determined by the probability distribution represented by the node with five branches emanating from it. It was assumed that the type of stress (pharmacological or exercise) that a patient receives for the second test would be the same type of stress used in the first test. As with the first test, there was a probability that the second test was uninterpretable. Patients with two uninterpretable test results were regarded as "undiagnosed".

Each patient in the model therefore received one of five possible diagnoses: true positive (where the test result is positive in the presence of CAD); true negative (where the test result is negative in the absence of CAD); false positive (where a test result is positive in the absence of CAD); false negative (where a test result is negative in the presence of CAD); and undiagnosed (where a patient cannot be diagnosed due to two uninterpretable test results).

Target populations

The stable outpatient population was defined as persons with suspected CAD presenting to an ambulatory setting with chest pain, with an intermediate risk of CAD following physical examination and a graded exercise test, as defined by the American College of Cardiology / American Heart Association 2002 Guideline Update for the Management of Patients with Chronic Stable Angina.(27)[30]

The acute inpatient population was defined as persons with suspected CAD presenting to the emergency department with an acute chest pain syndrome, of low-intermediate risk with a normal ECG and negative cardiac biomarker and who are admitted to hospital, as defined by the American College of Cardiology / American Heart Association 2007 Guidelines for the Management of Patients with Unstable Angina/Non-ST-Elevation Myocardial Infarction.(28)[29]

Outcomes

The short time frame in which the analysis was completed precluded the use of generic health outcomes such as the QALY – instead, the primary outcome measure was the incremental cost per additional "accurate diagnosis" of CAD resulting from non-invasive testing. This included patients with either a true positive or true negative diagnosis.

A secondary outcome measure (adopted only in the base case and primary sensitivity analyses) was the incremental cost per additional "true positive diagnosis" of CAD. This outcome measure differed from the primary outcome measure by not considering patients with a true negative diagnosis.

Test characteristics

The sensitivity and specificity of each cardiac imaging technology were obtained from a systematic review and meta-analysis conducted by the Medical Advisory Secretariat (MAS) of the Ontario MOHLTC (Table 8). The sensitivity of each test represents the proportion of persons with a disease who have a positive test for the disease (a true positive diagnosis). Highly sensitive tests are usually positive in the presence of a disease. Conversely, specificity represents the proportion of persons without a disease who have a negative test result (a true negative diagnosis). A very specific test will rarely misclassify persons without a disease as having the disease.

It follows that the primary outcome (accurate diagnosis) is dependent upon both the sensitivity and specificity of each test (implicitly weighting each equally), while the secondary outcome (true positive diagnosis) is dependent only upon each test's sensitivity.

Other estimates

The model assumed that acute inpatients would have to wait a short time in hospital before receiving each test. Estimates of these wait times were provided for each test by content experts in cardiology and cardiac imaging (Table 9). Simple averages of the estimates for each test were adopted in the base case analysis and all but one of the sensitivity analyses. Given the uncertainty around these estimates a single sensitivity analysis was carried out for acute inpatients only in which the hospital wait time for all tests was assumed to be the same (1.5 days, the average estimate for coronary angiography).

The probability of an uninterpretable test result for each of the five imaging tests in each of the two settings (inpatient and outpatient) was also obtained from these experts (Table 10).

The proportion of patients receiving pharmacological stress (as opposed to exercise stress) was assumed from expert opinion to be 30% for stable outpatients and 80% for acute inpatients.

Resource use and costs

Resource use and costs were derived from Ontario data sources: the OHIP and OCCI databases.(25, 26)[32,33] The cost of conducting each cardiac test was calculated as the sum of the test's respective professional fees and technical fees, as described in the Ontario Schedule of Benefits (Table 11).

The cost of conducting each cardiac test was calculated as the sum of the test's respective professional fees and technical fees. The professional fees shown in Table 11 represent physician costs for the specified cardiac imaging tests and the technical fees represent the corresponding hospital or clinic costs of performing the tests. In general, professional fees are paid to the physician who performs and interprets the test, whereas the technical fees are paid to the imaging facility (e.g. the hospital) to offset the costs associated with providing the imaging services (including the costs of paying technicians, overhead expenditures, capital outlays, amortization, etc.).

For stress contrast ECHO tests, the cost of the contrast medium was added only in the event of uninterpretable stress ECHO test result. The cost of this contrast medium was estimated as $170 per vial (single use) through consultation with industry experts. In the situation where an imaging test result was uninterpretable, an additional cost of follow-up with the patient (physician fee) was incurred, as well as the cost of conducting another cardiac imaging test. For stable outpatients, a one time assessment professional fee of $30.60 (OHIP code A608 for "partial assessment") was assumed after an uninterpretable test result.

For acute inpatients, the costs associated with hospitalization were also included in the model. The total cost of hospitalization was calculated based on the average wait time for each cardiac imaging test and a cost per diem for each day spent in hospital. Following consultations with experts in cardiology, the number of additional days spent in hospital for non-invasive cardiac tests assumed in the model ranged from 1.25 days for SPECT to 4.5 days for cardiac MRI (see Table 9). The average cost per diem for inpatient care was estimated using the 2007-08 OCCI database, where patients were identified by Case Mix Group 213 ("Unstable angina without cardiac catheterization, without specified cardiac conditions"), in combination with the list of 2009 CCI procedure codes(29) found in Table 12. The average of the technical fees associated with stress ECHO and SPECT tests ($213, Table 11) was subtracted from the average inpatient cost ($2,942). This was divided by the average length-of-stay (3.2 days) to obtain a per diem cost of $852. An additional consultation fee of $29.20 (OHIP code C602 for "subsequent visit- first five weeks") was also assumed for each inpatient day spent in hospital.

In the cases of CT angiography and cardiac MRI, where no OHIP fee codes currently exist for the technical components of the imaging tests, a technical fee was estimated and imputed by multiplying the respective professional fee by 2.04, a weighted average of the ratio of the technical to professional fees for each of the other tests. These imputed technical fees were validated against OCCI functional centre costs for diagnostic imaging for CCT and CMR, for the fiscal year 2007-08. Case Mix Groups 242 ("Chest pain") and 213 ("Unstable angina without cardiac catheterization, without specified cardiac conditions") were used to represent the outpatient and inpatient populations of interest, respectively. The final imputed technical fees for CCT and CMR were found to be consistent with the diagnostic imaging costs reported under the corresponding OCCI functional centres.

Willingness to pay

Since the short time horizon adopted in the model precluded the use of generic health outcomes such as the QALY, the analysis adopted as its primary outcome measure the incremental cost per additional "accurate diagnosis" of CAD resulting from non-invasive testing. Unlike the QALY, an accurate diagnosis of CAD has no commonly understood monetary value. However, such a monetary value is required in order to establish which technologies appear most cost-effective. This value represents the "willingness-to-pay" (WTP) of the relevant decision maker – in this case the Ontario MOHLTC – for an additional accurate diagnosis of CAD resulting from non-invasive imaging.

Several considerations which might be useful in determining this WTP are given in Appendix 2. These may be summarized as follows:

a) An "accurate diagnosis" of CAD can be obtained through a coronary angiography for $1433 – therefore one might expect the WTP for an accurate diagnosis through a non-invasive test to resemble this amount. However, it must be remembered that "accurate diagnosis" is an imperfect measure of the health consequences of diagnostic tests : both non-invasive imaging and coronary angiography provide far more information than a simple yes/no diagnosis of CAD, with each test providing different information useful to guide diagnosis and further treatment.

b) The Ministry currently pays $804 for a non-invasive test with less-than-perfect diagnostic accuracy – its willingness to pay for an “accurate diagnosis” from such a test may therefore be greater than $804.

c) These tests are non-invasive, whereas coronary angiography is invasive – if all else were equal this would presumably result in a higher WTP for non-invasive tests.

d) These tests are not perfectly accurate – an accurate diagnosis from such a test may therefore be valued less than one from a coronary angiography (an explanation for this is given in Appendix 2).

Given these uncertainties around the WTP, the results of the following analyses were considered across a wide range of WTP values. These results were then interpreted at two reasonable WTP “anchors”: the first representing the estimated cost of the most costly non-invasive test considered in our model (MRI perfusion, $804); the second representing the estimated cost of a coronary angiography ($1433). These anchors are intended to guide discussion only.

Finally, it should be noted that where “true positive” and “true negative” diagnoses are considered to be of equal value (implicit in the adoption of “accurate diagnosis” as an outcome measure), the WTP for a “true positive” diagnosis of CAD (the secondary outcome measure) is the same as that for an accurate diagnosis of CAD.

The prevalence of CAD in the presenting population

A critical parameter in the analysis was the prevalence of CAD in each of the two populations under consideration. Figures from the ACC guidelines [reference] suggest that the prevalence of CAD varies substantially by age, gender, and whether the patient presents with typical or atypical angina. However, no relevant Ontario-based data were identified for either population.

In the absence of specific data for Ontario, the prevalence of CAD in the base case analysis was assumed to be 50% for both populations. Given the uncertainty around this estimate, all of the subsequent analyses considered the cost-effectiveness of non-invasive imaging at a wide range of prevalence values from 5% to 95%.

Analyses

Base case analyses

Base case cost-effectiveness analyses were conducted in each population for both outcome measures. In each analysis only a single prevalence value was considered, as described above. For each non-invasive test, the incremental cost per accurate (or true positive) diagnosis was calculated and expressed in terms of an incremental cost-effectiveness ratio (ICER).

Primary sensitivity analyses

Given the uncertainty surrounding the prevalence of CAD in the population presenting with chest pain, a number of primary sensitivity analyses were carried out with this modeled as a variable rather than a fixed estimate. The prevalence of CAD was varied in 5% increments from 5% to 95%. Rather than reporting the results of each of these analyses as a series of tables of ICERs, the results were reported graphically, with the prevalence of CAD varying along the horizonal axis and the WTP for an accurate (or true positive) diagnosis of CAD varying along the vertical axis. The WTP was considered at a very wide range of values incorporating and extending beyond both proposed WTP anchors. These graphs identify the single most cost-effective non-invasive test at each combination of prevalence of CAD and WTP. Similar graphs were employed for all of the following analyses.

Additional sensitivity analyses

In stable outpatients, the results of the model appeared particularly sensitive to the proportion of stress ECHO tests assumed to be uninterpretable without the use of a contrast agent. As such, a sensitivity analysis was conducted where this proportion was taken from expert opinion (15%) rather than from a literature estimate (30%).

In acute inpatients, an important determinant of the model's results appeared to be the estimated number of additional days in hospital associated with each non-invasive imaging test. An additional sensitivity analysis was conducted based on the assumption that all tests were associated with the same additional stay in hospital (1.5 days, the average estimate from expert opinion for coronary angiography).

In a further sensitivity analysis, the estimates of the diagnositic sensitivity and specificity of CT angiography were altered to take account of preliminary results made available by Programs for Assessment of Technology in Health (PATH). These preliminary results were taken from the unpublished Ontario Multidetector Computed Tomographic Coronary Angiography Study (OMCAS) (29) and based only on "group 2" patients, defined as having an intermediate probability of CAD and 50% stenosis. The OMCAS sensitivity and specificity estimates for this group were 0.812 and 0.958, respectively. These were combined with the original estimates for CT angiography in a bivariate meta-analysis. The resulting values of 0.961 sensitivity and 0.815 specificity were used in the sensitivity analysis.

Further analyses to address feasibility issues

MAS expressed concern that there may be feasibility issues with implementing one or both of stress contrast ECHO and CT angiography more widely across the province. As such, each of the primary sensitivity analyses were re-run excluding one or both of these tests.

Isolated comparisons of stress ECHO and SPECT

Since stress ECHO and SPECT are currently the most widely adopted tests for the diagnosis of CAD in Ontario, MAS expressed interest in the results of pairwise comparisons between each of the stress ECHO strategies (either with or without the use of a contrast agent) and each of the SPECT technologies (gated, attenuated, or traditional) in stable outpatients only. This consisted of six comparisons in total:

1) Stress contrast ECHO vs attenuated SPECT;

2) Stress contrast ECHO vs gated SPECT;

3) Stress contrast ECHO vs traditional SPECT;

4) Stress ECHO vs attenuated SPECT;

5) Stress ECHO vs gated SPECT;

6) Stress ECHO vs traditional SPECT.

Results

Base case analyses

The base case results are summarized in Tables 13 to 16. The results are reported separately for the two patient populations (stable outpatients and acute inpatients) and for the two outcome measures (accurate diagnosis and true positive diagnosis).

In stable outpatients, CT angiography was found to dominate – that is, it was found to be less costly and more effective than – stress ECHO, SPECT and cardiac MRI, but not stress contrast ECHO. Stress contrast ECHO and CT angiography are the only non-dominated strategies – that is, they represent the only potentially cost-effective non-invasive imaging tests under the base case assumptions – with stress contrast ECHO the less costly and less effective of the two.

Which of stress contrast ECHO and CT angiography is the *more* cost-effective depends on the willingness to pay (WTP) for an additional unit of the preferred outcome measure (whether accurate diagnosis or true positive diagnosis).

The ICER of CT angiography versus stress contrast ECHO was found to be $1527 per accurate diagnosis or $1088 per additional true positive diagnosis. If accurate diagnosis is the preferred outcome measure then stress contract ECHO appears to be the most cost-effective non-invasive disgnostic test for stable outpatients at either WTP anchor – while CT angiography provides a higher proportion of accurate diagnoses, it does so at too high an additional cost per accurate diagnosis for it to appear cost-effective. However, it should be noted that the higher anchor falls only slightly below this ICER, suggesting that this finding may be very sensitive to the assumptions adopted in the base case. If true positive diagnosis is the preferred outcome measure then stress contract ECHO appears to be cost-effective at the lower WTP anchor but CT angiography appears to be cost-effective at the higher anchor.

In acute inpatients, CT angiography appeared much more costly due to its relatively long assumed hospital wait time (this assumption was relaxed in a sensitivity analysis). As such it appeared to dominate only cardiac MRI. The non-dominated strategies (in ascending order of cost) were stress contrast ECHO, SPECT and CT angiography. SPECT was found to have an ICER of $9489 per accurate diagnosis ($6999 per true positive diagnosis) versus stress contrast ECHO, while CT angiography had an ICER of $36,055 per accurate diagnosis ($25,763 per true positive diagnosis) versus SPECT. As such, stress contrast ECHO appears to be the most cost-effective non-invasive disgnostic test for acute inpatients at either WTP anchor.

Primary sensitivity analyses

The results of the primary sensitivity analysis are summarized in Figures 3 to 6.

In stable outpatients, stress contrast ECHO appears to be the most cost-effective non-invasive imaging test at lower prevalence rates of CAD and/or at lower WTP values, while CT angiography appears to be the most cost-effective non-invasive imaging test at higher prevalence rates of CAD and/or at higher WTP values.

Where the primary outcome measure of accurate diagnosis is adopted, stress contrast ECHO appears cost-effective at the lower WTP anchor of $804 per accurate diagnosis when the prevalence of CAD is less than 70%, with CT angiography appearing cost-effective otherwise. At the higher WTP anchor, this cut-point between stress contrast ECHO and CT angiography falls to around 50%. Where the secondary outcome measure of true positive diagnosis is adopted, these cut-points fall to 65% and 35% at the lower and higher WTP anchors respectively.

