BlueCross BlueShield of Alabama

Name of Policy:
Ultrasonographic Measurement of Carotid Intimal-Medial Thickness as an Assessment of Subclinical Atherosclerosis

Policy #: 245
Category: Medicine

Latest Review Date: July 2014
Policy Grade: C

Background/Definitions:

As a general rule, benefits are payable under Blue Cross and Blue Shield of Alabama health plans only in cases of medical necessity and only if services or supplies are not investigational, provided the customer group contracts have such coverage.

The following Association Technology Evaluation Criteria must be met for a service/supply to be considered for coverage:

1. *The technology must have final approval from the appropriate government regulatory bodies;*
2. *The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes;*
3. *The technology must improve the net health outcome;*
4. *The technology must be as beneficial as any established alternatives;*
5. *The improvement must be attainable outside the investigational setting.*

Medical Necessity means that health care services (e.g., procedures, treatments, supplies, devices, equipment, facilities or drugs) that a physician, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury or disease or its symptoms, and that are:

1. *In accordance with generally accepted standards of medical practice; and*
2. *Clinically appropriate in terms of type, frequency, extent, site and duration and considered effective for the patient's illness, injury or disease; and*
3. *Not primarily for the convenience of the patient, physician or other health care provider; and*
4. *Not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.*

Description of Procedure or Service:

Ultrasonographic measurement of carotid intima-medial (or intimal-media) thickness (CIMT) refers to the use of B-mode ultrasound to determine the thickness of the two innermost layers of the carotid artery wall, the intima and the media. Detection and monitoring of intima-medial thickening (atherosclerosis) may provide an opportunity to intervene earlier in atherogenic disease and/or monitor disease progression.

Coronary heart disease (CHD) accounts for 27% of all deaths in the United States. Established major risk factors for coronary artery disease (CHD) have been identified by the National Cholesterol Education Program (NCEP) Expert Panel. These risk factors include elevated serum levels of low density lipoprotein (LDL) cholesterol, total cholesterol, and low serum levels of high-density lipoprotein (HDL) cholesterol. Other risk factors include a history of cigarette smoking, hypertension, family history of premature CHD, and age.

The third report of the NCEP Adult Treatment Panel (ATP III) establishes various treatment strategies to modify the risk of CHD, based in part on target goals of LDL cholesterol. Pathology studies have demonstrated that levels of traditional risk factors are associated with the extent and severity of atherosclerosis. However, at every level of risk factor exposure, there is substantial variation in the amount of atherosclerosis, presumably related to genetic susceptibility and the influence of other risk factors. Therefore, there has been interest in identifying a technique that can improve the ability to diagnose those at risk of developing CHD, as well as measure disease progression, particularly for those at intermediate risk. ATP III recommends the use of the Framingham criteria to further stratify those patients with two or more risk factors for more intensive lipid management.

The carotid arteries can be well visualized by ultrasonography, and ultrasonographic measurements of the thickness of the carotid intimal-medial wall (CIMT) have been investigated as a technique to identify and monitor subclinical atherosclerosis. B-mode ultrasound is most commonly used, and the intimal-medial thickness is measured and averaged over six sites in each carotid artery. Imaging of the far wall of each common carotid artery yields more accurate and reproducible IMT measurements than imaging of the near wall. Two echogenic lines are produced, representing the lumen-intima interface and the media-adventitia interface. The distance between these two lines constitutes the IMT.

Policy:

Ultrasonographic measurement of carotid artery intimal-medial thickness (CIMT) as a technique for identifying subclinical atherosclerosis for use in the screening, diagnosis, or management of atherosclerosis **does not meet** Blue Cross and Blue Shield of Alabama's medical criteria for coverage and is considered **investigational**.

Blue Cross and Blue Shield of Alabama does not approve or deny procedures, services, testing, or equipment for our members. Our decisions concern coverage only. The decision of whether or not to have a certain test, treatment or procedure is one made between the physician and his/her patient. Blue Cross and Blue Shield of Alabama administer benefits based on the members' contract and corporate medical policies. Physicians should always exercise their best medical judgment in providing the care they feel is most appropriate for their patients. Needed care should not be delayed or refused because of a coverage determination.

Key Points:

This policy was originally created in 2003 and was updated regularly with searches of the MEDLINE database. The most recent literature review was performed for the period May 2013 through June 16, 2014.

