

## ASE CONSENSUS STATEMENT

# Use of Carotid Ultrasound to Identify Subclinical Vascular Disease and Evaluate Cardiovascular Disease Risk: A Consensus Statement from the American Society of Echocardiography Carotid Intima-Media Thickness Task Force *Endorsed by the Society for Vascular Medicine*

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Continuing Medical Education Course for "Use of Carotid Ultrasound to Identify Subclinical Vascular Disease and Evaluate Cardiovascular Disease Risk: A Consensus Statement for the American Society of Echocardiography Carotid Intima-Media Thickness Task Force"

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#### **Target Audience:**

1. Physicians, physicians' assistants, and nurses with an interest in cardiac and vascular imaging, preventive cardiology, and cardiovascular disease risk assessment. 2. Ultrasonographers with interest in vascular imaging and cardiovascular disease risk assessment.

#### **Objectives:**

Upon completing this activity, participants will be able to: 1. Describe the rationale for using carotid ultrasound to identify subclinical vascular disease and to evaluate cardiovascular disease risk. 2. Explain the application of carotid ultrasound to cardiovascular disease risk assessment. 3. Describe the scanning technique for identifying subclinical vascular disease using carotid ultrasound. 4. Explain the key components of interpreting carotid ultrasound studies for cardiovascular disease risk assessment.

#### **Authors Disclosures:**

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Research grants: Siemens Medical Solutions, Sonosite

Intellectual property: listed as the inventor of Patent #US 6,730,0235 "Ultrasonic Apparatus and Method for Providing Quantitative Indication of Risk of Coronary Heart Disease." It has been assigned to the Wisconsin Alumni Research Foundation.

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## SUMMARY

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There is great interest in identifying asymptomatic patients at high risk who might be candidates for more intensive, evidence-based medical interventions that reduce cardiovascular disease (CVD) risk. Measurement of carotid intima-media thickness (CIMT) with B-mode ultrasound is a noninvasive, sensitive, and reproducible technique for identifying and quantifying subclinical vascular disease and for evaluating CVD risk. To address issues of standardization and help improve the availability of experienced clinical laboratories that can perform high-quality CIMT studies, this consensus document provides recommendations for the use of carotid ultrasound for identifying and quantifying subclinical vascular disease and for evaluating CVD risk in clinical practice. Nine published prospective studies that included at least 1000 asymptomatic participants have examined CIMT and CVD risk. Each study demonstrated that CIMT was significantly associated with risk for myocardial infarction, stroke, death from coronary heart disease, or a combination of these events. In most of these studies, the ability of CIMT to predict future CVD events was independent of traditional risk factors. Furthermore, 9 large studies have demonstrated similar or greater predictive power for carotid plaque and CVD.

Measuring CIMT and identifying carotid plaque can be useful for refining CVD risk assessment in patients at intermediate CVD risk (ie, patients with a 6%-20% 10-year risk of myocardial infarction or coronary heart disease death who do not have established coronary heart disease or coronary disease risk equivalent conditions). Patients with the following clinical circumstances also might be considered for testing: (1) family history of premature CVD in a first-degree relative; (2) individuals younger than 60 years old with severe abnormalities in a single risk factor who otherwise would not be candidates for pharmacotherapy; or (3) women younger than 60 years old with at least two CVD risk factors. This test can be considered if the level of aggressiveness of therapy is uncertain and additional information about the burden of subclinical vascular disease or future CVD risk is needed. Imaging should not be performed unless the results would be expected to alter therapy. CIMT testing can reclassify patients at intermediate risk, discriminate between patients with and without prevalent CVD, and predict major adverse CVD events. Outcome data regarding the ability of a management strategy that includes CIMT or plaque screening tests to improve cardiovascular outcomes are limited to changes in patient or physician behavior that would be expected to reduce CVD risk. Consensus recommendations are highlighted in **bold** and are also presented in tables. Because a randomized, controlled trial studying the effectiveness of carotid ultrasound imaging as a tool to modify preventive therapies and improve CVD outcomes has not yet been performed, the clinical practice recommendations in this document are based on the best available observational data. For CVD risk assessment, carotid ultrasound imaging and measurement should follow the protocol from a large epidemiologic study that reported CIMT values in percentiles by age, sex, and race/ethnicity (eg, the Atherosclerosis Risk in Communities Study). The recommended carotid ultrasound scanning protocol is described in detail. CIMT measurements should be limited to the far wall of the common carotid artery and should be supplemented by a thorough scan of the extracranial carotid arteries for the presence of carotid plaque, to increase sensitivity for identifying subclinical vascular disease. Carotid plaque is defined as the presence of focal wall thickening that is at least 50% greater than that of the surrounding vessel wall or as a focal region with CIMT greater than 1.5 mm that protrudes into the lumen that is distinct from the adjacent boundary. The presence of carotid plaque or CIMT greater than or equal

to 75th percentile for the patient's age, sex, and race/ethnicity are indicative of increased CVD risk and may signify the need for more aggressive risk-reduction interventions. Serial studies of CIMT to address progression or regression are not recommended.

## INTRODUCTION

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Atherosclerotic vascular disease begins in childhood and progresses over decades.<sup>1</sup> Symptomatic, clinical cardiovascular disease (CVD) events generally occur when atherosclerosis progresses to flow-limiting disease that causes ischemia, or when a thrombus forms on an existing plaque as a result of rupture or erosion.<sup>2</sup> Although not everyone with underlying atherosclerotic plaque will experience a clinical CVD event, the greater the degree of subclinical atherosclerosis, the greater the risk for future cardiovascular events.<sup>3-7</sup> To prevent death and morbidity from CVD, there is great interest in identifying asymptomatic patients at high risk who would be candidates for more intensive, evidence-based medical interventions that reduce CVD risk.<sup>3,4</sup> Imaging of arteries to identify and quantify the presence of subclinical vascular disease has been suggested to further refine CVD risk assessment.<sup>3,4</sup> As a screening test, imaging must be safe, be sensitive, be affordable, and lead to interventions that can favorably alter the natural history of CVD. Measurement of carotid intima-media thickness (CIMT) with B-mode ultrasound is a noninvasive, sensitive, and reproducible technique for identifying and quantifying atherosclerotic burden and CVD risk. It is a well-validated research tool that has been translated increasingly into clinical practice.<sup>8-13</sup> The United States Centers for Medicare and Medicaid has established a *Current Procedural Terminology* code (0126T) for "Common CIMT study for evaluation of atherosclerotic burden or coronary heart disease risk factor assessment."

In 2000, the American Heart Association Prevention Conference V concluded that CIMT "can now be considered for further clarification of coronary heart disease (CHD) risk assessment at the request of a physician," provided that it is performed by an experienced laboratory.<sup>3</sup> In 2001, the National Cholesterol Education Program (NCEP) Adult Treatment Panel III stated that CIMT "could be used as an adjunct in CHD risk assessment . . . the finding of an elevated CIMT (eg,  $\geq 75$ th percentile for age and sex) could elevate a person with multiple risk factors to a higher risk category," while noting that "expense, lack of availability, and difficulties with standardization preclude a current recommendation for its use in routine risk assessment."<sup>14</sup> This expert panel concluded that "if carried out under proper conditions, CIMT could be used to identify persons at higher risk than that revealed by the major risk factors alone."<sup>14</sup> The clinical application of CIMT methodology recently was reviewed in a report from the American Society of Echocardiography (ASE) and the Society of Vascular Medicine and Biology.<sup>15</sup> To address issues of standardization and help improve the availability of experienced clinical laboratories that can perform high-quality CIMT studies, this consensus statement provides recommendations for the use of carotid ultrasound to assess subclinical vascular disease and CVD risk.

