

## Medical Policy



**Title: Computed Tomography (CT) to Detect Coronary Artery Calcification**

Related Policies:	▪ <i>Contrast-Enhanced CCTA for Coronary Artery Evaluation</i>
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<b>Professional / Institutional</b>
Original Effective Date: April 2002 / February 2005
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Populations	Interventions	Comparators	Outcomes
Individuals: • Who are asymptomatic with risk of coronary artery disease	Interventions of interest are: • Coronary artery calcium scoring in combination standard risk stratification	Comparators of interest are: • Coronary artery disease risk factor stratification based on standard risks	Relevant outcomes include: • Overall survival • Test accuracy • Test validity • Morbid events • Resource utilization
Individuals: • With signs and/or symptoms	Interventions of interest are:	Comparators of interest are:	Relevant outcomes include: • Overall survival

Populations	Interventions	Comparators	Outcomes
suggestive of coronary artery disease	<ul style="list-style-type: none"> <li>Coronary artery calcium scoring before other diagnostic testing</li> </ul>	<ul style="list-style-type: none"> <li>Standard diagnostic testing</li> </ul>	<ul style="list-style-type: none"> <li>Test accuracy</li> <li>Test validity</li> <li>Morbid events</li> <li>Resource utilization</li> </ul>

**DESCRIPTION**

Several types of fast computed tomography (CT) imaging, including electron-beam CT and spiral CT, allow the quantification of calcium in coronary arteries. Coronary artery calcium (CAC) is associated with coronary artery disease (CAD). The use of CAC scores has been studied in the prediction of future risk of CAD and in the diagnosis of CAD in symptomatic individuals.

**OBJECTIVE**

The objective of this evidence review is to evaluate the net health outcome of the use of computed tomography to detect coronary artery calcium in 2 settings:

1. For patients with risk of coronary artery disease, who are asymptomatic, does the use of coronary artery calcium scoring as an adjunct standard risk stratification to manage treatment result in improvement in cardiac risk factors?
2. For patients with chest pain symptoms suggestive of coronary artery disease, compared to standard diagnostic testing, does the use of coronary artery calcium scoring to rule out coronary artery disease reduce the use of unnecessary invasive coronary angiography?

**BACKGROUND**

**Coronary Artery Calcium**

Coronary artery calcium (CAC) is associated with coronary artery disease (CAD). The development of fast computed tomography (CT) scanners has allowed the measurement of CAC in clinical practice. Coronary artery calcium has been evaluated in several clinical settings. The most widely studied indication is for the use of CAC in the prediction of future risk of CAD in patients with subclinical disease, with the goal of instituting appropriate risk-reducing therapy (e.g., statin treatment, lifestyle modifications) to improve outcomes. Also, CAC has been evaluated in patients with symptoms potentially consistent with CAD, but in whom a diagnosis is unclear.

**Detection**

Electron-beam computed tomography (EBCT; also known as ultrafast CT) and spiral CT (or helical CT) may be used as an alternative to conventional CT scanning due to faster throughput. In both methods, the speed of image acquisition gives them unique value for imaging a moving heart. The rapid image acquisition time virtually eliminates motion artifact related to cardiac contraction, permitting visualization of the calcium in the epicardial coronary arteries. Electron-beam computed tomography software permits quantification of calcium area and density, which are translated into calcium scores. Calcium scores have been investigated as a technique for detecting CAC, both as a diagnostic technique in symptomatic patients to rule out an

atherosclerotic etiology of symptoms or, in asymptomatic patients, as an adjunctive method for risk stratification for CAD.

Electron-beam computed tomography and multidetector CT were initially the primary fast CT methods for measurement of CAC. A fast CT study for CAC measurement takes 10 to 15 minutes and requires only a few seconds of scanning time. More recently, computed tomography angiography has been used to assess coronary calcium. Because of the basic similarity between EBCT and computed tomography angiography in measuring coronary calcium, it is expected that computed tomography angiography provides information on coronary calcium that is similar to EBCT.

Computed tomography scan-derived coronary calcium measures have been used to evaluate coronary atherosclerosis. Coronary calcium is present in coronary atherosclerosis, but atherosclerosis detected may or may not be causing ischemia or symptoms. Coronary calcium measures may be correlated with the presence of critical coronary stenoses or serve as a measure of the patient's proclivity toward atherosclerosis and future coronary disease. Thus, coronary calcium could serve as a variable to be used in a risk assessment calculation to determine appropriate preventive treatment in asymptomatic patients. Alternatively, in other clinical scenarios, coronary calcium scores might help determine whether there is an atherosclerotic etiology or component to the presenting clinical problem in symptomatic patients, thus helping to direct further workup for the clinical problem. In this second scenario, a calcium score of 0 usually indicates that the patient's clinical problem is unlikely to be due to atherosclerosis and that other etiologies should be more strongly considered. In neither case does the test determine a specific diagnosis. Most clinical studies have examined coronary calcium for its potential use in estimating the risk of future coronary heart disease events.

### **Nomenclature**

Coronary calcium levels can be expressed in many ways. The most common method is the Agatston score, which is a weighted summed total of calcified coronary artery area observed on CT. This value can be expressed as an absolute number, commonly ranging from 0 (low-risk) to 400 (high-risk). These values can be translated into age- and sex-specific percentile values. Different imaging methods and protocols will produce different values based on the specific algorithm used to create the score, but the correlation between any 2 methods appears to be high, and scores from 1 method can be translated into scores from a different method.

### **REGULATORY STATUS**

Many models of CT devices, including EBCT and other ultrafast CT devices, have been cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process. U.S. FDA product code: JAK.

## **POLICY**

The use of computed tomography (CT) to detect coronary artery calcification (CAC) is considered **experimental / investigational**.

**Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.**

## **RATIONALE**

This evidence review has been updated regularly with searches of the PubMed database. The most recent literature update was performed through July 11, 2024.

Evidence reviews assess whether a medical test is clinically useful. A useful test provides information to make a clinical management decision that improves the net health outcome. That is, the balance of benefits and harms is better when the test is used to manage the condition than when another test or no test is used to manage the condition.

The first step in assessing a medical test is to formulate the clinical context and purpose of the test. The test must be technically reliable, clinically valid, and clinically useful for that purpose. Evidence reviews assess the evidence on whether a test is clinically valid and clinically useful. Technical reliability is outside the scope of these reviews, and credible information on technical reliability is available from other sources.

Of note, this review was informed, in part, by a TEC Assessment (1998).<sup>1</sup>

Promotion of greater diversity and inclusion in clinical research of historically marginalized groups (e.g., People of Color [African-American, Asian, Black, Latino and Native American]; LGBTQIA (Lesbian, Gay, Bisexual, Transgender, Queer, Intersex, Asexual); Women; and People with Disabilities [Physical and Invisible]) allows policy populations to be more reflective of and findings more applicable to our diverse members. While we also strive to use inclusive language related to these groups in our policies, use of gender-specific nouns (e.g., women, men, sisters, etc.) will continue when reflective of language used in publications describing study populations.

## **CORONARY ARTERY CALCIUM SCORING IN ASYMPTOMATIC INDIVIDUALS**

### **Clinical Context and Test Purpose**

The purpose of coronary artery calcium (CAC) scoring using computed tomography (CT) in asymptomatic individuals is to assess who may benefit from preventive interventions targeted to minimize the risk of atherosclerotic cardiovascular disease (ASCVD).