In acute inpatients, stress contrast ECHO appears to be the most cost-effective non-invasive imaging test at both WTP anchors, at any prevalence of CAD, and under either outcome measure. SPECT appears cost-effective only at implausibly high prevalence or WTP values.

The base case finding that stress contrast ECHO *dominates* stress ECHO (without the use of a contrast agent) was seen to hold across the entire range of prevalence values.

Additional sensitivity analyses

In stable outpatients, an additional sensitivity analyses was conducted in which the proportion of stress ECHO tests assumed to be uninterpretable without the use of a contrast agent was taken from expert opinion (15%) rather than from a literature estimate (30%). The results are reported in Figure 7. Such a change favours stress contrast ECHO, slightly raising the prevalence cut-points above which CT angiography appears more cost effective. Stress contrast ECHO still dominates stress ECHO at all prevalence values.

In acute inpatients, an additional sensitivity analysis was conducted based on the assumption that all tests were associated with the same additional stay in hospital. The results are given in Figure 8. Most notably, CT angiography appears to have been significantly disadvantaged by the estimates adopted in the base case and in this analysis appears to have replaced SPECT as the most cost-effective test at very high WTP and prevalence values. However, at the lower WTP anchor stress contrast ECHO remains the most cost-effective test at all prevalence values, while at the higher WTP anchor it appears cost-effective at all prevalence values below approximately 80%. CT angiography appears cost-effective at the higher WTP anchor only if the prevalence of CAD is greater than 80%.

Incorporating the preliminary results provided by OMCAS into the sensitivity and specificity of CT angiography had a negligible effect on the results of the cost-effectiveness analysis. The incorporation of these preliminary results changed the output of the bivariate meta-analysis from 0.972 to 0.961 for sensitivity and from 0.787 to 0.815 for specificity, which had little effect on the incremental cost per accurate or true positive diagnosis for CT angiography versus stress contrast ECHO. Figures 9 and 10 represent revisions of Figures 3 and 5 (for stable outpatients and acute inpatients respectively) with these updated sensitivity and specificity results incorporated.

Further analyses to address feasibility issues

The results of the further analyses to address feasibility issues are summarized in Figures 11 to 14.

In stable outpatients, if CT angiography is removed from the analysis, stress contrast ECHO appears cost-effective at both WTP anchors (and indeed at any reasonable WTP value) across the entire range of prevalence values. Similarly, if stress contrast ECHO is unavailable then CT angiography appears cost-effective at both WTP anchors across the entire range of prevalence values. If both CT angiography and stress contrast ECHO are unavailable then the most cost-effective test appears to be either stress ECHO or SPECT. At the lower WTP anchor stress ECHO appears cost-effective irrespective of the prevalence of CAD, while at the higher WTP anchor stress ECHO appears cost-effecitve if the prevalence of CAD is below 90%, with SPECT appearing cost-effective otherwise.

In acute inpatients, if stress contrast ECHO is removed from the analysis then SPECT appears cost-effective at both WTP anchors, for any prevalence of CAD.

Isolated comparisons of stress ECHO and SPECT

The results of the pairwise comparisons of stress ECHO and SPECT are summarized in Figures 15 to 20. Since each of these comparisons was conducted in isolation and excluded all other tests (one or more of which might have appeared cost-effective if included), these comparisons *do not* reveal which of the stress ECHO or SPECT technologies is *cost-effective*, but rather which technology in each comparison is *preferred* at particular WTP and prevalence values.

Critically, no SPECT technology was found to be preferred to stress contrast ECHO for any reasonable combination of WTP and prevalence rate. Furthermore, at the lower WTP anchor, no SPECT technology appeared to be preferred to stress ECHO at any prevalence rate of CAD. Only at relatively high WTP and prevalence values were any of the SPECT technologies preferred to stress ECHO – at the higher WTP anchor, attenuated, gated, and traditional SPECT were preferred to stress ECHO at prevalence rates above 55%, 85%, and 80% respectively.

Since stress contrast ECHO was previously found to dominate stress ECHO, and since attenuated SPECT weakly dominates gated and traditional SPECT, some weak orderings are possible. Denoting ">" as "preferred to":

1) At the lower WTP anchor, or at the higher WTP anchor with a prevalence of CAD below 55%, stress contrast ECHO > stress ECHO > attenuated SPECT > gated or traditional SPECT;

2) At the higher WTP anchor with a prevalence of CAD above 80%, stress contrast ECHO > attenuated SPECT > gated or traditional SPECT > stress ECHO.

Budget impact analysis

The budget impact analysis (BIA) was performed taking the perspective of the MOHLTC and includes both physician and hospital (clinic) costs of non-invasive cardiac imaging tests. Volumes of cardiac tests in Ontario were taken from administrative databases (OHIP, DAD, NACRS) for fiscal years 2004 to 2008 using methodology summarized in the MAS report Non-Invasive Cardiac Imaging Technologies for the Diagnosis of Coronary Artery Disease.(30)

The tests considered in the BIA were the same as those considered in the cost-effectiveness analysis: stress echocardiography (stress ECHO); stress echocardiography with the use of contrast agent if necessary for interpretation (stress contrast ECHO); single photon emission computed tomography (SPECT); cardiac magnetic resonance imaging (cardiac MRI); and cardiac computed tomography (CT angiography).

Methods

The volume of SPECT tests was estimated from all nuclear cardiac tests identified in OHIP according to specific professional and technical fees. According to experts in cardiology, the proportion of nuclear cardiac tests used for the diagnosis of CAD in Ontario was approximately 56.0% in 2008-09. Similarly, the proportion of all stress ECHO tests used for the diagnosis of CAD was estimated at 9.5%, with stress contrast ECHO estimated as comprising 10% of these tests. The volumes of CT angiography and cardiac MRI tests were specific to the diagnosis of CAD and were taken from DAD and NACRS databases. Note also that the volumes reported here represent the total number of cardiac imaging tests for the diagnosis of CAD in both populations modeled in the cost-effectiveness analysis ("stable outpatients" and "acute inpatients").

Table 17 shows the volume of cardiac tests in Ontario from FY2004 to FY2008, as well as the corresponding test costs used in the BIA. The costs listed represent an average cost of all tests and include physician and hospital / clinic (technical) costs for a given technology (see Table 11). Table 18 shows the projected volume of cardiac tests in Ontario for FY2010 to FY2014. The volume of tests was projected based on the average annual increase in technology-specific volume from Table 17. Note that in the case of cardiac tests involving stress contrast ECHO, the average test cost was calculated based on the standard cost of a stress ECHO, with the additional cost of contrast agent ($170) included only in 30% of cases (representing the proportion of uninterpretable stress ECHO tests).

In the current BIA, the effect of moving a certain proportion of the volume of specific tests to another, substitute technology was assessed for various scenarios. These scenarios are presented irrespective of whether a technology was found to be cost-effective and are reported as general reference tables. Tables 19 to 38 show the proportion of cardiac tests shifted, or moved to the corresponding substitute technology for the following percentages: 5%, 10%, 25%, and 50%. Total projected costs for 5 years are reported for each proportion of tests moved, together with corresponding 5-year cost differences and an average annual cost difference. Note that the costs shown are not discounted and are reported as 2009 CDN.

Results

The results of our budget impact analysis should be considered as complementing those of our cost-effectiveness analysis, rather than the other way around. Technologies found not to be cost-effective should not be adopted even if their adoption would free up the MOHLTC's budget for other activities; conversely, technologies regarded as cost-effective should be adopted even if their adoption has a detrimental impact on the budget. If there is a reluctance to impose additional costs on the budget – even if this is through the adoption of technologies with better diagnostic accuracy than are used at present – then this should be reflected by adopting a lower

WTP for an accurate diagnosis in the cost-effectiveness analysis, rather than by dismissing the results of the cost-effectiveness analysis out of hand. If the primary aim of policy is cost saving, this can be accomplished by adopting a much lower WTP for an accurate diagnosis – where this WTP is extremely low, the cost-effective technology will always be that which is cheapest.

Stress ECHO

Stress ECHO tests are the least costly of the cardiac imaging modalities we reviewed. When the volume of stress ECHO tests is shifted to other technologies, all scenarios result in higher projected costs (see Tables 19 to 22). If 25% of stress ECHO tests are moved to other imaging technologies, projected costs would be higher: from a small cost difference of about $166K per year for contrast available stress ECHO testing to a large difference of $10.2M for cardiac MRI testing. The largest possible cost difference corresponds to replacing 50% of stress ECHO tests with cardiac MRI ($20.5M per year); the smallest possible cost difference occurs by replacing 5% of stress ECHO tests with stress contrast ECHO tests ($33.2K per year).

Scress contrast ECHO

Stress contrast ECHO tests are the second least costly of the compared cardiac imaging modalities. When the volume of stress contrast ECHO tests is shifted to other technologies, all scenarios result in higher projected costs except for standard stress ECHO tests (see Tables 23 to 26). If 25% of stress contrast ECHO tests are switched to other imaging technologies, ensuing projected costs would be higher (excluding standard stress ECHO): from a small cost difference of about $14.6K per year for CT angiography testing to a large difference of $95.3K for cardiac MRI testing. The largest possible cost difference corresponds to replacing 50% of stress contrast ECHO tests with cardiac MRI imaging ($190.7K per year); the smallest cost difference occurs for replacing 5% of stress contrast ECHO tests with CT angiography ($2.9K per year), excluding standard stress ECHO.

SPECT

SPECT was found to be the second most costly of the compared cardiac imaging modalities. When the volume of SPECT tests is shifted to other technologies, all scenarios result in lower projected costs, except for cardiac MRI imaging (see Tables 27 to 30). If 25% of SPECT tests are moved to other imaging technologies, ensuing projected costs would be lower (excluding cardiac MRI): from the largest cost avoidance of about $10.8M per year for stress ECHO testing to the smallest cost avoidance of $5.8M for CT angiography. The largest possible cost avoidance corresponds to replacing 50% of SPECT tests with stress ECHO imaging ($21.7M per year); the smallest cost avoidance occurs by replacing 5% of SPECT tests with CT angiography imaging ($1.2M per year), excluding cardiac MRI.

Cardiac MRI

Cardiac MRI tests were found to be the most costly of the compared cardiac imaging modalities. When the volume of cardiac MRI tests is shifted to other technologies, all scenarios result in lower projected costs, however, the actual number of tests moved is relatively small (see Tables 31 to 34). If 25% of cardiac MRI tests are moved to other imaging technologies, ensuing projected costs would be lower: from the largest cost avoidance of about $62.1K per year for stress ECHO testing to the smallest cost avoidance of $28.3K for SPECT testing. The largest possible cost avoidance corresponds to replacing 50% of cardiac MRI tests with stress ECHO imaging ($124.2M per year); the smallest cost avoidance occurs by replacing 5% of cardiac MRI tests with nuclear cardiac imaging ($5.7K per year).

CT angiography

CT angiography lies in the mid-range of test costs of the compared cardiac imaging modalities. When the volume of CT angiography tests is shifted to other technologies, some scenarios result in higher projected costs, while others result in lower project costs (see Tables 35 to 38). If 25% of CT angiography tests are moved to other imaging technologies, ensuing projected costs would be as follows: the largest cost avoidance would be $53.8K per year for stress ECHO imaging, and the largest cost difference would be $156.7K per year for cardiac MRI (with cardiac MRI being the more costly option). The largest possible cost avoidance corresponds to replacing 50% of CT angiography tests with stress ECHO ($107.6K per year); the largest possible cost difference corresponds to replacing 50% of CT angiography tests with cardiac MRI ($313.4K per year).

Discussion

Overall, our economic evaluation suggests that stress contrast ECHO and CT angiography are the most cost-effective tests for stable outpatients, while stress contrast ECHO is the most cost-effective test for acute inpatients. In our cost-effectiveness analysis, it was very uncommon for any other technology to appear to be more cost-effective than either of these two tests. This finding was consonant with the previous studies identified in our systematic review.

Previous analyses found that CT angiography was cost-effective versus stress ECHO, that stress ECHO was cost effective versus SPECT, and that SPECT was cost-effective versus cardiac MRI (which, in turn, was not cost-effective against any other technology). In our base case and primary sensitivity analyses, we find that stress ECHO (without the use of contrast), SPECT and cardiac MRI are indeed not cost-effective technologies at our assumed WTP anchors. In addition, we find that stress contrast ECHO is a cost-effective alternative to CT angiography in acute inpatients (across all prevalence values) and in stable outpatients where the prevalence of CAD is low.

Adopting the lower (higher) WTP anchor, our analyses suggest that stress contrast ECHO is cost-effective for stable outpatients if the prevalence of CAD is below 70% (50%), with CT angiography cost-effective otherwise. The intuition is that CT angiography is more costly and has higher sensitivity than stress contrast ECHO, but stress contrast ECHO is more specific than CT angiography: a low prevalence of CAD therefore benefits stress contrast ECHO (since the sensitivity is less important than the specificity), while a high prevalence of CAD benefits CT angiography; meanwhile a higher WTP favours CT angiography (the more costly test) by lowering the prevalence value above which CT angiography appears cost-effective. Each of the other technologies is dominated by either stress contrast ECHO or CT angiography – that is, they are more costly and less effective.

For acute inpatients, stress contrast ECHO was found to be the most cost-effective strategy irrespective of the prevalence of CAD.

If CT angiography is unavailable, stress contrast ECHO appears to be cost-effective for stable outpatients, while if stress contrast ECHO is unavailable CT angiography appears cost-effective. Where both are unavailable, stress ECHO (without the use of a contrast agent) appears cost-effective at the lower WTP anchor (at all prevalence values) and at the higher WTP anchor if the prevalence of CAD is below 90% - due to its better sensitivity, attenuated SPECT appears cost-effective at the higher WTP anchor if the prevalence of CAD is 90% or higher. For acute inpatients, if stress contrast ECHO is unavailable then attenuated SPECT is found to be cost-effective.

An interesting finding of our analysis is that the use of a contrast agent in cases where a stress ECHO is uninterpretable dominates not using a contrast agent – that is, it is a less costly and more effective strategy. While the contrast agent itself costs $170, its higher interpretability negates the need for additional non-invasive testing in sufficient patients that its use appears cost saving overall. However, it should be noted that the economic analysis did not consider any potential adverse events associated with the contrast agent.

It must be noted that our analyses were subject to a number of limitations. We developed a short term model considering the diagnosis of CAD with non-invasive imaging only. Ideally our model would consider the downstream costs and health effects of each of the diagnostic outcomes (true positive, false positive, true negative, false negative, undiagnosed) and derive an incremental cost per QALY for each of the technologies under consideration. This would allow the consequences of a false positive diagnosis to differ from those of a false negative diagnosis, and a true positive to carry a different payoff to a true negative, and thus give a more accurate representation of the long-term costs and health outcomes associated with each technology. In addition to this limited scope, a number of parameters in the model lacked robust estimates. As mentioned earlier, we did not have estimates of the prevalence of CAD in the relevant populations in Ontario or the WTP of the MOHLTC for an accurate diagnosis; in addition, a number of other parameters in the model had to be derived (e.g. the technical fees for some technologies were derived from those for other technologies) or estimated from expert opinion (e.g. the estimates of hospital wait times, which were subject to such uncertainty that we conducted a sensitivity analysis specifically excluding them). There was also substantial heterogeneity in the pooled estimates of sensitivity and specificity, as discussed in the clinical reports.