## RATIONALE FOR USING CAROTID ULTRASOUND TO IDENTIFY SUBCLINICAL VASCULAR DISEASE AND EVALUATE CVD RISK: EVIDENCE FROM CLINICAL RESEARCH STUDIES

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Standard clinical carotid duplex ultrasound studies primarily are indicated to identify occlusive carotid plaques (ie, carotid artery

**Table 1** Prospective studies of carotid intima-media thickness and risk for cardiovascular disease events in individuals without known cardiovascular disease (N >1000 participants each)

Study	N	Age (y); F	Follow-up (y)	Measurement; site	Event	ΔCIMT (mm); adjusted RR (95% CI)*	CIMT cut point; adjusted RR (95% CI)*†
ARIC <sup>5</sup>	12,841	45-64; 57%	5.2	Mean of mean; CCA/bulb/ICA	MI, CHD death	0.19; F: 1.38 (1.21-1.58) M: 1.17 (1.04-1.31)	Highest tertile; F: 2.53 (1.02-6.26) M: 2.02 (1.32-3.09)
				Mean; CCA	MI, CHD death	0.19; F: 1.46 (1.22-1.74) M: 1.08 (0.91-1.1.27)	—
ARIC <sup>19</sup>	14,214	45-64; 55%	7.2	Mean of mean; CCA/bulb/ICA	Stroke	0.19; F: 1.36 (1.16-1.59) M: 1.21 (1.05-1.39)	Highest tertile; F: 2.32 (1.09-4.94) M: 2.24 (1.26-4.00)
				Mean; CCA	Stroke	0.18; F: 1.32 (1.10-1.58) M: 1.38 (1.16-1.65)	Highest tertile; F: 1.65 (0.85-3.19) M: 2.69 (1.49-4.87)
CAPS <sup>20</sup>	5056	19-90; 50%	4.2	Mean; far wall CCA	MI	0.16; 1.16 (1.05-1.27)	Highest quartile 1.83 (0.97-3.45)
				Mean; far wall CCA	Stroke	0.16; 1.11 (0.97-1.28)	Highest quartile 1.82 (0.64-5.16)
				Mean; far wall CCA	MI, stroke, death	0.16; 1.17 (1.08-1.26)	Highest quartile 1.85 (1.09-3.15)
CHS <sup>6</sup>	4476	>65; 39%	6.2	Mean of maximum; near + far CCA/ICA	MI	1 SD; 1.36 (1.23-1.52)	Highest quintile; 3.61(2.13-6.11)
				Maximum; near + far CCA	MI	0.20; 1.24 (1.12-1.38)	Highest quintile; 2.46 (1.51-4.01)
				Mean of maximum; near + far CCA/ICA	Stroke	1 SD; 1.33 (1.20-1.47)	Highest quintile; 2.57 (1.64-4.02)
				Maximum; near + far CCA	Stroke	0.20; 1.28 (1.16-1.42)	Highest quintile; 2.13 (1.38-3.28)
KIHD <sup>21</sup>	1257	42-60; 0%	3	Maximum; far wall CCA	MI	0.11; 1.11 (1.06-1.16)	>1.0 mm; 2.1 (0.8-5.2)
Yao City <sup>22</sup>	1289	60-74; 0%	4.5	Mean of maximum; near + far CCA/ICA	Stroke	—	Highest quartile; 4.9 (1.9-12.0)
				Maximum; near + far CCA	Stroke	—	Highest quartile; 4.9 (1.9-12.0)
MDCS <sup>23</sup>	5163	46-68; 60%	7	Maximum; far wall CCA	MI, CHD death	0.15; 1.23 (1.07-1.41)	Highest tertile; 1.50 (0.81-2.59)
Rotterdam <sup>24</sup>	6389	>55; 62%	7-10	Maximum; near + far CCA	MI	0.21; 1.28 (1.14-1.44)	Highest quartile; 1.95 (1.19-3.19)

CCA, Common carotid artery; CHD, coronary heart disease; CI, confidence interval; CIMT, carotid intima-media thickness; F, female; ICA, internal carotid artery; M, male; MI, myocardial infarction; RR, relative risk. ARIC, Atherosclerosis Risk in Communities Study; CAPS, Carotid Atherosclerosis Progression Study; CHS, Cardiovascular Health Study; KIHD, Kuopio Ischemic Heart Disease Study; MDCS, Malmö Diet and Cancer Study.

\*Adjusted for age, sex, and traditional risk factors.

†Highest tertile quartile or quintile compared with lowest.

stenosis), a manifestation of advanced atherosclerosis. For assessment of CVD risk, the carotid artery wall, rather than the degree of luminal narrowing, is examined to identify areas of increased thickness and nonocclusive atherosclerotic plaque, which represent early stages of arterial injury and atherosclerosis. Ultrasound imaging of the far wall of the carotid artery produces two echogenic lines. In situ anatomic and in vitro histologic studies have validated these lines as the lumen-intima interface and the media-adventitia interface.<sup>16-18</sup> The combined thickness of the intimal and medial layers of the arterial wall constitute the CIMT. Current ultrasound technology is not sufficiently sensitive to measure the thickness of the intima alone.

There are 8 published prospective studies of CIMT and CVD risk that included at least 1000 participants, and presented odds ratios or

relative risks adjusted for CVD risk factors (Table 1).<sup>5,6,19-24</sup> These studies recently have been reviewed in detail.<sup>25</sup> All 8 studies demonstrated that CIMT was significantly associated with risk for myocardial infarction, stroke, CHD death, or a combination of these.<sup>5,6,19-24</sup> An additional study with 10,000 participants had similar results.<sup>26</sup> In several studies, the adjusted relative risks associated with the greatest degrees of wall thickness (see cut points in Table 1) were sufficiently high (>2.0) that they would be expected to improve clinical risk prediction in appropriately selected patients.<sup>5,6,19,21,22</sup> CIMT values add additional information beyond traditional risk factors for classifying patients in regard to the likelihood of presence of significant angiographic coronary artery disease.<sup>27</sup> In two studies, CIMT values modestly increased the area

**Table 2** Prospective studies of carotid plaque presence and risk for cardiovascular disease events in individuals without known cardiovascular disease (N >1000 participants each)

Study	N	Age (y); F	Follow-up (y)	Event	Plaque presence adjusted HR (95% CI)*
ARIC <sup>38</sup>	12,375	45-64; 54%	7	MI, CHD death	With AS; 2.96 (1.54-3.30) Without AS: 2.02 (1.42-2.41)
KIHD <sup>39</sup>	1288	42-60; 0%	≤2 y	MI	4.15 (1.50-11.47)
Yao City <sup>22</sup>	1289	60-74; 0%	4.5	Stroke	3.2 (1.4-7.1)†
MDCS <sup>23</sup>	5163	46-68; 60%	7	MI, CHD death	1.81 (1.14-2.87)
Northern Manhattan <sup>40</sup>	1939	>40; 59%	6.2	Stroke	3.1 (1.1-8.5)
Rotterdam <sup>24</sup>	6389	>55; 62%	7-10	MI	Severe; 1.83 (1.27-2.62)

AS, Acoustic shadowing; CHD, coronary heart disease; CI, confidence interval; F, female; HR, hazard ratio; MI, myocardial infarction. ARIC, Atherosclerosis Risk in Communities Study; KIHD, Kuopio Ischemic Heart Disease Study; MDCS, Malmö Diet and Cancer Study.

\*Adjusted for age, sex, and traditional risk factors.