A summary of the key literature follows.

Evaluation of a diagnostic technology typically focuses on the following 3 parameters: technical performance; diagnostic parameters (sensitivity, specificity, positive and negative predictive value); and demonstration of clinical utility; the diagnostic information can be used to improve patient outcomes.

Literature Review

The literature on the use of carotid intima-media thickness (IMT) for cardiac risk stratification consists of numerous cohort studies and systematic reviews of these cohort studies. The following review includes the largest prospective cohort studies and the most important systematic reviews of these studies.

Diagnostic Utility

Systematic reviews

In a 2012 meta-analysis, the USE Intima-Media Thickness (USE-IMT) collaboration, investigators sought to determine whether common carotid intima-media thickness (CIMT) measurements could assist in estimating the 10-year risk of first-time myocardial infarction (MI) or first-time stroke when added to the Framingham Risk Score. Using individual data for 45,828 patients from 14 population-based cohort studies, Den Ruijter et al found risk of first-time MI or stroke was related positively to both the Framingham Risk Score and the adjusted common CIMT. The mean common CIMT was 0.73 mm and increased in every cohort with patient age during a median follow-up of 11 years. For every 0.1 mm difference in common CIMT, the hazard ratio (HR) for risk of MI or stroke, which occurred in 4007 patients, was 1.12 (95% confidence interval [CI], 1.09 to 1.14) for women and 1.08 (95% CI, 1.05 to 1.11) for men. However, adding common CIMT measurements to the Framingham Risk Score did not improve

risk prediction and resulted in reclassification of risk in only 6.6% of patients. The added value of mean common CIMT in reclassifying risk was only 0.8% (95% CI, 0.1% to 1.6%) and did not differ between men and women. The c-statistic of the Framingham Risk Score model with and without CIMT was similar (0.759; 95% CI, 0.752 to 0.766; and 0.757; 95% CI, 0.749 to 0.764), suggesting the addition of CIMT in risk assessment offered limited benefit.

A 2013 meta-analysis of 15 articles by van den Oord et al found similar results on the added value of CIMT. Six cohort studies totaling 32,299 patients were evaluated to examine the value of CIMT added to traditional cardiovascular risk factors. While a CIMT increase of 0.1mm was predictive for MI (HR=1.15; 95% CI, 1.12 to 1.18) and for stroke (HR=1.17; 95% CI, 1.15 to 1.21), the addition of CIMT did not statistically significantly increase risk prediction over traditional cardiovascular risk factors (p=0.8).

In a 2012 meta-analysis of individual participant data pooled from 16 studies with a total of 36,984 patients, Lorenz et al examined CIMT progression from two ultrasound screenings taken two to seven years apart (median, four years). Patients were followed for a mean of seven years, during which time 1339 strokes, 1519 MI, and 2028 combined end points (MI, stroke, vascular death) occurred. The mean CIMT of the two ultrasound results was predictive of cardiovascular risk using the combined end point (adjusted HR=1.16; 95% CI 1.10 to 1.22). In sensitivity analyses, no associations were found between cardiovascular risk and individual CIMT progression regardless of CIMT definition, end point, and adjustments. As an example, for the combined end points, an increase of 1 SD in mean common CIMT progression resulted in an overall estimated HR of 0.97 (95% CI, 0.94 to 1.00) when adjusted for age, sex, and mean common CIMT, and HR was 0.98 (95% CI, 0.95 to 1.01) when adjusted for vascular risk factors. These data confirm that CIMT is a predictor of cardiovascular risk, but do not demonstrate that changes in CIMT over time are predictive of future events.

In a 2012 systematic review of subclinical atherosclerosis imaging techniques, Peters et al reviewed 12 studies on CIMT that examined reclassification of risk. For the impact on the primary outcome of cardiovascular events, when CIMT was added to the prediction model, the range of increase in the c-statistic was 0.00 to 0.03 on a scale of 0 to 1.0. Net reclassification improvement with CIMT was reported in 5 of the studies included in the review and ranged from -1.4% to 12%.

Recent studies have found including carotid plaques in CIMT increases the predictive value of cardiovascular risk over CIMT assessed only in plaque-free sites. However, the meta-analysis by Lorenz found no difference in the main results between studies that included CIMT with carotid plaque and plaque-free CIMT. The systematic review by Peters found adding carotid plaque to the traditional CIMT model increased the c-statistic from 0.01 to 0.06.

