

## HERC Coverage Guidance – Coronary Artery Calcium Scoring Disposition of Public Comments

### General Comments

Stakeholder	#	Comment	Disposition
Society of Cardiovascular Computed Tomography Vienna, VA	1	It appears that the documents the committee reviewed, while appropriate, under-represented the data available regarding coronary calcium. Below please find some additional information related to the indications addressed. As Medicare and other payers including the California Technology Assessment Forum (Blue Cross/Blue Shield Tech Assessment) have made positive determinations in regarding coronary calcium coverage, we would hope you would consider the following information as supplemental. If it pleases the committee, we would be glad to provide a Professor of Medicine to present the data in a scientific forum to help address the specific questions regarding the science	Thank you for taking the time to comment. Medicare coverage policy as reported in the WA HTA report noted no national coverage decision, and a non-coverage local (Washington) coverage decision. We searched the Medicare Coverage Database and identified no positive coverage decision and one non-coverage local coverage decision from Minnesota. The California Technology Assessment Forum has made determinations on cardiac CT angiography, but we are unable to identify a determination on EBCT or CACS, or a BCBS Technology Assessment on those topics.
	2	Below are some specific comments regarding the document and some additional data. <b>UK NICE GUIDELINES</b> The SCCT would like to point out that the UK Guidelines are based upon very large observational cohorts (>1000 patients) and studies of >8 year follow up, not “One small retrospective study looked at 4 month follow up on 100 patients in ED where CACS score was taken, along with other tests and concluded that a score of 0 could permit a discharge.” There are numerous studies documenting efficacy, without the need of a functional test.	EbGS is aware of the literature used by the NICE guidelines, and that their rationale for coverage of CACS is based on a favorable cost-effectiveness evaluation that is specific to the UK healthcare delivery system.  The quote identified is directly from the WA HTA clinical committee findings, not from the EbGS. While the WA HTA clinical committee elected to comment on this one study in their findings report, EbGS agrees that there are other larger case series presented and discussed in the WA HTA report. A total of 5 case series that evaluated patients presenting to the ED were identified. Given that none used a control group, the ability to draw conclusions about the impact of CACS on clinical decisions is limited.
	3	Large studies have documented efficacy of CAC in the emergency department and the ability to safely discharge patients. In a study of 1031 patients that presented to the emergency room with chest pain and had a non-ischemic electrocardiogram, normal initial troponin, and no history of CAD, Nabi et al showed that a CAC score of 0 predicted a normal nuclear stress test and excellent short term outcome. <sup>1</sup> Event rate was 0.3% at 6 months for those persons who had a CAC of zero (>61% of the total cohort).	<sup>1</sup> Nabi is a case series (N=1031) of patients with chest pain suggestive of ischemia without elevated troponin or EKG changes admitted for observation. Outcomes were as described by the commenter.  As a case series, it is unclear how this compares with evaluation using other modalities.
	4	Furthermore, there have been studies with up to 8 years outcome after a negative CAC scan in the ED setting (without any functional testing), validating the safety of a CAC test, demonstrating no events in those with zero calcification. <sup>2</sup>	<sup>2</sup> Georgiou 2001 was published before the date of the WA HTA report and the NICE guideline. The EbGS bases their guidance documents on reviews of the literature that utilize the highest standards of evidence-based medicine. Studies are included or excluded based on transparent, reproducible

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			criteria; therefore the EbGS does not investigate individual studies. The EbGS assumes that the conclusions reached by the authors of these reviews weigh all the available evidence in accordance with the principles of evidence based medicine, and does not attempt to re-review the entire body of evidence to reach its own conclusions.
	5	A meta-analysis of 64,873 patients followed over 4.2 years similarly showed a 0.13% annual event rate for patients with 0 CAC scores. <sup>3</sup> This results in a negative predictive power of >99.5% for a score of zero (no detectable CAC) in symptomatic persons, which is higher than other advocated strategies such as stress testing or nuclear imaging in this setting. There are at least 6 prospective studies documenting the efficacy of the use of CAC testing in the ED or acute setting, all documenting the safety and efficacy of using coronary artery calcium in this setting.	<p><sup>3</sup>Sarwar 2009 was a systematic review that included a meta-analysis of 7 studies of symptomatic patients (N=3924). Inclusion criteria were broad and without limitations in study design. While not specifically stated, it appears that none of the seven had a control group, making this meta-analysis simply a large case series. It is unclear how CACS compares to evaluation of the symptomatic patient using other modalities.</p> <p>Of those with zero calcium, there was a 1.8% event rate over a mean follow up of 3.5 years. There was a much larger population of asymptomatic participants (71,595). (Unclear what the 64,873 number cited by the commenter refers to.)</p> <p>Citations for the 6 prospective studies not provided.</p>
	6	We would encourage you to consider this indication, given the support of the American Heart Association <sup>4</sup> ,	<p>AHA guidelines state the following: “Coronary calcium assessment may be reasonable for the assessment of symptomatic patients, especially in the setting of equivocal treadmill or functional testing (Class IIb, Level of Evidence: B). There are other situations when CAC assessment might be reasonable. CACP measurement may be considered in the symptomatic patient to determine the cause of cardiomyopathy (Class IIb, Level of Evidence: B). Also, patients with chest pain with equivocal or normal ECGs and negative cardiac enzyme studies may be considered for CAC assessment (Class IIb, Level of Evidence: B).”</p> <p>The AHA uses the following classification for their recommendations:</p> <ul style="list-style-type: none"> <li>• Class I: Conditions for which there is evidence, general agreement, or both that a given procedure or treatment is useful and effective.</li> <li>• Class II: Conditions for which there is conflicting evidence, a divergence of opinion, or both about the usefulness/efficacy of a procedure or treatment.</li> <li>• Class IIa: Weight of evidence/opinion is in favor of usefulness/efficacy.</li> </ul>