†Relative risk.

under the receiver operator characteristic curve for predicting cardiovascular events.<sup>28,29</sup> The relationship between increasing CIMT and incident CVD events has been established across a wide age range; however, the strongest data are for individuals between 42 and 74 years of age, because several studies of individuals in this age range show similar results (Table 1). For younger adults (18-42 years old), consistent, strong relationships between increasing risk factor burden, emerging risk factors, and CIMT have been demonstrated.<sup>30-37</sup> In the Carotid Atherosclerosis Progression Study (CAPS), CIMT predicted cardiovascular events even among the 2436 individuals younger than 50 years old (mean 38.7 years).<sup>20</sup> In that study, the relative risk associated with increased CIMT appeared to be higher among younger than older adults.<sup>20</sup>

Similarly, 6 observational studies that included at least 1000 participants and presented relative risks or hazard ratios adjusted for CVD risk factors have demonstrated the predictive power of the presence of carotid plaque (Table 2).<sup>22-24,38-40</sup> In these studies, the relative risks associated with plaque were similar to or slightly higher than those observed with increased CIMT. Three additional large studies had similar results.<sup>26,41,42</sup> In one study, the presence of carotid plaque significantly improved the area under the receiver operator characteristic curve for prediction of all-cause mortality even after considering risk factors and use of medications.<sup>41</sup> There was not a uniform definition of carotid plaque in these studies.<sup>43</sup> Most studies identified plaque as focal widening relative to adjacent segments with protrusion into the lumen and/or had a minimum wall thickness.<sup>43</sup> A previous ASE report defined nonobstructive plaque "as the presence of focal thickening at least 50% greater than that of the surrounding vessel wall."<sup>15</sup> The Mannheim CIMT Consensus Report suggested that plaque should be defined as "a focal structure that encroaches into the arterial lumen of at least 0.5 mm or 50% of the surrounding intima-media thickness or demonstrated a thickness of greater than or equal to 1.5 mm."<sup>44,45</sup> These definitions are similar to those used in the Atherosclerosis Risk in Communities (ARIC) Study, the largest prospective cohort study that demonstrated the predictive value of plaque in CVD risk assessment.<sup>38</sup>

#### THE RELATIONSHIP BETWEEN CIMT AND SUBCLINICAL VASCULAR DISEASE

CIMT is associated with CVD risk factors, prevalent CVD, incident CVD, and the degree of atherosclerosis in several different arterial beds.<sup>3,4,15,46,47</sup> Progression of CIMT may be attenuated or reversed

with risk factor interventions, in association with a reduced risk of future CVD events.<sup>48,49</sup> These findings provide support to the concept that CIMT measurements can be used as a surrogate marker of atherosclerosis. Increased CIMT may be related to intimal or medial hypertrophy or both, and may be an adaptive response to changes in flow, wall tension, or lumen diameter.<sup>50,51</sup> It is well-established that CIMT increases with advancing age, even in the absence of overt or occult atherosclerosis, as a result of thickening of both the intimal and medial layers. In human beings, CIMT increases nearly 3-fold between the ages of 20 and 90 years.<sup>52</sup> Postmortem studies indicate that age-associated increases in carotid wall thickening mainly are caused by an increase in intimal thickening.<sup>53</sup> In rodent and nonhuman primate models of aging, age-associated arterial changes are observed with advancing age, even though these animals tend not to develop atherosclerosis.<sup>54,55</sup> These alterations encompass many factors that have been implicated in the pathogenesis and progression of atherosclerotic plaques, such as endothelial dysfunction; increased endothelial cell adhesiveness and permeability; increases in procoagulant, vasoconstrictive, and inflammatory molecules; increases in cytokines and chemokines; increased oxidative stress; and proliferation and migration of smooth muscle cells.<sup>54,55</sup> Thus, intimal-medial thickening is a feature of arterial wall aging that is not synonymous with subclinical atherosclerosis, but is related to it because the cellular and molecular alterations that underlie intimal-medial thickening have been implicated in the development, progression, or both of atherosclerosis. Accordingly, carotid wall thickening is not synonymous with atherosclerosis, particularly in the absence of plaque. It represents subclinical vascular disease, the pathophysiologic substrate that explains why CIMT is a risk factor and a marker of CVD risk.<sup>56,57</sup>

#### APPLICATION OF CAROTID ULTRASOUND TO CVD RISK ASSESSMENT

The traditional approach to CVD risk assessment involves identifying and quantifying the presence or absence of CVD risk factors. The NCEP recommends estimating the 10-year risk for CHD death or myocardial infarction using the Framingham risk score (FRS) model.<sup>14</sup> Patients at intermediate risk may benefit most from measurement of subclinical vascular disease to further refine their CVD risk estimates, as decision-making about preventive therapies in this group may be uncertain.<sup>3,4,15,58,59</sup> Although the FRS accurately discriminates short-term CVD risk, it has some potential limitations. Because

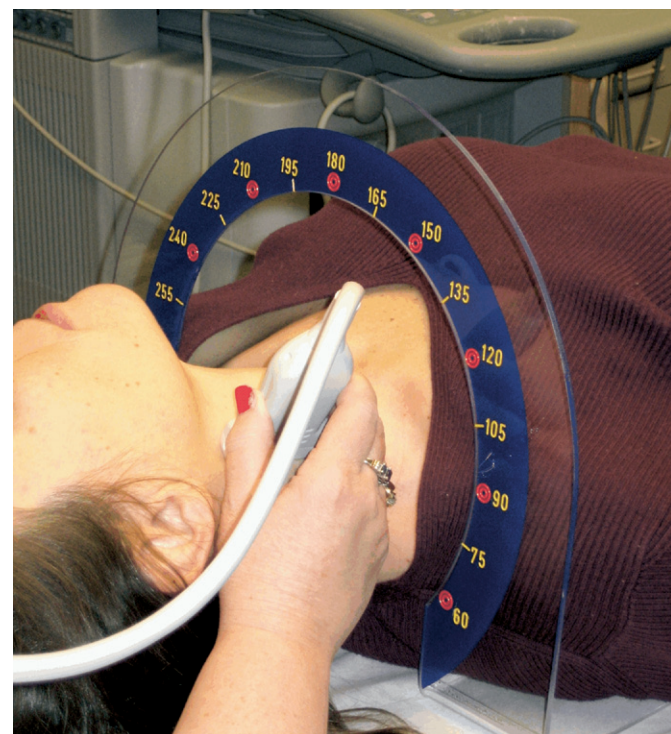


**Table 3** Study setup

Sonographer	Patient
Position at head of patient, with enough space to rest elbow on bed Adjust height and location of ultrasound system keyboard and monitor, examination bed, and chair to avoid ergonomic injuries	Position supine on scan bed with head resting comfortably Slightly hyperextend and rotate neck in direction opposite to probe Use 45-degree angle wedge pillow to help standardize lateral rotation During scan, sonographer may adjust neck position to optimize images, especially in anterior scanning planes Use rolled towels under neck and pillows under legs for comfort Use external landmarks such as the Meijer arc (Figure 1) <sup>91</sup> or similar devices can help standardize transducer angle

the FRS only predicts 10-year risk rather than lifetime risk<sup>60</sup> and women tend to develop CVD at older ages, women with significant subclinical vascular disease can be misclassified as being at lower risk based on the 10-year FRS alone, and therefore, may not receive appropriate preventive measures.<sup>61-63</sup> In addition, patients with extremely high levels of a single risk factor, such as genetic forms of dyslipidemia, may not be adequately classified based solely on their FRS.<sup>14,58,64</sup> In addition, the FRS does not account for family history of premature CVD, and some risk factors such as smoking and diabetes mellitus are considered only as present or absent, although epidemiologic data support a continuous relationship between CVD risk and tobacco exposure and glucose levels, respectively.<sup>64</sup> Finally, chronologic age is the overriding determinant of the FRS, ignoring great interindividual variation in atherosclerotic burden at older ages.<sup>65</sup>

The clinical usefulness of CIMT measurement and plaque detection is related to the patient's pretest CVD risk, which is altered by the relative risk based on the test results, as in Tables 1 and 2. **Measuring CIMT and identifying carotid plaque by ultrasound are most useful for refining CVD risk assessment in patients at intermediate CVD risk (FRS 6%-20% without established**



