



AMERICAN SOCIETY OF
NUCLEAR CARDIOLOGY

COST-EFFECTIVENESS OF MYOCARDIAL PERFUSION IMAGING

Information Statement
Approved by the Board of Directors – September 2005

Copies available from the American Society of
Nuclear Cardiology website (www.asnc.org)

This Information Statement is a summary of the currently available literature on the Cost-Effectiveness of Myocardial Perfusion Imaging.

We thank the following individuals for developing this statement.

Roger D. Des Prez, MD, Chair
Robert L. Gillespie, MD
Wael A. Jaber, MD
Gavin L. Noble, MD
Leslee J. Shaw, PhD
Prem Soman, MD, PhD
Kim A. Williams, MD
David G. Wolinsky, MD

This statement is a document of the Cost-Effectiveness of Myocardial Perfusion Imaging writing group and has been approved by the American Society of Nuclear Cardiology Board of Directors
September 2005

Cost-effectiveness of myocardial perfusion imaging: A summary of the currently available literature

Roger D. Des Prez, MD, Robert L. Gillespie, MD, Wael A. Jaber, MD, Gavin L. Noble, MD, Leslee J. Shaw, PhD, Prem Soman, MD, PhD, Kim A. Williams, MD, David G. Wolinsky, MD

EXECUTIVE SUMMARY

This literature review presents evidence that myocardial perfusion imaging (MPI), SPECT, is cost-effective when compared with other diagnostic modalities. This is particularly the case with respect to the patient who appears by clinical criteria to be at intermediate risk, in which SPECT can accurately both diagnose and risk stratify for coronary artery disease (CAD). By diagnosing and then stratifying risk, SPECT can efficiently distinguish patients with CAD who are most likely to benefit from cardiac catheterization and revascularization from those in whom medical therapy alone is likely to be the best initial strategy. Standard measures of this cost-effectiveness used in analyses include cost per correct diagnosis, cost per quality adjusted life years, and cost per event identified.

Studies comparing SPECT with stress ECG in intermediate risk patients indicate that SPECT is more cost-effective mostly because it is more accurate. Of the ten published cost effectiveness analyses comparing these two diagnostic modalities, seven favored the SPECT-guided testing approach. Although SPECT is more expensive as an initial diagnostic strategy, the extra cost is justified by conventional cost-effectiveness criteria. These studies indicate that SPECT costs between \$5,417 and \$20,550 per correct diagnosis of significant coronary artery disease. More importantly, the cost quality-adjusted life-year is estimated at \$38,000 to \$40,316. These values are below the conventionally accepted threshold for economic efficiency (i.e., set at <\$50,000 per life year saved). This is in contrast to the stress ECG, which has a cost quality-adjusted life-year above the accepted threshold. The greater accuracy and sensitivity of SPECT in the detection of prognostically important coronary pathology makes it possible to avoid costly false negative diagnoses and their associated down-stream economic and health consequences, such as result from potentially avoidable acute coronary syndromes or myocardial infarctions. In patients with a normal SPECT study the annual risk of myocardial infarction or cardiac death is approximately 1%. Data derived from actual observation demonstrate that in practice, patients who have a normal stress ECG are often referred for further costly testing, including cardiac catheterization. In contrast, the excellent negative predictive value of a normal SPECT study constitutes a strong deterrent to additional confirmatory testing. In patients with a normal SPECT study, only 1% undergo downstream coronary angiography.

The strategy of utilizing initial SPECT studies is also cost-effective in the intermediate risk patient when compared to the diagnostic strategy of initial cardiac catheterization. The highly favorable prognostic value of a negative or a low risk SPECT study in this situation makes it possible to avoid costly and unnecessary cardiac catheterization and revascularization procedures. This has been demonstrated in important large observational data base studies including the multicenter END registry in the United States and the multicenter EMPIRE study from Europe. These studies both showed that a diagnostic strategy beginning with SPECT and using catheterization only in patients with provokable ischemia on SPECT study resulted in a 30-41% savings when compared to a strategy of initial cardiac catheterization in all. Savings were in part due to the fact that patients with low to moderate risk on SPECT studies could be treated with medical therapy, avoiding the costs associated with catheterization and revascularization with equivalent health outcomes.

Comparison of the cost-effectiveness of SPECT with stress echo is complex. There are less relevant, high quality data available. The initial cost of stress echo is less. However, using a

hypothetical case analysis of an intermediate risk patient, the incremental cost-effectiveness ratios (ICERs) of SPECT and stress echo were found to be in a similar range: \$41,900 for stress echo and \$54,800 for SPECT, both modalities being compared with stress ECG. These analyses were in part based on SPECT methods (planar thallium data), which are outdated, limiting the relevance of the cost comparison. Concern has been raised about the false positive rate of SPECT studies. However, a recent evaluation by the Agency for Health-Related Quality evaluation reported that the false positive rate was similar for echocardiography and SPECT imaging. An analysis by Lee et al indicated that the lower occurrence of false negative tests with SPECT balanced the greater initial expense of this procedure relative to stress echocardiography in patients with an intermediate-risk pretest probability of coronary artery disease (i.e., $\geq 30\%$). The conclusion from the data available is that the techniques have similar cost effectiveness, and that choice between the two should be guided by local expertise. In addition patient risk profile and concerns may be important in this decision, with higher risk and/or concern favoring SPECT because of the excellent prognosis of a normal SPECT, and because this negative predictive value has been demonstrated to help reduce the need for further testing.

In summary, evidence is convincing that for the intermediate risk patient, initial investigation with SPECT studies is a cost-efficient approach. In special populations including the emergency room patient, diabetics, and women, there is additional information indicating the cost effectiveness of SPECT. For low risk patients, a cost effective strategy appears to be stress ECG, with the selective use of SPECT in patients in whom the initial test is abnormal. For high-risk patients cardiac catheterization is in most analyses found to be the most effective diagnostic approach. However, some believe that initial SPECT studies are nevertheless indicated even in stable patients with a high probability of coronary disease because it can provide additional data to help direct the most effective use of revascularization therapy.

BACKGROUND ON COST EFFECTIVENESS ANALYSIS (CEA)

Over the last decade there has been a movement in medicine towards requiring a sufficient evidence-base upon which to justify the cost of any procedure or therapy. This movement of evidence-based medicine was initiated as a result of dramatic increases in the costs of healthcare far outpacing inflation and encumbering greater percentages of our gross domestic product. Detailed analysis of healthcare costs over the past few decades has noted tremendous growth in the utilization of medical procedures. Recent updates from the American Heart Association reveal that, of the nearly \$50 billion dollars spent on professional and hospital services, the growth in diagnostic procedures has been dramatic.¹ Since 1979 cardiac catheterization utilization rates have increased 389%. Dramatic growth is not solely for invasive procedures but also, since 1998, the utilization rates for myocardial perfusion SPECT have increased from 10% to 30% per year in both the US and Europe.² From the epidemiologic evidence, a portion of the recent dramatic declines in cardiovascular disease mortality has been, in part, a result of patient management strategies that focus on an early and effective diagnosis of coronary artery disease. However, dramatic growth in utilization rates has led health care policy analysts to question the rationale and to consider strategies to constrain further diagnostic test growth.

