Washington State Health Care Authority

Health Technology Assessment

Cardiac Nuclear Imaging

Draft Evidence Report: Public Comment & Response

September 4, 2013

Health Technology Assessment Program (HTA)
Washington State Health Care Authority
PO Box 42712
Olympia, WA 98504-2712

(360) 725-5126

hta.hca.wa.gov

shtap@hca.wa.gov

Cardiac Nuclear Imaging

Draft Report
Public Comment and Response

September 4, 2013

Response to Public Comments

The Institute for Clinical and Economic Review (ICER) is an independent vendor contracted to produce evidence assessment reports for the Washington HTA program. For transparency, all comments received during the public comment period are included in this response document. Comments related to program decisions, process, or other matters not pertaining specifically to the draft key questions, project scope, or evidence assessment are acknowledged through inclusion only.

This document responds to comments from the following parties:

Draft Report

- Bryan E. Fuhs, MD, FACC, Invasive Non-Interventional Cardiologist, Providence Spokane Cardiology & Joint Operating Committee Member, Providence Spokane Heart Institute; Braden W. Batkoff, MD, FACC, President, Providence Spokane Heart Institute and Providence Spokane Cardiology, & Joint Operating Committee Chair, Providence Spokane Heart Institute; Janice D. Christensen, MD, FACC, Non-Invasive Director, Providence Spokane Cardiology
- James H. Caldwell, MD, FACC, FAHA, Professor of Medicine and Radiology, Adjunct Professor of Bioengineering, and Director of Nuclear Cardiology, UW Medicine
- Washington Health Care Authority Agency Medical Directors

	Comment	Response
Bryan E. Fuhs, MD, FACC, Invasive Non-Interventional Cardiologist, Providence Spokane Cardiology & Joint Operating Committee Member, Providence Spokane Heart Institute; Braden W. Batkoff, MD, FACC, President, Providence Spokane Heart Institute and Providence Spokane Cardiology, & Joint Operating Committee Chair, Providence Spokane Heart Institute; Janice D. Christensen, MD, FACC, Non-Invasive Director, Providence Spokane Cardiology		
1	The preamble to the final key questions explicitly lists that there are differences in both "…their diagnostic and prognostic capabilities…" but then the first key question completely focuses on the diagnostic portion of the test. An important and well-validated use of SPECT is the prognostic power of the test, independent of whether CAD is present or absent.	*Thank you for your comments. The populations and questions were defined as those of most interest to the HCA. Of note, question 1E does relate to prognostic uses of nuclear imaging, and we identified comparative prognostic studies in both patients with known CAD and "mixed" populations.*
2	Nuclear cardiology for over two decades has been a well-validated tool for either diagnosis or prognosis in low to high-risk populations. Not only has the data been validated, but through the use of statistical quantitative analysis of the images, significant intra-observer variability has been reduced, which is not the case with Stress echocardiography. Academic studies suggest that consensus core reading reduces this variability, but rarely are stress echos interpreted that way in practice.	*The focus of the report was on nuclear imaging's impact on patient management and outcomes.*
3	Academic studies comparing stress echo to MPI, usually exclude patients that were technically suboptimal (an echo problem) to match the diagnostic accuracy in nuclear studies. This is usually about 20% of patients presenting, and had they been analyzed in an intention to treat fashion, Stress echo would not be as accurate as MPI, particularly in the group that can not adequately exercise.	*Unfortunately, exclusions due to technical issues with tests were rarely reported in any study of any modality, making adjustments to an "intent to treat" analysis untenable. We do note that a higher rate of "equivocal" findings was assumed for stress ECHO vs. the nuclear tests in the model based on patients with conditions likely to affect imagery.*
4	Radiation exposure carries risk that is not present in stress echo (without contrast) but the misleading portion of this statement is that underdiagnosis of CAD is not a riskless event. Interestingly, this report is being generated because of increasing use of these tests, without addressing the root cause of the increasing use. One of the strongest variables for the development of CAD is age, and demographics in the state of Washington show that the aging baby boomer population is almost completely responsible for this increased utilization. However, the older the patient, the less lifetime risk from the radiation in a	*We believe that we have presented the risks associated with radiation exposure in an appropriate context, noting the tradeoffs that must be considered in older vs. younger patients, single vs. repeat testing, etc.* *As noted in the report, concerns regarding nuclear imaging are associated not only with increasing utilization of these tests but also with an apparent decline in the rate of abnormal findings.*