Our budget impact analysis suggests that replacement of tests that are currently used very widely in Ontario has the potential for substantial cost savings. For example, replacing 25% of SPECTs with stress contrast ECHO would save the MOHLTC an estimated $42.2m over five years, while replacing the same number of tests with CT angiography would save an estimated $28.8m over the same time frame.

Clinical policy regarding implementation and wider use of these tests, however, must also consider additional factors. These include radiation-related risk. Many of the technologies we evaluated offer very substantial radiation exposure. Our analysis does not distinguish between technologies with respect to radiation risk.

In addition, future policy should consider how these tests will be used in practice. It is quite possible that the introduction of new diagnostic tests may result in their use being complementary to, rather than as a replacement for, existing technologies. If this were to be the case, no cost savings may be realized, and there may be additional adverse health consequences associated with unnecessary testing. Finally, clinical policy should consider the importance of operator skill and quality standards in the use of these new technologies. Neither stress contrast ECHO nor CT angiography are widely used in the province at present. Obtaining excellent clinical and economic outcomes will depend on maintenance of quality standards in the wide implementation and use of these technologies.

Tables

Table 1: List of studies excluded from the systematic review of selected diagnostic strategies for coronary arterial disease

First author	Year	Reason for exclusion
Hayashino	2007	Duplicate of Hayashino 2004
Kreis	2009	CT angiography compared to CA
Ladapo	2008	CT angiography compared to "standard of care=stress test" (no definition given for "stress test")
Lorenzoni	2003	ECHO compared to ECG
Maddahi	1997	SPECT compared to PET or CA
Medical Advisory Secretariat (OMHLTC)	2005	Different diagnosis (myocardial viability)
Mowatt	2004	SPECT compared to PET or CA
Patterson	1995	SPECT compared to PET or CA
Shaw	1999	No comparators of interest
Stacul	2009	CT angiography versus CA
Moir	2007	No comparators of interest
Wyrick	2008	No comparators of interest
Yong	2002	Different setting (intensive care unit)

CA = Coronary angiography, CT = Computed tomography, ECHO = Echocardiography, OMHLTC = Ontario Ministry of Health and Long-Term Care, SPECT = Single-photon emission computed tomography.

Table 2: Summary of diagnostic strategies compared from the selected economic studies

First author	Year	Comparators*
Bedetti	2008	1. Exercise stress ECHO 2. Pharmacological stress ECHO 3. SPECT
Dewey	2007	1. Multi-slice CT 2. Electron-beam CT 3. Exercise stress ECHO 4. Pharmacological stress ECHO 5. MRI
Garber	1999	1. Stress ECHO (combination of pharmacological and exercise stress) 2. SPECT
Hayashino	2004	1. Exercise stress ECHO 2. SPECT
Hernandez	2007	1. SPECT 2. ECHO (not defined)
Khare	2008	1. Multi-detector CT 2. ECHO (not defined)
Kuntz	1999	1. Exercise stress ECHO 2. SPECT
Lee	2002	1. Exercise stress ECHO 2. Pharmacological stress ECHO 3. SPECT
Rumberger	1999	1. Eletron-beam CT 2. Exercise stress ECHO
Sharples	2007	1. Pharmacological stress ECHO 2. SPECT 3. MRI
Shaw	2006	1. Exercise stress ECHO 2. SPECT
Tardif	2002	1. Contrast stress ECHO 2. SPECT

CT = Computed tomography, ECHO = Echocardiography, SPECT = Single-photon emission computed tomography.

* Comparators reported based on inclusion/exclusion criteria

Table 3: Summary incremental cost-effectiveness ratios across selected studies evaluating echocardiography

Technology of interest	Comparator	First author	Year	Outcome of interest	Reported as cost-effective?	ICER
Stress ECHO	CT angio	Dewey	2007	Cost per successful diagnosis	No	Not reported*
	CT angio	Khare	2008	Cost per QALY	No	Dominated
	CT angio	Rumberger	1999	Cost per correct diagnosis	No	Not reported†
	MRI	Dewey	2007	Cost per successful diagnosis	Yes	Not reported‡
	MRI	Sharples	2007	Cost per QALY	Yes	GBP (2006) £13,200
	SPECT	Bedetti	2008	Cost per correct diagnosis	Yes	Dominant
	SPECT	Garber	1999	Cost per QALY	Yes	USD (1996) $78,444**
	SPECT	Hayashino	2004	Cost per QALY	Yes	Dominant
	SPECT	Hernandez	2007	Cost per QALY	Yes	Dominant
	SPECT	Kuntz	1999	Cost per QALY	Yes	USD (1996) $62,800**
	SPECT	Lee	2002	Cost per QALY	No	Not reported§
	SPECT	Sharples	2007	Cost per QALY	No	More costly, same QALYs
	SPECT	Shaw	2006	Cost per LYS	Yes	USD (2003) $72,187**
	SPECT	Tardif	2002	Cost per correct diagnosis	ND	CDN (2000) $5,029

Angio = Angiography, CDN = Canadian dollars, CT = Computed tomography, ECHO = Echocardiography, ICER = Incremental cost-effectiveness ratio, LYS = Life years saved, MRI = Magnetic resonance imaging, ND = Not defined; QALY = Quality adjusted life years, SPECT = Single-photon emission computed tomography, USD = United States dollars.

* At a pre-test likelihood of 60%, CT angiography was cost-effective.
† For prevalence of disease <=70%, CT angiography was considered cost-effective.
‡ Both not cost effective when compared to CT angiography.
§ SPECT was cost-effective when the probability of CAD was >=30%. Stress ECHO was cost-effective when the probability of CAD was <=20%.
** Stress ECHO was the alternative reporting lower cost and worst outcome.

Table 4: Summary incremental cost-effectiveness ratios across selected studies evaluating single-photon emission computed tomography

Technology of interest	Comparator	First author	Year	Outcome of interest	Reported as cost-effective?	ICER
SPECT	MRI	Sharples	2007	Cost per QALY	Yes	Dominant
	Stress ECHO	Bedetti	2008	Cost per correct diagnosis	No	Dominated
	Stress ECHO	Garber	1999	Cost per QALY	No	USD (1996) $78,444
	Stress ECHO	Hayashino	2004	Cost per QALY	No	Dominated
	Stress ECHO	Hernandez	2007	Cost per QALY	No	Dominated
	Stress ECHO	Kuntz	1999	Cost per QALY	No	USD (1996) $62,800
	Stress ECHO	Lee	2002	Cost per QALY	Yes	Not reported*
	Stress ECHO	Sharples	2007	Cost per QALY	Yes	Less costly, same QALYs
	Stress ECHO	Shaw	2006	Cost per LYS	No	USD (2003) $72,187
	Stress ECHO	Tardif	2002	Cost per correct diagnosis	ND	CDN (2000) $5,029

CDN = Canadian dollars; ECHO = Echocardiography, ICER = Incremental cost-effectiveness ratio, LYS = Life years saved, MRI = Magnetic resonance imaging, ND = Not defined, QALY = Quality adjusted life years, SPECT = Single-photon emission computed tomography, USD = United States dollars.

* SPECT was cost-effective when the probability of CAD was >=30%. Stress ECHO was cost-effective when the probability of CAD was <=20%.

Table 5: Summary incremental cost-effectiveness ratios across selected studies evaluating computed tomography angiography

Technology of interest	Comparator	First author	Year	Outcome of interest	Reported as cost-effective?	ICER
CT angio	MRI	Dewey	2007	Cost per QALY	Yes	Not reported*
	Stress ECHO	Dewey	2007	Cost per QALY	Yes	Not reported†
	Stress ECHO	Khare	2008	Cost per QALY	Yes	Dominant
	Stress ECHO	Rumberger	1999	Cost per correct diagnosis	Yes	Not reported‡

Angio = Angiography, CT = Computed tomography, ECHO = Echocardiography, ICER = Incremental cost-effectiveness ratio, MRI = Magnetic resonance imaging, QALY = Quality adjusted life years.

* At a pre-test likelihood of 60%, CT angiography was cost-effective.
† At a pre-test likelihood of 60%, CT angiography was cost-effective.
‡ For prevalence of disease <=70%, CT angiography was considered cost-effective.

Table 6: Summary incremental cost-effectiveness ratios across selected studies evaluating cardiac magnetic resonance imaging

Technology of interest	Comparator	First author	Year	Outcome of interest	Reported as cost-effective?	ICER
MRI	CT angio	Dewey	2007	Cost per correct diagnosis	No	Not reported*
	SPECT	Sharples	2007	Cost per QALY	No	Dominated
	Stress ECHO	Dewey	2007	Cost per correct diagnosis	No	Not reported†
	Stress ECHO	Sharples	2007	Cost per QALY	No	GBP (2006) £13,200‡

Angio = Angiography, CT = Computed tomography, ECHO = Echocardiography, ICER = Incremental cost-effectiveness ratio, GBP = Great Britain pounds, MRI = Magnetic resonance imaging, QALY = Quality adjusted life years, SPECT = Single-photon emission computed tomography.

* Invasive coronary angiography using CT reported lower costs.
† Both not cost effective when compared to CT angiography.
‡ MRI was the alternative reporting lower cost and worst outcome.

Table 7: Summary of cost-effectiveness findings*

Strategy	Cost-effectiveness comparator: CT angio	MRI	SPECT	Stress ECHO	Overall
CT angio	-	1/1	NA	3/3	**4/4**
MRI	0/1	-	0/1	0/2	**0/4**
SPECT	NA	1/1	-	2/8	**3/9**
Stress ECHO	0/3	2/2	6/8	-	**8/13**

Angio = Angiography, CT = Computed tomography, ECHO = Echocardiography, MRI = Magnetic resonance imaging, NA = Not available, SPECT = Single-photon emission computed tomography.

* Table 7 reads from left to right. The numerator indicates the number of times a strategy was considered cost-effective over its respective comparator. Whereas the denominator indicates the number of cost-effectiveness comparisons between a strategy versus its respective comparator.

Table 8: Pooled estimates of sensitivity and specificity for the cost-effectiveness models

Technology	Pooled Sensitivity: Point Estimate	95% Lower	95% Upper	Pooled Specificity: Point Estimate	95% Lower	95% Upper
Stress ECHO	0.795	0.774	0.816	0.842	0.819	0.865
Stress contrast ECHO	0.844	0.792	0.896	0.800	0.725	0.874
SPECT (Attenuation)	0.861	0.812	0.910	0.821	0.748	0.895
SPECT (Gated)	0.840	0.795	0.884	0.782	0.715	0.849
SPECT (Traditional)	0.861	0.839	0.883	0.712	0.668	0.756
CT Angiography	0.977	0.955	0.999	0.788	0.708	0.868
Cardiac MRI	0.907	0.878	0.936	0.809	0.750	0.868

Table 9: Additional days needed to wait for specific cardiac tests (compared to GXT) for the inpatient model

Technology	Additional time for test (days) Average	Range
Inpatient population (model 2)		
Stress ECHO	1.50	1.0 - 2.0
Stress contrast ECHO contrast	1.50	1.0 - 2.0
SPECT	1.25	1.0 - 2.0
CT Angiography	3.00	0.0 - 7.0
Cardiac MRI	4.50	3.0 - 7.0

Note: Above estimates are based on consultations with experts in cardiology

Table 10: Proportion of non-invasive tests considered uninterpretable in the outpatient and inpatient models

Technology	Uninterpretable test (%) Average	Range
Outpatient population (model 1)		
Stress ECHO	15.0%	10.0 - 30.0%
Stress contrast ECHO	4.3%	1.0 - 5.0%
SPECT	6.9%	0.0 - 10.0%
CT Angiography	5.3%	3.0 - 8.0%
Cardiac MRI	5.0%	
Inpatient population (model 2)		
Stress ECHO	20.0%	15.0 - 30.0%
Stress contrast ECHO	4.0%	1.0 - 5.0%
SPECT	7.0%	0.0 - 10.0%
CT Angiography	7.5%	5.0 - 10.0%
Cardiac MRI	5.0%	

Note: Above estimates are based on consultations with experts in cardiology

Table 11: List of cardiac imaging tests and associated OHIP 2009 costs

Technology		List of professional fees					Subtotal	List of technical fees					Subtotal	Total
Cardiac CT	Fee code	X125	X417					Imputed						
	Cost	$89.20	$64.00				$153.20	$336.52					$336.52	$489.72
Cardiac MRI-dobutamine stress, gadolinium contrast	Fee code	X441	X445	X487	G319			Imputed	G315	G174				
	Multiplier	1.0	3.0	1.0	1.0			1.0	1.0	1.0				
	Cost	$75.55	$37.80	$37.75	$62.65		$289.35	$463.06	$33.65	$37.00			$533.71	$823.06
Cardiac SPECT-exercise stress	Fee code	J866	J811	J807	G319			J866	J811	J807	G315			
	Cost	$28.70	$55.30	$47.00	$62.65		$193.65	$44.60	$97.55	$223.15	$33.65		$398.95	$592.60
Cardiac SPECT-dobutamine stress	Fee code	J866	J811	J807	G319			J866	J811	J807	G315	G174		
	Cost	$28.70	$55.30	$47.00	$62.65		$193.65	$44.60	$97.55	$223.15	$33.65	$37.00	$435.95	$629.60
Cardiac SPECT-dipyramidole stress	Fee code	J866	J811	J807	G112			J866	J811	J807	G111			
	Cost	$28.70	$55.30	$47.00	$75.00		$206.00	$44.60	$97.55	$223.15	$41.10		$406.40	$612.40
Echocardiography-exercise stress	Fee code	G571	G578	G575	G319			G570	G577	G574	G315			
	Cost	$74.10	$36.90	$17.45	$62.65		$191.10	$76.45	$45.15	$16.45	$33.65		$171.70	$362.80
Echocardiography-dobutamine stress	Fee code	G571	G578	G575	G319			G570	G577	G574	G315	G174		
	Cost	$74.10	$36.90	$17.45	$62.65		$191.10	$76.45	$45.15	$16.45	$33.65	$37.00	$208.70	$399.80
Echocardiography-dipyramidole stress	Fee code	G571	G578	G575	G112			G570	G577	G574	G111			
	Cost	$74.10	$36.90	$17.45	$75.00		$203.45	$76.45	$45.15	$16.45	$41.10		$179.15	$382.60
Coronary angiography	Fee code	A605	J021	Z442	G297	Z440		Lab						
	Multiplier	1.0	1.0	1.0	0.5	0.5		1.0						
	Cost	$132.50	$121.40	$289.55	$118.70	$210.55	$708.08	$725.00					$725.00	$1,433.08

Notes: Imputed technical fees were based on the proportion of average technical fees associated with above ECHO and SPECT fee code combinations. For cardiac SPECT and ECHO stress tests, an average test cost was calculated using dobutamine and dipyramidole fee codes. Coronary angiography costs are listed above as a reference costs and include an average catheterization lab cost / fee of approximately $725.