The following PICO was used to select literature to inform this review.

### ***Populations***

The population of interest is individuals who are asymptomatic with risk of CAD.

**Interventions**

The intervention of interest is CAC scoring using fast CT imaging, including electron-beam computed tomography (EBCT) and spiral CT, in combination with standard risk stratification.

Coronary artery calcium scoring is usually initiated or used to modify cardiac risk-reduction interventions in individuals asymptomatic for CAD.

**Comparators**

The following tool is currently being used to make decisions about managing cardiovascular disease (CVD) in asymptomatic patients: CAD risk factor stratification based on standard risks, such as the Framingham Risk Score (FRS).

**Outcomes**

The outcomes of interest include overall survival (OS), test accuracy, test validity, morbid events (e.g., major adverse cardiac events [MACEs]), as well as the need for invasive coronary angiography (ICA) and revascularization.

Intermediate or surrogate outcomes of interest are changes in cardiac risk profile indicators such as smoking, hyperlipidemia, or hypertension.

**Study Selection Criteria**

For the evaluation of clinical validity of CAC scoring using CT, studies that meet the following eligibility criteria were considered:

- Reported on the accuracy of the marketed version of the technology;
- Included a suitable reference standard;
- Patient/sample clinical characteristics were described;
- Patient/sample selection criteria were described;
- The study reported on a minimum of 1000 patients.

**Clinically Valid**

A test must detect the presence or absence of a condition, the risk of developing a condition in the future, or treatment response (beneficial or adverse).

**REVIEW OF EVIDENCE****Systematic Reviews**

Bell et al (2022) evaluated the incremental gain of CAC scoring in addition to traditional cardiovascular risk assessments for primary prevention in a systematic review and meta-analysis of cohort studies.<sup>2</sup> Six studies (N=17,961) were included. Mean patient age ranged from 50 to 75.1 years; 38.4% to 59.4% of patients in each study were women and 38% to 100% were white. The C statistic for the traditional CVD risk assessments ranged from 0.693 (95% confidence interval [CI], 0.661 to 0.726) to 0.80. The addition of CAC scoring resulted in a gain of 0.036 (95% CI, 0.020 to 0.052). When CAC score reclassified low risk patients to intermediate or high risk, 85.5% to 96.4% of patients did not have a CVD event during follow-up (range, 5.1 to 10 years). Of those originally classified as high risk and reclassified as low risk after CAC scoring, 91.4% to 99.2% did not have a CVD event during follow-up. Although the CAC score did

add some additional discrimination to traditional CVD risk assessment, the authors cautioned that costs, rates of incidental findings, and radiation risks may offset the benefit.

Sarwar et al (2009) conducted a systematic review and meta-analysis to examine the prognostic utility of CAC scoring in categorizing asymptomatic patients according to their risk for adverse events.<sup>3</sup> Thirteen studies assessing the relation between CAC and adverse cardiovascular outcomes (N=71,595 asymptomatic patients; 65% men) were included in the analysis. Among the participants, 29,312 (41%) did not have any evidence of CAC (range, 22% to 80% of patients per study). During a mean follow-up of 50 months (range, 32 to 102 months), 154 (0.47%) of 29,312 patients without CAC and 1749 (4.14%) of 42,283 patients with CAC had cardiovascular events. The pooled relative risk was 0.15 (95% CI, 0.11 to 0.21;  $p < .001$ ).

### **Observational Studies**

From a pool of 27,125 patients who had had coronary computed tomography angiography (CCTA) for CAD, Han et al (2018) evaluated 3145 asymptomatic elderly patients between 52 and 62 years of age to compare the prognostic value of CCTA and CAC score.<sup>4</sup> In this multicenter, prospective, observational study, the authors found that adding CCTA improved the level of discrimination of a model that only included FRS and CAC score (C statistic: 0.75 vs. 0.70;  $p = .015$ ). The authors did not correlate the potential impact of CCTA results with treatment choices and downstream events. The study had a relatively short follow-up, and substantial disparity in the duration of risk prediction, FRS in particular.

Numerous observational studies have used data available from the Multi-Ethnic Study of Atherosclerosis (MESA) cohort to evaluate CAC in patients asymptomatic for CVD.<sup>5</sup> The MESA cohort of 6814 asymptomatic men and women 45 to 84 years of age is designed to study the characteristics of subclinical CVD and the risk factors that predict progression to symptomatic CVD. Approximately 38% of the patients in MESA were white, 28% African American, 22% Hispanic, and 12% Asian. Cainzos-Achirica et al (2020) assessed whether use of CAC improved appropriate aspirin use for primary prevention compared with other risk calculators.<sup>6</sup> In multivariable regression analysis, a CAC score  $\geq 100$  was independently associated with an increased risk of CVD events compared with those with a CAC score of 0 (hazard ratio [HR], 3.9; 95% CI, 2.5 to 6.1]. The pooled cohort equations and an estimated cardiovascular risk threshold of  $>20\%$  failed to identify optimal candidates for aspirin; however, a CAC score of at least 100 was able to identify subgroups of patients where aspirin would yield benefit. Gepner et al (2017) prospectively compared the use of CAC with carotid plaque scores in order to predict CVD, coronary heart disease (CHD), and stroke/transient ischemic attack (TIA) events.<sup>7</sup> After 11.3 years of follow-up among 4955 participants (mean age, 61.6 years), 709 CVD, 498 CHD, and 262 stroke/TIA events had occurred. Coronary artery calcium score significantly reclassified non-CVD events (3%; 95% CI, 2% to 5%) and CHD events (13%; 95% CI, 5% to 18%). Carotid plaque score did not consistently reclassify CVD or CHD events or nonevents. Budoff et al (2018) evaluated the relationship between CAC and incident ASCVD (stroke, cardiovascular death or nonfatal myocardial infarction [MI]).<sup>8</sup> After a median follow-up of 11.1 years, there were 498 total CHD events in the cohort (7.3%). Results were stratified by categories of race/ethnicity, age, sex, and education. Event rates increased with increasing CAC levels across all demographic subgroups and tests for interaction with age, sex, or race/ethnicity were all non-significant, demonstrating that CAC was independently associated with events. Event rates in the CAC=0 group ranged from 1.3% to 5.6%, and in the CAC  $>300$  group ranged from 13.1% to 25.6%.

Blaha et al (2016) evaluated the accuracy of change in risk classification by calculating the net reclassification improvement (NRI) for each of the 13 negative risk markers.<sup>9</sup> During a median of 10.3 years of follow-up among a cohort of 6814, 710 CVD events occurred. Among all the negative risk markers, a CAC score of 0 was the strongest, with an adjusted mean diagnostic likelihood ratio of 0.41 for all CHD. Net reclassification improvement for downward reclassification (10-year CVD risk, <7.5%) of CVD events with CAC scores of 0 in participants with a pretest 10-year CVD risk of 7.5% or higher (n=3833 [3227 participants without events and 606 with events]) was 0.14, higher than other negative risk markers included in the study. Polonsky et al (2010) also used data from MESA to determine whether incorporation of calcium score into a risk model based on traditional risk factors would improve the classification of risk.<sup>10</sup> During a median of 5.8 years of follow-up among a final cohort of 5878, 209 CHD events occurred, of which 122 were MI, death from CHD, or resuscitated cardiac arrest. Addition of CAC score in the model resulted in significant improvements in risk prediction compared with the model without CAC score (NRI=0.25; 95% CI, 0.16 to 0.34; p<.001). Subjects reclassified to high-risk had a similar risk of CHD events as those originally classified as high-risk.