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			<ul style="list-style-type: none"> <li>Class IIb: Usefulness/efficacy is less well established by evidence/opinion.</li> <li>Class III: Conditions for which there is evidence, general agreement, or both that the procedure/treatment is not useful/effective and in some cases may be harmful.</li> </ul> <p>The AHA uses the following classification for their Level of Evidence</p> <ul style="list-style-type: none"> <li>Level of Evidence A: Data derived from multiple randomized clinical trials</li> <li>Level of Evidence B: Data derived from a single randomized trial or nonrandomized studies</li> <li>Level of Evidence C: Consensus opinion of experts</li> </ul> <p>EbGS makes their decisions based on the best available evidence of effectiveness and harms as represented in the source evidence documents, not on the basis of guidelines that are of unknown quality. In addition, the recommendation on the use of CACS is rated class IIb, for which “efficacy is less well established”.</p>
	7	American College of Cardiology <sup>5</sup> ,	<p>The ACC consensus statement states the following for symptomatic patients: “In direct-comparison studies, CAC detection in the symptomatic person has been shown to be comparable to nuclear exercise testing in the detection of obstructive CAD. Given the prognostic information that is implicit in exercise capacity, even when it is combined with imaging, fast CT starts with a disadvantage compared with existing modalities in symptomatic patients who can exercise. Anatomic testing, such as cardiac CT (whether with contrast in the form of CT angiography or without contrast, such as CAC assessment), should be relegated to second line testing or considered when functional testing is either not possible or indeterminate.”</p> <p>“Considerable discussion among the group focused on the best and most proper way to assess clinical appropriateness of tests such as CAC measurement <i>since there have been no clinical trials to evaluate the impact of CAC testing on clinical outcomes</i> [italics added] in either symptomatic or asymptomatic patients.”</p>

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			<p>Also: “Is there evidence that coronary calcium measurement is better than other potentially competing tests in intermediate risk patients for modifying cardiovascular disease risk estimate?”</p> <p>In general, CAC measurement has not been compared to alternative approaches to risk assessment in head-to-head studies. This question cannot be adequately answered from available data.”</p> <p>And: “Is there a role of CAC testing in patients with atypical cardiac symptoms?”</p> <p>Evidence indicates that patients considered to be at low risk of coronary disease by virtue of atypical cardiac symptoms may benefit from CAC testing to help in ruling out the presence of obstructive coronary disease. Other competing approaches are available, and most of these competing modalities have not been compared head-to-head with CAC.”</p> <p>EbGS makes their decisions based on the best available evidence of effectiveness and harms as represented in the source evidence documents, not on the basis of guidelines that are of unknown quality.</p>
	8	UK NICE Guidelines and European guidelines <sup>6</sup> in this regard.	<p>The NICE guidelines are included in the guidance document; EbGS is aware of their recommendations and that their rationale for coverage of CACS is based on a favorable cost-effectiveness evaluation that is specific to the UK healthcare delivery system.</p> <p>The European guidelines use essentially the same classification system for their recommendations and evidence levels as the AHA. In addition they include suggested wording based on the Class as follows:</p> <ul style="list-style-type: none"> <li>• Class I – Is recommended</li> <li>• Class IIa – Should be considered</li> <li>• Class IIb – May be considered</li> <li>• Class III – Is not recommended</li> </ul>