**Figure 1** Patient position for carotid ultrasound study.

**CHD, peripheral arterial disease, cerebrovascular disease, diabetes mellitus, or abdominal aortic aneurysm). Patients with the following clinical circumstances also might be considered for CIMT measurement and carotid plaque detection: (1) family history of premature CVD in a first-degree relative (men < 55 years old, women < 65 years old); (2) individuals younger than 60 years old with severe abnormalities in a single risk factor (eg, genetic dyslipidemia) who otherwise would not be candidates for pharmacotherapy; or (3) women younger than 60 years old with at least two CVD risk factors.** This test can be considered if the level of aggressiveness of preventive therapies is uncertain and additional information about the burden of subclinical vascular disease or future CVD risk is needed. **Imaging should not be performed in patients with established atherosclerotic vascular disease or if the results would not be expected to alter therapy. Serial studies of CIMT to address progression or regression are not recommended for use in clinical practice.**

Fast computed tomography to measure coronary artery calcium also evaluates subclinical vascular disease<sup>66</sup>; however, carotid ultrasound has some potential advantages compared with this test. Carotid ultrasound does not involve exposure to ionizing radiation, an important consideration when imaging healthy young and middle-aged adults.<sup>67</sup> In addition, CIMT has the advantage of being a continuous measure that could be used to stratify risk in women and younger men, and in African American individuals, where coronary artery calcium scoring may have limited discriminatory power because of a high prevalence of a zero calcium score.<sup>68</sup>

**Table 4** Instrumentation and display

State-of-the-art ultrasound system
Digital image acquisition and storage, preferably DICOM
Phantom scans every 6 months and after any system changes
Semiannual routine preventive maintenance
Transducer
Linear array
Minimal compression (<10:1)
Fundamental frequency ≥ 7 MHz
Footprint ≥ 3 cm
Display
Depth 4 cm
Single focal zone
Frame rate ≥ 25 Hz
High dynamic range
Clear 3-lead electrocardiographic signal
Annotate images to describe segments, angles, and other findings
Carefully adhere to predefined scanning protocol

DICOM, Digital Imaging and Communications in Medicine.

**Table 5** Recommend scanning protocol for evaluation of common carotid artery carotid intima-media thickness and detection of carotid plaques

Step	View	Area of interest	Technique	Use
1	Transverse B-mode scan (3-5 beat cine-loop in each segment)	From proximal CCA through middle of the internal carotid artery	Notch of transducer oriented to right of patient Slowly advance probe, keep vessel in center of screen, show double lines on near and far walls	Overview of vessel orientation, wall thickness, plaques, and surrounding structures
2	Internal and external carotid artery Doppler recordings (one frame of each)	Pulsed wave Doppler of proximal 1 cm of each branch	Sample volume parallel to flow by beam steering and angle correction of $\leq 60$ degrees If narrowing is seen, obtain pre- and post-velocities to document severity	Verifies anatomic orientation and may identify significant stenosis if present
3	Longitudinal plaque screen scan (3-5 beat cine-loop from at least 3 different angles in each segment)	Near and far walls of CCA, bulb, and internal carotid artery segments	Rotate 90 degrees from transverse plane with notch of transducer oriented toward head of patient Circumferential plaque screen scan from anterior, lateral, and posterior imaging planes Return to transverse plane to corroborate maximum plaque size in orthogonal plane Document location and angle that plaque has greatest encroachment into lumen	Identification and description of plaques
4	CIMT imaging (3-5 beat cine-loop and optimized R-wave gated still frames at each angle)	Distal 1 cm of each CCA	Longitudinal images from 3 imaging planes: optimal angle of incidence and two complementary angles (anterior, lateral, and posterior) (Figure 2) Use cursor to mark location of bifurcation Display clear images of distal CCA perfectly horizontal with double lines on near and far walls, indicating true perpendicular scanning plane (Figure 3) Optimize transducer depth (usually 4 cm) to avoid slice thickness artifacts	Segments for CIMT measurement

CCA, Common carotid artery; CIMT, carotid intima-media thickness.  
By convention, the right carotid artery is imaged first.

#### **PUBLISHED EXPERIENCE OF CAROTID ULTRASOUND FOR CVD RISK PREDICTION IN CLINICAL PRACTICE**

Several clinical CVD risk assessment programs have used carotid ultrasound to measure CIMT.<sup>8-13,69,70</sup> In clinical practice, CIMT values can help reclassify patients at intermediate risk,<sup>8-10</sup> discriminate between patients with and without prevalent CVD,<sup>69</sup> and predict major adverse cardiovascular events.<sup>12</sup> Most of these studies incorporated the patient's age and sex by using normative percentile values.<sup>8,9,11-13</sup> Outcome data describing the ability of a management strategy that includes CIMT or plaque screening tests to improve CVD outcomes are limited to changes in patient or physician behavior that would be expected to lead to reduced CVD risk. In a small (N = 50) interventional study, physicians were more likely to prescribe aspirin and lipid-lowering therapy to patients who were found to have carotid plaque during an office screening examination.<sup>71</sup> In a small (n = 74) randomized study, smokers shown images of their carotid plaques were more likely to stop smoking at 6 months.<sup>72</sup> In a study of 210 individuals described in a review article, patients were more likely to adhere to recommendations regarding diet, exercise, and smoking cessation 12 months after seeing pictures of their CIMT examination.<sup>73</sup> **More research is needed to determine whether improved risk prediction observed with CIMT or carotid plaque imaging translates into improved patient outcomes. Because a randomized, controlled trial studying the effectiveness of carotid ultrasound imaging as a tool to**

**modify preventive therapies and improve CVD outcomes has not yet been performed, the clinical practice recommendations in this document are based on the best available observational data.** The Measuring Effects on Intima-Media Thickness: An Evaluation of Rosuvastatin (METEOR) Study demonstrated that middle-aged adults at apparently low to intermediate CVD risk but with increased CIMT (N = 984) benefited from statin therapy that they otherwise would not have qualified for based on current treatment guidelines.<sup>14,74</sup> In this prospective, randomized multicenter clinical trial, the magnitude of the difference in CIMT progression rates ( $-0.145$  mm/y) was similar to that observed in secondary prevention trials that were associated with a reduction in cardiovascular events.<sup>48,74</sup> Although not definitive, this study suggests that using CIMT to modify preventive treatment strategies is feasible and associated with a delay in the progression of vascular injury. **Appropriately designed prospective studies to investigate the effectiveness of carotid ultrasound imaging as a strategy to help improve CVD outcomes are recommended.**

#### **CAROTID ULTRASOUND SCANNING TECHNIQUE**

Patient and Sonographer Preparation (Table 3, Figure 1)

Both the sonographer and patient should be positioned properly to facilitate high-quality, reproducible images. Allow sufficient time for the scan to facilitate positioning and to avoid rushing.<sup>75</sup>

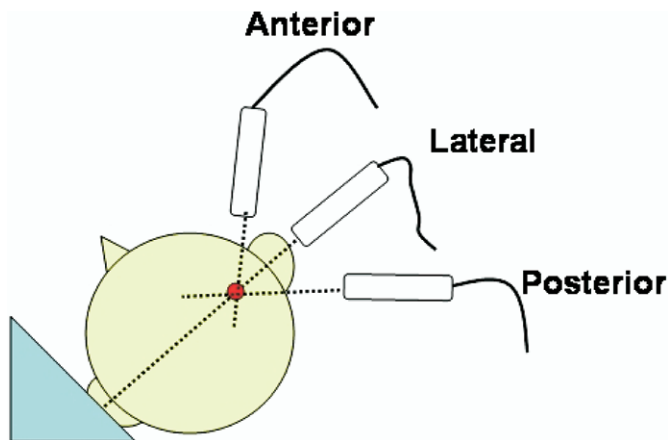


Figure 2 Head position and probe orientation for carotid ultrasound scanning, right-side example.