In 2010, Mookadam et al conducted a systematic review of the role of CIMT in predicting individual cardiovascular event risk and as a tool in assessing therapeutic interventions. The authors concluded that CIMT is an independent risk factor for cardiovascular events and may be useful in determining treatment when there is uncertainty regarding the approach or patient reluctance. However, further studies are needed to identify the best approaches to screening and interventions to prevent progression of atherosclerosis.

Prospective cohort studies

In the Atherosclerosis Risk in Communities (ARIC) study, the authors evaluated risk factors associated with increased CIMT in 15,800 subjects. CIMT had a graded relationship with increasing quartiles of plasma total cholesterol, low-density lipoprotein (LDL) cholesterol, and triglycerides. CIMT was then also correlated with the incidence of CHD in a subgroup of patients enrolled in the trial after four to seven years of follow-up. Among the 12,841 subjects studied, there were 290 incident events. The HR rate for men and women, adjusted for age and gender, comparing extreme CIMT (ie, ≥1 mm) to non-extreme CIMT (ie, <1 mm) was 5.07 for women and 1.85 for men. The strength of the relationship was reduced by including major coronary heart disease (CHD) risk factors but remained elevated for higher measurements of CIMT. The authors concluded that mean CIMT is a noninvasive predictor of future CHD incidence.

The Rotterdam study was a prospective cohort study that started in 1989 and recruited 7983 men and women aged 55 years and older. The main objective of the Rotterdam study was to investigate the prevalence and incidence of risk factors for chronic diseases, including cardiovascular disease, in elderly people. One aspect of the study sought to determine whether progression of atherosclerosis in asymptomatic elderly subjects is a prelude to cardiovascular events. Measurements of CIMT were used to assess the progression of atherosclerosis. Increasing CIMT was associated with increasing risks of stroke and MI. O'Leary et al performed CIMT in 4476 asymptomatic subjects aged 65 years or older without clinical cardiovascular disease. The incidence of cardiovascular events correlated with measurements of CIMT; this association remained significant after adjustment for traditional risk factors. The authors concluded that increases in CIMT are directly associated with an increased risk of MI and stroke in older adults without a history of cardiovascular disease.

The Carotid Atherosclerosis Progression Study (CAPS) was a longitudinal study of 4904 subjects. All subjects received a baseline CIMT measurement, as well as traditional risk factor analysis, and were followed over a 10-year period (mean follow-up, 8.5 years; range 7.1-10.0 years). Adverse outcome events were MI in 73 patients (1.5%), angina or MI in 271 patients (5.5%), and death in 72 subjects (1.5%). Lorenz et al have recently published a retrospective review of the data from CAPS. The authors modeled the predictive value of CIMT on the cardiovascular adverse events within that decade. Because the thresholds of CIMT measurements that would lead to reclassification of risk are unknown, the authors used 24 different models of reclassification and five statistical tests. Each model compares the predictive value of traditional risk factors alone with those risk factors with the addition of CIMT. The authors were unable to find significance in the reclassification models with the addition of CIMT measurements. They concluded that this retrospective analysis does not support the use of CIMT as a clinically useful risk classification tool when used in conjunction with traditional risk factor analysis.

Several other studies have, in fact, used CIMT measurements as outcome measures. In this setting, serial measurements of CIMT are performed, as opposed to a single measure. For example, the Asymptomatic Carotid Artery Progression Study (ACAPS) was designed to evaluate the role of lovastatin (an HMG-CoA reductase inhibitor, i.e., a statin drug) in patients asymptomatic for cardiovascular disease and with LDL cholesterol levels at or below the limits

established by the National Cholesterol Education Program. A total of 919 asymptomatic men and women were randomly assigned to receive various combinations of lovastatin, warfarin, and placebo over a three-year period. The principal outcome measurement was the progression of CIMT, tested at six sites in both carotid arteries. Lovastatin treatment was associated with a reduction in the progression of mean maximum CIMT. The Monitored Atherosclerosis Regression Study also included measurements of CIMT every six months for four years in a subset of enrolled subjects. The authors concluded that lipid-lowering therapy resulted in a regression of CIMT.