	Comment	Response
	SPECT examination, and should be considered when formulating this policy.	
5	The final comment is that in elderly populations, where the exercise test is often converted to chemical stress test (either ischemia producing, or blood flow discordance) SPECT has a much more robust database and validated outcomes. Data presented (Table ES3) appears to show that as the studies include more patients, SPECT outperforms Stress Echo, and yet analysis suggested that the testing strategies were equal. An alternative interpretation of the presented data would be, that as long as not many patients are tested, the difference between the two techniques is not as evident.	*The studies presented in Table ES3 were quite heterogeneous in many ways beyond sample size, including outcome definition, duration of follow-up, and statistical methods used. Given these differences, we feel that it is inappropriate to comment on any "trend" in findings based on sample size alone.*
James H. Caldwell, MD, FACC, FAHA, Professor of Medicine and Radiology, Adjunct Professor of Bioengineering, and Director of Nuclear Cardiology, UW Medicine		
1	*The primary objective of this decision analytic model was to evaluate the short-term effectiveness and economic outcomes of cardiac nuclear imaging tests and comparator strategies for diagnosing functionally-significant CAD.* a) While diagnosing functionally-significant CAD is important, it is only part of the equation in providing comprehensive cardiac care. b) The review states that the target population has "stable symptoms of myocardial ischemia (i.e., atypical or typical chest pain or other symptoms such as dyspnea) who were at varying risks of functionally-significant CAD". HOWEVER, as a clinician I need to know if the symptoms are associated with a small or moderate or large amount of myocardium at risk and whether it is mild, moderate or severe ischemia. This is not addressed adequately in the decision analytic model. For example, in Figure D2 of the appendix, only severe stenosis based on the ICA results are used and as the FAME trial (ref 157) has shown, the ICA is a poor predictor of outcome.	*Thank you for your comments.* *We recognize that limitations in available data precluded use of functional reference standard information for all tests, and that anatomic data alone correlates poorly with functional information. Nevertheless, we do note that many treatment decisions are still made based on anatomic data from angiography. We have clarified this in several sections of our description of the model.* *In addition, we conducted sensitivity analyses in which the functional reference standard data for PET and SPECT were used.*
2	*With regard the model assumptions:* a) It is assumed that all patients are fit enough to undergo exercise stress (use of pharmacologic stress for PET is a function of	*We understand that there are clinical realities such those noted that were not reflected in the model. We had to make a number of simplifying*

	Comment	Response
	the device) i) Not a realistic assumption since in my practice only 52% of referred outpatients are able to exercise. b) All patients are able to complete each test (exercise patients achieve target heart rate, stressor infusion is successful, there are no technical failures) i) Again, not a realistic assumption. We start out trying to exercise even those we suspect may not be capable of achieving target heart rate and when they fail (20%) convert them to vasodilator stress while still walking on the treadmill. So the referring provider gets the physiologic information of the patients maximal exercise performance plus the imaging information that can be obtained from vasodilator stress. This is easy to accomplish with SPECT and not possible with echo. c) ICA is assumed to have sensitivity and specificity of 100% (i.e., the "gold" standard) i) Another false assumption since it is well established that stenosis and physiology do not correlate well. See comments regarding FAME trial above.	*assumptions to ensure that the model remained transparent and parsimonious, and note the limitations of these assumptions in the report.* *Please see above for our discussion and treatment of the poor correlation between anatomic and functional data.*
3	*Table 14 and related discussion:* a) The value judgments statement is very important. This population is one that has a high probability of known CAD and already revascularized. What drives the clinical decision process in this population is what is the location and functional severity of a failing CABG or stent in a patient with multi-vessel disease and probably abnormal regional function. This is a situation in which PET really excels since it has the resolution to separate out individual coronary beds and quantify stress myocardial blood flow (mL/m/g) and coronary flow reserve and thus does not have to assume one myocardial region is normal which is required for SPECT and not as subject to trying to determine if abnormal function got worse as a marker of ischemia as is required by echo. Very difficult to include such	*We feel that this comment may be the result of misinterpretation. While the "basecase" population had a high underlying prevalence of CAD and it is likely that some of these patients were known to have disease, we did not make any explicit assumptions about this and it would therefore be impossible to estimate how many of these patients had prior revascularization vs. medical management.*