Cost effectiveness analysis (CEA) is one analytical approach that integrates a test's clinical effectiveness with its economic value.³⁻⁴ In this era of limited resources, the calculation of marginal or incremental cost effectiveness provides a rational means to balance health care quality and clinical value in terms of the best outcomes at a reasonable price. In the case of gated SPECT imaging, it has been used to evaluate whether its use is worth the additional cost when compared with other diagnostic test modalities. Using traditional definitions put forth by the US Preventive Services Taskforce, CEA is defined as an incremental comparison of the cost per life year saved. In cardiovascular medicine, disease-specific CEA have also been defined as the cost

per correct disease classification or cost per event detected. Thus, the global equation that may be applied for any CEA is $\Delta \text{ cost} / \Delta \text{ outcome}$. In this manner, a CEA relates the economic resources consumed in relation to their benefits attained.

The purpose of the current statement is twofold: 1) to provide a synopsis of available economic data on the value of myocardial perfusion SPECT and 2) to identify additional guidelines and other reviews available on the subject, such as the recently exhaustive technology assessment published by the UK's National Institute of Clinical Excellence (NICE).^{2,5} This report will focus on the comparative costs for an array of diagnostic procedures, as well as on a synthesis of available evidence concerning the cost effectiveness of myocardial perfusion SPECT as compared with the exercise electrocardiogram (ECG), echocardiography, and coronary angiography.

METHODS

The journals *Circulation*, *American Journal of Cardiology*, *Journal of Nuclear Cardiology (JNC)*, *Journal of the American Society of Echocardiography (JASE)*, *Journal of the American College of Cardiology*, and *The Journal of Nuclear Medicine* were surveyed for articles relating to topics on cost-effectiveness and myocardial perfusion imaging or SPECT imaging, using conventional search engines such as PubMed and OVID. Two journals, *JNC* and *JASE*, were surveyed for the period 1996 to 2004; the remaining journals were surveyed for the period 1993 to 2004. This journal survey was supplemented by references contained in several recent review articles. Special mention is made here of a recent publication from the UK National Health Service Health Technology Assessment Programme which presents a systematic review of the effectiveness and cost-effectiveness of myocardial perfusion SPECT.⁵

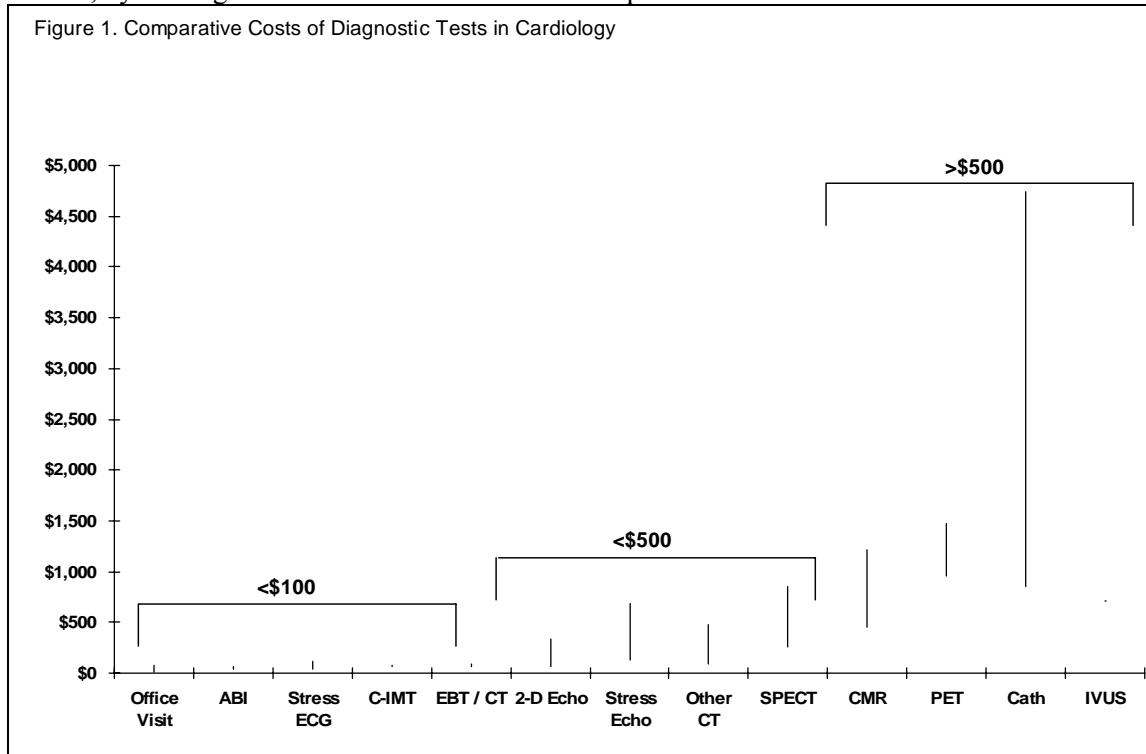
Data Quality

In general, the quality of economic analysis, including myocardial perfusion SPECT, is heterogeneous. A few are complex mathematical analyses, with multiple assumptions. Most of the studies are decision (or simulation) models while a few represent observational cohorts comprising clinically mixed populations. In the NICE evaluation of myocardial perfusion SPECT, a total of 22 economic evaluations were utilized to evaluate the CEA of SPECT. And, although they noted that a number used poor methodologies, there was a notable proportion that employed accepted and strong analytical approaches for their economic models.² In some studies, disease specific economic analyses were employed, such as the incremental cost-to-diagnosis of coronary disease; others used clinical outcomes as endpoints and included cardiac-specific (i.e., cost per event detected) and traditional CEA, including cost per life year saved or cost per quality-adjusted life year saved.

Diagnostic Costs of SPECT

There are a number of diagnostic testing modalities for the assessment of suspected myocardial ischemia. These include the "low-tech" but low-cost exercise electrocardiogram and increase in cost up to an invasive coronary angiogram. Costs for available diagnostic tests are listed in **Figure 1**. It should be noted that **Figure 1** details *direct costs that vary from charges or reimbursement*. Costs have been estimated using traditional "bottom up" or "top down" approaches and have been synthesized from statements of the American College of Cardiology (ACC) and European Society of Cardiology.^{4,6} In reviewing this evidence, it appears that SPECT imaging is a moderately priced diagnostic modality with costs lower than those for PET, MR, and X-ray coronary angiography. However, SPECT costs are uniformly higher than an office visit, exercise electrocardiogram, or echocardiography. In devising cost structures, cardiac SPECT

costs may be minimized in centers with higher volumes (i.e., economies of scale) and, in many centers, by sharing of fixed costs across non-cardiac procedures.



Frequently, diagnostic cost differences between modalities are used as a deciding metric for test choice. However, diagnostic costs must also evaluate the economic burden throughout the episode of care. That is, not only the upfront test costs, but also any downstream or induced costs directly emanating from the procedure must be considered. For many diagnostic modalities including SPECT, this would include notably the false positive and negative results that may define cost inefficiency for a diagnostic procedure. One method to quantify cost waste with SPECT is to examine the diagnostic accuracy statistics in order to garner some insight into the common rates of false positive and negative tests. In a recent review, the overall diagnostic sensitivity and specificity is 87% and 73% (n=19 studies) for exercise, and 89% and 75% (n= 24 studies) for pharmacologic stress SPECT⁷ (**Figure 2a** and **2b**). This would mean that in nearly 9 of every 10 patients with a significant coronary stenosis by coronary arteriography, a perfusion abnormality is noted on SPECT.