#### Instrumentation and Image Display

**The carotid arteries should be interrogated using a state-of-the-art ultrasound system with a linear-array transducer operating at a fundamental frequency of at least 7 MHz.** Use of nonfundamental frequencies can increase wall thickness. Use of ultrasound contrast is a research technique that is not recommended for clinical assessment of CIMT at this time. Most patients can be scanned at a standard depth of 4 cm, however, increased depth may be necessary in some patients with larger necks or deeper vessels. Resolution decreases with increasing imaging depth. The typical pixel size when imaging at a 4-cm depth is approximately 0.11 mm. Because CIMT measurements are extremely small, differences of 1 digital pixel can classify patients in different risk categories, so close attention to instrumentation and standardized imaging and reading protocols are critical. Use of the zoom function is discouraged because most studies relating CIMT to CVD events did not use zoomed images. The zoom function on some commercial ultrasound systems increase the pixel size, rather than increasing resolution. When viewing zoomed images, the location of external landmarks for standardized image acquisition may be lost and it is easier for the probe to drift off the optimal image and location. If used, zoom functions should be relegated to very standardized protocols, where internal and external landmarks are kept constant. These considerations require a very experienced operator who can avoid subtle drifting. Protocol deviations from those published require validation, including evaluation of reproducibility.

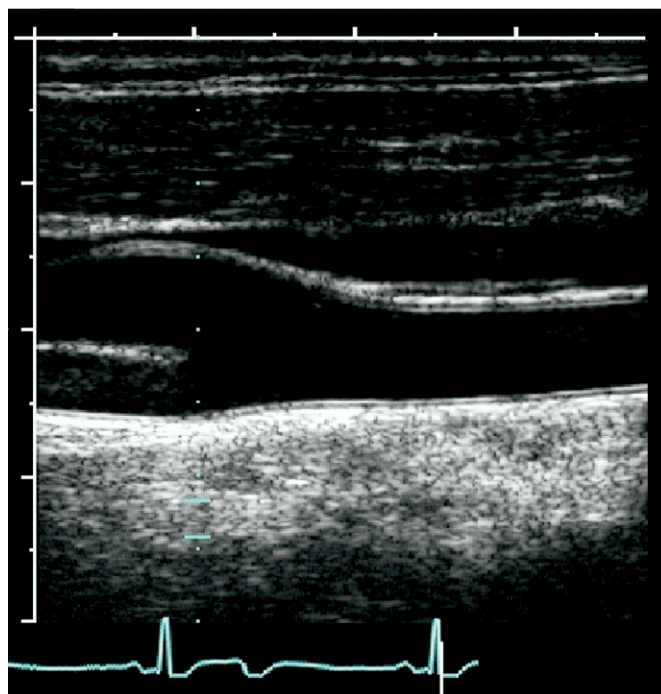


Figure 3 True longitudinal plane simultaneously demonstrating double lines on the near and far walls of the common carotid artery (“double-line” sign).

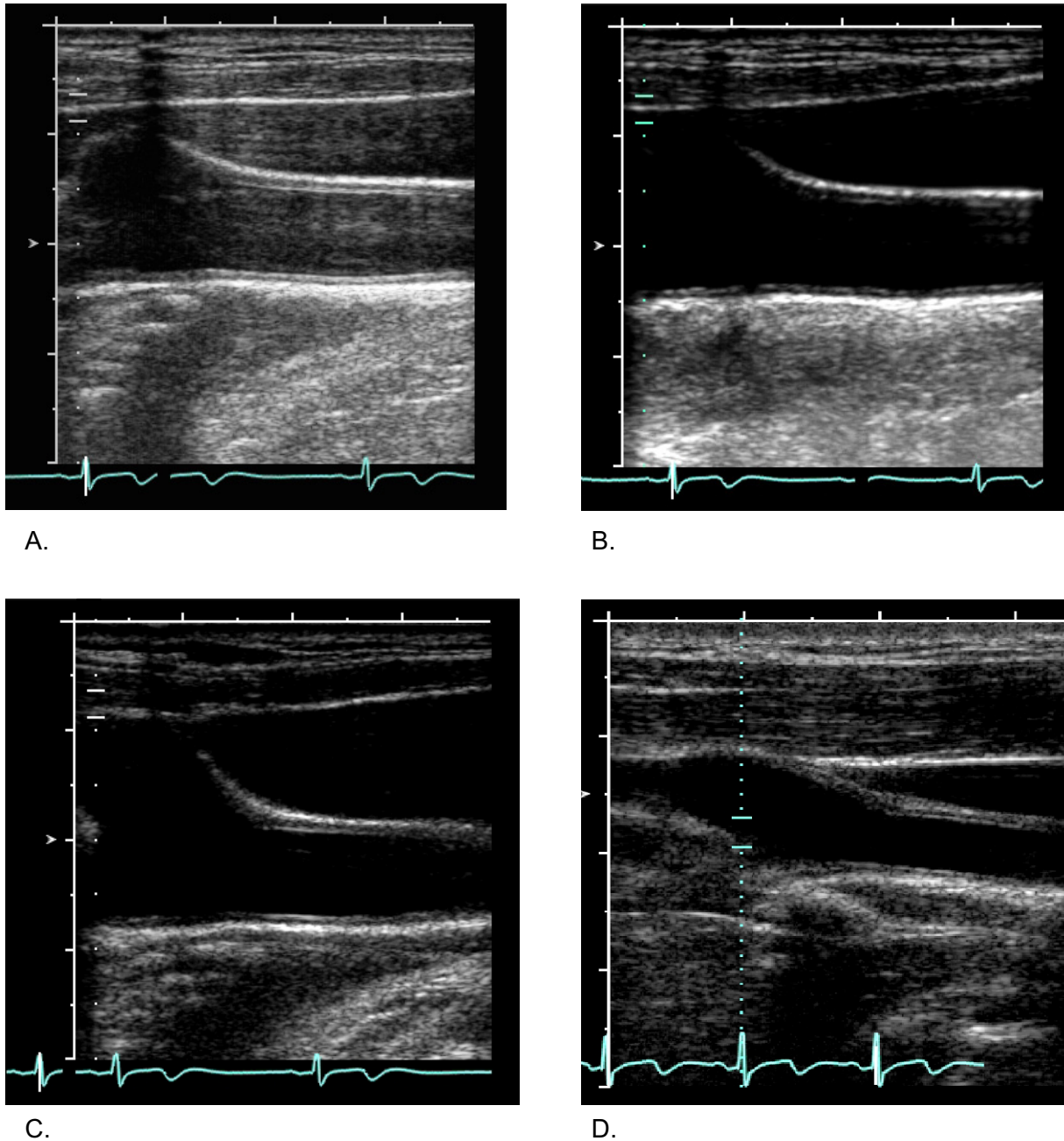
**B-mode imaging is preferred over M-mode imaging.** Although M-mode has superior temporal resolution, it provides measurement of only a single point of thickness, rather than a segmental value. Carotid wall thickening is not uniform, so a single value without considering a wider region is difficult to reproduce and may not accurately represent arterial changes. Perpendicular imaging also is challenging using M-mode. Because M-mode measurements or point-to-point measurements of B-mode images are limited multiples of the pixel size, measurement precision is reduced unless multiple (several hundred) points are measured. Multiple measurements of several extended segment lengths permit expression of CIMT values with higher precision (subpixel level) instead of simple multiples of the pixel size. All reported observational studies relating CIMT values to cardiovascular events used B-mode measurements, usually averaged over at least a 1-cm segment.