	Comment	Response
	considerations in a decision analytic model. *Imaging cost data*	
4	a) Since the HCA costs for PET are totally driven by charges from the UW cardiac PET program, they are artificially high since radiotracer charges are high because of low volumes. That is, much of the cost is driven by the cost of sterility testing and other QC testing that is required each day that a radiotracer is synthesized and is fixed regardless of the number synthesis done that day. Thus if larger number of studies were performed per day, the cost per synthesis would be less. Medicare (and subsequently other insurers) in this region has been very restrictive in its indications for cardiac PET and thus have limited the number of studies even though the data (as demonstrated in the current review) indicates that PET is better than SPECT in a number of different aspects (see Tables 11-17). We try to perform studies on a limited number of days per week to increase efficiency but urgency of patient studies and patient satisfaction as to scheduling requires more flexibility than cost considerations allow. The review should at least obtain radiotracer costs from other regions of the country where stress PET volumes are much larger and per-dose costs less and re-run the cost analysis models as a comparison. For example, Brigham and Women's Hospital in Boston does almost 1,000 stress PET's per year.	*As with our prior reviews for the HCA, we chose to model costs based on agency payments for services rendered. While it is likely the case that payments for cardiac PET vary in other areas of the country, it is likely the case that payments for comparator tests also vary regionally.*
5	The review also didn't examine the difference in image quality/diagnostic accuracy of PET vs SPECT or echo in the obese population.	*As noted in the review's Methods section, we focused attention on studies explicitly comparing the tests of interest. We found no studies of obese patients that involved use of both PET and SPECT and measurement of the outcomes of interest.*
6	In the paragraph (page 11) related to the Chang, 2010 reference, in which stress only vs rest/stress was compared, the review failed to note that this required SPECT with **attenuation correction** and attenuation correction is currently not widely used in the nuclear cardiology community. Doing stress only in appropriate populations would reduce the study costs but impact on model would have to be tested since there would be added equipment costs and	*We have modified this section of the review to note that attenuation correction is not in widespread use, and that use of attenuation correction would have both clinical and economic impacts.*