CIMT is frequently used in the research setting but application or widespread use is uncertain. In the Multi-Ethnic Study of Atherosclerosis (MESA) trial, an ongoing cohort study of atherosclerosis, CIMT was found to be a modestly better predictor of stroke but a worse predictor of CHD than coronary artery calcium score at a median follow-up of 3.9 years among 6698 adults asymptomatic at baseline. In a 2010 article from MESA, CIMT results in 4792 healthy, nondiabetic adults who were not on lipid-lowering medications were compared in six different lipid groups, including normolipemic and several types of common dyslipidemias. The mean CIMT values were increased only for the combined hyperlipidemia (defined as any high-density lipoprotein [HDL]-C level, LDL-cholesterol [C] ≥160 and triglyceride ≥150) and simple hypercholesterolemia (defined as any HDL-C level, LDL-C ≥160 and triglyceride <150) groups. In another MESA report, in 2011, on 6760 patients with elevated high-sensitivity C-reactive protein (hsCRP) as defined by the JUPITER study, CIMT increases correlated with obesity but only mildly with hsCRP. In the Bogalusa Heart Study of 991 subjects, obesity along with overweight and elevated metabolic risk were also associated with increased CIMT. In this study population, 41% of patients were found to have increased CHD risk. In the CARDIA study, clotting factor VII was associated with increases in CIMT in 1254 subjects. CIMT is also used as a surrogate outcome measure in atherosclerosis treatment research studies.

In 2010, Raiko et al compared cardiovascular disease risk-scoring tools for identification of CHD risk to CIMT results in 2204 healthy adults, aged 24 to 39 years, from the Cardiovascular Risk in Young Finns study. The cardiovascular disease risk scoring tools evaluated included the Framingham, Reynolds Risk Score, Systematic Coronary Risk Evaluation (SCORE), PROCAM, and Finrisk cardiovascular risk scores. In this population-based follow-up study, the authors found all of the cardiovascular disease risk scores performed equally in being able to predict subclinical atherosclerosis, as measured by high CIMT six years later.

Section Summary
Evidence from large, prospective cohort studies has established that CIMT is an independent risk factor for cardiovascular disease. However, systematic reviews have concluded that the ability of CIMT to reclassify patients into clinically relevant categories is modest and may not be clinically important. The uncertainty around the ability to reclassify patients into clinically relevant categories limits the potential for CIMT to improve health outcomes

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Clinical Utility
In a 2011 study by Johnson et al, 355 patients, aged 40 years with one or more cardiovascular disease risk factors, received carotid ultrasound screenings to prospectively determine whether abnormal results would change physician and patient behaviors. Results were considered

abnormal (when CIMT was greater than the 75th percentile or the presence of carotid plaque) in 266 patients. Self-reported questionnaires were completed before the carotid ultrasound, immediately after the ultrasound, and 30 days later to determine behavioral changes. Physician behavior in prescribing aspirin and cholesterol medication changed significantly ($p<0.001$ and $p<0.001$, respectively) after identification of abnormal carotid ultrasound results. Abnormal ultrasound results predicted reduced dietary sodium (odds ratio [OR], 1.45; $p=0.002$) and increased fiber intake (OR=1.55; $p=0.022$) in patients but no other significant changes. Health outcomes were not evaluated in this study, and the short-term follow-up limits interpretation of results.

The evidence on reclassification of cardiovascular risk offers a potential indirect chain of evidence to improve outcomes. If a measure is able to reclassify patients into risk categories that have different treatment approaches, then clinical management changes may occur that lead to improved outcomes. Because the ability to reclassify patients into clinically relevant categories with CIMT is modest at best, the clinical utility of this measure for reclassification is uncertain.

Section Summary
There is no direct evidence on the clinical utility of measuring CIMT for cardiac risk stratification. The available evidence on reclassification into clinically relevant categories does not support that the use of CIMT will improve health outcomes.

Practice Guidelines and Position Statements
A 2013 guideline on the assessment of cardiovascular risk from the American College of Cardiology and the American Heart Association (ACC/AHA) does not recommend CIMT for routine risk assessment of a first atherosclerotic cardiovascular disease event. (Grade N, not recommendation for or against) ACC/AHA Class III: no benefit, LOE: B. (based on new evidence during ACC/AHA update of evidence). This differs from the previous 2010 version of the ACC/AHA guidelines for assessment of cardiovascular risk, which indicated CIMT might be reasonable for assessing cardiovascular risk in intermediate risk asymptomatic adults.