In 2017, Ferencik et al evaluated whether the distribution of CAC in individual coronary arteries and segments, as well as CAC in the proximal dominant coronary artery, as detected by cardiac CT predicts incident major CHD events independent of traditional CAC score in 1268 asymptomatic subjects without prevalent major CHD from the offspring and third generation cohorts of the Framingham Heart Study.<sup>11</sup> Results revealed a total of 42 major CHD events occurring during a median follow-up period of 7.4 years. Both the number of coronary arteries with CAC (HR, 1.68 per artery, 95% CI, 1.10 to 2.57; p=.02) and the presence of CAC in the proximal dominant coronary artery (HR, 2.59; 95% CI, 1.15 to 5.83; p=.02) were associated with major CHD events after multivariable adjustment.

Nakanishi et al (2016) conducted a study among 13,092 consecutive asymptomatic individuals without known CAD (mean age, 58 years) clinically referred for a CAC scan between 1997 and 2011 at a university medical center; the study examined the predictive value of CAC for 5- and 15-year mortality rates among men and women.<sup>12</sup> Coronary artery calcium showed an incremental prognostic value over traditional risk factors among men at 5 years (area under curve [AUC], 0.702 vs. 0.655; p=.002) as well as at 15 years (AUC, 0.723 vs. 0.656; p<.001). In women, the incremental prognostic value of CAC was not statistically significant at 5 years (AUC, 0.650 vs. 0.612; p=.065), but was statistically significant at 15 years (AUC, 0.690 vs. 0.624; p<.001).

Elias-Smale et al (2011) conducted a study among 2153 asymptomatic participants (69.6 years) who underwent a multidetector CT scan in the Rotterdam Study.<sup>13</sup> During a median follow-up of 3.5 years, 58 CHD events (MI or death) occurred. Participants were classified into low (<5%), intermediate (5% to 10%), and high (>10%) 5-year risk categories based on a refitted Framingham risk model. For the outcome of CHD, the C statistic improved from 0.693 for the refitted Framingham model to 0.743 by addition of coronary calcium. Reclassification of subjects occurred most substantially in the intermediate-risk group (5-year risk, 5% to 10%) where 56% of persons were reclassified. Addition of CAC scoring reclassified 56% of persons: 36% moved to low-risk while 20% moved to high-risk, leading to a net gain in reclassification of 18% in persons with an event and a net decline in reclassification of 3% in persons without an event, resulting in an NRI of 15% (p<.01).

Erbel et al (2010) assessed NRI and risk prediction based on CAC scoring in comparison with traditional risk factors in 4129 subjects without overt CAD at baseline in the Heinz Nixdorf Recall study.<sup>14</sup> Results revealed that 93 coronary deaths and nonfatal MIs occurred after 5 years of follow-up (cumulative risk 2.3%; 95% CI, 1.8% to 2.8%). Reclassifying intermediate risk subjects with CAC <100 to the low risk category and with CAC ≥400 to the high risk category yielded a NRI of 21.7% (p=.0002) and 30.6% (p<.0001) for the FRS, respectively. Adding CAC scores to the FRS and National Cholesterol Education Panel ATP III categories improved the AUC from 0.681 to 0.749 (p<.003) and from 0.653 to 0.755 (p=.001), respectively. The authors concluded that limiting CAC scoring to intermediate risk subjects assists in correctly identifying a high proportion of individuals at highest risk and may contribute to reducing the number of coronary events in the general population; however, clinicians need to be aware that this may not be applicable across the board, particularly for patients in a low risk category. In 2018, Lehmann et al published additional 10 year follow-up data from Heinz Nixdorf and concluded that CAC progression is associated with coronary and CV event rates, but only weakly adds to risk prediction.<sup>15</sup> The authors stated that what counts is the most recent CAC value and risk factor assessment.

A number of additional studies have reported that CAC scoring adds predictive information.<sup>16,17,18,19,20,21,22,23,24,</sup>

### **Clinically Useful**

A test is clinically useful if the use of the results informs management decisions that improve the net health outcome of care. The net health outcome can be improved if patients receive correct therapy, more effective therapy, or avoid unnecessary therapy or testing.

### **Direct Evidence**

Direct evidence of clinical utility is provided by studies that have compared health outcomes for patients managed with and without the test. Because these are intervention studies, the preferred evidence would be from randomized controlled trials (RCTs).

### **Systematic Reviews**

Tables 1 and 2 summarize, respectively, the characteristics and results of systematic reviews relevant to the assessment of the clinical utility of CAC scoring.

Gupta et al (2017) performed a systematic review and meta-analysis evaluating the odds of initiating or continuing pharmacological (i.e., aspirin, lipid-lowering, and blood pressure lowering medications) and lifestyle preventive therapies in asymptomatic CAD patients with nonzero versus 0 CAC scores as detected on cardiac CT.<sup>25</sup> Results revealed that the odds of aspirin, lipid-lowering, and blood pressure lowering medication initiation, lipid-lowering medication continuation, an increase in exercise, and dietary changes were significantly higher in patients with nonzero CAC versus 0 CAC scores. However, the odds of aspirin or blood pressure-lowering medication continuation were not significantly increased in the nonzero CAC group. Statistical heterogeneity was present across studies for many of the outcomes; potential sources of heterogeneity included variations in sample size and the proportion of patients with 0 versus nonzero CAC, whether patients were shown their CAC scan, and differences in clinical characteristics of study populations.



Mamudu et al (2014) conducted a systematic review of studies evaluating the effects of CAC screening on behavioral modification, risk perception, and medication adherence in asymptomatic adults.<sup>26</sup> Fifteen studies were selected (3 RCTs, 12 observational studies). The size of the study populations ranged from 56 to 6814 individuals. Reviewers primarily provided descriptive results of the studies given the lack of standardization across studies regarding CAC measures and outcome variables. Coronary artery calcium screening improved medication adherence. However, the impact of CAC screening on behavioral and lifestyle factors (body mass index, diet, exercise, smoking), the perception of CAD risk, and psychosocial effects were not statistically significant compared with baseline.

Whelton et al (2012) published a meta-analysis of RCTs that evaluated the impact of CAC scores on cardiac risk profiles and cardiac procedures.<sup>27</sup> Four trials were identified (N=2490 ); the individual trials ranged in size from 50 to 1934 patients. Reviewers pooled data from 4 trials on the impact of calcium scores on blood pressure, from 3 to evaluate the impact on low-density lipoprotein, and from 2 to determine the impact on high-density lipoprotein. Pooled analysis did not show a significant change in any of these parameters when incorporating calcium scores. Similarly, in 4 studies that looked at the rates of smoking cessation following calcium scores, no significant change was found. Two studies included rates of coronary angiography and 2 included rates of revascularization. Pooled analysis of these studies did not show a significant change after the measurement of coronary calcium.