**A small parts ultrasound phantom should be used to determine whether the ultrasound system is calibrated**

Table 6 Frequently observed carotid ultrasound imaging pitfalls and potential solutions

Pitfall/problem	Potential solutions
Lack of “double-line” sign	Place vessel horizontal on screen, move transducer perpendicular to vessel, adjust focus and gain
Tortuous vessel	Further extend and slightly rotate neck to elongate segment
Image too deep, blurry posterior angles	Adjust focus, add gel, press sternocleidomastoid muscle and slowly decrease pressure until ideal acoustic impedance is achieved, showing clear double lines
Image too shallow, slice thickness artifact	Increase distance of vessel from near field, add more gel, use less pressure, stack over jugular vein
Under-gained images	Adjust time-gain compensators and overall gain, ensure proper monitor settings
Over-gained images (falsely thick)	Adjust time-gain compensators and overall gain, ensure proper monitor settings
Translation artifact from pulsatile jugular vein	Have patient hold breath at midinspiration to stabilize image





**Figure 4** Common carotid artery intima-media thickness imaging pitfalls and potential solutions. **(A)**, Image is over-gained. Reduce overall gain. **(B)**, Persistence is too high. Turn down persistence. **(C)**, Image not well aligned; double lines lost at right of common carotid artery segment. Re-align transducer with vessel. **(D)**, Image not horizontal. Use heel-toe motion of transducer to re-align.

**accurately and to help determine the axial and lateral resolutions of the transducer.** Phantoms also provide information on gray-scale ranges, help the sonographer select postprocessing maps, and provide an objective tool to compare different systems and transducers. **Routine ultrasound system preventive maintenance should be performed at least biannually.**

Early carotid ultrasound images were recorded on videocassette tapes for subsequent offline image capture and digitization. Although this approach yielded reproducible measurements in highly specialized laboratories, image degradation was inevitable. Current ultrasound technology enables direct storage of digital images on digital

media. **Digital images should be stored directly from the ultrasound system, rather than digitized video captures.** Most current ultrasound systems store images in a Digital Imaging and Communication in Medicine (DICOM) format or one that maintains study organization and internal image calibration, thus eliminating errors caused by manual calibration (Table 4).

#### Imaging Protocol

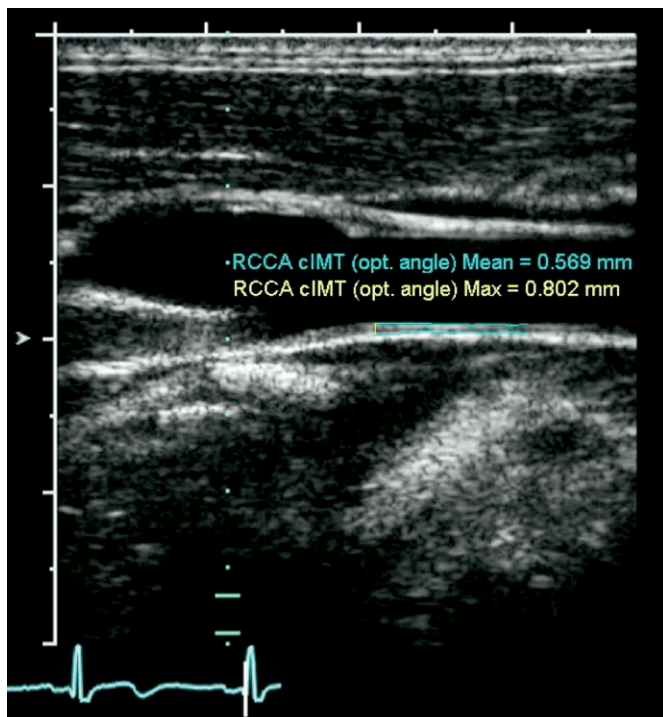
**Carotid ultrasound imaging should follow a scanning protocol from a large epidemiologic study that reported CIMT values in percentiles by age, sex, and race/ethnicity (eg,**



**Table 7** Interpretation of carotid ultrasound studies for cardiovascular disease risk assessment

Step	Action	Rationale
1	Review images on high-quality monitor (resolution $\geq 1024 \times 768$ pixels)	Preserve image quality Accurate display of boundaries
2	Review study images for overall image quality, wall thickness, plaque presence	Corroborate settings Identify incidental findings
3	Evaluate for presence of carotid plaques -Use transverse and longitudinal views to distinguish between plaque presence and imaging artifacts -Report location of plaques (near or far wall, segment, side)	Describing plaque presence improves description of extent of subclinical vascular injury Carotid plaque presence predicts future CVD events
4	Select best images of distal 1 cm of CCA far wall from each of 3 angles; review loops, then measure from R-wave gated still frames	Complementary angles better represent overall wall thickness
5	Measure images in triplicate by tracing far wall blood-intima and media-adventitia interfaces using leading edge-to-leading edge method (Figure 5) -Measure 1-cm length -Assure that measurements from each angle are within 0.05 mm of others -Plaques should be traced as part of CIMT	Triplicate measurements insure consistency, averaging increases precision If more variation is identified, critically review images; only trace images with clear boundaries that are over-gained and are imaged perpendicular to artery
6	Measurement data should automatically enter report -Measured images should be saved digitally to document tracing for later review -Images and measurements should be stored in database -Report mean CIMT values from far walls of right and left CCAs (mean-mean)	Avoids manual entry errors Permits later review and facilitates quality assurance Mean CIMT values are reproducible and predict future CVD events

CCA, Common carotid artery; CIMT, carotid intima-media thickness; CVD, cardiovascular disease.



**Figure 5** Example measurement of far wall common carotid artery (CCA) carotid intima-media thickness (CIMT).

**ARIC Study or others listed in Table 1 and Appendices 1 and 2).** The 4 studies described in Appendix 1 were selected because they are large, cross-sectional, high-quality studies that reported common carotid artery (CCA) CIMT values by age, sex, and race/ethnicity and were conducted in North America (Alice M. Arnold, PhD, personal communication, December 2006; and Robyn L. McClelland, PhD, personal communication, January 2007).<sup>6,76,77</sup> The 50th percentile mean far wall CCA CIMT values for white and black men and women between 45 and 64 years of age in ARIC and Multi-Ethnic Study of Atherosclerosis (MESA) are remarkably similar given the differences between the studies (Robyn L. McClelland, PhD, personal communication, January 2007).<sup>76</sup> For older patients, the 50th percentile maximum CCA CIMT values in the Cardiovascular Health Study (CHS) Study tended to be higher than in MESA, likely because individuals with known CVD were excluded from MESA, but not CHS (Alice M. Arnold, PhD, personal communication, December 2006; Robyn L. McClelland, PhD, personal communication, January 2007).<sup>6,78</sup> Four additional large studies from Europe that reported CCA CIMT values are described in Appendix 2 (Matthias W. Lorenz, MD, personal communication, December 2006; F. Gerald R. Fowkes, MBChB, PhD, personal communication, November 2006; Maria Rosvall, MD, PhD, Bo Hedblad, MD, PhD, and Goran Berglund, MD, PhD, personal communication, December 2006).<sup>20,23,79-81</sup> These studies did not provide information about race/ethnicity, but were conducted mostly in white individuals. In general, CIMT values in studies such as the Carotid Atherosclerosis Progression Study (CAPS) and Malmö Diet and Cancer Study (MDCS) tended to be higher than in the North American studies, so

**Table 8** Components of the carotid ultrasound study for cardiovascular disease risk assessment report

Patient information	
	Name, date of birth, medical record/identification number
	Sex
	Race/ethnicity
	Ordering health care provider
	Indication
Statements	
	This is a screening carotid ultrasound study for CVD risk assessment
	This study is not a replacement for a clinically indicated carotid duplex ultrasound
	This study measures the thickness of the walls of the carotid arteries and identifies the presence of carotid plaques
	Percentile values do represent percent stenosis
	Summary of scanning protocol and reference database (ie, ARIC Study, right and left CCA)
Data reporting	
	Describe carotid plaques
	Presence/absence
	Location (ie, side, segment, near/far wall)
	Acoustic shadowing (optional)
	State mean CIMT values for each side (a composite value is optional)*
	State percentile range for each CIMT value, relative to the patient's age, sex, and race/ethnicity (Appendices 1 and 2)
	Describe other clinically relevant findings (eg, possible obstructive carotid artery disease, thyroid abnormalities, lymphadenopathy)
Interpretation	
	Level of CVD risk (ie, increased, unchanged, lower)
	Relative risk associated with findings (optional)
Recommendations (optional)	

ARIC, Atherosclerosis Risk in Communities; CCA, common carotid artery; CIMT, carotid intima-media thickness; CVD, cardiovascular disease.