In October 2009, the U.S. Preventive Services Task Force (USPSTF) published a systematic review of CIMT within the scope of a larger recommendation statement entitled "Using Nontraditional Risk Factors in Coronary Heart Disease Risk Assessment". On the basis of one fair- and two good-quality studies, the USPSTF states that CIMT, independently of Framingham risk factors, predicts coronary heart disease (CHD) in asymptomatic patients. These studies were longitudinal, population-based studies conducted in the U.S. and the Netherlands. USPSTF reviewed the Atherosclerosis Risk in Communities (ARIC) study and concluded that CIMT measurement can result in risk prediction that is modestly improved, particularly in adult men. However, the review cautions that the studies that did show an association were all done in a research setting, and therefore one cannot draw conclusions on the applicability of CIMT to the intermediate-risk population at large. The studies which USPSTF referenced are further detailed within this policy.

The Summary of Recommendation specific to CIMT is stated as: "The U.S. Preventive Services Task Force (USPSTF) concludes that the current evidence is insufficient to assess the balance of benefits and harms of using…[CIMT]…to screen asymptomatic men and women

with no history of CHD to prevent CHD events." The USPSTF identifies the following research need: "The predictive value…of carotid IMT…should be examined in conjunction with traditional Framingham risk factors for predicting CHD events and death."

The American Society of Echocardiography Consensus Statement endorsed by the Society for Vascular Medicine, states that CIMT is a feature of arterial wall aging "that is not synonymous with atherosclerosis, particularly in the absence of plaque." The statement recommends measurement of both CIMT and carotid plaque by ultrasound "for refining CVD risk assessment in patients at intermediate cardiovascular disease risk (Framingham Risk Score 6–20%) without established CHD, peripheral arterial disease, cerebrovascular disease, diabetes mellitus, or abdominal aortic aneurysm." However, the authors acknowledge that, "More research is needed to determine whether improved risk prediction observed with CIMT or carotid plaque imaging translates into improved patient outcomes."

The ATP III does not recommend using "emerging risk factors" in the assessment of persons for primary prevention. It does state that "emerging risk factors" may be useful in certain patient-centered circumstances.

Key Words:

Carotid intimal medial thickness (CIMT), B-mode ultrasound, intimal medial thickness, IMT

Approved by Governing Bodies:

In February 2003, SonoCalc® (SonoMetric Health, LLC, Bountiful UT) was cleared for marketing by the FDA through the 510(k) process. The FDA determined that this software was substantially equivalent to existing image display products for use in the automatic measurement of the intima media thickness of the carotid artery from images obtained from ultrasound systems. Subsequently, several other devices have been approved through the 510(k) process.

Benefit Application:

Coverage is subject to member's specific benefits. Group specific policy will supersede this policy when applicable.

ITS: Home Policy provisions apply
FEP contracts: FEP does not consider investigational if FDA approved. Will be reviewed for medical necessity.
Pre-certification requirements: Not applicable

Current Coding:

CPT code:

0126T	Carotid intima media thickness
93799	Unlisted cardiovascular service or procedure

References:

1. Adolphe A, et al. A cross-sectional study of intima-media thickness, ethnicity, metabolic syndrome, and cardiovascular risk in 2,268 study participants. Mayo Clinical Proceedings, March 2009; 84(3): 221-228.
2. Anand SS, et al. Relationship of metabolic syndrome and fibrinolytic dysfunction to cardiovascular disease, Circulation, July 2003; 108(4): 420-425.
3. Blaha MJ, Rivera JJ, Budoff MJ et al. Association Between Obesity, High-Sensitivity C-Reactive Protein >=2 mg/L, and Subclinical Atherosclerosis: Implications of JUPITER from the Multi-Ethnic Study of Atherosclerosis. Arterioscler Thromb Vasc Biol 2011; 31(6):1430-8.
4. Blue Cross Blue Shield Association. Ultrasonographic measurement of carotid intimal-medial thickness as an assessment of subclinical atherosclerosis. Medical Policy Reference Manual, July 2010.
5. Bots ML, et al. Common carotid intima-media thickness and risk of stroke and myocardial infarction: The Rotherdam Study, Circulation, September 1997; 96(5): 1432-1437.
6. Bots ML, et al. Intensive lipid lowering may reduce progression of carotid atherosclerosis within 12 months of treatment: the METEOR study. Journal of Internal Medicine, June 2009; 265(6): 698-707.
7. Burke GL, et al. Arterial wall thickness is associated with prevalent cardiovascular disease in middle-aged adults. The Atherosclerosis Risk in Communities (ARIC), Stroke, March 1995; 26(3): 386-391.
8. Byington RP, et al. Effects of lovastatin and warfarin on early carotid atherosclerosis: Sex-specific analyses. Asymptomatic Carotid Artery Progression Study (ACAPS) Research Group, Circulation, July 1999; 100(3): E14-17.
9. Camhi SM, Katzmarzyk PT, Broyles ST et al. Subclinical atherosclerosis and metabolic risk: role of body mass index and waist circumference. Metab Syndr Relat Disord 2011; 9(2):119-25.
10. Chambless LE, et al. Association of coronary heart disease incidence with carotid arterial wall thickness and major risk factors: The Atherosclerosis Risk in Communities (ARIC) Study, 1987-1993, American Journal of Epidemiology, September 1997; 146(6): 483-494.
11. Chambless LE, et al. Carotid wall thickness is predictive of incident clinical stroke: The Atherosclerosis Risk in Communities (ARIC) Study, American Journal of Epidemiology, March 2000; 151(5): 478-487.
12. Chambless LE, et al. Prediction of ischemic stroke in the Atherosclerosis Risk in Communities Study, American Journal of Epidemiology, August 2004; 160(3): 259-269.
13. Den Ruijter HM, Peters SA, Anderson TJ et al. Common carotid intima-media thickness measurements in cardiovascular risk prediction: a meta-analysis. JAMA 2012; 308(8):796-803.
14. Dobs AS, et al. Risk factors for popliteal and carotid wall thickness in the Atherosclerosis Risk in Communities (ARIC) Study, American Journal of Epidemiology, November 1999; 150(10): 1055-1067.
15. Espeland MA, et al. Associations of risk factors with segment-specific intimal-medial thickness of the extracranial carotid artery, Stroke, May 1999; 30(5): 1047-1055.

16. Fernandes VR, Polak JF, Edvardsen T, et al. Subclinical atherosclerosis and incipient regional myocardial dysfunction in asymptomatic individuals: the Multi-Ethnic Study of Atherosclerosis (MESA). J Am Coll Cardiol 2006; 47(12):2420-8.
17. Folsom AR, et al. Coronary artery calcification compared with carotid intima-media thickness in the prediction of cardiovascular disease incidence: the Multi-Ethnic Study of Atherosclerosis (MESA). Archives of Internal Medicine, June 2008; 168(12): 1333-1339.
18. Goff DC, Jr., Lloyd-Jones DM, Bennett G et al. 2013 ACC/AHA Guideline on the Assessment of Cardiovascular Risk: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation 2013.
19. Green D, Foiles N, Chan C et al. An association between clotting factor VII and carotid intima-media thickness: the CARDIA study. Stroke 2010; 41(7):1417-22.
20. Greenland P, Alpert JS, Beller GA et al. 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. J Am Coll Cardiol 2010; 56(25):e50-103.
21. Hodis HN, et al. Reduction in carotid arterial wall thickness using lovastatin and dietary therapy: A randomized controlled clinical trial, Annals of Internal Medicine, March 1996; 124(6): 548-556.
22. Hodis HN, et al. The role of carotid arterial intima-media thickness in predicting clinical coronary events, Annals of Internal Medicine, February 1998; 128(4): 262-269.
23. Howard G, et al. Carotid artery intimal-medial thickness distribution in general populations as evaluated by B-mode ultrasound. ARIC investigators, Stroke, September 1993; 24(3): 1297-1304.
24. Howard G, et al. Relations of intimal-medial thickness among sites within the carotid artery as evaluated by B-mode ultrasound. ARIC investigators. Atherosclerosis Risk in Communities, Stroke, August 1994; 25(8): 1581-1587.
25. Iglesias del Sol A, et al. Carotid intima-media thickness at different sites : Relation to incident myocardial infarction: The Rotterdam Study, European Heart Journal, June 2002; 23(12): 934-940.
26. Johnson HM, Turke TL, Grossklaus M et al. Effects of an office-based carotid ultrasound screening intervention. J Am Soc Echocardiogr 2011; 24(7):738-47.
27. Kanwar M, Rosman HS, Fozo PK, et al. Usefulness of carotid ultrasound to improve the ability of stress testing to predict coronary artery disease. Am J Cardiol 2007; 99(9):1196-200.
28. Keo HH, Baumgartner I, Hirsch AT et al. Carotid plaque and intima-media thickness and the incidence of ischemic events in patients with atherosclerotic vascular disease. Vasc Med 2011; 16(5):323-30.
29. Lorenz MW, Markus HS, Bots ML, et al. Prediction of clinical cardiovascular events with carotid intima-media thickness: A systematic review and meta-analysis. Circulation 2007; 115(4):459-67.
30. Lorenz MW, Polak JF, Kavousi M et al. Carotid intima-media thickness progression to predict cardiovascular events in the general population (the PROG-IMT collaborative project): a meta-analysis of individual participant data. Lancet 2012; 379(9831):2053-62.