**Table 1. Characteristics of Systematic Reviews Assessing the Clinical Utility of CAC Score for Asymptomatic Patients**

Study	Dates	Trials	Participants	N (Range)	Design	Duration (Range)	Outcomes
Gupta et al (2017) <sup>25</sup> ,	2006-2011	6	Asymptomatic for CAD	11,256 (505 to 6814)	SR and MA of RCTs and observational cohorts	1.6 to 6 y (mean follow-up)	Initiation or continuation of pharmacological and lifestyle preventive therapies
Mamudu et al (2014) <sup>26</sup> ,	1996-2014	15	Asymptomatic for CAD	16,983 (56 to 6814)	SR of RCTs and prospective cohorts	3 mo to >8 y	Positive behavioral change, risk perception, medication adherence
Whelton et al (2012) <sup>27</sup> ,	2003-2011	4	Asymptomatic for CAD	2490 (50 to 1934)	MA of RCTs	1 to 4 y	CVD and CAD risk factors, 10-y FRS event rate, incident clinical disease

CAC: coronary artery calcium; CAD: coronary artery disease; CVD: cardiovascular disease; FRS: Framingham Risk Score; MA: meta-analysis; RCT: randomized controlled trial; SR: systematic review.

**Table 2. Results of Systematic Reviews Assessing the Impact of CAC Score on Clinical Risk Profile, Cardiac Procedures, and Pharmacological and Lifestyle Preventive Therapies Among Asymptomatic Patients**

Study	Treatment	Comparator	Trials	Measure	Association	95% CI
Gupta et al (2017) <sup>25,</sup>	CAC score of 0	Nonzero CAC score	4	Aspirin initiation	2.61	1.81 to 3.78
	CAC score of 0	Nonzero CAC score	3	Lipid lowering medication initiation	2.86	1.85 to 4.41
	CAC score of 0	Nonzero CAC score	2	Blood pressure lowering medication initiation	1.94	1.61 to 2.33
	CAC score of 0	Nonzero CAC score	3	Aspirin continuation	1.28	0.75 to 2.18
	CAC score of 0	Nonzero CAC score	4	Lipid lowering medication continuation	2.26	1.56 to 3.28
	CAC score of 0	Nonzero CAC score	2	Blood pressure lowering medication continuation	1.38	0.86 to 2.23
	CAC score of 0	Nonzero CAC score	3	Increased exercise	1.84	1.41 to 2.41
	CAC score of 0	Nonzero CAC score	2	Dietary change	1.94	1.52 to 2.49
Whelton et al (2012) <sup>27,</sup>	CAC screen	No CAC screen	4	Mean change in systolic BP	0.23	-2.25 to 2.71
	CAC screen	No CAC screen	3	Mean change in diastolic BP	-0.42	-1.18 to 0.35
	CAC screen	No CAC screen	3	Mean change in LDL	0.23	-5.96 to 6.42
	CAC screen	No CAC screen	2	Mean change in HDL	-1.18	-5.50 to 3.14
	CAC screen	No CAC screen		RR of smoking cessation	1.15	0.77 to 1.71
	CAC screen	No CAC screen		RR of angiography	1.17	0.68 to 1.99
	CAC screen	No CAC screen		RR of revascularization	1.35	0.69 to 2.63

BP: blood pressure; CAC: coronary artery calcium; CI: confidence interval; HDL: high-density lipoprotein; LDL: low-density lipoprotein; RR: relative risk.

### Randomized Controlled Trials

Randomized controlled trials by Rozanski et al (2011)<sup>28</sup>, and O'Malley et al (2003)<sup>29</sup>, both included in the Whelton et al (2012)<sup>27</sup>, systematic review, captured the effect of incorporating CAC scoring in clinical practice on CAD risk factors and overall CAD risk.

Rozanski et al (2011) conducted an RCT to evaluate the impact of CT scanning for CAC on cardiac risk factors.<sup>28</sup> A total of 2137 healthy volunteers were randomized in a 2:1 ratio to CT scanning (n=1424) or no CT scanning (n=713) and followed for 4 years. At baseline, both groups received 1 session of risk factor counseling by a nurse practitioner. The primary endpoint was a 4-year change in CAD risk factors and FRS. At the 4-year follow-up, there was a differential dropout among the groups, with 88.2% (1256/1424) of follow-up in the scan group and 81.9% (584/713) in the no-scan group. Compared with the no-scan group, the scan group showed a net favorable change in systolic blood pressure (p=.02), low-density lipoprotein cholesterol (p=.04), and waist circumference for those with increased abdominal girth (p=.01), and a tendency to weight loss among overweight subjects (p=.07). While there was a mean rise in FRS in the no-scan group (0.7), FRS remained static in the scan group (0.002; p=.003). Downstream medical testing in the scan group was comparable with those of the no-scan group, balanced by lower and higher resource utilization for subjects with normal CAC scans and CAC scores of 400 or higher, respectively.

This trial highlights the potential benefit of CAC screening in modifying the cardiac risk profile but is not definitive in demonstrating improved outcomes. Trial limitations included differing intensities of interventions between groups and differential dropout. It is possible that the small differences reported in the trial resulted from bias related to these methodologic limitations. Also, this trial did not compare the impact of other types of risk factor intervention, most notably more intensive risk factor counseling.

O'Malley et al (2003) conducted an RCT among a consecutive sample of 450 asymptomatic active-duty U.S. Army personnel ages 39 to 45 years to assess the effects of incorporating EBCT as a motivational factor into a cardiovascular screening program.<sup>29</sup> The program offered intensive case management or usual care and assessed treatment impact on 10-year FRS over 1 year. The authors used a 2 x 2 factorial design and patients were randomized to 1 of the 4 intervention arms: EBCT results provided in the setting of intensive case management (n=111) or usual care (n=119) or EBCT results withheld in the setting of intensive case management (n=124) or usual care (n=96). Mean absolute risk change in 10-year FRS between groups receiving and not receiving results was +0.30 and +0.36 (p=.81), respectively. The trial was not powered for clinical endpoints. EBCT did not produce any benefits regarding a difference in FRS at 1 year.

### Chain of Evidence

Indirect evidence on clinical utility rests on clinical validity. If the evidence is insufficient to demonstrate test performance, no inferences can be made about clinical utility.

### Section Summary: Coronary Artery Calcium Scoring in Asymptomatic Individuals

Multiple observational cohort studies and systematic reviews of these studies have consistently demonstrated the incremental prognostic value of CAC scoring in predicting CVD events compared to standard risk stratification alone among asymptomatic populations over the

intermediate and long-term; however, studies have reported mixed findings on whether the use of the score is key to improved cardiovascular outcomes or improvements in other clinical outcomes that lead to cardiovascular risk reduction.

### **Coronary Artery Calcium Scoring in Symptomatic Patients**

In certain clinical situations, such as individuals presenting with chest pain, it is uncertain whether the symptoms are due to CAD. Coronary calcium measurement has been proposed as a method to rule out CAD in certain individuals if their CAC score is 0. The presence of any coronary calcium can be a sensitive, but not specific, test for coronary disease because CAD rarely occurs in the absence of coronary calcium. False-positives occur because the calcium may not be associated with an ischemic lesion. The absence of any coronary calcium can be a specific test for the absence of coronary disease and direct the diagnostic workup toward other causes of the patient's symptoms. In this context, coronary calcium measurement is not used to make a positive diagnosis, but as a diagnostic "filter" to rule out an atherosclerotic cause for the patient's symptoms.