\*Clearly state if a different scanning protocol is used or maximum values are reported.

they are reported separately (Matthias W. Lorenz, MD, personal communication, December 2006; and Maria Rosvall, MD, PhD, Bo Hedblad, MD, PhD, and Goran Berglund, MD, PhD, personal communication, December 2006).<sup>20,23</sup> Reasons for the thicker CIMT values observed in these studies include different population characteristics, instrumentation, imaging and recording standards, and measurement techniques, including whether segments with plaque were included in the measurement protocol. Nevertheless, the relative risks associated with increasing CIMT were similar across the studies in Table 1, so the studies in Appendix 2 may provide more appropriate reference values for clinical sites in Europe.

**Within the context of the protocols and nomograms from large epidemiologic studies, the task force recommends that ultrasound images of the distal 1 cm of the far wall of each CCA should be obtained and compared with values from a normative data set.** Because of its size, superficial location, ease of accessibility, and limited movement, the far wall of the CCA provides a convenient window to study arterial structure using B-mode ultrasound. The distal CCA is easy to image, as it is straight and relatively superficial. With current ultrasound technology, it is difficult to reliably discern the intima-media interface of the near wall of the CCA, however, far wall CCA CIMT measurements predict future cardiovascular events (Table 1). Although near wall measure-

ments and those from other segments also have been used in some studies, they are more challenging technically, less reproducible, and do not appreciably improve risk prediction.<sup>15</sup> In addition, near wall CIMT is less accurate because the ultrasound beam is traveling from more echogenic to less echogenic layers at the adventitia-media and intima-lumen interfaces of the near wall. In one study, the ultrasound measurement of the near wall CIMT was 20% lower than the corresponding histologic measurement.<sup>18</sup> Although atherosclerosis and CIMT progress more rapidly in the bulb and internal carotid segments, **limiting CIMT measurements to the far wall of the CCA is the preferred strategy for clinical testing; however, it should be supplemented by a thorough scan of the extracranial carotid arteries for the presence of carotid plaques, to increase sensitivity for identifying subclinical vascular disease.** A circumferential scan of both carotid arteries to identify plaque can compensate for reduced sensitivity that may result from only measuring CCA CIMT.<sup>15,70,82</sup>

**The CIMT and carotid plaque scanning protocol recommended for most adults (40-70 years old) is in Table 5.** The CIMT portion of the recommended scanning protocol is based on the ARIC Study protocol because it was a large study with published nomograms for CIMT values in the age range that usually is most appropriate for screening (Appendix 1).<sup>76</sup> Furthermore, in the ARIC Study, both increasing CIMT and carotid plaque presence independently predicted CVD events (Tables 1 and 2), and the scanning methods are reproducible in most clinical laboratories.<sup>5,19,38,76,83</sup> **Scanning protocols from observational studies with published nomograms may be used if they are more germane to the age, sex, and race/ethnicity of the clinical population being investigated, however, the clinical laboratory must have sufficient expertise to perform them accurately and reproducibly.** Decisions as to which segments of the carotid artery are interrogated, at which angles, and which measurements are obtained must match those in the normative data set of the representative epidemiologic study (Appendices 1 and 2). For example, the CIMT measurements in the Bogalusa Heart Study have not yet been related to future CVD events; however, they are the only normative CIMT values in young adults from North America.<sup>77</sup> Similarly, the CIMT measurements in the MESA Study have not yet been related to future CVD events; however, they are the only normative values for CIMT in Chinese and Hispanic Americans (Robyn L. McLelland, PhD, personal communication, January 2007). Based on the similar relative risk associated with increasing CIMT across the age ranges described in Table 1, it can be inferred that increased CIMT in these patient groups (as determined by comparison with these data sets) is associated with increased CVD risk. **Use of values from clinically referred populations are discouraged, because of the high likelihood of referral bias and inaccurate risk estimates.**

#### Tips for Carotid Plaque Screening

Because of the eccentric nature of plaques, a circumferential scan ranging from anterior to posterior angles, and imaging the near or far walls of the CCA, bulb, and internal carotid artery segments is required (Table 5, Figure 2). During the plaque screen, the bulb and internal carotid arterial segments are carefully interrogated because plaque typically develops earliest in these segments. In some cases, plaques are present in the proximal or middle segments of the CCA or further than the proximal 1-cm segment of the internal carotid artery, so the full extracranial carotid arterial bed should be interrogated. Small plaques can be missed if images are obtained too quickly

**Table 9** Requirements for training and certification of sonographers and readers

	Sonographers	Readers
Ultrasound background	Registered diagnostic cardiac sonographer, medical sonographer, or vascular technician Certification in cardiopulmonary resuscitation and institutional emergency procedures	Appropriate credentials and institutional privileges to interpret cardiac and/or vascular ultrasound studies
Content areas (minimum 8 h of didactic or online training)	Pathophysiology of atherosclerosis, histopathologic correlations between ultrasound and healthy and diseased arteries, carotid artery anatomy CVD risk assessment and rationale for noninvasive testing with carotid ultrasound Clinical use of carotid ultrasound to identify subclinical vascular injury and predict CVD risk, including evidence base from epidemiologic and clinical trials and advantages and limitations of testing Scanning technique, instrumentation, protocol selection, and imaging pitfalls, including limited hemodynamic evaluation of stenotic lesions, recognition of common cardiac arrhythmias, and blood pressure monitoring Ultrasound principles and quality assurance Measurement and reporting Training standards for readers and sonographers	
Initial hands-on, supervised training	Scanning (minimum 8 h, in-person) -Protocol, image acquisition, best image -Demonstrate knowledge of content areas above Reading (minimum 2 h, in-person)—demonstrate proficiency with reading program	Scanning (minimum 2 h, in-person) -Understand image generation and pitfalls -Familiarity with scanning protocol Reading (minimum 2 h, in-person)—demonstrate proficiency with reading program
Follow-up of initial training	Submit at least 3 paired mock studies for review by an experienced sonographer 2 sets of images obtained at least 1 day apart, from 3 patient models Demonstrate protocol adherence, image quality, and image reproducibility	Submit at least 10 measured scans to a core laboratory with published accuracy and reproducibility data -Mean $\Delta$ reader core laboratory < 0.11 mm -95% of CIMT values within 0.11 mm of core laboratory <sup>87, 88, 95</sup>
Maintenance of certification and quality assurance	Perform least 25 CIMT studies/y Annual retesting of repeatability* Quarterly detailed, objective feedback If inactivity > 2 months, perform two mock studies to show continued competence	Read at least 25 CIMT studies/y Annual testing of intraobserver and interobserver repeatability*

*CIMT*, Carotid intima-media thickness; *CVD*, cardiovascular disease; h, hour; y, year.

\*Benchmarks for interscan/interread repeatability are a mean absolute difference of less than 0.055 mm and a coefficient of variation of less than 6%, where the coefficient of variation is calculated as SD divided by the mean using the root mean square (or equivalent) approach and is based on a minimum of 10 studies.<sup>96</sup>

or if the artery is imaged from only a few angles of incidence, rather than the recommended continuous screen of all the available circumferential angles. Careful evaluation of near wall boundaries helps avoid missing homogenous plaques on the near wall of the bulb and internal carotid artery. Regions where the arterial diameter changes abruptly and the images are not perpendicular to the scan lines, such as at the transition of the CCA into the bulb, can give a false appearance of focal thickening. Artifacts are common and the sonographer has to consider possible surrounding structures that can cause them. Color Doppler can be used with careful adjustment of the velocity scale to demonstrate a complete lumen filling, or an irregular arterial interface. Because of the complex shape of plaque, accurate measurement of size is difficult with the current tools. Some groups have used the measurement of total plaque area.<sup>10,42</sup> This promising approach deserves further study and validation, but is not recom-

mended because its generalizability and incremental predictive value are not known.