However, nearly 1 in 4 patients would have a “false positive” SPECT. Most often these were due to: 1) perfusion abnormalities being elicited in the setting of an intermediate stenosis with endothelial dysfunction (i.e., physiological true positive, but anatomically “false positive”), and 2) body tissue-related attenuation artifacts occurring in women and obese patients. With regards to the latter, recent improvements in the field have resulted in reductions in this “false positive” rate. These improvements include the use of attenuation correction algorithms, the use of the higher energy isotope Tc-99m rather than thallium-201 in many laboratories, and the inclusion of gated SPECT assessment of left ventricular regional function (i.e., a perfusion abnormality with abnormal wall motion/thinning and reduced function has an increased likelihood of being a true positive).

Figure 2a. Rates of False Negative Rates for Exercise (n=19 studies) and Pharmacologic Stress (n=24 studies) Myocardial Perfusion SPECT Imaging Using all 3 Approved Tracers

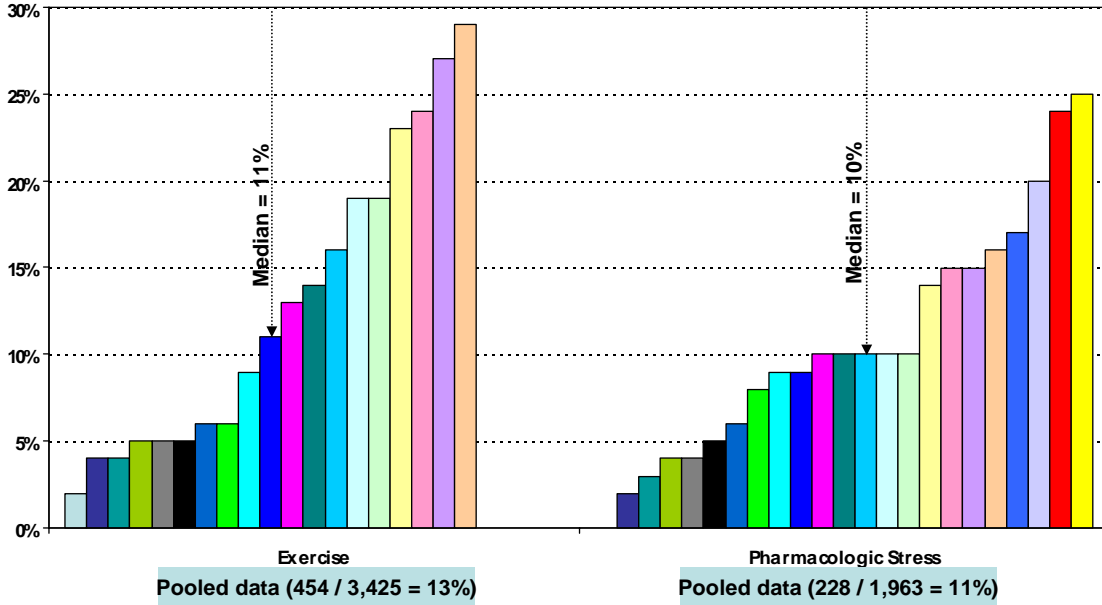
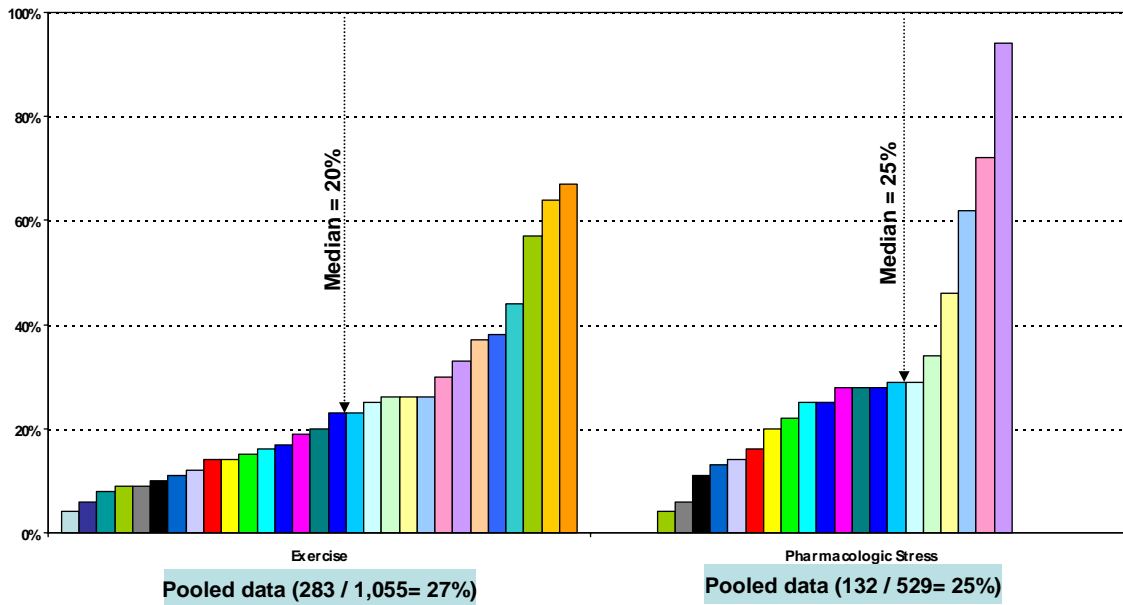


Figure 2b. Rates of False Positive Rates by Exercise (n=19 Studies) Adenosine / Dipyridamole (n=24 studies) Myocardial Perfusion SPECT Imaging



Economic Principles Applicable to SPECT

There are a number of economic principles that may be garnered by reviewing the SPECT evidence. First of all, a high diagnostic sensitivity reveals that costly false negative SPECT scans (e.g., downstream myocardial infarction or death in a patient with normal perfusion) are rare. In fact, from the prognostic literature, a normal myocardial perfusion SPECT is associated with an annual rate of cardiac death or myocardial infarction of 0.7% (exercise) to 1.2% (pharmacologic stress).⁸ This avoidance of future cardiac events in undiagnosed patients is a particular strength of this modality.

Available prognostic data lend considerable insight into the value of a positive study. From guidelines from the ACC, the American Heart Association, and the American Society of Nuclear Cardiology, there is a direct linear relationship between the extent and severity of perfusion abnormalities and clinical outcome.⁹⁻¹⁰ That is, as the extent and severity of perfusion defects worsen, so does a patient's risk of cardiac death or myocardial infarction. From this evidence we may also see that risk and cost have a directly proportional relationship. That is, high-risk SPECT results are associated with high-cost care, as events have direct economic consequences. Additionally, high-risk patients also have a greater frequency of significant obstructive coronary disease and require more therapeutic intervention leading to even greater costs of care. For the high-risk patient, this relationship of risk to expenditures is the result of diagnostic modalities and therapeutic interventions aimed at improving life expectancy and quality of life. It is the economic aim of current diagnostic strategies that the high cost care would be justified, as it is effective at reducing premature morbidity and mortality and, thus, is both clinically and cost effective.