### **Clinical Context and Test Purpose**

The use of CAC scoring with CT in symptomatic individuals can rule out the atherosclerotic etiology of CAD.

The following PICO was used to select literature to inform this review.

### ***Populations***

The population of interest is individuals who have signs and/or symptoms suggestive of CAD.

### ***Interventions***

The intervention of interest is CAC scoring using fast CT imaging, including EBCT and spiral CT. Computed tomography CAC scoring is utilized when individuals require evaluation for persistent stable angina or experience onset of acute chest pain.

### ***Comparators***

The following test is currently being used to make decisions about managing CAD: standard diagnostic testing, which includes functional testing and exercise electrocardiography.

### ***Outcomes***

The outcomes of interest include OS, test accuracy, test validity, and morbid events (e.g., MACEs, need for ICA and revascularization).

### **Study Selection Criteria**

For the evaluation of clinical validity of CAC scoring using CT, studies that meet the following eligibility criteria were considered:

- Reported on the accuracy of the marketed version of the technology;
- Included a suitable reference standard;
- Patient/sample clinical characteristics were described;
- Patient/sample selection criteria were described;
- The study reported on a minimum of 1000 patients.

**Clinically Valid**

A test must detect the presence or absence of a condition, the risk of developing a condition in the future, or treatment response (beneficial or adverse).

**REVIEW OF EVIDENCE****Systematic Reviews**

Chaikriangkrai et al (2016) conducted a systematic review and meta-analysis to examine the prognostic value and accuracy of a CAC score of 0 for identifying patients presenting with acute chest pain at acceptable low-risk for future cardiovascular events.<sup>30</sup> The systematic review included only prospective cohort studies that used multidetector CT or EBCT to calculate CAC scores using the Agatston method and reported MACEs at 1 month and beyond the index emergency department visit. Eight studies evaluating 3556 patients with a median follow-up of 10.5 months were selected. Reviewers conducted a subgroup analysis of 6 studies in predominantly white patients (N=2432 ) to estimate the prognostic accuracy indices of CAC scores (0, >0) for cardiovascular events (MACEs, all-cause deaths, nonfatal MI). Pooled sensitivity, specificity, as well as positive and negative likelihood ratios were 96% ( $I^2=0\%$ ), 60% ( $I^2=15.1\%$ ), 2.36 ( $I^2=0\%$ ), and 0.07 ( $I^2=0\%$ ), respectively (Table 3).

The systematic review by Sarwar et al (2009), mentioned prior in this review examined the clinical, diagnostic, and prognostic significance of a CAC score of 0.<sup>3</sup> Eighteen studies from 1992 to 2007, in which 10,355 symptomatic patients with suspected CAD underwent CAC testing as well as ICA, were selected in the analysis to examine the diagnostic accuracy of CAC scoring for stenosis on ICA. A total of 5805 (56%) patients had significant coronary stenosis (defined as >50%) on ICA. Pooled data revealed that the presence of calcium had a sensitivity, a specificity, as well as a positive and a negative likelihood ratio of 98%, 40%, 1.63, and 0.06, respectively, for predicting coronary artery stenosis. The summary negative predictive value was 92% (95% CI, 88% to 95%;  $p<.001$ ). The summary positive predictive value was 68% (95% CI, 64% to 72%;  $p<.001$ ) (Table 3).

Lo-Kioeng-Shioe et al (2019) conducted a systematic review and meta-analysis of 18 observational studies (N=34,041) to assess the ability of CAC to predict risk of major cardiac events (MACE, defined as the composite of late cardiac revascularization, hospitalization for unstable angina pectoris or heart failure, nonfatal MI, and cardiac death or all-cause mortality) in stable patients with suspected CAD.<sup>31</sup> Of 1601 cardiovascular events, 158 occurred in patients with a CAC score of 0. The pooled risk ratio for MACE in patients with CAC >0 was 5.71 (95% CI 3.98 to 8.19), and risk increased with increasing levels of CAC. The pooled relative risk for incidence of all-cause mortality or nonfatal MI was 3.64 (95% CI 2.68 to 4.96).

**Table 3. Pooled Diagnostic Performance of CAC Score for CAD Among Symptomatic Individuals**

Test	Studies	N	Sensitivity (95% CI), %	Specificity (95% CI), %	LR+ (95% CI)	LR- (95% CI)
Chaikriangkrai et al (2016) <sup>30</sup> ,						
CAC score (0, >0)	6	2432	96 (93 to 98)	60 (58 to 62)	2.36 (2.22 to 2.51)	0.07 (0.04 to 0.14)
Sarwar et al (2009) <sup>3</sup> ,						
CAC score (0, >0)	18	10,355	98 (97 to 98)	40 (38 to 41)	1.63 (1.59 to 1.67)	0.06 (0.05 to 0.07)

CAC: coronary artery calcium; CAD: coronary artery disease; CI: confidence interval; LR: likelihood ratio.

### Randomized Controlled Trials

Lubbers et al (2016) conducted a multicenter RCT to compare the effectiveness and safety of a cardiac CT algorithm with functional testing in patients with symptoms (stable chest pain or angina equivalent symptoms) suggestive of CAD.<sup>32</sup> A total of 350 patients with stable angina were prospectively randomized 2:1 to cardiac CT or functional testing, such as exercise electrocardiography, myocardial perfusion imaging, or stress echocardiography. Patients in the cardiac CT arm (n=242) initially underwent calcium scanning followed by CCTA if the Agatston score was between 1 and 400. Coronary artery disease was ruled out if the patients had a CAC score of 0. The original primary endpoint of the trial was the proportion of patients undergoing catheter angiography followed by revascularization, but because of insufficient funding, the authors could not assess that endpoint and chose clinical effectiveness as the alternative primary outcome, defined as the absence of chest pain complaints after 1 year. After 1 year, fewer patients randomized to CT reported angina symptoms than those in the functional testing group (39% vs. 25%; p=.012), although the proportion of patients with similar or worsened symptoms was comparable (26% vs. 29%; p=.595). The tiered protocol study design is a strength of this trial, but the unplanned change in endpoints limits analysis and conclusions.