Table 12: List of CCI procedure codes used in combination with CMG 213 to estimate an inpatient hospital per diem cost

Technology	Procedure code	Description 1	Description 2
Cardiac CT	3.IP.20.WA	Computerized tomography [CT], heart with coronary arteries	without enhancement (contrast)
	3.IP.20.WC	Computerized tomography [CT], heart with coronary arteries	with enhancement (contrast)
	3.IP.20.WE	Computerized tomography [CT], heart with coronary arteries	with and without enhancement (contrast)
Cardiac MRI	3.IP.40.WA	Magnetic resonance imaging [MRI], heart with coronary arteries	without enhancement (contrast)
	3.IP.40.WC	Magnetic resonance imaging [MRI], heart with coronary arteries	with enhancement (contrast)
	3.IP.40.WE	Magnetic resonance imaging [MRI], heart with coronary arteries	with and without enhancement (contrast)
	3.KV.40.WA	Magnetic resonance imaging [MRI], artery NEC	without enhancement
	3.KV.40.WC	Magnetic resonance imaging [MRI], artery NEC	with enhancement
	3.KV.40.WE	Magnetic resonance imaging [MRI], artery NEC	with and without enhancement
	3.LZ.40.WA	Magnetic resonance imaging [MRI], circulatory system NEC	without enhancement
	3.LZ.40.WC	Magnetic resonance imaging [MRI], circulatory system NEC	with enhancement
	3.LZ.40.WE	Magnetic resonance imaging [MRI], circulatory system NEC	with and without enhancement
Cardiac SPECT	3.IP.70.CC	Diagnostic nuclear (imaging) study, heart with coronary arteries	using SPEC tomography (SPECT)
	3.IP.70.KS	Diagnostic nuclear (imaging) study, heart with coronary arteries	using SPEC tomography (SPECT) and blood pool imaging
	3.IP.70.KG	Diagnostic nuclear (imaging) study, heart with coronary arteries	using scintigraphy perfusion imaging
	3.IP.70.KP	Diagnostic nuclear (imaging) study, heart with coronary arteries	using scintigraphy blood pool imaging
Echocardiography	3.IP.30.DA	Ultrasound, heart with coronary arteries	transcutaneous ultrasound alone
	3.IP.30.DB	Ultrasound, heart with coronary arteries	transcutaneous with color flow
	3.IP.30.DC	Ultrasound, heart with coronary arteries	transcutaneous with Doppler
	3.IP.30.DD	Ultrasound, heart with coronary arteries	transcutaneous with color flow and Doppler ;
	3.IP.30.HA	Ultrasound, heart with coronary arteries	endoscopic [EUS] (transesophageal) NOS
	3.IP.30.HB	Ultrasound, heart with coronary arteries	endoscopic [EUS] (transesophageal) with color flow
	3.IP.30.HC	Ultrasound, heart with coronary arteries	endoscopic [EUS] (transesophageal) with Doppler
	3.IP.30.HD	Ultrasound, heart with coronary arteries	endoscopic [EUS] (transesophageal) with color flow and Doppler

Table 13: Base case results for stable outpatients (outcome: accurate diagnosis)

Technology	Cost (C)	Δ Cost	Effect (E)	Δ Effect	C / E	ICER
Stress contrast ECHO	$433.49		81.83%		$530	N/A
CT angiography	$517.73	$84.24	87.35%	5.52%	$593	$1,527
Stress ECHO	$551.58		81.06%		$680	(Dominated)
SPECT	$634.63		82.80%		$766	(Dominated)
Cardiac MRI	$835.47		85.15%		$981	(Dominated)

Table 14: Base case results for stable outpatients (outcome: true positive diagnosis)

Technology	Cost (C)	Δ Cost	Effect (E)	Δ Effect	C / E	ICER
Stress contrast ECHO	$433.49		40.42%		$1,072	N/A
CT angiography	$517.73	$84.24	48.17%	7.75%	$1,075	$1,088
Stress ECHO	$551.58		40.17%		$1,373	(Dominated)
SPECT	$634.63		42.38%		$1,497	(Dominated)
Cardiac MRI	$835.47		44.94%		$1,859	(Dominated)

Table 15: Base case results for acute inpatients (outcome: accurate diagnosis)

Technology	Cost (C)	Δ Cost	Effect (E)	Δ Effect	C / E	ICER
Stress contrast ECHO	$1,794.58		81.94%		$2,190	N/A
SPECT	$1,982.91	$188.32	83.92%	1.99%	$2,363	$9,489
Stress ECHO	$2,550.87		81.53%		$3,129	(Dominated)
CT angiography	$3,267.39	$1,284.48	87.49%	3.56%	$3,735	$36,055
Cardiac MRI	$4,918.02		85.55%		$5,749	(Dominated)

Table 16: Base case results for acute inpatients (outcome: true positive diagnosis)

Technology	Cost (C)	Δ Cost	Effect (E)	Δ Effect	C / E	ICER
Stress contrast ECHO	$1,794.58		40.51%		$4,430	N/A
SPECT	$1,982.91	$188.32	43.20%	2.69%	$4,590	$6,999
Stress ECHO	$2,550.87		41.00%		$6,222	(Dominated)
CT angiography	$3,267.39	$1,284.48	48.18%	4.99%	$6,781	$25,763
Cardiac MRI	$4,918.02		45.28%		$10,862	(Dominated)

Table 17: Historical volume of cardiac tests in Ontario with average annual volume increases and average unit costs per test

Technology category	Average unit cost per test	2004	2005	2006	2007	2008	Annual increase
Nuclear (MPI, SPECT)	$612	131,108	139,373	146,773	152,092	157,208	4.6%
Stress ECHO	$382	37,094	41,378	49,413	54,864	59,539	12.6%
Stress contrast ECHO	$552	393	438	524	581	631	12.6%
Cardiac MRI	$804	100	146	211	260	237	24.1%
CT angiography	$501	87	178	236	273	389	45.4%
Total volume of tests		**186,614**	**200,605**	**217,674**	**229,588**	**240,445**	**6.5%**
Total cost		$94.6M	$101.4M	$109.1M	$114.5M	$119.5M	

Table 18: Projected volume of cardiac tests with a 5-year total (2010 to 1014) and projected average annual volume

Technology category	2010	2011	2012	2013	2014	Total (5 yr)	Annual
Nuclear (MPI, SPECT)	172,146	180,140	188,504	197,257	206,416	944,462	188,892
Stress ECHO	75,430	84,902	95,563	107,563	121,070	484,528	96,906
Stress contrast ECHO	799	900	1,013	1,140	1,283	5,134	1,027
Cardiac MRI	365	453	562	697	865	2,941	588
CT angiography	823	1,196	1,739	2,529	3,678	9,965	1,993
Total volume of tests	**249,563**	**267,590**	**287,381**	**309,186**	**333,311**	**1,447,030**	**289,406**
Total cost (discounted)	$135.1M	$143.9M	$153.5M	$164.0M	$175.5M	$772.0M	$154.4M

Table 19: Effect of moving Stress ECHO volume to Nuclear cardiac tests

% of ECHO tests moved	Total 5-year costs (all tests)	5-year cost difference	Annual cost difference
0%	$771,964,247	-	-
5%	$777,530,746	$5,566,499	$1,113,300
10%	$783,097,245	$11,132,999	$2,226,600
25%	$799,796,744	$27,832,497	$5,566,499
50%	$827,629,240	$55,664,994	$11,132,999

Table 20: Effect of moving Stress ECHO volume to Stress contrast ECHO tests

% of ECHO tests moved	Total 5-year costs (all tests)	5-year cost difference	Annual cost difference
0%	$771,964,247	-	-
5%	$772,130,543	$166,296	$33,259
10%	$772,296,839	$332,593	$66,519
25%	$772,795,729	$831,482	$166,296
50%	$773,627,211	$1,662,964	$332,593

Table 21: Effect of moving Stress ECHO volume to Cardiac MRI tests

% of ECHO tests moved	Total 5-year costs (all tests)	5-year cost difference	Annual cost difference
0%	$771,964,247	-	-
5%	$782,198,688	$10,234,442	$2,046,888
10%	$792,433,130	$20,468,883	$4,093,777
25%	$823,136,455	$51,172,209	$10,234,442
50%	$874,308,664	$102,344,417	$20,468,883

Table 22: Effect of moving Stress ECHO volume to CT Angiography tests

% of ECHO tests moved	Total 5-year costs (all tests)	5-year cost difference	Annual cost difference
0%	$771,964,247	-	-
5%	$774,580,398	$2,616,151	$523,230
10%	$777,196,549	$5,232,302	$1,046,460
25%	$785,045,002	$13,080,756	$2,616,151
50%	$798,125,758	$26,161,512	$5,232,302

Table 23: Effect of moving Stress contrast ECHO volume to Nuclear cardiac tests

% of ECHO tests moved	Total 5-year costs (all tests)	5-year cost difference	Annual cost difference
0%	$771,964,247	-	-
5%	$772,010,137	$45,891	$9,178
10%	$772,056,028	$91,782	$18,356
25%	$772,193,701	$229,454	$45,891
50%	$772,423,155	$458,909	$91,782

Table 24: Effect of moving Stress contrast ECHO volume to Stress ECHO tests

% of ECHO tests moved	Total 5-year costs (all tests)	5-year cost difference	Annual cost difference
0%	$771,964,247	-	-
5%	$771,951,155	-$13,092	-$2,618
10%	$771,938,063	-$26,184	-$5,237
25%	$771,898,787	-$65,459	-$13,092
50%	$771,833,328	-$130,919	-$26,184

Table 25: Effect of moving Stress contast ECHO volume to Cardiac MRI tests

% of ECHO tests moved	Total 5-year costs (all tests)	5-year cost difference	Annual cost difference
0%	$771,964,247	-	-
5%	$772,059,599	$95,353	$19,071
10%	$772,154,952	$190,705	$38,141
25%	$772,441,009	$476,763	$95,353
50%	$772,917,772	$953,525	$190,705

Table 26: Effect of moving Stress contrast ECHO volume to CT Angiography tests

% of ECHO tests moved	Total 5-year costs (all tests)	5-year cost difference	Annual cost difference
0%	$771,964,247	-	-
5%	$771,978,875	$14,629	$2,926
10%	$771,993,504	$29,258	$5,852
25%	$772,037,391	$73,145	$14,629
50%	$772,110,536	$146,289	$29,258

Table 27: Effect of moving Nuclear cardiac volume to Stress ECHO tests

% of Nuclear cardiac tests moved	Total 5-year costs (all tests)	5-year cost difference	Annual cost difference
0%	$771,964,247	-	-
5%	$761,113,792	-$10,850,454	-$2,170,091
10%	$750,263,338	-$21,700,909	-$4,340,182
25%	$717,711,975	-$54,252,272	-$10,850,454
50%	$663,459,703	-$108,504,544	-$21,700,909

Table 28: Effect of moving Nuclear cardiac volume to Stress contrast ECHO tests

% of Nuclear cardiac tests moved	Total 5-year costs (all tests)	5-year cost difference	Annual cost difference
0%	$771,964,247	-	-
5%	$763,522,171	-$8,442,076	-$1,688,415
10%	$755,080,095	-$16,884,151	-$3,376,830
25%	$729,753,868	-$42,210,378	-$8,442,076
50%	$687,543,490	-$84,420,757	-$16,884,151

Table 29: Effect of moving Nuclear cardiac volume to Cardiac MRI tests

% of Nuclear cardiac tests moved	Total 5-year costs (all tests)	5-year cost difference	Annual cost difference
0%	$771,964,247	-	-
5%	$781,063,196	$9,098,949	$1,819,790
10%	$790,162,145	$18,197,898	$3,639,580
25%	$817,458,992	$45,494,746	$9,098,949
50%	$862,953,738	$90,989,492	$18,197,898

Table 30: Effect of moving Nuclear cardiac volume to CT Angiography tests

% of Nuclear cardiac tests moved	Total 5-year costs (all tests)	5-year cost difference	Annual cost difference
0%	$771,964,247	-	-
5%	$766,213,304	-$5,750,943	-$1,150,189
10%	$760,462,361	-$11,501,885	-$2,300,377
25%	$743,209,533	-$28,754,713	-$5,750,943
50%	$714,454,820	-$57,509,427	-$11,501,885

Table 31: Effect of moving Cardiac MRI to Nuclear cardiac tests

% of Cardiac MRI tests moved	Total 5-year costs (all tests)	5-year cost difference	Annual cost difference
0%	$771,964,247	-	-
5%	$771,935,914	-$28,332	-$5,666
10%	$771,907,582	-$56,665	-$11,333
25%	$771,822,584	-$141,662	-$28,332
50%	$771,680,922	-$283,324	-$56,665

Table 32: Effect of moving Cardiac MRI volume to Stress ECHO tests

% of Cardiac MRI tests moved	Total 5-year costs (all tests)	5-year cost difference	Annual cost difference
0%	$771,964,247	-	-
5%	$771,902,128	-$62,119	-$12,424
10%	$771,840,009	-$124,237	-$24,847
25%	$771,653,653	-$310,593	-$62,119
50%	$771,343,060	-$621,187	-$124,237

Table 33: Effect of moving Cardiac MRI to Stress contrast ECHO tests

% of Cardiac MRI tests moved	Total 5-year costs (all tests)	5-year cost difference	Annual cost difference
0%	$771,964,247	-	-
5%	$771,909,627	-$54,619	-$10,924
10%	$771,855,008	-$109,239	-$21,848
25%	$771,691,149	-$273,097	-$54,619
50%	$771,418,052	-$546,195	-$109,239

Table 34: Effect of moving Cardiac MRI to CT Angiography tests

% of Cardiac MRI tests moved	Total 5-year costs (all tests)	5-year cost difference	Annual cost difference
0%	$771,964,247	-	-
5%	$771,918,007	-$46,240	-$9,248
10%	$771,871,767	-$92,480	-$18,496
25%	$771,733,048	-$231,199	-$46,240
50%	$771,501,849	-$462,398	-$92,480

Table 35: Effect of moving CT Angiography volume to Nuclear cardiac tests

% of CT Angiography tests moved	Total 5-year costs (all tests)	5-year cost difference	Annual cost difference
0%	$771,964,247	-	-
5%	$772,024,925	$60,679	$12,136
10%	$772,085,604	$121,357	$24,271
25%	$772,267,639	$303,393	$60,679
50%	$772,571,032	$606,785	$121,357

Table 36: Effect of moving CT Angiography volume to Stress ECHO tests

% of CT Angiography tests moved	Total 5-year costs (all tests)	5-year cost difference	Annual cost difference
0%	$771,964,247	-	-
5%	$771,910,441	-$53,805	-$10,761
10%	$771,856,636	-$107,610	-$21,522
25%	$771,695,220	-$269,026	-$53,805
50%	$771,426,194	-$538,052	-$107,610

Table 37: Effect of moving CT Angiography to Stress contrast ECHO tests

% of CT Angiography tests moved	Total 5-year costs (all tests)	5-year cost difference	Annual cost difference
0%	$771,964,247	-	-
5%	$771,935,852	-$28,394	-$5,679
10%	$771,907,458	-$56,789	-$11,358
25%	$771,822,275	-$141,971	-$28,394
50%	$771,680,304	-$283,943	-$56,789