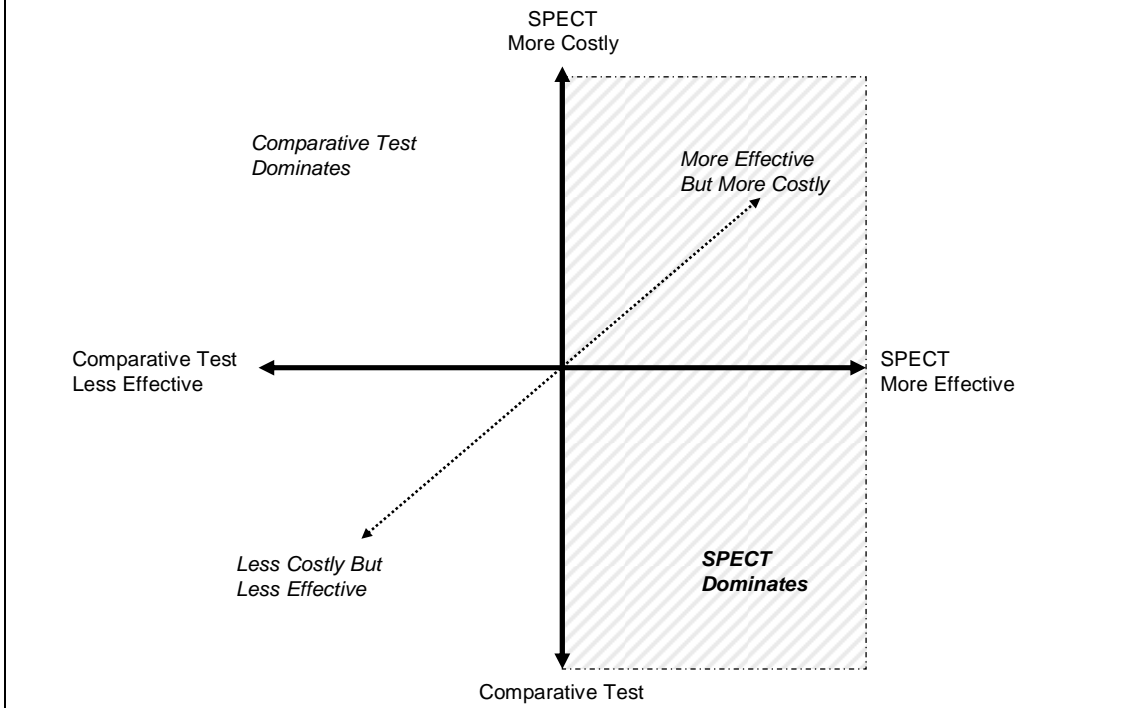
One additional principle may be seen in reviewing this data and that is the idea of allocative efficiency. Discerning the extent and severity of SPECT perfusion abnormalities (normal, mildly abnormal, and moderate-severely abnormal) is effective at classifying patients into corresponding risk groups (low, intermediate, and high) allowing one to envision a strategy of expected costs of care for each subset of patients. When applied, this concept is that the estimation of risk directs the allocation of resources to focus high-cost care to those who will benefit from it the most. For the low-risk patient, low-costs of care are expected for the ensuing 2-3 years post-SPECT imaging. This would entail minimal use (~1%) of downstream coronary angiography for patients with normal stress perfusion results.¹¹⁻¹³ For the patient with moderate-severely abnormal SPECT results, high-cost interventional care is focused on a cohort with more advanced coronary disease and on those who have the most to gain in terms of life expectancy.

Thus, myocardial perfusion SPECT may be cost effective, even if more costly than another diagnostic modality, by being substantially more effective at identifying risk, improving outcome detection, and more efficiently directing the allocation of resources (**Figure 3**). SPECT may also be more cost effective, when compared to more expensive diagnostic modalities, by being at least equally as effective at identifying those diseased patients and resulting in equivalent (at a minimum) rates of major adverse cardiovascular events.

Economic Modeling Evidence on SPECT by Pretest Risk Patient Subsets

Although earlier analysis,¹⁴⁻¹⁸ such as that by Patterson et al.¹⁴ and Maddahi et al.,¹⁵ employed the use of decision or simulation models, more recent economic data has been derived from "real world" effectiveness data.¹⁹⁻²⁵ These earlier models focused on the application of diagnostic accuracy statistics as drivers for evaluating economic efficiency, and were built upon the principles described above of minimizing cost waste through higher diagnostic sensitivity and lower false positive rates. Although these models often rely upon unrealistic assumptions,

Figure 3. Simplistic View of Cost Effectiveness Plane When compared with another modality. SPECT can become cost effective (hatched area) by being more effective than a less expensive test but also by being both less expensive and more effective than a comparative modality.



such as 100% of patients with abnormal tests proceed to coronary angiography, they do provide some insight into developing economic efficiencies and may provide the groundwork for future cost models in imaging.

The lion's share of current CEA evidence is in the routine use of myocardial perfusion SPECT as compared with the exercise ECG, echocardiography, or angiography in the evaluation of chest pain symptoms, especially for the intermediate-risk patient. In general, several reports have noted that SPECT is economically superior to the exercise electrocardiogram (ECG) primarily due to its improved accuracy.² For the stress ECG, a diminished accuracy has been noted leading to greater (unnecessary) downstream costs. In a related report by Marwick and colleagues,²⁶ a normal stress ECG often did not prevent additional diagnostic testing, which was performed based on clinical risk profiles, and resulted in an unexpected increase in the rate of coronary angiography. Thus, normal stress perfusion results are strong deterrents for additional confirmatory testing. Applying a SPECT perfusion-based strategy has been shown to result in a 23% to 41% cost savings when compared to direct coronary angiography.^{19,20,25}

These results are consistent with the evidence put forth in the NICE appraisal that the use of myocardial perfusion imaging, followed by selective coronary angiography, is cost effective for intermediate-risk patients. In fact, of the 10 published CEA reports cited by the NICE appraisal, 7 noted economic favorability of a SPECT-guided testing approach over the stress ECG alone. Using mostly disease-specific CEA, the results ranged from a cost of \$5,417 per correct disease classification to \$20,550 per correct cardiac event classified.² In two other reports, myocardial perfusion SPECT had an incremental cost effectiveness ratio (ICER) of \$38,000 to \$40,316 dollars per quality-adjusted life years, values below the threshold for economic efficiency (i.e., set at <\$50,000 per life year saved) when compared with the stress ECG.¹⁷⁻¹⁸

However, for low-risk patients, a sequential testing strategy that included initial testing by the stress ECG followed by SPECT and (possibly) coronary angiography if the results were positive, allowed for a more selective use of higher cost tests. This has been shown to be a more cost effective approach than direct imaging strategies.² This economic evidence is further supported by ACC/AHA guidelines⁹⁻¹⁰ that recommend against the use of initial SPECT for low-risk patients.

Additionally, there are also several reports that compared stress SPECT to coronary angiography in high-risk patients.² These results consistently reveal that, for diagnosis, direct angiography is economically favorable. In a report by Jacklin²⁷ for high-risk patients, SPECT was more costly and less effective than direct coronary angiography. The resulting ICER exceeded \$100,000 for SPECT versus coronary angiography in the decision model by Garber.¹⁷

It is reasonable to conclude that direct coronary angiography is cost effective when the pretest risk of coronary artery disease is high (>75%). However, at lower levels of pretest risk, non-invasive strategies are a better use of resources than a strategy of direct coronary angiography. Furthermore, a synthesis of available evidence in intermediate-risk patients reveals that SPECT-based strategies are likely to economically dominate (i.e., defined as less costly and more effective) or result in economic favorability when compared with a stress ECG strategy.²

When stress echocardiography (a lower cost procedure) has been compared with SPECT, exercise ECG, and angiography, several decision models have concluded that using a case-based analysis of a 55-year-old man with atypical angina, the ICER of echocardiography versus exercise ECG was <\$50,000 per quality-adjusted life years saved.¹⁹⁻²⁰ Additionally, the ICER for SPECT versus ECG was similar at \$54,800 per quality-adjusted life years saved. From the report by Garber and Solomon,¹⁷ the ICER of echocardiography vs. outdated planar Tl-201 imaging was marginal at \$75,000 per quality-adjusted life years saved. Furthermore, direct angiography was not cost effective when compared with SPECT with an ICER of \$94,000 per quality-adjusted life years saved. Garber concluded that echocardiography, SPECT, and direct angiography were all cost-effective alternatives as compared to other diagnostic modalities and that optimal test selection should be guided by local expertise. However, questions have been raised about such analyses, since there is a significant degree of selection bias in the populations referred for each test (with practitioners referring a lower-risk subset to stress echocardiography), and the existing direct cross-over comparison database is small.