31. Lorenz MW, Schaefer C, et al. Is carotid intima media thickness useful for individual prediction of cardiovascular risk? Ten-year results from the Carotid Atherosclerosis Progression Study (CAPS). Eur Heart J, June 2010. [epub ahead of print]
32. Manolio TA, Arnold AM, Post W, et al. Ethnic differences in the relationship of carotid atherosclerosis to coronary calcification: The Multi-Ethnic Study of Atherosclerosis. Atherosclerosis, March 2008; 197(1): 132-138.
33. McNeill AM, et al. Prevalence of coronary heart disease and carotid arterial thickening in patients with the metabolic syndrome (The ARIL Study). American Journal of Cardiology, November 2004; 94(10): 1249-1254.
34. Minino AM, Heron MP, Murphy SL and Kochanek KD. Deaths: Final data for 2004. Centers for Disease Control and Prevention (CDC). National Vital Statistics Reports, Vol. 55, No. 19, pp. 1-119, www.cdc.gov. Accessed June 30, 2010.
35. Mookadam F, Moustafa SE, Lester SJ et al. Subclinical atherosclerosis: evolving role of carotid intima-media thickness. Prev Cardiol 2010; 13(4):186-97.
36. Naghavi M, Falk E, Hecht HS, et al. From vulnerable plaque to vulnerable patient – Part III: Executive summary of the Screening for Heart Attack Prevention and Education (SHAPE) Task Force Report. Am J Cardiol 2006; 98(2A):2H-15H.
37. Nambi V, Chambless L, He M et al. Common carotid artery intima-media thickness is as good as carotid intima-media thickness of all carotid artery segments in improving prediction of coronary heart disease risk in the Atherosclerosis Risk in Communities (ARIC) study. Eur Heart J 2012; 33(2):183-90.
38. National Cholesterol Education Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults, www.nhlbi.nih.gov/guidelines/cholesterol/atp3xsum.pdf.
39. O'Leary DH, et al. Carotid-artery intima and media thickness as a risk factor for myocardial infarction and stroke in older adults. Cardiovascular Health Study Collaborative Research Group, New England Journal of Medicine, January 1999; 340(1): 14-22.
40. Paramsothy P, Knopp RH, Bertoni AG et al. Association of combinations of lipid parameters with carotid intima-media thickness and coronary artery calcium in the MESA (Multi-Ethnic Study of Atherosclerosis). J Am Coll Cardiol 2010; 56(13):1034-41.
41. Pasternak RC. Report of the adult treatment panel III: The 2001National Cholesterol Education Program guidelines on the detection, evaluation and treatment of elevated cholesterol in adults. Cardiol Clin, August 2003; 21(3): 393-398.
42. Peters SA, den Ruijter HM, Bots ML et al. Improvements in risk stratification for the occurrence of cardiovascular disease by imaging subclinical atherosclerosis: a systematic review. Heart 2012; 98(3):177-84.
43. Plichart M, Celermajer DS, Zureik M et al. Carotid intima-media thickness in plaque-free site, carotid plaques and coronary heart disease risk prediction in older adults. The Three-City Study. Atherosclerosis 2011; 219(2):917-24.
44. Prati P, et al. Carotid intima media thickness and plaques can predict the occurrence of ischemic cerebrovascular events. Stroke, September 2008; 39(9): 2470-2476.
45. Probstfield JL, et al. Results of the primary outcome measure and clinical events from the Asymptomatic Carotid Artery Progression Study, American Journal of Cardiology, September 1995; 76(9): 47C-53C.