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			<p>Their recommendations are as follows:</p> <p>“Computed tomography for coronary calcium should be considered for cardiovascular risk assessment in asymptomatic adults at moderate risk.” Class IIa Recommendation, Level of Evidence: B, GRADE: Weak</p> <p>EbGS makes their decisions based on the best available evidence of effectiveness and harms as represented in the source evidence documents, not on the basis of guidelines that are of unknown quality.</p>
	9	<p>“The committee noted that national guidelines do not endorse the use of CACS, though some have permissive statements for use of the test.”</p> <p>There are actually several national guidelines that endorse the use of CACS, that perhaps were not made available to the committee.</p>	<p>As above, this is a direct quote from the findings of the WA HTA Clinical Committee. The WA HTA report that served as their evidence source (and was also one of the source documents for this guidance) included guidelines from the following entities:</p> <p>ACCF/AHA 2007 Clinical Expert Consensus document on CACS by CT in global CV risk assessment and in evaluation of patients with chest pain. (see comment #7).</p> <p>AHA Committee on CV Imaging and Intervention: Assessment of coronary artery disease by CCT 2006 (see comment #6).</p> <p>ACC/AHA expert consensus document on EBCT for the diagnosis and prognosis of CAD (2000).</p> <p>American College of Radiology Appropriateness Criteria (2008): CACS received a score of 3 (most appropriate = 9, least appropriate = 1)</p>
	10	<p>The most notable and specific guideline covering this indication is the 2010 ACCF/AHA Guideline for Assessment of Cardiovascular Risk in Asymptomatic Adults: A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines.<sup>7</sup> This statement advocates for the use of coronary calcium testing for intermediate risk asymptomatic persons, as well as for those with diabetes. This was reinforced by another guideline in 2012 from the European Guidelines on cardiovascular disease prevention in clinical practice (version</p>	<p>The ACCF/AHA guideline (2010) referenced by the commenter makes the following recommendations regarding asymptomatic patients:</p> <p>CLASS IIa (is reasonable to perform)</p> <p>1. Measurement of CAC is reasonable for cardiovascular risk assessment in asymptomatic adults at intermediate risk (10% to 20% 10-year risk). (<i>Level of Evidence: B</i>)</p> <p>CLASS IIb (may be considered)</p> <p>1. Measurement of CAC may be reasonable for cardiovascular risk</p>

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		2012). <sup>6</sup>	<p>assessment in persons at low to intermediate risk (6% to 10% 10-year risk). (<i>Level of Evidence: B</i>)</p> <p>CLASS III: NO BENEFIT (should not be done)</p> <p>1. Persons at low risk (&lt;6% 10-year risk) should not undergo CAC measurement for cardiovascular risk assessment. (<i>Level of Evidence: B</i>)</p> <p>CLASS IIa (is reasonable to perform)</p> <p>1. In asymptomatic adults with diabetes, 40 years of age and older, measurement of CAC is reasonable for cardiovascular risk assessment. (<i>Level of Evidence: B</i>)</p> <p>For European guidelines, see comment #8.</p> <p>Class IIb recommendations are used when “efficacy is less well established”.</p> <p>EbGS makes their decisions based on the best available evidence of effectiveness and harms as represented in the source evidence documents, not on the basis of guidelines that are of unknown quality.</p>
	11	In 2010, the ACCF, AHA, and other organizations, including the Society for Cardiovascular Computed Tomography and the American College of Radiology published appropriate use criteria for cardiac CT for selected patient indications. <sup>8</sup> They rated calcium scoring as appropriate in patients at low or intermediate risk but uncertain (optional) in high risk patients.	<p>The referenced guideline states, in summary, patients: “Use of noncontrast computed tomography (CT) for calcium scoring was rated as appropriate within intermediate- and selected low-risk patients.”</p> <p>For asymptomatic patients, appropriateness ranged from appropriate to inappropriate depending on global CHD risk estimate. They consider it appropriate for patients at low risk (&lt;10%) with a positive family history of premature CHD, or for patients with intermediate risk (10-20%). Appropriateness was uncertain for high risk asymptomatic patients, and inappropriate for low risk asymptomatic patients (&lt;10%). For symptomatic patients, no appropriateness scores were provided for CACS (only for CCTA).</p> <p>EbGS makes their decisions based on the best available evidence of effectiveness and harms as represented in the source evidence documents, not on the basis of guidelines that are of unknown quality.</p>
	12	The 2007 ACC Expert Consensus document on Coronary Artery Calcium also endorsed the use of CAC testing for asymptomatic persons, stating “CAC scoring has an increasingly high level of quality evidence on its role in	<p>With regard to asymptomatic patients at intermediate risk, the guideline states the following: “The Committee judged that it may be reasonable to consider use of CAC</p>