	Comment	Response
	potentially larger number of extra-cardiac findings.	
7	A limitation of several of the studies referenced (example Danand 2013 and Kajander 2010) during the discussion comparing SPECT or PET to FFR is that within an individual study, the reference standard was **either** FFR **or** stenosis 50-70%. It is well recognized that there is a poor correlation between FFR and 50-70% stenosis (see FAME trial) so using either FFR or 50-70% stenosis potentially biases the results against SPECT or PET. Perfusion imaging reflects total of hemodynamic stenosis plus microvascular dysfunction which is not measured by stenosis severity. Thus the comparison should be SPECT or PET vs FFR alone. Furthermore, abnormal perfusion is probably a better predictor of outcome than stenosis severity.	*We have also noted that use of a "hybrid" reference standard provides limited information with which to judge the accuracy of these tests to detect important ischemia.*
8	It would benefit the review if Appendix F also contained the HCA costs for echo during the same time period as well as figures for echo utilization by PEBB similar to Figures 1b and 1c.	*Data on trends in stress ECHO utilization have been added to the "Agency Experience" section of the report.*
Washington Health Care Authority Agency Medical Directors		
1	"Low, intermediate and high risk coronary artery disease" is utilized throughout this report. There does not appear to be a standardized definition included in the report.	*Thank you for these comments. Our consideration of risk was based on pretest probability as first defined by Diamond & Forrester. This has been clarified in the report.*
2	Was the same risk assessment score utilized for all studies and referenced guidelines? If no standardized definition exists, and these terms are utilized in heterogeneous populations, then this needs to be clarified in the report.	*Risk assessment algorithms differed by study; where available, data on the system utilized was abstracted and included in the full evidence tables (Appendix C).*
3	Is known coronary artery disease the same as high risk for coronary artery disease?	*We attempted to separate the evidence on high-risk individuals with suspected CAD vs. those with known CAD, but as noted in the report, many study populations were mixed. Individuals would prior revascularization were considered to have known CAD in our report.*
4	Do post procedure PTCA with stent or CABG patients fall in the high risk category for coronary artery disease?	
5	If the use of low, intermediate and high risk was used because that was the term utilized in the referenced study, without any additional clinical clarification, please include a comment in the report.	*When determination of CAD risk was noted in the study but no information on how risk was categorized was available, this was noted in our data abstraction.*
6	If risk is defined only in terms of pretest probability	*Numeric ranges associated with pretest*

	Comment	Response
	of disease, please include the associated numeric values and whether or not this definition of "risk" is uniform throughout the referenced studies and guidelines.	*probability have been added to the report, along with commentary that these algorithms tend to overstate underlying prevalence (this is described in detail in the model section).*
7	"Consistency," "Directness," and "Precision" are used throughout the report. A definition of these terms and how they are utilized in the majority of summary tables was not identified in the body of report. Please elucidate these terms.	*These terms are defined in the section of the report dealing with the ICER rating system.*
8	ICA is the medical acronym for internal carotid artery and not invasive coronary angiography. Use of ICA in the body of the text is confusing.	*We have changed the reference from "ICA" to "angiography" throughout the report.*
9	**p.30** the derived model estimates utilized systematic reviews for derivation of diagnostic accuracy for ECHO, SPECT and PET. How was diagnostic accuracy defined? Presence or absence of ischemia or presence or absence of coronary artery disease?	*As noted in previous responses, accuracy for the model was defined based on presence of CAD. We note the limitations of this approach in the Model section.*
10	What was the reference test for these systematic reviews?	*Angiography was the gold standard for all systematic reviews used for the model.*
11	In addition, why were these reviews chosen if the probability of inconclusive tests needed to be derived from alternative sources?	*Systematic reviews were used as a source of robust pooled estimates of accuracy for the model. Accuracy studies rarely report the proportion of tests with inconclusive findings, however, so alternative studies focusing on this outcome were utilized.*
12	**p. 31** The Decision-Analytic Model is based on invasive coronary angiography as being the "gold" standard with sensitivity and specificity of 100%. This model is fundamentally flawed because of this assumption. Invasive coronary angiography is the anatomic gold standard but is not considered to be the functional gold standard for detection of myocardial ischemia.	*Please see our responses to comments from UW Medicine above.*
13	Does "stable symptoms of myocardial ischemia" mean symptomatic? Atypical chest pain and dyspnea are used as examples of "stable symptoms."	*Yes. The phrase was added at the suggestion of one of the Agency medical directors, as ischemia does not always present with traditional chest pain as its major symptom.*
14	**p. 31** How was the rate of "ICA negative" determined?	*By definition, these patients had positive results on one or more non-invasive tests but were negative for CAD on angiography (i.e., false-positives).*
15	Were ICA related deaths merely a set percentage of	*Yes, a constant risk of 0.6% was applied to all*