46. Raiko JR, Magnussen CG, Kivimaki M et al. Cardiovascular risk scores in the prediction of subclinical atherosclerosis in young adults: evidence from the cardiovascular risk in a young Finns study. Eur J Cardiovasc Prev Rehabil 2010; 17(5):549-55.
47. Riley WA, et al. Reproducibility of non-invasive ultrasonic measurement of carotid atherosclerosis. The Asymptomatic Carotid Artery Plaque Study, Stroke 1992, Vol. 23, pp. 1062-1068.
48. Roman MJ, Moeller E, Davis A, et al. Preclinical carotid atherosclerosis in patients with rheumatoid arthritis. Ann Intern Med 2006; 144(4):249-56.
49. Salonen JT and Salonen R. Ultrasound B-mode imaging in observational studies of atherosclerotic progression, Circulation, March 1993; 87(3 Suppl): II 56-65.
50. Singh TP, et al. Vascular function and carotid intimal-medial thickness in children with insulin-dependent diabetes mellitus, Journal of the American College of Cardiology, February 2003; 41(4): 661-665.
51. Stein JH, et al. Use of carotid ultrasound to identify subclinical vascular disease and evaluate cardiovascular disease risk? A Consensus Statement from the American Society for Echocardiography Carotid Intima-Media Thickness Task Force. Endorsed by the Society for Vascular Medicine. Journal of the American Society of Echocardiography, February 2008, Vol. 21, Issue 2.
52. U.S. Preventive Services Task Force. Using nontraditional risk factors in coronary heart disease risk assessment: US Preventive Services Task Force Recommendation Statement. Ann Intern Med 2009; 151: 474-482.
53. U.S. Preventive Services Task Force. Screening for Coronary Heart Disease: Recommendation Statement. Agency for Healthcare Research and Quality, Rockville, MD, February 2004. Accessible at www.ahrq.gov/clinic/3rduspstf/chd/chdrs.htm .
54. Using nontraditional risk factors in coronary heart disease risk assessment: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med 2009; 151(7):474-82.
55. van den Oord SC, Sijbrands EJ, ten Kate GL et al. Carotid intima-media thickness for cardiovascular risk assessment: systematic review and meta-analysis. Atherosclerosis 2013; 228(1): 1-11.
56. van der Meer IM, et al. Predictive value of non-invasive measures of atherosclerosis for incident myocardial infarction: The Rotterdam Study, Circulation, March 2004; 109(9): 1089-1094.
57. Wagenknecht LE, et al. Diabetes and progression of carotid atherosclerosis: The insulin resistance atherosclerosis study, Arteriosclerosis, Thrombosis and Vascular Biology, June 2003; 23(6): 1035-1041.
58. Xie W, Liang L, Zhao L et al. Combination of carotid intima-media thickness and plaque for better predicting risk of ischaemic cardiovascular events. Heart 2011; 97(16):1326-31.

Policy History:

Medical Policy Group, August 2005 **(3)**
Medical Policy Administration Committee, August 2005
Available for comment August 27-October 10, 2005
Medical Policy Group, August 2006 **(1)**
Medical Policy Group, August 2007**(1)**

Medical Policy Group, March 2009 **(4)**
Medical Policy Group, July 2009 **(3)**
Medical Policy Group, July 2010 **(1)**: Policy updated, no coverage change
Medical Policy Group, July 2011 (**1)**: Update to Description, Key Points and References
Medical Policy Group, July 2012 **(1)**: Update to Key Points and References related to MPP update; no change to policy statement
Medical Policy Group, July 2013 **(4)**: 2013 Update to Key Points and References related to Diagnostic Utility
Medical Policy Panel, July 2014
Medical Policy Group, July 2014 **(4):** Updated Key Points, Practice Guidelines and References. No change to policy statement at this time.