Table 38: Effect of moving CT Angiography volume to Cardiac MRI tests

% of CT Angiography tests moved	Total 5-year costs (all tests)	5-year cost difference	Annual cost difference
0%	$771,964,247	-	-
5%	$772,120,929	$156,682	$31,336
10%	$772,277,611	$313,364	$62,673
25%	$772,747,657	$783,410	$156,682
50%	$773,531,067	$1,566,821	$313,364

Figures

Figure 1: Literature search strategy applied and results obtained

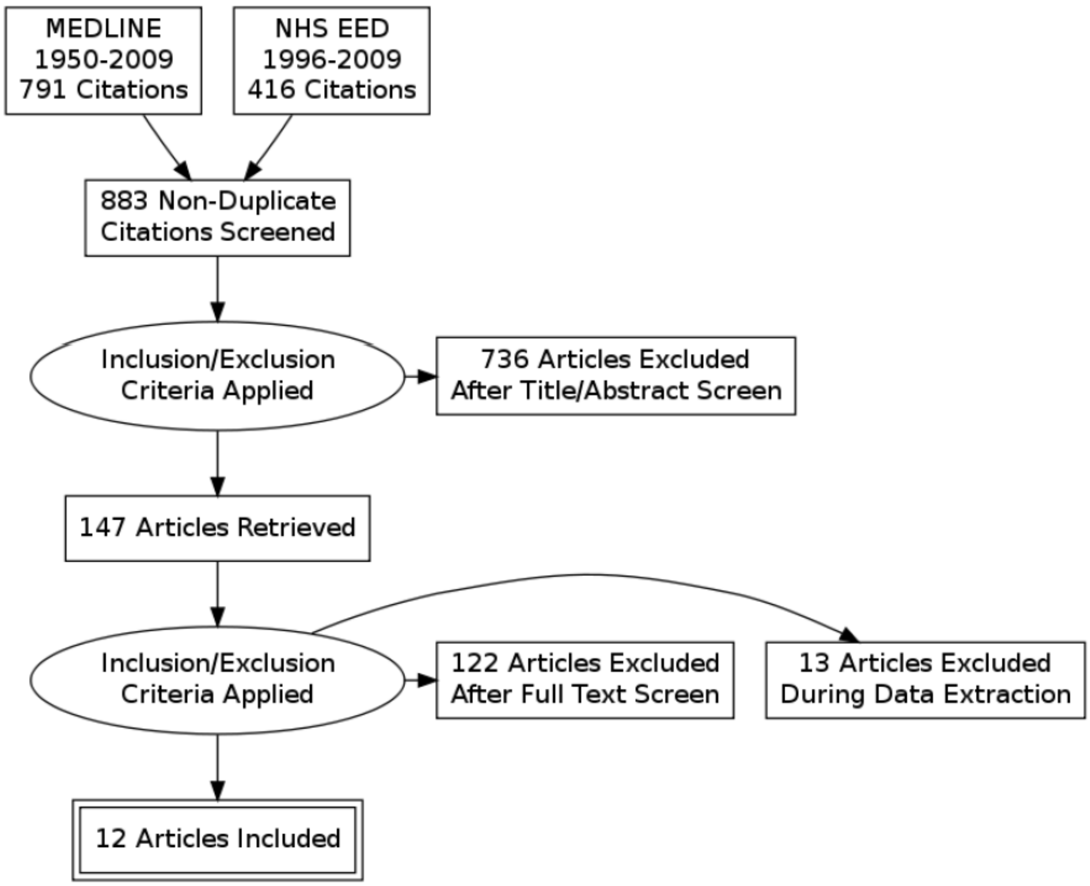


Figure 2: Simplified view of the decision-analytic model used in the cost-effectiveness analysis

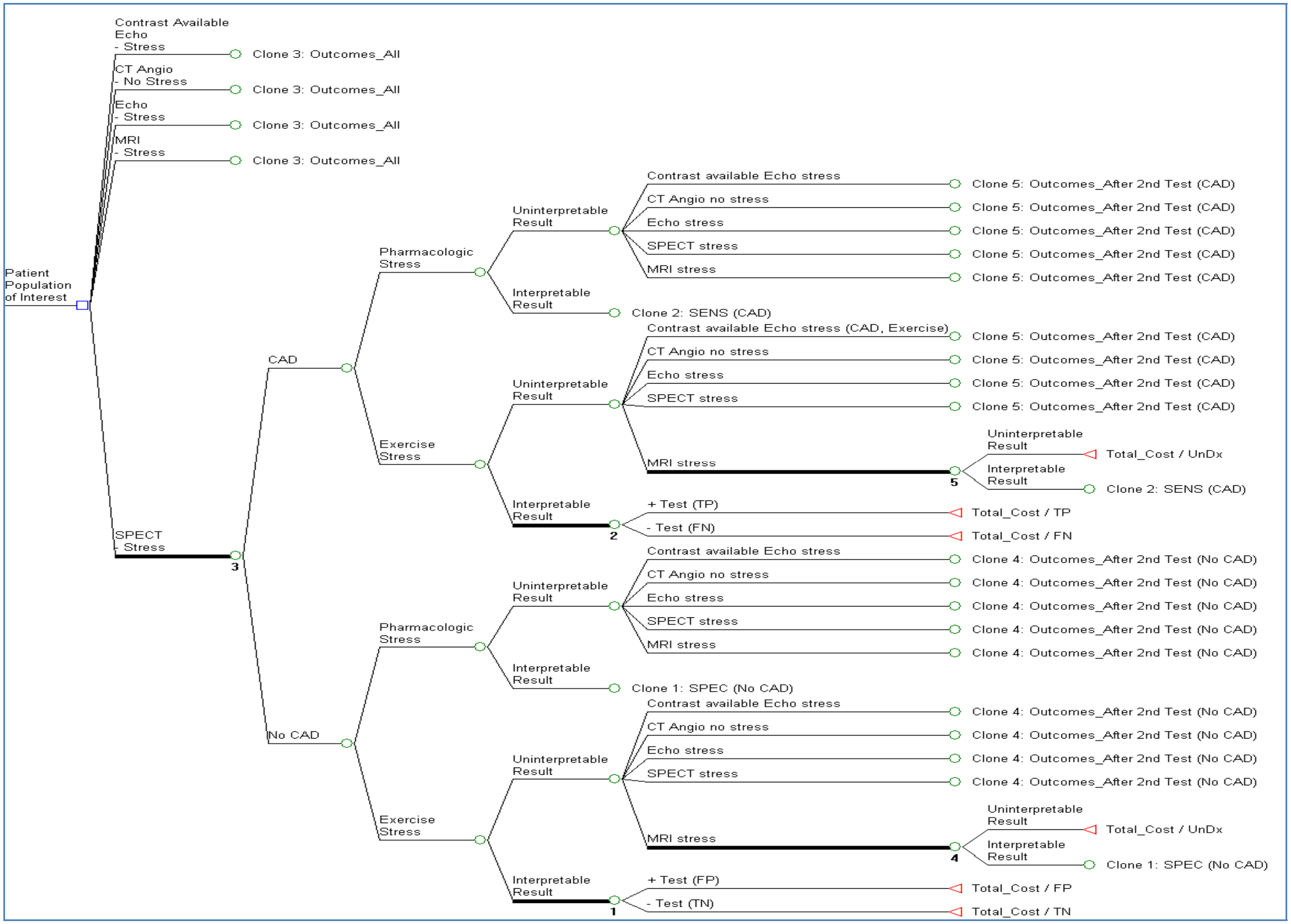


Figure 3: Cost-effective technology for stable outpatients by prevalence of CAD in the population presenting with chest pain and willingness-to-pay for an *accurate* diagnosis from a non-invasive diagnostic test

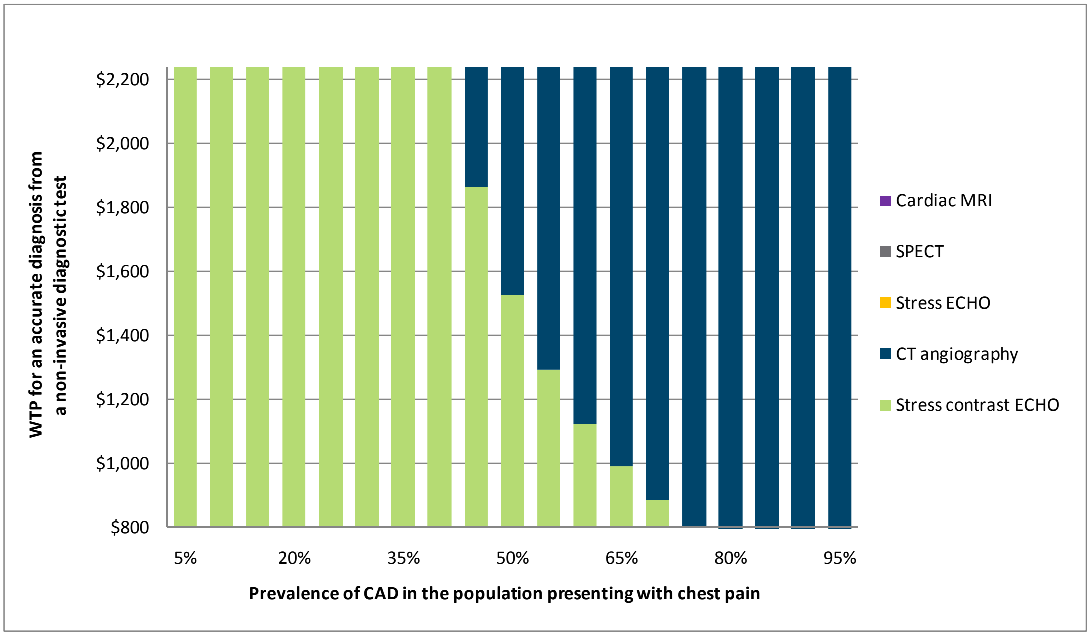


Figure 4: Cost-effective technology for stable outpatients by prevalence of CAD in the population presenting with chest pain and willingness-to-pay for a *true positive* diagnosis from a non-invasive diagnostic test

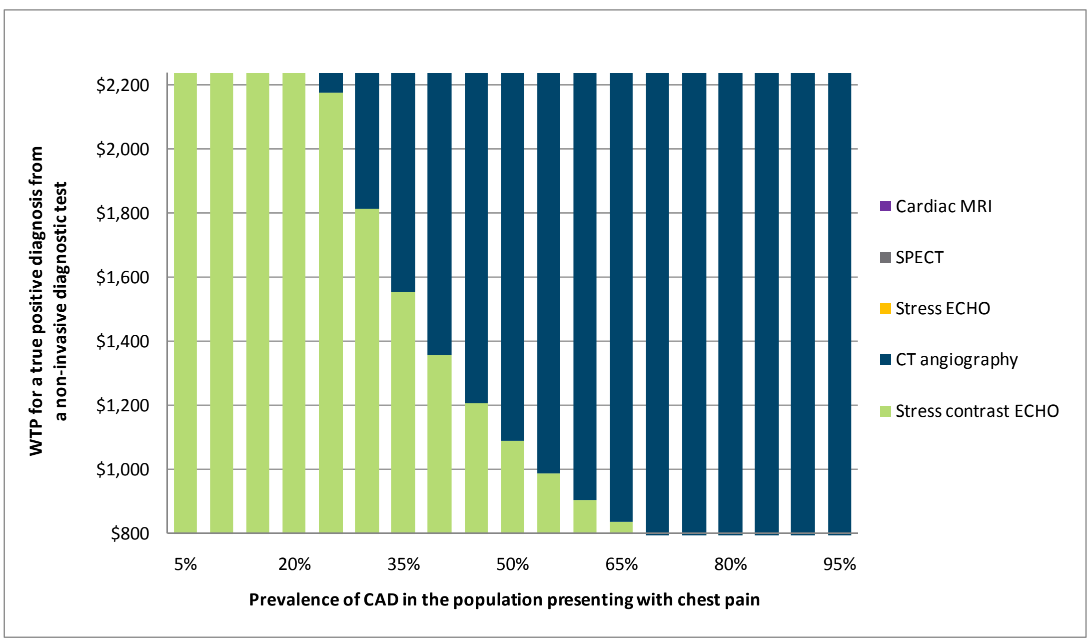


Figure 5: Cost-effective technology for acute inpatients by prevalence of CAD in the population presenting with chest pain and willingness-to-pay for an *accurate* diagnosis from a non-invasive diagnostic test

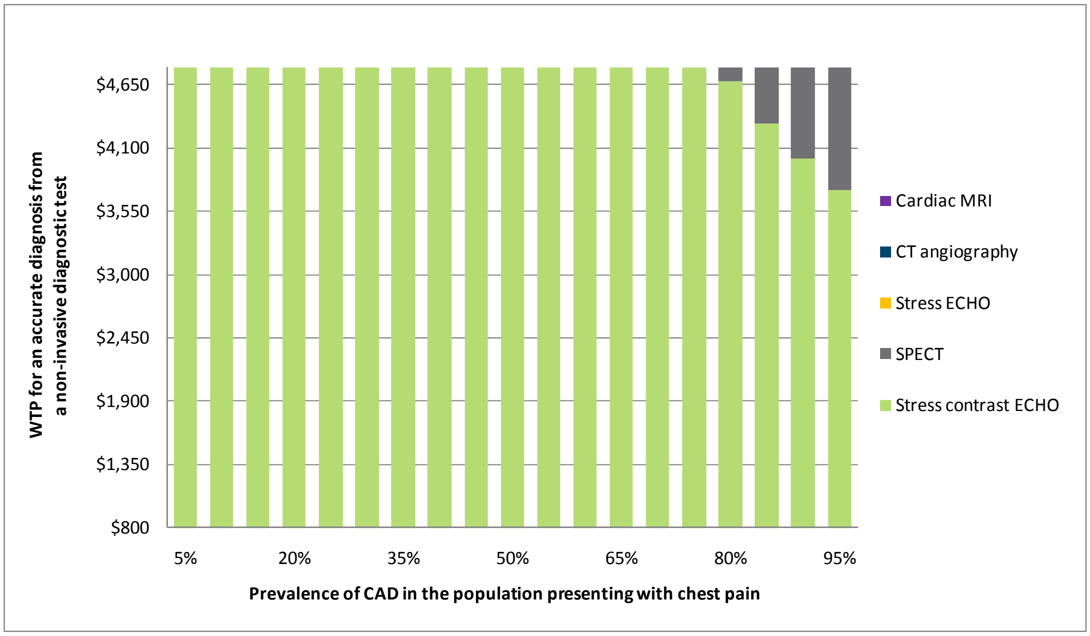


Figure 6: Cost-effective technology for acute inpatients by prevalence of CAD in the population presenting with chest pain and willingness-to-pay for a *true positive* diagnosis from a non-invasive diagnostic test