	Comment	Response
	the number of ICA tests performed, or cumulative risks of all tests performed?	*angiographies performed for a given strategy.*
16	**Tables ES 11-13.** Does Low/intermediate/high risk of functionally significant CAD correlate with the low/intermediate/high risk in other tables, eg Table ES2?	*To some extent yes, but as previously noted, pretest probability overstates risk/prevalence, so the assumed risk levels in the model were intended to approximate low, intermediate, and high pretest probability.*
17	**p. 39** Which evidence rating addresses key question 1(e): patients with known CAD who have no changes in symptoms? (prognosis) Symptomatic individuals at high CAD risk or Known CAD?	*We have clarified the evidence ratings to provide separate ratings for patients with known CAD who do and do not have changes in symptoms.*
18	**p. 116** The cost information for treatments considered appears to be for UMP rather than Medicaid? Are these total costs for the tests, eg including facility charge as well as technical component?	*These were PEBB allowed amounts, and did include facility charges unless charges were bundled under a global code.*
19	**pp. 122-125** Is the target population for these tables patients with "stable symptoms of ischemia?"	*Yes.*
20	Do these tables exclude patients with previous stents/grafts?	*Not necessarily, although as noted previously, we did not assume a set percentage would have been revascularized previously.*
21	Does this population include both men and women?	*Yes.*

Heart Institute Office
122 West 7th Ave Suite 450
Spokane, WA 99204
tel: 509.455.8820
fax: 509.838.4978
www.PSHeart.org

Spokane Cardiology

PROVIDENCE
Spokane Heart Institute

July 22, 2013

Re: Public Comment on Final Questions:

The preamble to the final key questions explicitly lists that there are differences in both "…their diagnostic and prognostic capabilities…" but then the first key question completely focuses on the diagnostic portion of the test. An important and well-validated use of SPECT is the prognostic power of the test, independent of whether CAD is present or absent.

Nuclear cardiology for over two decades has been a well-validated tool for either diagnosis or prognosis in low to high-risk populations. Not only has the data been validated, but through the use of statistical quantitative analysis of the images, significant intra-observer variability has been reduced, which is not the case with Stress echocardiography. Academic studies suggest that consensus core reading reduces this variability, but rarely are stress echos interpreted that way in practice.

Academic studies comparing stress echo to MPI, usually exclude patients that were technically suboptimal (an echo problem) to match the diagnostic accuracy in nuclear studies. This is usually about 20% of patients presenting, and had they been analyzed in an intention to treat fashion, Stress echo would not be as accurate as MPI, particularly in the group that can not adequately exercise.

Appropriate Use Criteria have been established for both modalities and have been widely adopted. MPI studies are required to be performed in accredited labs, thereby institutionalizing ongoing quality improvement and standard reporting. Diagnostic accuracy in comparison with Cath is routinely collected to remain accredited.

Radiation exposure carries risk that is not present in stress echo (without contrast) but the misleading portion of this statement is that underdiagnosis of CAD is not a riskless event. Interestingly, this report is being generated because of increasing use of these tests, without addressing the root cause of the increasing use. One of the strongest variables for the development of CAD is age, and demographics in the state of Washington show that the aging baby boomer population is almost completely responsible for this increased utilization. However, the older the patient, the less lifetime risk from the radiation in a SPECT examination, and should be considered when formulating this policy.

The final comment is that in elderly populations, where the exercise test is often converted to chemical stress test (either ischemia producing, or blood flow discordance) SPECT has a much more robust database and validated outcomes. Data presented (Table ES3) appears to show that as the studies include more patients, SPECT outperforms Stress Echo, and yet analysis suggested that the testing strategies were equal.