### Observational Studies

Purnani et al (2015) published results from a subgroup analysis of the Rule Out Myocardial Infarction using Computed Assisted Tomography II trial.<sup>33</sup> This analysis evaluated the incremental diagnostic value of CAC scoring plus CCTA in low- to intermediate-risk patients presenting to the emergency department with symptoms (chest pain or angina equivalent of  $\geq 5$  minutes duration within 24 hours) suggesting acute coronary syndrome (ACS). The Rule Out Myocardial Infarction using Computed Assisted Tomography II trial randomized patients with possible ACS to CCTA as part of an initial evaluation or to the standard emergency department evaluation strategy, as directed by local caregivers. As part of the trial protocol, all patients undergoing CCTA had a CAC scan; the present analysis included 473 patients who underwent both CCTA and CAC scanning. Among these patients, the ACS rate (defined as unstable angina and MI during the index hospitalization) was 8% (n=38). Patients with lower CAC scores were less likely to have a discharge diagnosis of ACS. Among 253 patients with a CAC score of 0, 2 (0.8%) patients were diagnosed with ACS (95% CI, 0.1% to 2.8%). Receiver operating characteristic curve analysis was used to predict the risk of ACS by CAC score greater than 0,

continuous CAC score, CCTA results, and combined CAC and CCTA score. The optimal cut-point of CAC for ACS detection was 22 (C statistic, 0.81), with 318 (67%) patients having a CAC score of less than 22. All CCTA strategies had high sensitivity for ACS detection, without significant differences in stenosis thresholds. Coronary artery calcium was inferior to CCTA for predicting ACS (C range, 0.86 vs. 0.92;  $p=.03$ ). The addition of CAC score to CCTA (i.e., using selective CCTA only for patients with CAC score  $>22$  or  $>0$ ) did not significantly improve the detection of ACS (CAC plus CCTA  $C=0.93$  vs. CCTA  $C=0.92$ ;  $p=.88$ ). Overall, this trial suggested that CAC scoring did not provide incremental value beyond CCTA in predicting the likelihood of ACS in a low- to intermediate-risk population presenting to the emergency department.

Chaikriangkrai et al (2015) retrospectively evaluated whether CAC added incremental value to CCTA for predicting coronary artery stenosis in 805 symptomatic patients without known CHD.<sup>34</sup> Coronary artery calcium score was significantly associated with the presence of coronary artery stenosis on CCTA. Both CAC score and the presence of CCTA stenosis were significantly associated with MACE rates, including cardiac death, nonfatal MI, and late coronary revascularization. Patients with more than 50% stenosis on CCTA had higher MACE rates, compared with those who had a normal CCTA (4.5% vs. 0.1%;  $p<.001$ ) and with those who had less than 50% stenosis (4.5% vs. 1.4%;  $p=.002$ ). Those with a CAC score of more than 400 had higher MACE rates than those with scores between 1 and 100 (4.2% vs. 1.4%;  $p=.014$ ) and those with scores of 0 (4.2% vs. 0%;  $p<.001$ ). The addition of CAC score to a risk prediction model for MACE, which included clinical risk factors and CCTA stenosis, significantly improved the model's predictive performance (global  $c^2$  score, 108 vs. 70;  $p=.019$ ).

Hulten et al (2014) published results from a retrospective cohort study among symptomatic patients without a history of CAD to evaluate the accuracy of CAC scoring for excluding coronary stenosis, using CCTA as the criterion standard.<sup>35</sup> The study included 1145 patients who had symptoms possibly consistent with CAD who underwent noncontrast CAC scoring and contrast-enhanced CCTA from 2004 to 2011. For detection of greater than 50% stenosis, CAC had a sensitivity, specificity, and negative predictive value of 98%, 55%, and 99%, respectively. For the prediction of cardiovascular death or MI, the addition of either or both CAC and CCTA to a clinical prediction score did not significantly improve prognostic value.

Dharampal et al (2013) retrospectively evaluated a cohort of 1975 symptomatic patients (those with chest pain referred by their cardiologist for CCTA) who underwent a clinical evaluation and CAC scoring and CCTA or ICA.<sup>36</sup> The primary outcome was obstructive CAD ( $\geq 50\%$  stenosis) on ICA or CCTA (if ICA was not done). The authors evaluated the NRI with the addition of CAC score to a clinical prediction model for patients who had an intermediate probability of CHD (10% to 90%) after clinical evaluation based on chest pain characteristic, age, sex, risk factors, and electrocardiogram. Discrimination of CAD was significantly improved by incorporating the CAC score into the clinical evaluation (AUC, 0.80 vs. 0.89;  $p<.001$ ).

Yoon et al (2012) conducted a prospective study among 136 Korean men (58% men; age, 56 years) who presented to the emergency department with acute chest pain and nondiagnostic electrocardiograph to examine the diagnostic usefulness of the "zero calcium score criteria" as a decision-making strategy to rule out significant CAD as the etiology of acute chest pain.<sup>37</sup> All patients underwent 64-slice CT for calcium scoring and CCTA. Ninety-two (68%) of 136 patients did not show detectable CAC, and 14 (15%) of these 92 without CAC had 50% or more stenosis

on CCTA. Sensitivity, specificity, positive predictive value, and negative predictive value of a CAC score of 0 for the detection of 50% or more stenosis were 66% (95% CI, 50% to 80%), 83% (95% CI, 74% to 90%), 64% (95% CI, 48% to 77%), and 85% (95% CI, 75% to 91%), respectively. A calcium score of 0 did not necessarily guarantee the absence of significant CAD in an Asian population presenting to the emergency department with chest pain.

Gottlieb et al (2010) conducted a prospective multicenter study to evaluate whether the absence of coronary calcium could be used to rule out 50% or more coronary stenosis or the need for revascularization.<sup>38</sup> The authors compared the diagnostic performance of 64-detector CT with that of ICA. Among 291 patients with suspected CAD included in the study, 214 (73%) were male, and the mean age was 59.3 years. Fifty-six percent of the patients had 50% or more stenosis. Among 72 patients with a CAC score of 0, 14 (19%) had at least 1 coronary artery with 50% or more stenosis. The overall sensitivity for a CAC score of 0 to predict the absence of 50% or more stenosis was 45%, specificity was 91%, the negative predictive value was 68%, and the positive predictive value was 81%. Additionally, 9 (12.5%) patients with a CAC score of 0 underwent revascularization within 30 days of calcium scoring.

### **Clinically Useful**

A test is clinically useful if the use of the results informs management decisions that improve the net health outcome of care. The net health outcome can be improved if patients receive correct therapy, more effective therapy, or avoid unnecessary therapy or testing.

### **Direct Evidence**

Direct evidence of clinical utility is provided by studies that have compared health outcomes for patients managed with and without the test. Because these are intervention studies, the preferred evidence would be from RCTs.

### **Observational Studies**

Yerramasu et al (2014) prospectively assessed an evaluation algorithm including CAC scoring for patients presenting to a rapid access chest pain clinic with stable chest pain possibly consistent with CHD.<sup>39</sup> Three hundred patients presenting with acute chest pain to 1 of 3 chest pain clinics underwent CAC scoring. If the CAC score was 1000 or more Agatston units, ICA was performed; if the CAC score was less than 1000, CCTA was performed. All patients with a CAC score of 0 and low pretest likelihood of CHD had no obstructive CHD on CCTA and were event-free during follow-up. Of the 18 patients with CAC scores from 400 to 1000, 17 (94%) had greater than 50% obstruction on subsequent CCTA and were referred for further evaluation, 14 (78%) of whom had obstructive CHD. Of 15 patients with CAC scores 1000 or more and who were referred for coronary angiography, obstructive CHD was present in 13 (87%). This study suggested that CAC scoring can be used in the acute chest pain setting to stratify decision-making for further testing.

ten Kate et al (2013) prospectively evaluated the accuracy of cardiac CT, including CAC scoring with or without CCTA, in distinguishing heart failure due to CAD from heart failure due to non-CAD causes.<sup>40</sup> Data on the predictive ability of a negative CAC score in ruling out CAD was also included. The study included 93 symptomatic patients with newly diagnosed heart failure of unknown etiology, all of whom underwent CAC scoring. Those with a CAC score greater than 0 underwent CCTA and, if the CCTA was positive for CAD (>20% luminal diameter narrowing), ICA was recommended. Forty-six percent of patients had a CAC score of 0. At a mean follow-up of 20



months, no patient with a CAC score of 0 had a MI, underwent percutaneous coronary intervention, had a coronary artery bypass graft, or had signs of CAD.