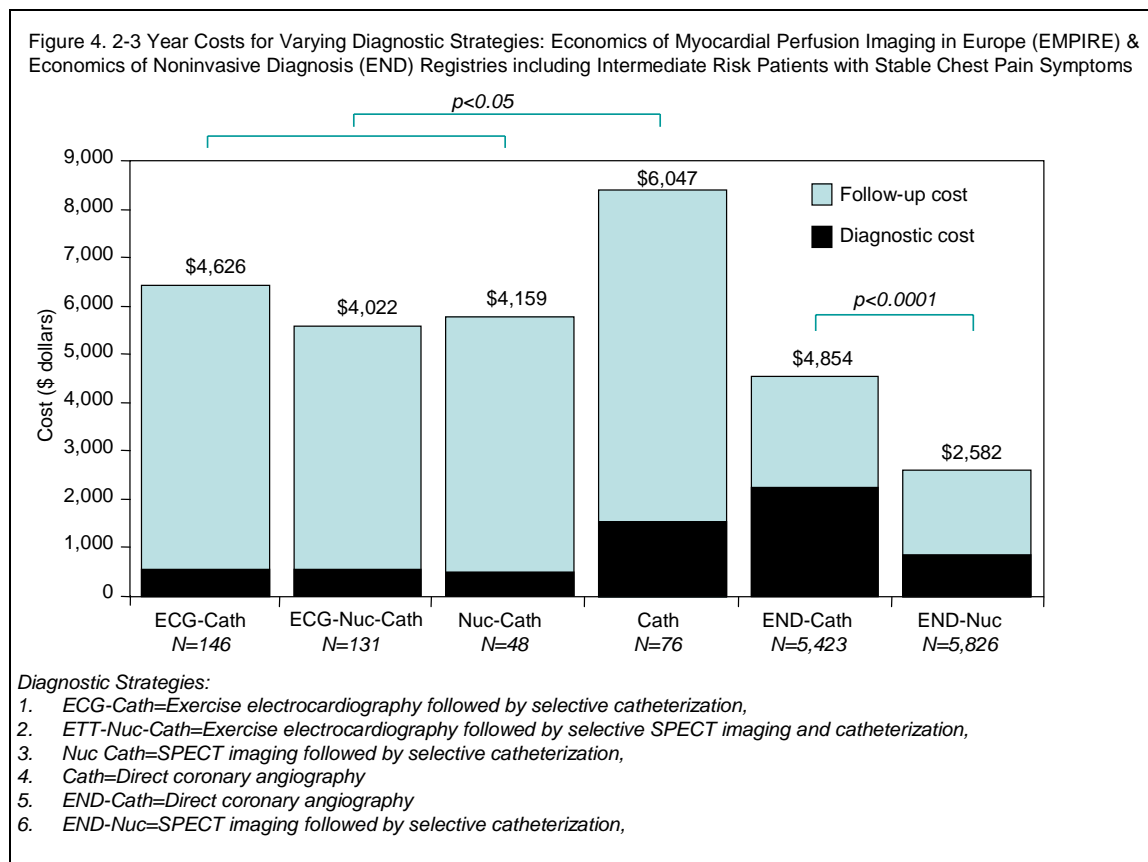
From the recent Agency for Health-Related Quality evaluation of diagnostic testing modalities, the false positive rate was similar for echocardiography and SPECT imaging.²⁸ Further research in the field should focus on decreasing the false positive rate and creating greater economic efficiency in a SPECT diagnostic testing strategy. In a preliminary report by Lee et al.,²⁹ the lower occurrence of false negative tests with stress SPECT balanced the greater initial expense associated with nuclear perfusion imaging resulting in cost efficiency when compared to stress echocardiography in patients with an intermediate-risk pretest probability of coronary artery disease (i.e., $\geq 30\%$).

A compilation of simulation evidence is mixed but often favorable with regards to SPECT, although models often mix planar and SPECT data. As a result, more contemporary evidence, such as that from the NICE appraisal, is increasingly supportive of diagnostic testing strategies employing myocardial perfusion SPECT imaging.^{2,17-18} A key to the transition in this evidence has been the unfolding of several large observational cohorts that have detailed the economic efficiency of SPECT.¹⁹⁻²⁵

Observational Economic Evidence on SPECT

The Economics of Noninvasive Diagnosis (END) registry compiled a consecutive series of patients with stable angina presenting for a diagnostic evaluation that included either direct coronary angiography or SPECT imaging.²⁰ A total of 5,826 SPECT imaging patients were

matched to a cohort of 5,423 patients referred for direct diagnostic cardiac catheterization. Extensive statistical matching was employed so that the 3-year risk of death or myocardial infarction was similar between the two groups. That is, the two cohorts were matched according to their pretest clinical risk.³⁰ As the outcome between these two groups was equal, the analysis focused on a cost minimization (or savings) approach. In this cohort with stable angina, the use of myocardial perfusion SPECT resulted in a 30%-41% cost savings when compared with direct cardiac catheterization (**Figure 4**). From this analysis, several factors appear to drive cost efficiency, including 1) the fact that cardiac catheterization was rarely used for patients with normal stress perfusion imaging results; and 2) direct coronary angiography resulted in a greater frequency of revascularization, without an added outcome benefit. Thus, from this series, direct coronary angiography resulted in substantial cost waste when compared with a SPECT approach which included selective coronary angiography for those with provokable ischemia. Similar findings were reported from the Economics of Myocardial Perfusion Imaging in Europe (EMPIRE) study of 396 patients.²⁵



In a related report by Mishra et al.,²¹ myocardial perfusion SPECT (n=2,022) was compared with direct coronary angiography (n=4,572), and resulted in an average cost of care which was nearly half of that incurred by a strategy employing direct cardiac catheterization (i.e., \$1,420 per patient lower in the SPECT group). Of the 557 patients with abnormal MPI images, only 313 (66%) underwent cardiac catheterization, suggesting risk stratification by the extent and severity of perfusion abnormalities is cost efficient by creating selective resource consumption. Of interest, in the SPECT cohort, the ratio of catheterization / revascularization for those with

significant coronary disease was 38%, revealing that medical therapy was employed in patients with modest perfusion abnormalities. By comparison, in the catheterization cohort, the catheterization / revascularization ratio was 51% for those with significant coronary disease ($p < 0.001$). These results demonstrate that when perfusion imaging is used as an initial diagnostic strategy, both cardiac catheterization and revascularization are used more selectively, resulting in lower costs.