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		<p>risk stratification of asymptomatic patients. Recent evidence is supportive that measurement of CAC is predictive of CHD death or MI at 3 to 5 years... The accumulating evidence suggests that asymptomatic individuals with an intermediate FRS may be reasonable candidates for CHD testing using CAC as a means of modifying risk prediction and altering therapy.”<sup>5</sup></p>	<p>measurement in such patients based on available evidence that demonstrates incremental risk prediction information in this selected (intermediate risk) patient group. This conclusion is based on the possibility that such patients might be reclassified to a higher risk status based on high CAC score, and subsequent patient management may be modified.”</p> <p>Despite the statement cited by the commenter and the theoretical possibility, there remains no firm evidence to support use of CACS “as a means of modifying risk prediction and altering therapy.”</p> <p>EbGS makes their decisions based on the best available evidence of effectiveness and harms as represented in the source evidence documents, not on the basis of guidelines that are of unknown quality.</p>
	13	<p>Furthermore, the 2010 ACC/AHA Guidelines and the 2012 European guidelines both advocate for the test, with Class IIA recommendations for CAC in asymptomatic persons. This is a stronger recommendation than most other tests evaluated, including advanced lipid testing, C-reactive protein testing, homocysteine testing and treadmill testing, all covered services in your system. It is not consistent to reimburse tests with lower recommendations by the ACC/AHA Guidelines without covering CAC in the same setting. There is no standard to show that a diagnostic test should improve outcomes, it is up to the treatment modality to cover the test.</p>	<p>See comments #8 and #10. While the EbGS appreciates the recommendations from the ACC/AHA, they make their decisions based on the best available evidence of effectiveness and harms as represented in the source evidence documents, not on the basis of guidelines that are of unknown quality. In addition, the cost of CACS is substantially higher than the tests mentioned by the commenter, and potentially higher risk given the radiation exposure incurred by the patient. Further, a number of these tests will be evaluated in a subsequent coverage guidance.</p>
	14	<p>Several randomized prospective trials have demonstrated that undergoing CAC testing has resulted in lower event rates or lower Framingham Risk (Eisner study and St Francis Randomized Trial). This documents that those undergoing CAC testing have evidence of improved health status. This is more substantial and validated data than is available for algorithms that involve Framingham risk assessment, lipid testing or other commonly covered tests. Thus again, this test has or exceeds the necessary evidence for coverage, and exceeds that of many other covered tests used in similar context.</p>	<p>Citations not provided, unable to confirm findings.</p>
	15	<p>All current guidelines, from the European Society of Cardiology,<sup>1</sup> American College of Cardiology and American Heart Association<sup>2</sup>, all give coronary artery calcium a Class IIA recommendation for use in asymptomatic modest (intermediate) risk patients. Regarding CAC, the Joint ESC Statement<sup>1</sup></p>	<p>EbGS disagrees that “all current guidelines” recommend use of CACS in asymptomatic intermediate risk patients, since the USPSTF does NOT recommend use of CACS in asymptomatic patients, regardless of risk.</p>

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		concludes “Although calcium scanning is widely applied today, it is especially suited for patients at moderate risk. The radiation exposure with the properly selected techniques is <1 mSv.” (Class IIa Recommendation).	
	16	<p>The European Working Group made separate guidelines in 2011<sup>9</sup> also recommending this test in asymptomatic persons at intermediate risk, and made the very succinct statement “In summary, there is overwhelming evidence that coronary calcification represents a strong marker of risk for future cardiovascular events in asymptomatic individuals and has prognostic power above and beyond traditional risk factors.” We agree that demonstrating improved mortality in those undergoing a CAC scan would be optimal, but not practical. The sample size for such a study has been estimated around 100,000 persons. We have no outcome data showing improved mortality or morbidity with <b>ANY</b> cardiac test currently available. There is <b>NO</b> data that exercise treadmill testing, echocardiography, stress imaging or even cardiac catheterization improve outcomes; yet we understand as clinicians the important role they each play. Even total risk assessment (such as calculating Framingham Risk) has not been validated to improve outcomes.<sup>3</sup> Thus, the cumulative evidence is very strong supporting CAC testing in the specific population of intermediate risk, and consistent with every published guideline, should be covered and applied in this population.</p> <p>Thank you for your time and consideration.</p>	<p>EbGS agrees that there is no evidence of improved outcomes with the use of CACS, and it has the potential to be more costly and less safe than alternative diagnostic modalities. With regard to asymptomatic patients, EbGS disagrees that “every published guideline” supports coverage, since the USPSTF does NOT recommend use of CACS in asymptomatic patients.</p>