North Spokane Office
212 East Central Ave, Suite 240
Spokane, WA 99208
tel: 509.482.2025
fax: 509.482.2915

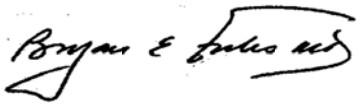
Spokane Valley Office
1215 North McDonald Rd, Suite 202
Spokane, WA 99216
tel: 509.922.0136
fax: 509.922.7976

Lewiston Office
2315 Eighth Street
Lewiston, ID 83501
tel: 208.298.0720
fax: 208.298.0727

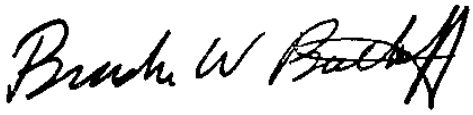
An alternative interpretation of the presented data would be, that as long as not many patients are tested, the difference between the two techniques is not as evident.

Although stress nuclear imaging and stress echocardiography are similar this is one time where redundancy of testing is useful and the decision should be left to the clinician. It is clear that centers of excellence perform similarly. But there is no clear way to predict which center has developed expertise. Leaving that decision to the clinician with continuing feedback is probably an important and necessary way to continue to ensure the best care for patients locally.

Respectfully submitted:



Bryan E Fuhs MD, FACC
Invasive Non-Interventional Cardiologist, Providence Spokane Cardiology
Joint Operating Committee Member, Providence Spokane Heart Institute



Braden W Batkoff, MD, FACC
President, Providence Spokane Heart Institute & Providence Spokane Cardiology
Joint Operating Committee Chair, Providence Spokane Heart Institute

Janice D Christensen, MD, FACC
Non-Invasive Director, Providence Spokane Cardiology
Providence Spokane Heart Institute

UW Medicine
DEPARTMENT OF MEDICINE
DIVISION OF CARDIOLOGY

James H. Caldwell, MD
Director, Nuclear Cardiology
Professor, Medicine and Radiology

September 6, 2013

Washington State Health Care Authority
P.O. Box 42712
Olympia, Washington 98504

Re: UW Medicine Comments on the Health Technology Assessment of Cardiac Nuclear Imaging

Dear HCA Director;

In response the HTA Draft Evidence Report dated 21 June 2013 and as active members of the UW Medicine cardiovascular imaging community, I have the following comments.

The review is for the most part comprehensive and tries to deal with literature that at best is suboptimal because of lack of randomized control trials, changing technology and changing approaches to risk-factor modifications which changes patient populations (not even considered) during the time period covered by the review. I have a few specific comments about the articles referenced but will focus my primary remarks on the decision analytic model, recognizing the challenges of the decision-analytic model approach.

1) *The primary objective of this decision analytic model was to evaluate the short-term effectiveness and economic outcomes of cardiac nuclear imaging tests and comparator strategies for diagnosing functionally-significant CAD.*
   a) While diagnosing functionally-significant CAD is important, it is only part of the equation in providing comprehensive cardiac care.
   b) The review states that the target population has "stable symptoms of myocardial ischemia (i.e., atypical or typical chest pain or other symptoms such as dyspnea) who were at varying risks of functionally-significant CAD". HOWEVER, as a clinician I need to know if the symptoms are associated with a small or moderate or large amount of myocardium at risk and whether it is mild, moderate or severe ischemia. This is not addressed adequately in the decision analytic model. For example, in Figure D2 of the appendix, only severe stenosis based on the ICA results are used and as the FAME trial (ref 157) has shown, the ICA is a poor predictor of outcome.

2) With regard the model assumptions:
   a) It is assumed that all patients are fit enough to undergo exercise stress (use of pharmacologic stress for PET is a function of the device)
      i) Not a realistic assumption since in my practice only 52% of referred outpatients are able to exercise.
   b) All patients are able to complete each test (exercise patients achieve target heart rate, stressor infusion is successful, there are no technical failures)
      i) Again, not a realistic assumption. We start out trying to exercise even those we suspect may not be capable of achieving target heart rate and when they fail (20%) convert them to vasodilator stress while still walking on the treadmill. So the referring provider gets the

physiologic information of the patients maximal exercise performance plus the imaging information that can be obtained from vasodilator stress. This is easy to accomplish with SPECT and not possible with echo.

c) ICA is assumed to have sensitivity and specificity of 100% (i.e., the "gold" standard)

i) Another false assumption since it is well established that stenosis and physiology do not correlate well. See comments regarding FAME trial above.