Economic Analysis in Special Populations

There is economic evidence for the use of SPECT in special populations including those evaluated with acute chest pain symptoms in the Emergency Department,³¹⁻³⁹ diabetics,⁴⁰ and women.⁴¹

Emergency Department (ED) Imaging of Chest Pain

SPECT imaging is one of many strategies employed as a gatekeeper to hospitalization for acute chest pain. Of the approximately 6 million patients evaluated for chest pain in an emergency department in the US, only one third will be found to have symptoms of cardiac origin.⁴²⁻⁴³ It is estimated that nearly 3 million of these patients are hospitalized unnecessarily at an annual cost of 5 to 8 billion dollars.⁴⁴ Additionally, 4% to 7% of patients with an acute coronary syndrome will be inappropriately sent home from the ED each year.³¹⁻³³

Several studies have demonstrated that the use of SPECT imaging in the ED reduces costs by avoiding hospitalization in certain patient subsets without compromising patient outcome. A study by Weissman et al.³³ documented changes in physicians' decision-making in a group of ED chest pain patients before and after the physicians were given MPI data. They found that 68% of physician decisions were influenced by the SPECT imaging results generating a potential cost savings of \$786 per patient from reduced admissions for patients with low-risk SPECT findings. Radensky et al.³⁶ used a decision model comparing use versus no use of myocardial perfusion SPECT and calculated a potential cost savings of \$796 per patient in a similar clinical setting.

When SPECT imaging is introduced into a chest pain work-up, rates of hospitalization (i.e., 53% to 41%) and the ensuing admission diagnosis of "rule out MI" (i.e., 32% to 18%) decline as recently reported by Abbott et al. and others.^{35,39} They concluded that the use of SPECT imaging to guide admissions resulted in a decrease in the rate of unnecessary hospitalizations by 29%, as well as resulting in a 6% reduction in inappropriate discharges from the ED. In a similar report, Kontos et al.³⁴ demonstrated significant cost savings, a lower angiography rate, and a shorter average length of stay for patients initially undergoing SPECT imaging when compared to a control population.

These results are supportive of the high negative predictive value for SPECT in ruling out an acute myocardial infarction (99%) or future adverse cardiac event (97%).³¹ Based on these data, the ACC/AHA/ASNC Guidelines assign a Class IA indication to the assessment of myocardial risk in possible acute coronary syndrome patients with a nondiagnostic ECG and initial normal serum markers and enzymes, and a Class IB indication to the diagnosis of coronary artery disease in these patients.⁹

A substantial cost benefit of perfusion imaging is also evident in hospitalized patients, a finding which extends the benefits demonstrated in the emergency department. A prospective, randomized study by Stowers et al.³⁷ assessed differences in hospital costs between a conventional and MPI-guided strategy. The median hospital costs per patient were \$1,843 lower in the perfusion imaging-guided arm compared with the conventional arm. Heller et al.³¹ estimated savings of a similar magnitude. From an additional study by Kosnik et al.³⁸ (n=69 admitted patients), however, the use of myocardial perfusion SPECT resulted in a more appropriate patient triaging in 42%, but at an added cost of \$307 per patient.

Overall, the majority of these small studies support the potential for significant cost savings for the use of SPECT in patients with low to moderate risk chest pain, non-diagnostic ECG, and/or negative biomarkers.

Diabetic Patients

Coronary artery disease is prevalent in diabetics, accounting for 50% of deaths in this population and encumbering substantial economic resources to care for diabetic patients.^{1,45} Myocardial perfusion SPECT has been demonstrated to effectively diagnose coronary disease and predict future cardiac risk in patients with diabetes.⁴⁶⁻⁴⁷ Giri et al.⁴⁰ demonstrated that the use of myocardial perfusion SPECT was highly effective at identifying at-risk diabetic and non-diabetic patients. From this END substudy, the 3-year risk-adjusted costs were decidedly higher in diabetics (\$2,705 vs. \$1,688), in large part because of increased follow-up costs for diabetics. Importantly, diabetes itself only accounted for approximately 1% of the variance in costs. The most important drivers of cost were based upon ischemic burden and the extent of coronary disease. Thus, from this evidence, the intensity of resource consumption may be predicted based upon the results of SPECT to a greater extent than diabetes. We await additional results on the cost implications of varying SPECT imaging strategies in diabetics, such as that from the Bypass, Angioplasty, Revascularization Investigation in Diabetics (BARI 2-D) and Detection of Ischemia in Asymptomatic Diabetics (DIAD) study.⁴⁷

Women and Coronary Artery Disease

As women present more often with more atypical symptoms, clinicians often disproportionately rely upon imaging to guide further medical decision-making. Several reports have noted the cost effectiveness of myocardial perfusion SPECT in women.^{2,41} Notably, in a subset analysis from the END database, the use of SPECT (n=1,263) resulted in substantial cost savings when compared with direct coronary angiography (n=3,375).⁴¹ These findings mirrored the overall findings from the END study, noting cost saving in the range of 35% over 3 years of care. The composite cost was greater in the direct catheterization group when compared with SPECT while achieving equivalent patient outcomes (i.e., for the intermediate-risk woman, cost for catheterization ≈\$3,000 vs. \$1,700 for SPECT, p<0.01). However, of the data reported to date, a decision model developed within the NICE appraisal revealed that the ICER for SPECT in women was moderately favorable in the \$50,000-\$75,000 per life year saved range when compared to other diagnostic testing modalities. As a result, the NICE report concluded that evidence supported the use of SPECT imaging in women presenting for evaluation of suspected coronary disease. This model is consistent with a recent imaging statement from the AHA that supports cardiac imaging for diabetic and functionally impaired women.⁴⁸ We also await additional results from the ongoing WOMENs study (**W**hat is the **O**ptimal **M**ethod for Ischemia **E**valuation in **W**ome**N**) that is enrolling over 1,008 women who are randomized to exercise ECG versus SPECT imaging and where CEA is a secondary endpoint.

CONCLUSIONS

The cost-effectiveness of myocardial perfusion imaging has been demonstrated in a number of clinical studies and in a variety of patient populations. Although some simulation models are mixed with regards to the benefit of employing SPECT versus echocardiography, contemporary research increasingly highlights the greater accuracy of SPECT as a prominent factor reducing downstream costs when compared with the exercise ECG. Large cohort studies (e.g., END, EMPIRE) are also available comparing SPECT with an array of other diagnostic modalities. The results consistently note significant cost savings when SPECT is employed as a gatekeeper by limiting angiography to only patients with provokable ischemia. There are also data

to support favorable cost models for special populations, including those patients evaluated with acute chest pain in the ED, diabetics, and women.

The economic evidence is reflective of the prognostic data (i.e., clinical effectiveness) that SPECT imaging provides independent prognostic value incremental to that derived from a clinical history, ECG, or angiographic variables.⁴⁹ From a recent independent appraisal, 3 studies note that a strategy employing SPECT and selective coronary angiography resulted in revascularization rates ranging from 6% to 21%, as compared to rates of 16% to 44% for direct coronary angiography, without a negative impact on outcomes. Thus, there is a potential for significant cost savings when SPECT-guided diagnostic strategies are employed.

The quality of the economic evidence regarding SPECT myocardial perfusion imaging has improved over time. However, a large proportion of the reports employ simplistic analyses. We attempted to highlight those reports of higher quality and to include more contemporary evaluations of the role of SPECT imaging in the diagnosis of suspected myocardial ischemia. We await the completion of several large controlled clinical trials that may provide further economic evidence on the role of myocardial perfusion SPECT in a variety of populations, including those with established coronary disease, women, and diabetics.

Acknowledgments

Dr. Shaw reported that she has grant support from Fujisawa Healthcare, GE-Amersham, and BMS – Medical Imaging. Dr. Williams reported that he has grant support from Astellas, GE-Amersham, BMS-Medical Imaging, CV Therapeutics, and King Pharmaceuticals.