### **Chain of Evidence**

Indirect evidence on clinical utility rests on clinical validity. If the evidence is insufficient to demonstrate test performance, no inferences can be made about clinical utility.

Because the clinical validity of CAC scoring for symptomatic patients has not been established, a chain of evidence supporting the clinical utility of CAC scoring in this population cannot be constructed.

### **Section Summary: Coronary Artery Calcium Scoring in Symptomatic Patients**

Systematic reviews and meta-analyses have reported a very low negative likelihood ratio for CAC score in predicting MACEs and significant coronary stenosis, suggesting the potential value of a calcium score of 0 in ruling out an atherosclerotic etiology of the disease. However, multiple observational studies with angiographic (CCTA or ICA) interventions have suggested that a CAC score of 0 may not rule out the presence of significant atherosclerotic CAD among symptomatic patients. Currently, evidence from nonrandomized, observational studies has suggested a very low short- or long-term risk of cardiovascular events or death in patients having calcium scores of 0 compared with those having positive (>0) calcium scores. However, considering the inconsistency in evidence regarding the diagnostic accuracy of calcium scoring and lack of evidence from RCTs, further research is needed to examine the clinical utility of ruling out atherosclerotic CAD based on a CAC score of 0.

### **Supplemental Information**

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.

### **Practice Guidelines and Position Statements**

Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

### **Practice Guideline - American Heart Association/American College of Cardiology**

The American College of Cardiology and American Heart Association (2018) Clinical Practice Guidelines on the Management of Blood Cholesterol state, "When risk status is uncertain, a coronary artery calcium (CAC) score is an option to facilitate decision making in adults 40 to 75 years of age."<sup>41</sup> The guidelines further note, "One purpose of CAC scoring is to reclassify risk identification of patients who will potentially benefit from statin therapy. This is especially useful when the clinician and patient are uncertain whether to start a statin. Indeed, the most important recent observation has been the finding that a CAC score of 0 indicates a low ASCVD risk for the subsequent 10 years. Thus, measurement of CAC potentially allows a clinician to withhold statin therapy in patients showing 0 CAC."

With regard to the prognostic significance of CAC, the guideline "makes use of the available data to predict the risk associated with CAC."<sup>41</sup> The guideline notes that "these data need to be amplified by new and ongoing studies to guide treatment decisions" and that "particular uncertainty exists about the predictive value of intermediate CAC scores." Additionally, there are concerns regarding the predictive significance of a CAC score of 0, which must be further verified in follow-up studies. For patients with a 0 score, "it is currently uncertain when and if follow-up CAC measurements should be done to reassess risk status."

The American College of Cardiology and American Heart Association (2019) Guideline on the Primary Prevention of Cardiovascular Disease is in line with the blood cholesterol guideline stating that adults (40 to 75 years of age) who are being evaluated for cardiovascular disease prevention should initially undergo 10-year atherosclerotic cardiovascular disease (ASCVD) risk estimation with a clinician-patient risk discussion before starting pharmacological therapy.<sup>42</sup> The guideline also notes that assessing for other risk-enhancing factors can help guide decision making "about preventive interventions in select individuals, as can CAC scanning." The guideline specifically states the following recommendation regarding assessment of cardiovascular risk and CAC:

- In adults at intermediate risk ( $\geq 7.5\%$  to  $< 20\%$  10-year ASCVD risk) or selected adults at borderline risk ( $5\%$  to  $< 7.5\%$  10-year ASCVD risk), if risk-based decisions for preventive interventions remain uncertain, it is reasonable to measure a CAC score to guide clinician-patient risk discussion [Class (Strength) of Recommendation: IIa; Level (Quality) of Evidence: B-NR]. A IIa class of recommendation is of moderate strength based on moderate quality nonrandomized studies.

The American Heart Association, American College of Cardiology (2021) Guideline on Evaluation and Diagnosis of Chest Pain includes a recommendation for CAC as first-line testing in patients with stable chest pain with no known coronary artery disease and low likelihood of obstruction.<sup>43</sup> The guidelines recommend the addition of CAC may also be useful for intermediate-high risk patients with stable chest pain and no known coronary artery disease undergoing stress testing.

### **Special Report - American Heart Association/American College of Cardiology**

The American Heart Association and the American College of Cardiology (2019) issued a special report on the use of risk assessment tools to guide decision-making in the primary prevention of ASCVD.<sup>44</sup> This report includes an algorithm of clinical approaches to incorporate CAC measurement in risk assessment for borderline- and intermediate-risk patients:

"For borderline-risk (10-year risk  $5\%$  to  $< 7.5\%$ ) and intermediate-risk ( $7.5\%$  to  $< 20\%$ ) patients who are undecided regarding statin therapy, or when there is clinical uncertainty regarding the net benefit, consider the value of additional testing with measurement of CAC. If CAC is measured, interpret results as follows:

- a. CAC score of 0 indicates that a borderline- or intermediate-risk individual is reclassified to a 10-y event rate lower than predicted, and below the threshold for benefit from a statin. Consider avoiding or postponing statin therapy unless there is a strong family history of premature ASCVD, history of diabetes mellitus, or heavy cigarette smoking. Consider repeat CAC measurement in 5 years if patient remains at borderline or intermediate risk.

b. CAC score 1 to 99 and <75th percentile for age/sex/race/ethnicity indicates that there is subclinical atherosclerosis present. This may be sufficient information to consider initiating statin therapy, especially in younger individuals, but does not indicate substantial reclassification of the 10-y risk estimate. Consider patient preferences and, if statin decision is postponed, consider repeat CAC scoring in 5 years.

c. CAC score 100 or >75th percentile for age/sex/race/ethnicity indicates that the individual is reclassified to a higher event rate than predicted, that is above the threshold for statin benefit. Statin therapy is more likely to provide benefit for such patients."

**National Institute for Health and Care Excellence**

For patients with "stable chest pain who cannot be excluded by clinical assessment alone," the National Institute for Health and Care Excellence recommended CT using 64-slice imaging.<sup>45,</sup>

**U.S. Preventive Services Task Force Recommendations**

The U.S. Preventive Services Task Force (2018) updated its recommendations on the use of nontraditional or novel risk factors in assessing coronary heart disease risk in asymptomatic adults with no known cardiovascular disease.<sup>46,47</sup> Calcium score was 1 of 3 nontraditional risk factors considered. Reviewers concluded the current evidence was insufficient to assess the balance of benefits and harms of adding any of the nontraditional risk factors studied to traditional risk assessment in asymptomatic adults with no known cardiovascular disease.

**Ongoing and Unpublished Clinical Trials**

Some ongoing trials that might influence this review are listed in Table 4.