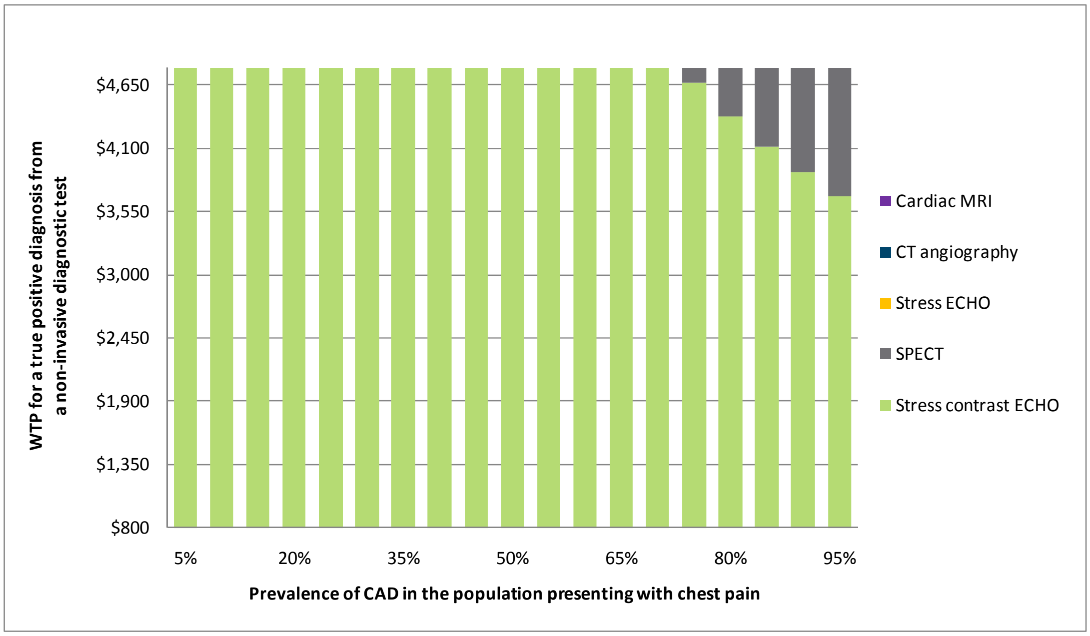


Figure 7: Cost-effective technology for stable outpatients by prevalence of CAD in the population presenting with chest pain and willingness-to-pay for an accurate diagnosis from a non-invasive diagnostic test where the proportion of stress ECHO tests which are uninterpretable without contrast is 15% rather than 30%

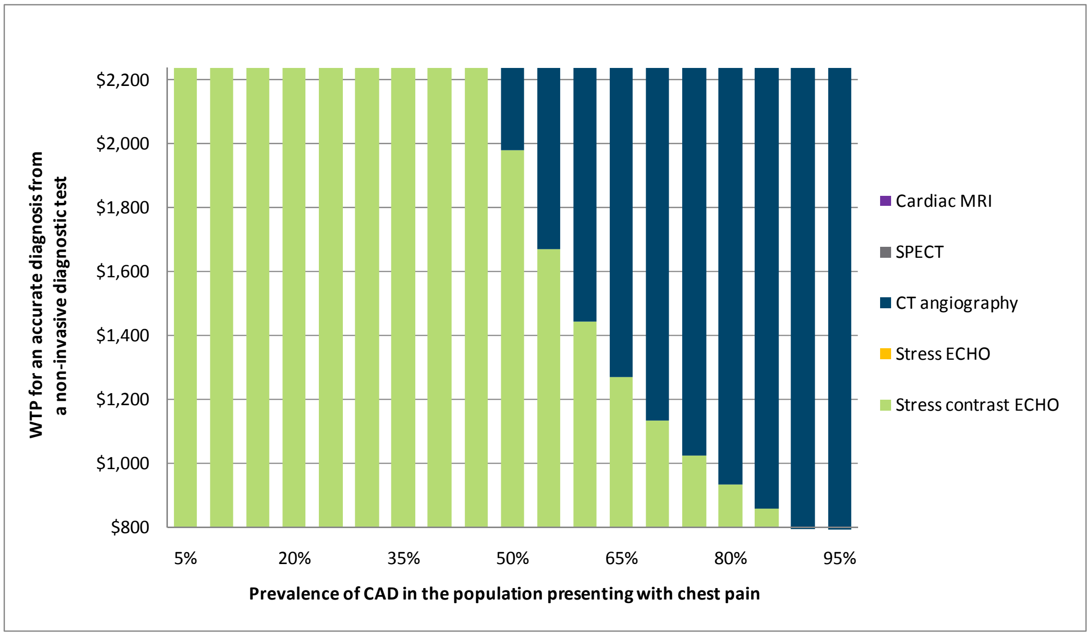


Figure 8: Cost-effective technology for acute inpatients by prevalence of CAD in the population presenting with chest pain and willingness-to-pay for an accurate diagnosis from a non-invasive diagnostic test where all technologies are associated with the same additional hospital wait time (1.5 days)

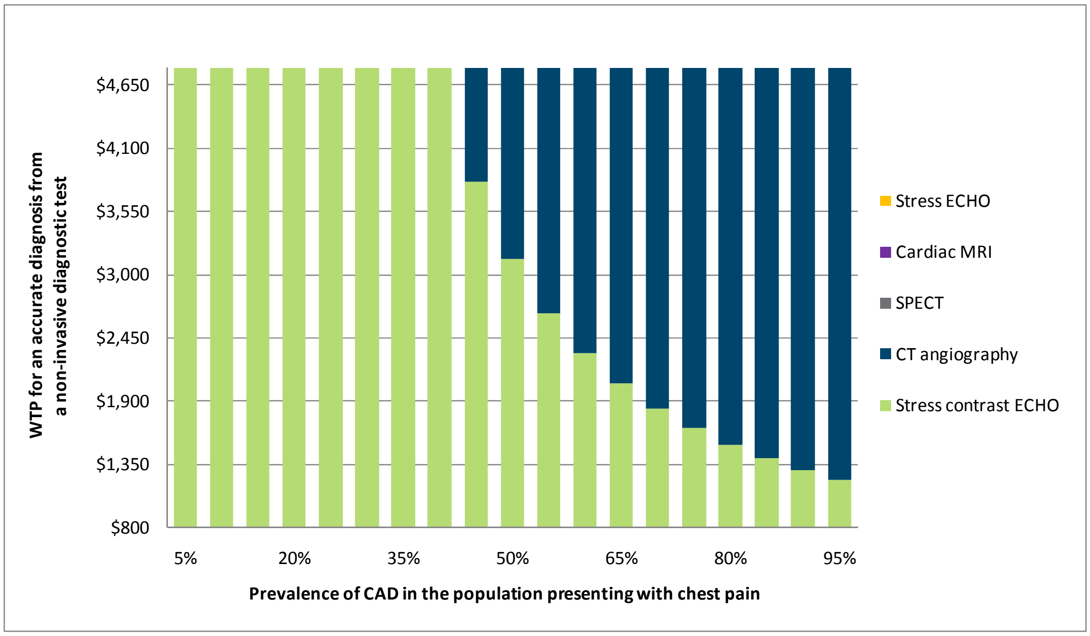


Figure 9: Cost-effective technology for stable outpatients by prevalence of CAD in the population presenting with chest pain and willingness-to-pay for an accurate diagnosis from a non-invasive diagnostic test where sensitivity and specificity of CT angiography incorporates provisional results from OMCAS study

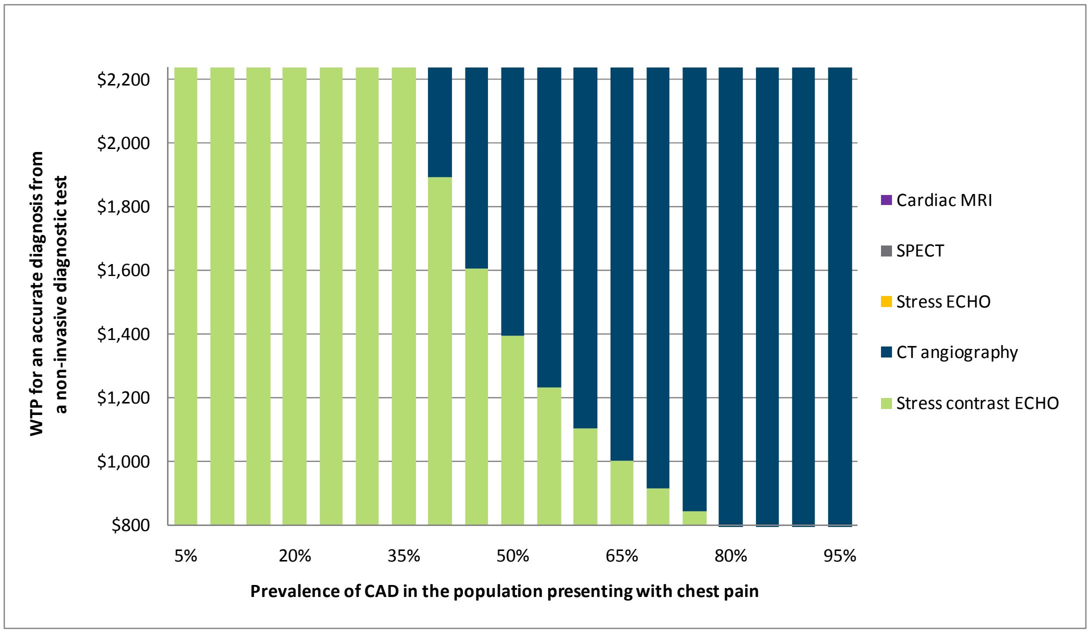


Figure 10: Cost-effective technology for acute inpatients by prevalence of CAD in the population presenting with chest pain and willingness-to-pay for an accurate diagnosis from a non-invasive diagnostic test where sensitivity and specificity of CT angiography incorporates provisional results from OMCAS study

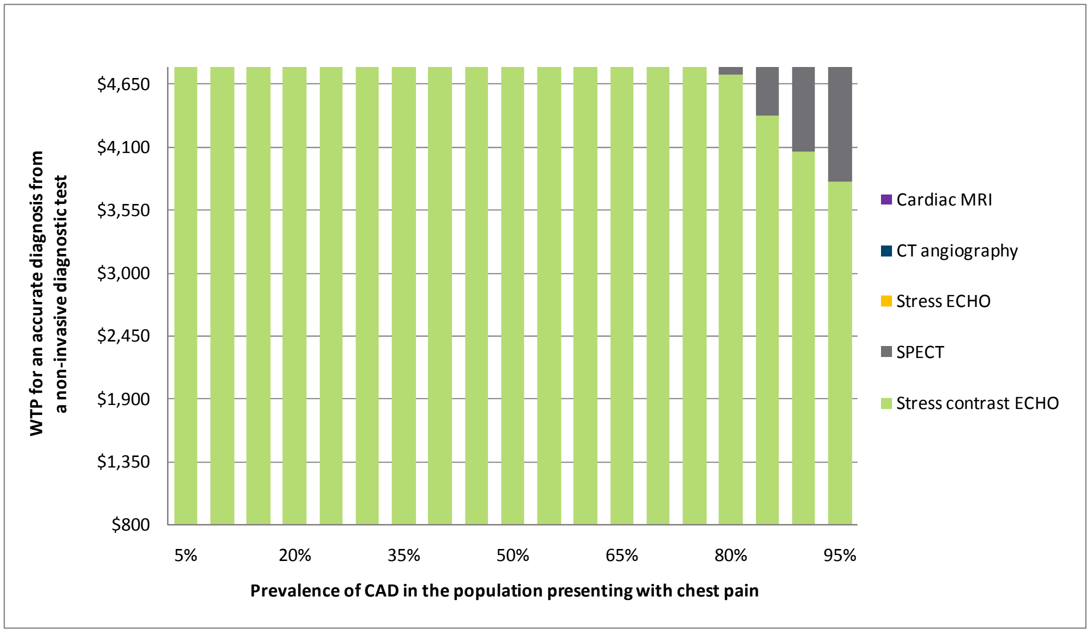


Figure 11: Cost-effective technology for stable outpatients by prevalence of CAD in the population presenting with chest pain and willingness-to-pay for an accurate diagnosis from a non-invasive diagnostic test where CT angiography is unavailable

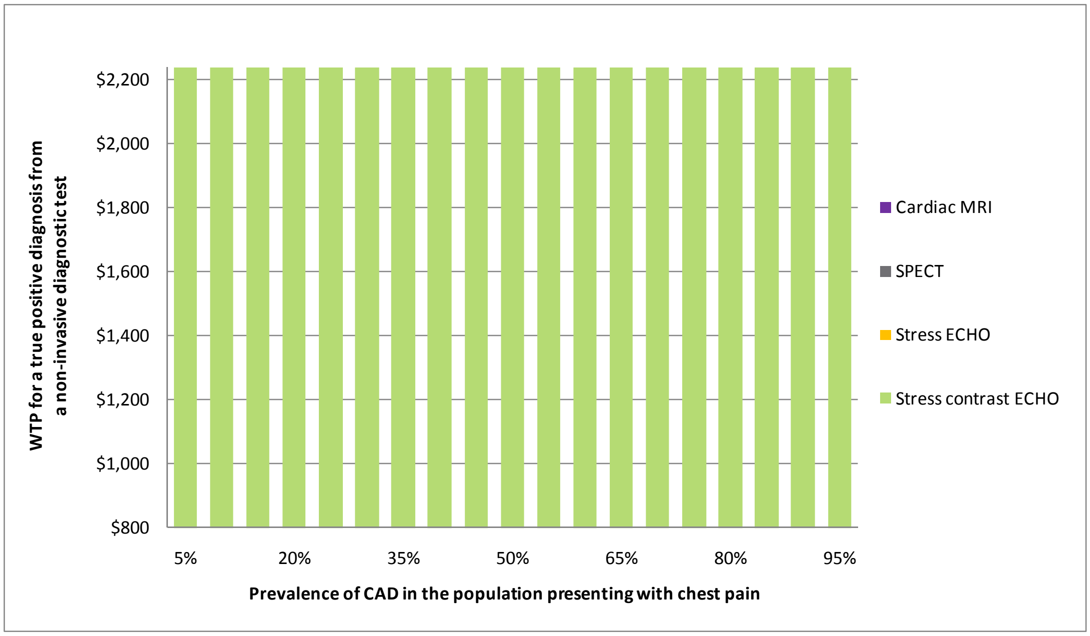


Figure 12: Cost-effective technology for stable outpatients by prevalence of CAD in the population presenting with chest pain and willingness-to-pay for an accurate diagnosis from a non-invasive diagnostic test where stress contrast ECHO is unavailable