References

1. Available from URL: <http://www.americanheart.org/downloadable/heart/1105390918119HDSStats2005Update.pdf>. Accessed April 1, 2005.
2. National Health Service–National Institute for Clinical Excellence, Technology Appraisal Consultation Document: Myocardial perfusion scintigraphy for the diagnosis and management of CAD. Available from: URL: <http://www.nice.org.uk/article.asp?a=80521>. Accessed August 15, 2003.
3. Mark DB, Hlatky MA. Medical economics and the assessment of value in cardiovascular medicine: Part I. *Circulation* 2002;106:516-20.
4. Mark DB, Shaw LJ, Lauer MS, O'Malley P, Heidenreich P. 34th Bethesda Conference: Task force #5 - Is atherosclerotic imaging cost effective? From the 34th Bethesda Conference on Atherosclerotic Imaging. *J Am Coll Cardiol* 2003;41:1906-17.
5. Mowatt G, Vale L, Brazzelli M, Hernandez R, Murray A, Scott N, Fraser C, McKenzie L, Gemmell H, Hillis G, Metcalfe M. Systematic review of the effectiveness and cost-effectiveness, and economic evaluation, of myocardial perfusion scintigraphy for the diagnosis and management of angina and myocardial infarction. Available from: URL: <http://www.hta.nhsweb.nhs.uk>. *Health Technol Assess* 2004;8:1-222.
6. Pennell DJ, Sechtem UP, Higgins CB, Manning WJ, Pohost GM, Rademakers F, van Rossum, Shaw LJ, Yucel EK. Clinical indications for cardiovascular magnetic resonance (CMR): Consensus panel report. *Eur Heart J* 2004;25:1940-65.
7. Underwood SR, Anagnostopoulos C, Cerqueira M, Ell PJ, Flint J, Harbinson M, Kelion A, Al-Mohammad A, Prvulovich EM, Shaw LJ, Tweddel AC. Myocardial perfusion scintigraphy: the evidence. A consensus conference organised by the British Cardiac Society, the British Nuclear Cardiology Society and the British Nuclear Medicine Society, endorsed by the Royal College of Physicians of London and the Royal College of Radiologists. *Eur J Nuc Med Mol Imaging* 2004;31:261-91.
8. Shaw LJ, Iskandrian AE. Prognostic value of stress gated SPECT in patients with known or suspected coronary artery disease. *J Nucl Cardiol* 2004;11:171-85.

9. Klocke FJ, Baird MG, Lorell BH, Bateman TM, Messer JV, Berman DS, O’Gara PT, Carabello BA, Russell RO, Cerqueira MD, St John Sutton MG, DeMaria AN, Udelson JE, Kennedy JW, Verani MS, Williams KA, Antman EM, Smith SC, Alpert JS, Gregoratos G, Anderson JL, Hiratzka LF, Faxon DP, Hunt SA, Fuster V, Jacobs AK, Gibbons RJ, Russell RO; American College of Cardiology; American Heart Association Task Force on Practice Guidelines; American Society of Nuclear Cardiology. ACC/AHA/ASNC guidelines for the clinical use of cardiac radionuclide imaging—executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/ASNC Committee to Revise the 1995 Guidelines for the Clinical Use of Cardiac Radionuclide Imaging). *Circulation* 2003;108:1404-18.
10. Gibbons RJ, Abrams J, Chatterjee K, Daley J, Deedwania PC, Douglas JS, Ferguson TB Jr, Fihn SD, Fraker TD Jr, Gardin JM, O’Rourke RA, Pasternak RC, Williams SV; American College of Cardiology; American Heart Association Task Force on practice guidelines (Committee on the Management of Patients With Chronic Stable Angina). ACC/AHA 2002 guideline update for the management of patients with chronic stable angina—summary article: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines (Committee on the Management of Patients With Chronic Stable Angina). *J Am Coll Cardiol* 2003;41:159-68.
11. Bateman TM, O’Keefe JH Jr, Dong VM, Barnhart C, Ligon RW. Coronary angiographic rates after stress single-photon emission computed tomographic scintigraphy. *J Nucl Cardiol* 1995;2:217-23.
12. Shaw LJ, Berman DS, Hachamovitch R, Heller GV, Travin M, Kesler K, Miller DD. Noninvasive strategies for the estimation of cardiac risk: An observational assessment of outcome in stable chest pain patients. *Am J Cardiol* 2000;86:1-7.
13. Thomas GS, Miyamoto MI, Morello AP, Majmundar H, Thomas JJ, Sampson CH, Hachamovitch R, Shaw LJ. Technetium-99m sestamibi myocardial perfusion imaging predicts clinical outcome in the community outpatient setting. The Nuclear Utility in the Community (NUC) Study. *J Am Coll Cardiol* 2004;43:213-23.
14. Patterson RE, Eisner RL, Horowitz SF. Comparison of cost-effectiveness and utility of exercise ECG, single photon emission computed tomography, positron emission tomography, and coronary angiography for diagnosis of coronary artery disease. *Circulation* 1995;91:54-65.
15. Maddahi J, Gambhir SS. Cost-effective selection of patients for coronary angiography. *J Nucl Cardiol* 1997;4:S141-51.
16. Rumberger JA, Behrenbeck T, Breen JF, Sheedy, PF. Coronary calcification by electron beam computed tomography and obstructive coronary artery disease: a model for costs and effectiveness of diagnosis as compared with conventional cardiac testing methods. *J Am Coll Cardiol* 1999;33:453-62.
17. Garber AM, Solomon NA. Cost-effectiveness of alternative test strategies for the diagnosis of coronary artery disease. *Ann Intern Med* 1999;130:719-28.
18. Kuntz KM, Fleischmann KE, Hunink MG, Douglas PS. Cost-effectiveness of diagnostic strategies for patients with chest pain. *Ann Intern Med* 1999;130:709-18.
19. Hachamovitch R, Berman DS, Shaw LJ, Kiat H, Cohen I, Cabico JA, Friedman J, Diamond GA. Incremental prognostic value of myocardial perfusion single photon emission computed tomography for the prediction of cardiac death: differential stratification for risk of cardiac death and myocardial infarction. *Circulation* 1998;97:535-43.
20. Shaw LJ, Hachamovitch R, Berman DS, Marwick TH, Lauer MS, Heller GV, Iskandrian AE, Kesler KL, Travin MI, Lewin HC, Hendel RC, Borges-Neto S, Miller DD. The economic consequences of available diagnostic and prognostic strategies for the evaluation of stable angina patients: an observational assessment of the value of pre-catheterization ischemia. *J Am Coll Cardiol* 1999;33:661-9.
21. Mishra JP, Acio E, Heo J, Narula J, Iskandrian AE. Impact of stress single-photon emission computed tomography perfusion imaging on downstream resource utilization. *Am J Cardiol* 1999;83:1401-3, A8.
22. Hachamovitch R, Hayes SW, Friedman JD, Cohen I, Berman DS. Stress myocardial perfusion single-photon emission computed tomography is clinically effective and cost-effective in risk stratification of patients with a high likelihood of coronary artery disease (CAD) but no known CAD. *J Am Coll Cardiol* 2004;43:200-8.
23. Hachamovitch R, Berman DS, Kiat H, Cohen I, Friedman JD, Shaw LJ. Value of stress myocardial perfusion single photon emission computed tomography in patients with normal resting electrocardiograms: an evaluation of incremental prognostic value and cost-effectiveness. *Circulation* 2002;105:823-9.