**Table 4. Summary of Key Trials**

<b>NCT No.</b>	<b>Trial Name</b>	<b>Planned Enrollment</b>	<b>Completion Date</b>
<i>Ongoing</i>			
NCT05700877	Screening and Intervention for Subclinical Coronary Artery Disease in Patients With Type 2 Diabetes: THE STENO INTEN-CT STUDY	7300	Mar 2029
NCT03972774	Assessment of Patients With Suspected Coronary Artery Disease by Coronary Calcium First Strategy Versus Usual Care Approach	2500	Nov 2029
NCT04075162	Community Benefit of No-charge Calcium Score Screening Program	77,000	Dec 2032
NCT03439267	Effectiveness of a Proactive Cardiovascular Primary Prevention Strategy, With or Without the Use of Coronary Calcium Screening, in Preventing Future Major Adverse Cardiac Events	9000	Aug 2024
NCT05314140	Towards Optimal Screening and Management of Coronary Artery Disease in Diabetes: TOSCANA Study	2000	Jun 2026
NCT05267990	Impact of a Coronary Artery Calcium-guided Primary Prevention of Major CoronaryHeart Disease for	2000	Dec 2028

<b>NCT No.</b>	<b>Trial Name</b>	<b>Planned Enrollment</b>	<b>Completion Date</b>
	Asymptomatic Coronary Artery Disease in Diabetes: a Prospective Cohort Study		

NCT: national clinical trial.

**CODING**

**The following codes for treatment and procedures applicable to this policy are included below for informational purposes. This may not be a comprehensive list of procedure codes applicable to this policy.**

**Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.**

**The code(s) listed below are medically necessary ONLY if the procedure is performed according to the "Policy" section of this document.**

<b>CPT/HCPCS</b>	
75571	Computed tomography, heart, without contrast material, with quantitative evaluation of coronary calcium
75572	Computed tomography, heart, with contrast material, for evaluation of cardiac structure and morphology (including 3D image postprocessing, assessment of cardiac function, and evaluation of venous structures, if performed)
75573	Computed tomography, heart, with contrast material, for evaluation of cardiac structure and morphology in the setting of congenital heart disease (including 3D image postprocessing, assessment of LV cardiac function, RV structure and function, and evaluation of vascular structures, if performed)
75574	Computed tomographic angiography, heart, coronary arteries and bypass grafts (when present), with contrast material, including 3D image postprocessing (including evaluation of cardiac structure and morphology, assessment of cardiac function, and evaluation of venous structures, if performed)
0710T	Noninvasive arterial plaque analysis using software processing of data from non-coronary computerized tomography angiography; including data preparation and transmission, quantification of the structure and composition of the vessel wall and assessment for lipid-rich necrotic core plaque to assess atherosclerotic plaque stability, data review, interpretation and report
0711T	Noninvasive arterial plaque analysis using software processing of data from non-coronary computerized tomography angiography; data preparation and transmission
0712T	Noninvasive arterial plaque analysis using software processing of data from non-coronary computerized tomography angiography; quantification of the structure and composition of the vessel wall and assessment for lipid-rich necrotic core plaque to assess atherosclerotic plaque stability
0713T	Noninvasive arterial plaque analysis using software processing of data from non-coronary computerized tomography angiography; data review, interpretation and report
S8092	Electron beam computed tomography (also known as ultrafast CT, cine CT)

- When quantitative assessment is performed as part of the same encounter as contrast-enhanced cardiac CT (codes 75572-75573) or coronary CT angiography (code 75574), it is included in the service.
- The primary fast CT methods for this determination are electron beam computed tomography (EBCT) and multi-detector computed tomography (MDCT).

<b>REVISIONS</b>	
11-14-2008	<ul style="list-style-type: none"> <li>▪ Changed title from Electron Beam Computerized Tomography (EBCT) Screening for Cardiovascular Calcium Deposits also known as Ultrafast CT, CT angiography and CINE CT to Computed Tomography to Detect Coronary Artery Calcification.</li> <li>▪ Added a rationale section to the policy.</li> <li>▪ In Coding section, added CPT codes: 0144T, 0147T, 0149T.</li> </ul>
09-18-2009	<p>In Header:</p> <ul style="list-style-type: none"> <li>▪ Added reference policies: Contrast-Enhanced CTA for Coronary Artery Evaluation, CTA and MRA of the Chest (excluding the heart), CTA and MRA of the Head, Neck, Abdomen, Pelvis, Lower Extremity, and Upper Extremity, and Cardiac Computed Tomography (CT).</li> </ul> <p>Updated Rationale and References sections</p>
01-01-2010	<p>In Coding Section:</p> <ul style="list-style-type: none"> <li>▪ Added CPT Code: 75571</li> <li>▪ Removed CPT Codes: 0144T, 0147T, 0149T</li> </ul>
09-20-2011	<p>Description section updated.</p> <p>Rationale section added.</p> <p>References section updated.</p>
11-06-2012	<p>Rationale section added.</p> <p>In Coding Section:</p> <p>Added a Diagnosis section and the following wording, "Experimental/Investigational for all diagnoses related to this policy." As no reference to diagnosis was previously reflected in the policy.</p> <p>References section updated.</p>
11-24-2015	<p>Description section updated</p> <p>In Policy section:</p> <ul style="list-style-type: none"> <li>▪ Added "(CAC)" the abbreviation for coronary artery calcification. No change in policy intent is made by this addition.</li> </ul> <p>Rationale section updated</p> <p>References updated</p>
01-18-2017	<p>Description section updated</p> <p>Rationale section updated</p> <p>In Coding section:</p> <ul style="list-style-type: none"> <li>▪ Coding notations updated</li> </ul> <p>References updated</p>
11-15-2017	<p>Description section updated</p> <p>Rationale section updated</p> <p>References updated</p>
01-17-2020	<p>Description section updated</p> <p>Rationale section updated</p> <p>References updated</p>
04-16-2021	<p>Description section updated</p> <p>Rationale section updated</p> <p>In Coding section:</p> <ul style="list-style-type: none"> <li>• Added codes 0623T, 0624T, 0625T, 0626T that became effective 1/1/21</li> </ul> <p>References updated</p>
11-5-2021	<p>In Related Policy section</p> <p>Deleted <i>CTA and MRA of the Head, Neck, Abdomen, Pelvis, and Extremities- archived 052421</i></p> <p>Updated Description section</p>

<b>REVISIONS</b>	
	Updated Rationale section
	Updated Reference section
04-25-2022	In Code Section: <ul style="list-style-type: none"> <li>▪ Updated nomenclature for 75573</li> </ul>
12-09-2022	Updated Description Section
	Updated Rationale Section
	Updated Coding Section <ul style="list-style-type: none"> <li>▪ Removed: 0623T, 0624T, 0625T, 0626T</li> <li>▪ Added: 75572, 75574, 0710T, 0711T, 0712T, 0713T</li> </ul>
	Updated References Section
10-24-2023	Updated Description Section
	Updated Rationale Section
	Updated Coding Section <ul style="list-style-type: none"> <li>▪ Removed ICD-10 Diagnosis Box</li> </ul>
	Updated References Section
11-20-2024	Updated Description Section
	Updated Rationale Section
	Updated References Section

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