3) Table 14 and related discussion:
   a) The value judgments statement is very important. This population is one that has a high probability of known CAD and already revascularized. What drives the clinical decision process in this population is what is the location and functional severity of a failing CABG or stent in a patient with multi-vessel disease and probably abnormal regional function. This is a situation in which PET really excels since it has the resolution to separate out individual coronary beds and quantify stress myocardial blood flow (mL/m/g) and coronary flow reserve and thus does not have to assume one myocardial region is normal which is required for SPECT and not as subject to trying to determine if abnormal function got worse as a marker of ischemia as is required by echo. Very difficult to include such considerations in a decision analytic model.
4) Imaging cost data
   a) Since the HCA costs for PET are totally driven by charges from the UW cardiac PET program, they are artificially high since radiotracer charges are high because of low volumes. That is, much of the cost is driven by the cost of sterility testing and other QC testing that is required each day that a radiotracer is synthesized and is fixed regardless of the number synthesis done that day. Thus if larger number of studies were performed per day, the cost per synthesis would be less. Medicare (and subsequently other insurers) in this region has been very restrictive in its indications for cardiac PET and thus have limited the number of studies even though the data (as demonstrated in the current review) indicates that PET is better than SPECT in a number of different aspects (see Tables 11-17). We try to perform studies on a limited number of days per week to increase efficiency but urgency of patient studies and patient satisfaction as to scheduling requires more flexibility than cost considerations allow. The review should at least obtain radiotracer costs from other regions of the country where stress PET volumes are much larger and per-dose costs less and re-run the cost analysis models as a comparison. For example, Brigham and Women's Hospital in Boston does almost 1,000 stress PET's per year.
5) The review also didn't examine the difference in image quality/diagnostic accuracy of PET vs SPECT or echo in the obese population.

Additional comments:

1. In the paragraph (page 11) related to the Chang, 2010 reference, in which stress only vs rest/stress was compared, the review failed to note that this required SPECT with **attenuation correction** and attenuation correction is currently not widely used in the nuclear cardiology community. Doing stress only in appropriate populations would reduce the study costs but impact on model would have to be tested since there would be added equipment costs and potentially larger number of extra-cardiac findings.
2. A limitation of several of the studies referenced (example Danand 2013 and Kajander 2010) during the discussion comparing SPECT or PET to FFR is that within an individual study, the reference standard was **either** FFR **or** stenosis 50-70%. It is well recognized that there is a poor correlation between FFR and 50-70% stenosis (see FAME trial) so using either FFR or 50-70% stenosis potentially biases the results against SPECT or PET. Perfusion imaging reflects total of hemodynamic stenosis plus microvascular dysfunction which is not measured

by stenosis severity. Thus the comparison should be SPECT or PET vs FFR alone. Furthermore, abnormal perfusion is probably a better predictor of outcome than stenosis severity.

3. It would benefit the review if Appendix F also contained the HCA costs for echo during the same time period as well as figures for echo utilization by PEBB similar to Figures 1b and 1c.
4. I concur completely with recommendations regarding additional research studies needed for stress nuclear myocardial perfusion imaging. The same can be said for stress echo and for stress cardiac MR which is evolving quickly into a clinically realistic modality.