24. Mattera JA, Arain SA, Sinusas AJ, Finta L, Wackers FJ. Exercise testing with myocardial perfusion imaging in patients with normal baseline electrocardiograms: cost savings with a stepwise diagnostic strategy. *J Nucl Cardiol* 1998;5:498-506.
25. Underwood SR, Godman B, Salvani S, Ogle JR, Ell PJ. Economics of Myocardial Perfusion Imaging in Europe—the EMPIRE study. *Eur Heart J* 1999;20:157-66.
26. Marwick TH, Shaw LJ, Case C, Vasey, Thomas JD. Clinical and economic impact of exercise electrocardiography and exercise echocardiography in clinical practice. *Eur Heart J* 2003;24:1153-63.
27. Jacklin PB, Barrington SF, Roxburgh JC, Jackson G, Sariklis D, West PA, Maisey MN. Cost-effectiveness of preoperative positron emission tomography in ischemic heart disease. *Ann Thorac Surg* 2002;73:1403-9.
28. Available from: URL: www.ahrq.gov/clinic/epcsums/chdwomsum.htm. Accessed June 15, 2004.
29. Lee DS, Jang MJ, Cheon GJ, Chung J-K, Lee CL. Comparison of the cost-effectiveness of stress myocardial SPECT and stress echocardiography in suspected coronary artery disease considering the prognostic value of false-negative results. *J Nucl Cardiol* 2002;9:515-22.
30. Pryor DB, Shaw L, McCants CB, Lee KL, Mark DB, Harrell FE Jr., Muhlbaier LH, Califf RM. Value of the history and physical in identifying patients at increased risk for coronary artery disease. *Ann Intern Med* 1993;118:81-90.
31. Heller GV, Stowers SA, Hendel RC, Herman SD, Daher E, Ahlberg AW, Baron, JM, Mendes dLC, Rizzo JA, Wackers FJ. Clinical value of acute rest technetium-99m tetrofosmin tomographic myocardial perfusion imaging in patients with acute chest pain and nondiagnostic electrocardiograms. *J Am Coll Cardiol* 1998;31:1011-17.
32. Udelson JE, Beshansky JR, Ballin DS, Feldman JA, Griffith JL, Handler J, Heller GV, Hendel RC, Pope JH, Ruthazer R, Spiegler EJ, Woolard RH, Selker HP. Myocardial perfusion imaging for evaluation and triage of patients with suspected acute cardiac ischemia: a randomized controlled trial. *JAMA* 2002;288:2693-700.
33. Weissman IA, Dickinson CZ, Dworkin HJ, O'Neill WW, Juni JE. Cost-effectiveness of myocardial perfusion imaging with SPECT in the emergency department evaluation of patients with unexplained chest pain. *Radiology* 1996;199:353-7.
34. Kontos MC, Schmidt KL, McCue M, Rossiter LF, Jurgensen M, Nicholson CS, Jesse RL, Ornato JP, Tatum JL. A comprehensive strategy for the evaluation and triage of the chest pain patient: a cost comparison study. *J Nucl Cardiol* 2003;10:284-90.
35. Knott JC, Baldey AC, Grigg LE, Cameron PA, Lichtenstein M, Better N. Impact of acute chest pain Tc-99m sestamibi myocardial perfusion imaging on clinical management. *J Nucl Cardiol* 2002;9:257-62.
36. Radensky PW, Hilton TC, Fulmer H, McLaughlin BA, Stowers SA. Potential cost-effectiveness of initial myocardial perfusion imaging for assessment of emergency department patients with chest pain. *Am J Cardiol* 1997;79:595-9.
37. Stowers SA, Eisenstein EL, Wackers FJ, Berman DS, Blackshear JL, Jones ADJ, Szymanski TJJ, Lam LC, Simons TA, Natale D, Paige KA, Wagner GS. An economic analysis of an aggressive diagnostic strategy with single photon emission computed tomography myocardial perfusion imaging and early exercise stress testing in emergency department patients who present with chest pain but nondiagnostic electrocardiograms: results from a randomized trial. *Ann Emerg Med* 2000;35:17-25.
38. Kosnik JW, Zalenski RJ, Grzybowski M, Huang R, Sweeny PJ, Welch RD. Impact of technetium-99m sestamibi imaging on the emergency department management and costs in the evaluation of low-risk chest pain. *Acad Emerg Med* 2001;8:315-23.
39. Abbott BG, Abdel-Aziz I, Nagula S, Monico EP, Schriver JA, Wackers FJ. Selective use of single-photon emission computed tomography myocardial perfusion imaging in a chest pain center. *Am J Cardiol* 2001;87:1351-5.
40. Giri S, Shaw LJ, Murthy DR, Travin MI, Miller DD, Hachamovitch R, Borges-Neto S, Berman DS, Waters DD, Heller GV. Impact of diabetes on the risk stratification using stress single-photon emission computed tomography myocardial perfusion imaging in patients with symptoms suggestive of coronary artery disease. *Circulation* 2002;105:32-40.
41. Shaw LJ, Heller GV, Travin MI, Lauer M, Marwick T, Hachamovitch R, Berman DS, Miller DD. Cost analysis of diagnostic testing for coronary artery disease in women with stable chest pain. Economics of Noninvasive Diagnosis (END) Study Group. *J Nucl Cardiol* 2002;9:515-22.

42. Fineberg HV, Scadden D, Goldman L. Care of patients with a low probability of acute myocardial infarction. Cost-effectiveness of alternatives to coronary-care-unit admission. *N Engl J Med* 1984;310:1301-7.
43. Lee TH, Rouan GW, Weisberg MC, Brand DA, Acampora D, Stasiulewicz C, Walshon J, Terranova G, Gottlieb L, Goldstein-Wayne B. Clinical characteristics and natural history of patients with acute myocardial infarction sent home from the emergency room. *Am J Cardiol* 1987;60:219-24.
44. Pope JH, Aufderheide TP, Ruthazer R, Woolard RH, Feldman JA, Beshansky JR, Griffith JL, Selker HP. Missed diagnoses of acute cardiac ischemia in the emergency department. *N Engl J Med* 2000;342:1163-70.
45. Hogan P, Dall T, Nikolov P. Economic costs of diabetes in the U.S. in 2002. *Diabetes Care* 2003;26:917-32.
46. Kang X, Berman DS, Lewin H, Miranda R, Erel J, Friedman JD, Amanullah AM. Comparative ability of myocardial perfusion single-photon emission computed tomography to detect coronary artery disease in patients with and without diabetes mellitus. *Am Heart J* 1999;137:949-57.
47. Wackers FJ, Young LH, Inzucchi SE, Chyun DA, Davey JA, Barrett EJ, Taillefer R, Wittlin SD, Heller GV, Filipchuk N, Engel S, Ratner RE, Iskandrian AE. Detection of silent myocardial ischemia in asymptomatic diabetic subjects: the DIAD study. *Diabetes Care* 2004;27:1954-61.
48. Mieres JH, Shaw LJ, Arai A, Budoff M, Hundley G, Flamm SD, Marwick TH, Mosca L, Patel AR, Redberg RF, Taubert K, Thomas G, Wenger NK, for the Cardiovascular Imaging Committee. American Heart Association – Cardiac Imaging Committee Consensus Statement: The role of cardiac imaging in the clinical evaluation of women with known or suspected coronary artery disease. *Circulation* 2005;111:682-96.
49. Mowatt G, Brazzelli M, Gemmell H, Hillis GS, Metcalfe M, Vale L; Aberdeen Technology Assessment Group. Systematic review of the prognostic effectiveness of SPECT myocardial perfusion scintigraphy in patients with suspected or known coronary artery disease and following myocardial infarction. *Nuc Med Comm* 2005;26:217-29.