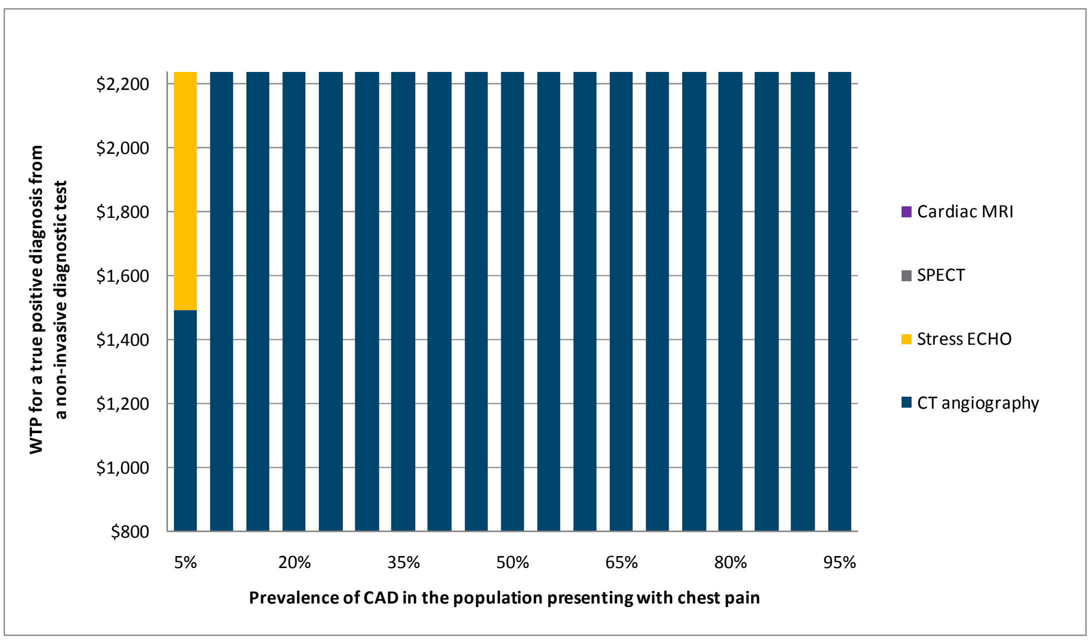


Figure 13: Cost-effective technology for stable outpatients by prevalence of CAD in the population presenting with chest pain and willingness-to-pay for an accurate diagnosis from a non-invasive diagnostic test where both CT angiography and stress contrast ECHO are unavailable

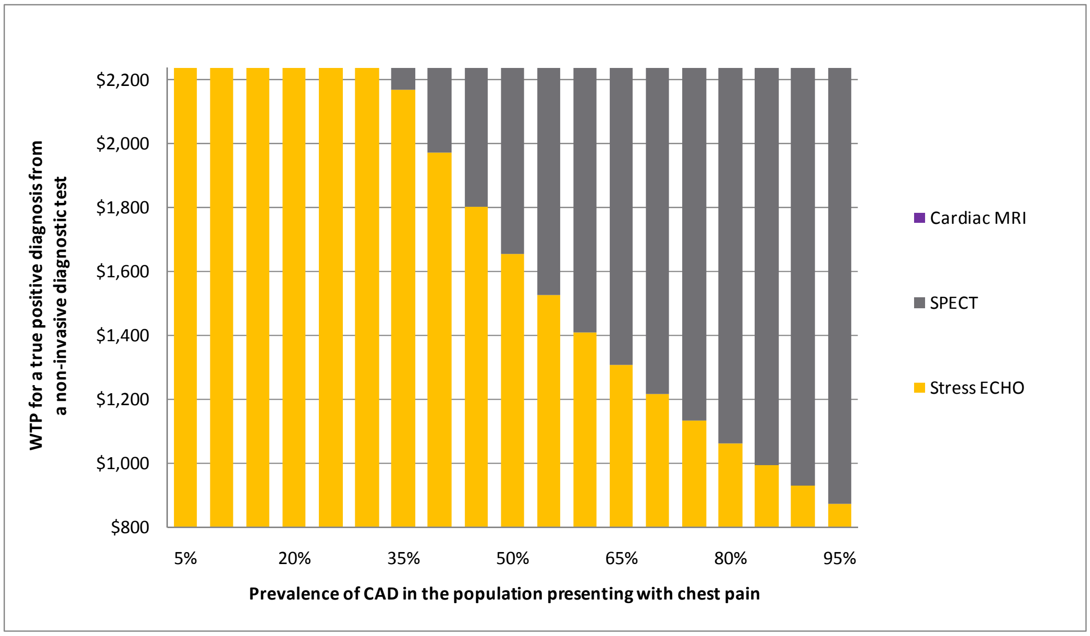


Figure 14: Cost-effective technology for acute inpatients by prevalence of CAD in the population presenting with chest pain and willingness-to-pay for an accurate diagnosis from a non-invasive diagnostic test where stress contrast ECHO is unavailable

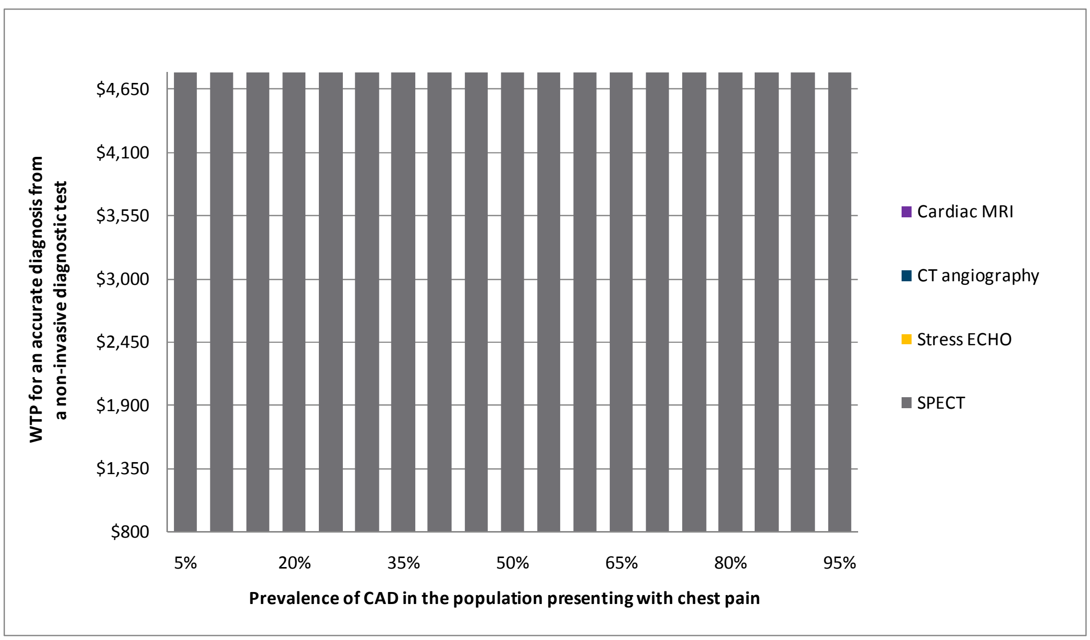


Figure 15: Preferred stress ECHO or SPECT technology for stable outpatients by prevalence of CAD in the population presenting with chest pain and willingness-to-pay for an accurate diagnosis from a non-invasive diagnostic test: stress contrast ECHO versus attenuated SPECT

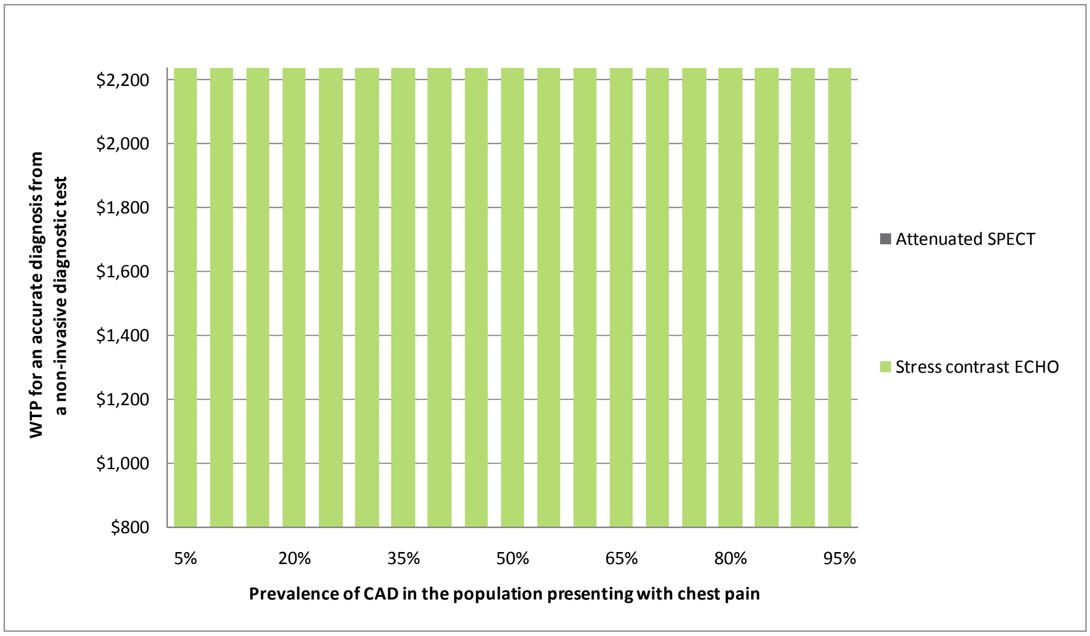


Figure 16: Preferred stress ECHO or SPECT technology for stable outpatients by prevalence of CAD in the population presenting with chest pain and willingness-to-pay for an accurate diagnosis from a non-invasive diagnostic test: stress contrast ECHO versus gated SPECT

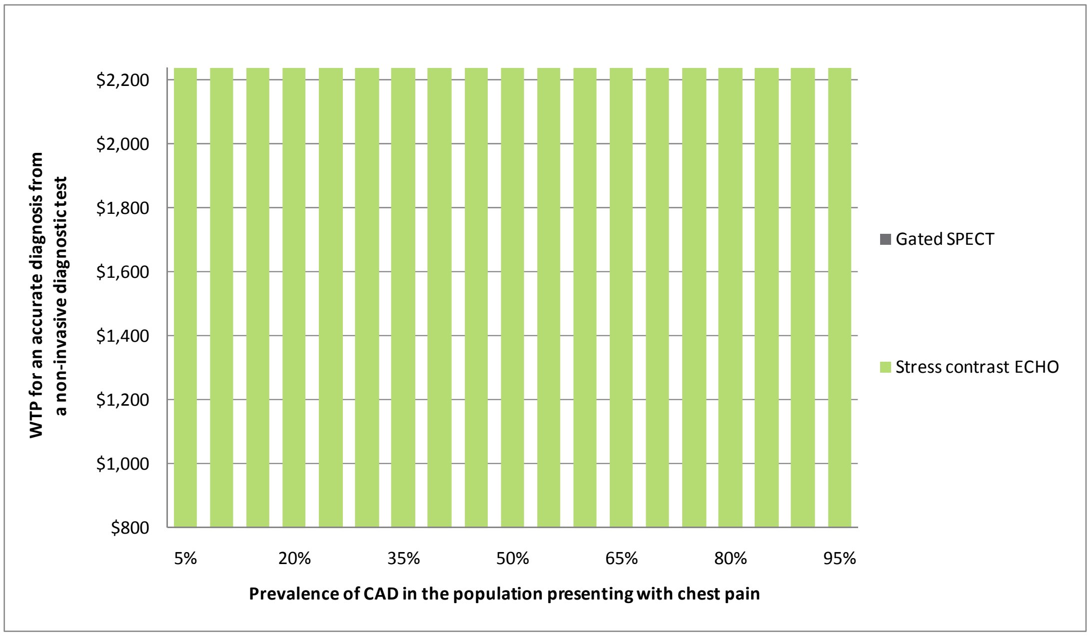


Figure 17: Preferred stress ECHO or SPECT technology for stable outpatients by prevalence of CAD in the population presenting with chest pain and willingness-to-pay for an accurate diagnosis from a non-invasive diagnostic test: stress contrast ECHO versus traditional SPECT

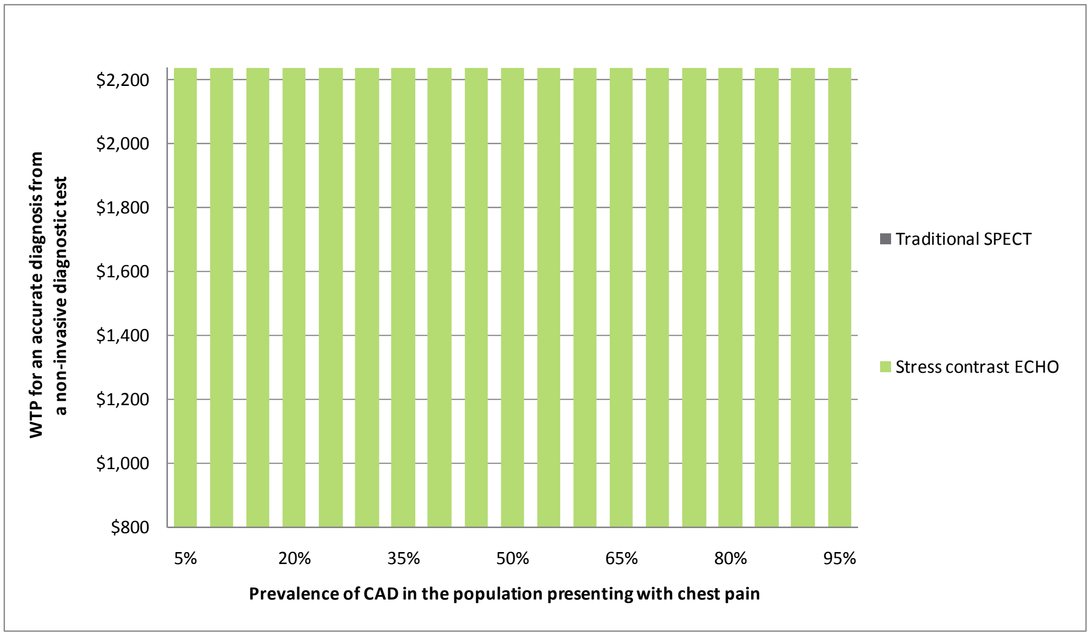


Figure 18: Preferred stress ECHO or SPECT technology for stable outpatients by prevalence of CAD in the population presenting with chest pain and willingness-to-pay for an accurate diagnosis from a non-invasive diagnostic test: stress ECHO versus attenuated SPECT

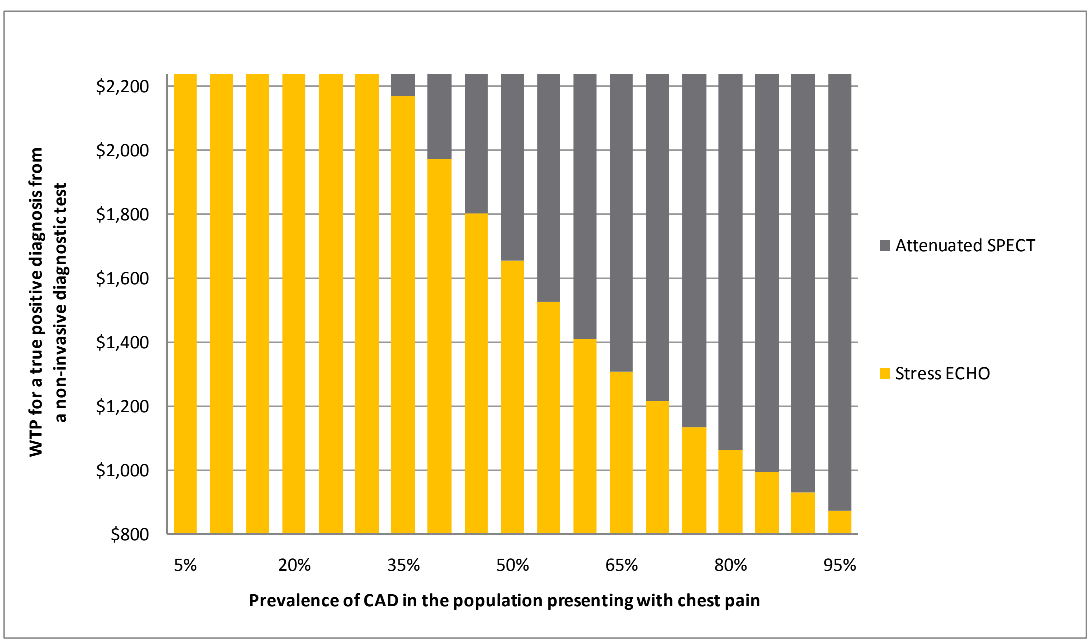


Figure 19: Preferred stress ECHO or SPECT technology for stable outpatients by prevalence of CAD in the population presenting with chest pain and willingness-to-pay for an accurate diagnosis from a non-invasive diagnostic test: stress ECHO versus gated SPECT