Sincerely,

James H. Caldwell, MD, FACC, FAHA
Professor of Medicine and Radiology
Adjunct Professor of Bioengineering
Director Nuclear Cardiology
UW Medicine

Agency Medical Directors Comments on Draft Report: Cardiac Nuclear Imaging

Evidence Researcher: Institute for Clinical & Economic Review
Report Date: June 21, 2013

Specifically gated single-photon emission computed tomography myocardial perfusion imaging (SPECT) and positron emission tomography (PET), have become the standard of care for evaluation of myocardial perfusion. Detailed "appropriate use" criteria have been jointly published by the American College of Cardiology Foundation, American Heart Association, American College of Physicians, American Society of Nuclear Cardiology, American College of Radiology, American Society of Echocardiography, American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association, Society for Cardiovascular Angiography and Interventions, and the Society of Thoracic Surgeons. Given the widely accepted use of these published criteria, the AMDG work group requested an evidence evaluation in order to aid in the selection of conditions of coverage for use of these imaging modalities in patients with known or suspected coronary artery disease, comparative effectiveness of different myocardial perfusion imaging modalities, cost effectiveness of these noninvasive modalities, impact on downstream imaging and clinical outcomes. The evidence summary for varying risk groups is effective and helpful. There are several flaws in the assumptions made for the decision-analytic model, and thus this model does not appear to add tremendous value to the report. Comments are as follows:

"Low, intermediate and high risk coronary artery disease" is utilized throughout this report. There does not appear to be a standardized definition included in the report. Was the same risk assessment score utilized for all studies and referenced guidelines? If no standardized definition exists, and these terms are utilized in heterogeneous populations, then this needs to be clarified in the report. If the final committee decision is dependent upon low/intermediate/high risk for coronary artery disease the agencies will not be able to implement the coverage decision without a clear definition of the risk categories. Is known coronary artery disease the same as high risk for coronary artery disease? Do post procedure PTCA with stent or CABG patients fall in the high risk category for coronary artery disease? If the use of low, intermediate and high risk was used because that was the term utilized in the referenced study, without any additional clinical clarification, please include a comment in the report. If risk is defined only in terms of pretest probability of disease please include the associated numeric values and whether or not this definition of "risk" is uniform throughout the referenced studies and guidelines.

"Consistency," "Directness," and "Precision" are used throughout the report. A definition of these terms and how they are utilized in the majority of summary tables was not identified in the body of report. Please elucidate these terms. Eg does "consistency" mean consistency of findings within the study or consistency of findings across studies?

ICA is the medical acronym for internal carotid artery and not invasive coronary angiography. Use of ICA in the body of the text is confusing.

p.30 the derived model estimates utilized systematic reviews for derivation of diagnostic accuracy for ECHO, SPECT and PET. How was diagnostic accuracy defined? Presence or absence of ischemia or presence or absence of coronary artery disease? What was the reference test for these systematic reviews? In addition, why were these reviews chosen if the probability of inconclusive tests needed to be derived from alternative sources?

p. 31 The Decision-Analytic Model is based on invasive coronary angiography as being the "gold" standard with sensitivity and specificity of 100%. This model is fundamentally flawed because of this assumption. Invasive coronary angiography is the anatomic gold standard but is not considered to be the functional gold standard for detection of myocardial ischemia. Does "stable symptoms of myocardial ischemia" mean symptomatic? Atypical chest pain and dyspnea are used as examples of "stable symptoms."

p. 31 How was the rate of "ICA negative" determined? Were ICA related deaths merely a set percentage of the number of ICA tests performed, or cumulative risks of all tests performed?

Tables ES 11-13. Does Low/intermediate/high risk of functionally significant CAD correlate with the low/intermediate/high risk in other tables, eg Table ES2?

p. 39 Which evidence rating addresses key question 1(e): patients with known CAD who have no changes in symptoms? (prognosis) Symptomatic individuals at high CAD risk or Known CAD?

p. 116 The cost information for treatments considered appears to be for UMP rather than Medicaid? Are these total costs for the tests, eg including facility charge as well as technical component?

pp. 122-125 Is the target population for these tables patients with "stable symptoms of ischemia?" Do these tables exclude patients with previous stents/grafts? Does this population include both men and women?