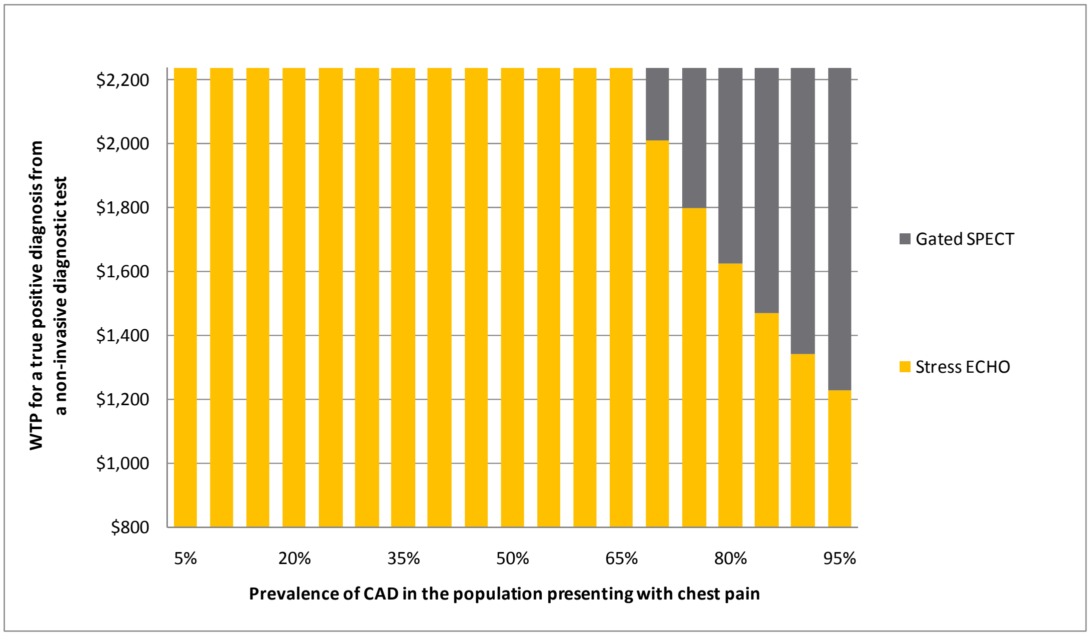
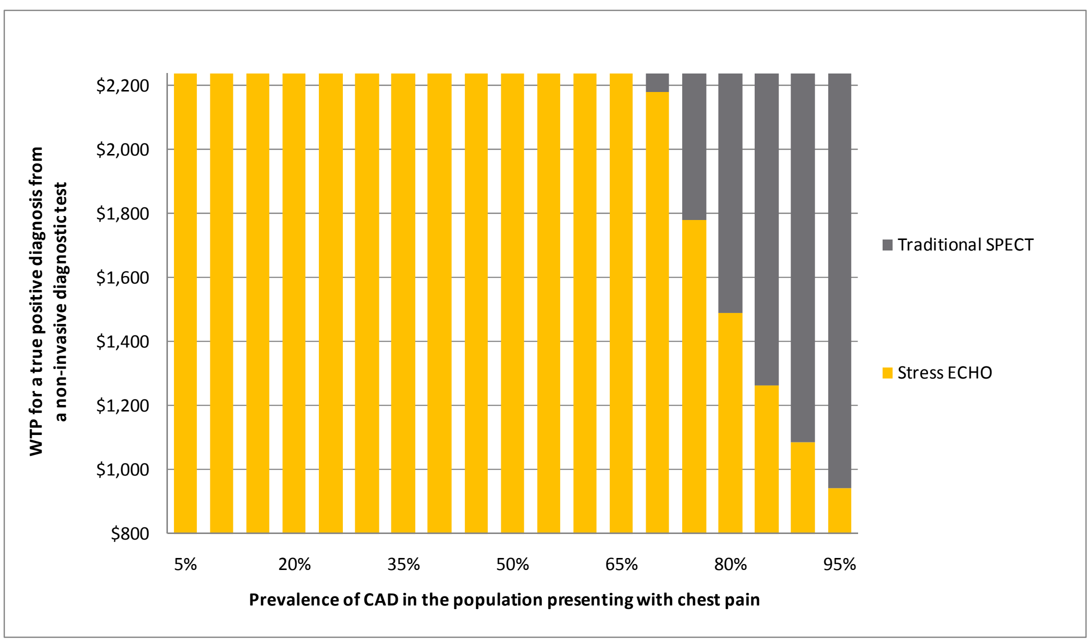


Figure 20: Preferred stress ECHO or SPECT technology for stable outpatients by prevalence of CAD in the population presenting with chest pain and willingness-to-pay for an accurate diagnosis from a non-invasive diagnostic test: stress ECHO versus traditional SPECT



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Appendix 1

Economic literature search criteria

Search segment specific to health economics:

[Economics - MEDLINE]
exp Economics/
Economics.mp.
exp "costs and cost analysis"/
(cost$ adj analysis).mp.
exp Cost allocation/
cost allocation.mp.
exp "Cost-benefit analysis"/
(cost-benefit adj analysis).mp.
exp Cost control/
cost control.mp.
exp Cost savings/
cost savings.mp.
exp "Cost of illness"/
(cost adj2 illness).mp.
exp Cost sharing/
cost sharing.mp.
exp "deductibles and coinsurance"/
(deductibles adj coinsurance).mp.
exp Medical savings accounts/
medical savings accounts.mp.
exp Health care costs/
health care costs.mp.
exp Direct service costs/
Direct service costs.mp.
exp Drug costs/
drug costs.mp.
exp Employer health costs/
Employer health costs.mp.
exp Hospital costs/
hospital costs.mp.
exp Health expenditures/
Health expenditures.mp.
exp Capital expenditures/
Capital expenditures.mp.
exp "Value of life"/
(value adj life).mp.
exp economics, hospital/
exp economics, medical/

exp Economics, nursing/
exp Economics, pharmaceutical/
exp "fees and charges"/
exp budgets/
(low adj cost).mp.
(high adj cost).mp.
(health?care adj cost$).mp.
(fiscal or funding or financial or finance).tw.
(cost adj estimate$).mp.
(unit adj cost$).mp.
(economic$ or pharmacoeconomic$ or price$ or pricing).tw.
(cost adj variable).mp.
(cost-effect* or "cost effect*").mp.
exp Quality-Adjusted Life Years/
"quality-adjusted life years".mp.
"quality adjusted life years".mp.
qaly.mp.
(life adj years).mp.
cost utili*.mp.
(cost adj2 utili*).mp.
(cost adj2 effect*).mp.
exp models, economic/
(economic$ adj2 model$).mp.
(cost adj2 utilit*).mp.
(cost adj2 consequenc*).mp.
net benefit.mp.
(willingness adj pay).mp.

Search segment specific to coronary artery disease and cardiac diagnosis:

[Cardiac]
exp Myocardial Ischemia/
exp Heart Failure/
exp Ventricular Dysfunction/
exp Myocardial Infarction/
exp Angina Pectoris/
Myocardial Ischemia.mp.
(Heart adj Failure).mp.
Ventricular Dysfunction.mp.
myocardial infarction.mp.
angina.mp.
(myocardi* or heart or cardiac or coronary or ventric*).mp.
(viable or viability or perfusion or function or isch?emi* or atheroscleros* or arterioscleros* or infarct* or occlu* or stenos* or thrombosis or stun or hibernat*).mp.
((myocardi* or heart or cardiac or coronary or ventric*) adj2 (viable or viability or perfusion or function or isch?emi* or atheroscleros* or arterioscleros* or infarct* or

occlu* or stenos* or thrombosis or stun or hibernat*)).mp.
exp Coronary Angiography/
angiography.mp.
exp Acute Coronary Syndrome/
Acute Coronary Syndrome.mp.
(coronary adj artery adj disease).mp.
exp Coronary Artery Disease/
exp Coronary Aneurysm/
Coronary Aneurysm.mp.
exp Coronary Care Units/
Coronary Care Units.mp.
exp Coronary Circulation/
Coronary Circulation.mp.
exp Coronary Disease/
(Coronary adj Disease).mp.
exp Coronary Occlusion/
Coronary Occlusion.mp.
exp Coronary Stenosis/
Coronary Stenosis.mp.
exp Coronary Thrombosis/
Coronary Thrombosis.mp.
exp Coronary Vessels/
Coronary Vessels.mp.
exp myocardial revascularization/
myocardial revascularization.mp.
revasculari?ation.tw.
exp myocardial reperfusion/
myocardial reperfusion.mp.
reperfusion.tw.

Search segments used to specify the technologies of interest:

Computed tomography

[CT]
exp Tomography, X-Ray Computed/
exp Tomography, X-Ray/
ct.mp.
(multisice or multi-slice or multi-detector or multidetector or spiral or helical).mp.
mdct.mp.
cat.mp.
computer assisted tomography.mp.

Echocardiography

[Cardiac Echo]

exp Ultrasonography/
Ultrasonography.mp.
ultrasound.mp.
exp Echocardiography/
Echocardiograph*.mp.
exp Contrast Media/
exp Microbubbles/
exp microspheres/
exp Fluorocarbons/
contrast media.mp.
microbubbles.mp.
microspheres.mp.
(fluorocarbon* or perflutren or perfluoropropane or octafluoropropane or aerosome*).mp.
(contrast adj2 (enhancement or dye* or medium* or agent* or media or material*)).mp.
[Manufacturers]
Luminity.mp.
albunex.mp.
Cardiosphere.mp.
definity.mp.
Optison.mp.
levovist.mp.
SonoVue.mp.
imagify.mp.

Magnetic Resonance Imaging

[MRI]
exp Magnetic Resonance Imaging/
magnetic resonance imaging.mp.
(magnetic adj2 resonance).mp.

Single photon emission computed tomography

exp Tomography, Emission-Computed, Single-Photon/
single photon emission computed tomography.mp.
spect.mp.
(single photon adj2 emi*).mp.

Appendix 2

Suggested considerations for the Ontario MOHLTC when determining its willingness to pay (WTP) for an accurate diagnosis of CAD from non-invasive testing

A primary consideration of the Ontario MOHLTC when determining the WTP should be that the cost of obtaining an accurate diagnosis of CAD through an invasive coronary angiography is approximately $1433 – it may therefore appear reasonable to assume that the WTP for an accurate diagnosis of CAD resulting from a non-invasive imaging test should also be approximately $1433. However, there are a number of reasons why this might not be the case. It must be remembered that “accurate diagnosis” is a flawed metric: both non-invasive imaging and coronary angiography provide far more information than a simple yes/no diagnosis of CAD, with each test providing different information useful to prognosis. Furthermore, coronary angiography is considered the gold standard diagnostic instrument – by definition it has 100% sensitivity and specificity – whereas these non-invasive tests all have less than perfect accuracy, leading to the possibility of false positive and false negative results. Since patients and doctors tend to be risk adverse, this may result in a patient being sent for a coronary angiography (incurring a further cost of $1433) to confirm the result of the non-invasive test – this in turn lowers the value of the accurate diagnosis from the non-invasive test. This can be seen by considering two extreme scenarios: if *all* patients undergoing a non-invasive test are sent for a coronary angiography to confirm the result (extreme risk aversion) then the diagnosis of CAD from the non-invasive test has no value – an accurate diagnosis will result from the coronary angiography in any case; alternatively, if *none* of the results of the non-invasive tests is confirmed through coronary angiography and patients and doctors are content to accept that there will be false positive and false negative test results (perfect risk neutrality) then an additional *accurate* diagnosis of CAD from non-invasive testing has the same value as a diagnosis of CAD from a coronary angiography – since a coronary angiography costs approximately $1433, the WTP for an additional accurate diagnosis from a non-invasive test would also be $1433. In reality the risk aversion is likely to be somewhere between these two extremes, which suggests that a reasonable initial estimate of this WTP would be somewhere between $0 and $1433.

A second consideration should be that a coronary angiography is invasive, while these tests are non-invasive. On the assumption that doctors and patients have a preference for non-invasive procedures where possible, this would presumably result in a higher WTP for an accurate diagnosis of CAD from a non-invasive test (all other things equal). However, many of these non-invasive tests have safety concerns of their own (such as radiation exposure or adverse reaction to contrast agents), which would imply a lower WTP perhaps even differing between the technologies due to their different safety profiles).

A final consideration is the potential for inconsistency between the MOHLTC’s stated and revealed preferences. For example, the estimated cost of the most costly non-invasive test considered in this analysis, cardiac MRI, is $804. As with the other non-invasive tests, this test does not guarantee an accurate diagnosis of CAD. As such, if the MOHLTC is willing to pay for this test then it follows that it is willing to pay *at least* this amount for an additional *accurate* diagnosis of CAD from a non-invasive imaging test. Indeed, the MOHLTC has revealed a willingness to pay for a *sequence* of non-invasive tests in an attempt to obtain an accurate diagnosis of CAD. As such, *if* the MOHLTC were to state that its willingness to pay for a non-invasive imaging test is less than $804 then a conflict would appear to arise between the MOHLTC’s stated and revealed preferences. The MOHLTC may therefore wish to consider what WTP value might be revealed from its previous funding decisions and to decide whether it finds this to be acceptable – if not, the MOHLTC may state an alternative WTP value but it may wish first to address any inconsistencies in its funding decisions to avoid contradiction between its stated and revealed preferences.

In summary, there is no straightforward answer to what the WTP should be. It should be kept in mind that an accurate diagnosis of CAD can be obtained via a coronary angiography for $1433 – this requires an invasive procedure but at the same time many of the non-invasive tests have safety concerns of their own. Importantly, since none of the non-invasive tests have perfect accuracy and society is risk-adverse, the results of these tests have less value than those of a coronary angiography – this presumably lowers the WTP, although it is not known to what extent. On the other hand, the MOHLTC has revealed a preference for paying up to $804 for such non-invasive tests, suggesting its WTP for an accurate diagnosis from such tests to be at least this amount, and possibly higher when one considers sequences of non-invasive tests which are currently funded.

Leslie Dan Pharmacy Building
University of Toronto
6th Floor, Room 658
144 College Street
Toronto, Ontario Canada M5S 3M2

T 416 946 3718
F 416 946 3719
E info@theta.utoronto.ca

www.theta.utoronto.ca