## OVERVIEW AND TIPS FOR CIMT IMAGING

After the plaque screen, longitudinal images of the CCA at 3 different angles are acquired for CIMT measurement (Table 5 and Figure 2). A cine-loop of 3 to 5 beats' duration should be recorded with selection of 3 optimized R-wave gated still frames from each angle of interrogation. Loops and still frames provide temporal information and insure good image quality at the crucial time of the cycle when measurements are performed, since cine-loops typically are compressed and still frames usually are not. The plane in which the bifurcation of the carotid bulb into the internal and external carotid

arteries at the tip of the flow divider can be visualized simultaneously with the bulb and distal CCA can be defined as the optimal angle of incidence (OAI) or "tuning fork" view. It is a reproducible view in most patients and relies on internal landmarks. If the head rotation is standardized, the OAI can be easily reproduced. The OAI can be determined during the transverse scan when the orientation of the internal and external carotid arteries is noted. Although a reliable point to start CIMT scanning, it often is not the best window to scan the bulb and internal carotid arterial segments.

The region to be measured includes the far wall of the distal 1 cm of the CCA. The distal CCA should be perfectly horizontal on the screen with simultaneous double lines in the near and far walls of the CCA ("double-line" sign) (Figure 3). This is accomplished by a combination of small adjustments in transducer tilt, rotation, and differential pressure of proximal-to-distal end of the probe (heel-toe movement). After the OAI is identified, the distal 1 cm of the CCA should be imaged from two additional complimentary angles, approximately 45 degrees anteriorly and posteriorly to cover a representative range of the neck circumference (anterior, lateral, and posterior) (Figure 3). If the patient's OAI is extremely anterior or posterior, two additional images approximately 45 degrees apart should be obtained. Applying different degrees of pressure and use of gel as an acoustic standoff will improve resolution and reduce artifacts. Some frequently observed pitfalls and possible solutions to CIMT image acquisition problems are listed in Table 6 (Figure 4).

#### INTERPRETATION OF CAROTID ULTRASOUND STUDIES FOR CVD RISK ASSESSMENT

The main steps for evaluating carotid ultrasound studies for CVD risk assessment are described in Table 7. **Evaluating for the presence or absence of plaque in conjunction with measuring CCA CIMT offers a better representation of subclinical vascular disease and CVD risk than only measuring CIMT. Carotid plaque is defined as the presence of focal wall thickening that is at least 50% greater than that of the surrounding vessel wall or as a focal region with CIMT greater than 1.5 mm that protrudes into the lumen that is distinct from the adjacent boundary.**<sup>15,38,44,45</sup> The presence of shadowing also may be reported; however, further plaque quantification and characterization by B-mode ultrasound is not sufficiently reproducible outside of research settings and does not appear to add significantly to the predictive value of carotid plaque presence.<sup>84</sup> Because of the complex, asymmetric nature of plaques, risk stratification based on plaque diameter or area is not recommended, as it may misrepresent plaque burden.<sup>15,85</sup>

Measurement of CIMT involves tracing the blood-intima and media-adventitia interfaces of the far wall using a leading edge-to-leading edge technique (Figure 5). The best image for CIMT measurement demonstrates the blood-intima and media-adventitia boundaries clearly. The reader should be able to see these interfaces on both near and far walls of the carotid artery to ensure that the sonographer has imaged the vessel through its truest diameter ("double-line" sign) (Figure 3), otherwise the CIMT may be thicker or thinner than is anatomically correct.<sup>75,86</sup> If the images do not show a complete 1-cm segment, the tracing maybe shortened. Avoid tracing interfaces that are not clearly visualized. If plaques are detected in the segment being measured, they should be traced as part of the CIMT because they appear to have been included in CIMT measurements in most of the epidemiologic studies in Table 1.<sup>25</sup> An alternate

reading protocol, based on published nomograms and risk prediction associations, also may be used (Table 1, and Appendices 1 and 2). In general, segments should be measured in triplicate and CIMT values averaged. Most studies that provided reference values in Appendices 1 and 2 used manual reading techniques; however, semiautomated border detection programs were used by some. Semiautomated border detection programs are widely available and, when used on high-quality images, tend to improve reproducibility and shorten reading time, especially among newer readers.<sup>87-90</sup> **The task force recommends use of a semiautomated border detection program with validated accuracy.** Border detection programs should allow the reader to edit the tracked borders if those generated by the program's algorithm are not optimal. These programs tend to produce somewhat thicker CIMT values than manual tracing, especially if the generated borders are left unedited. Software that assists with manual tracing using electronic calipers also is an option, especially considering that most outcome data are based on studies that used manual tracings. Simple point-to-point measurements of CIMT are not acceptable.

**Mean CIMT values from the far walls of the right and left CCAs (mean-mean) should be reported.** Use of additional segments or maximum values is an alternative if there is local expertise and these measurements can be mapped to normative values with published associations to CVD risk (Table 1, and Appendices 1 and 2). Most reading software will report mean-mean (average of segmental mean CIMT values) and mean-maximum (average of segmental maximum CIMT values) CIMT values. Mean-mean values are more reproducible because multiple points along the traced segment are averaged, but are less sensitive to change. Mean-maximum values are more sensitive to change, but less reproducible, because they are derived from a single point (or regional maximum) measurement along the 1-cm region.

#### REPORTING CAROTID ULTRASOUND STUDY RESULTS

Study results should be provided to the ordering provider in an understandable and clinically applicable fashion. **Recommended components of the report are described in Table 8.** The report should clearly identify the type of study being performed (ie, "carotid ultrasound study for cardiovascular risk assessment"), that it is not a replacement for a clinically indicated carotid duplex ultrasound, and that the results do not indicate the presence or absence of clinically significant obstruction, unless noted otherwise.

Because semiautomated border detection programs tend to produce somewhat thicker CIMT values than seen with manual tracing, their use should be considered by the reader when making recommendations concerning the findings of the study, especially if the normative data set was obtained using manual tracing. Current ultrasound instrumentation and digital imaging also provide better resolution, which may make CIMT values somewhat smaller. **Communication of CIMT results is facilitated by qualitatively describing broad ranges of percentiles. This avoids the appearance of greater precision than is achievable when mapping CIMT values to a reference population.** Because percentile estimates in the population studies have confidence intervals, and because the instrumentation, scanning, and measurement techniques in a clinical laboratory will not be exactly the same as used in these studies, reporting ranges helps mitigate some of these differences. The normative reference values used in the report must describe the same CIMT measurement (ie, mean or maximum) because these values differ substantially.



**CIMT values greater than or equal to 75th percentile are considered high and indicative of increased CVD risk. Values in the 25th to 75th percentile are considered average and indicative of unchanged CVD risk. Values less than or equal to 25th percentile are considered lower CVD risk, but whether or not they justify less aggressive preventive therapy than standard care is not known. These broad levels of risk should be reported.** Relative risk estimates for key percentile values (eg, the upper quartile or quintile) or the presence of carotid plaque also may be included (Tables 1 and 2).

Incidental findings that may require further evaluation such as the possibility of high-grade carotid artery stenosis (ie, visual appearance of obstructive plaque, increased color or spectral Doppler flow velocities), carotid tumor, carotid dissection, a large thyroid mass (1 cm or per local thresholds), lymphadenopathy, or others should be described. Each laboratory should have a mechanism for reporting urgent findings in a timely manner. Although carotid ultrasound for CVD risk assessment is not meant to screen for these findings or to replace a medically indicated diagnostic ultrasound study of these structures, the reader and sonographer should be able to recognize significant pathology if it is discovered incidentally during the course of the examination.

#### **TRAINING AND CERTIFICATION OF SONOGRAPHERS AND READERS**

To date, there is no clinical standard for training and certification for sonographers or readers. A training program for sonographers participating in clinical research has been published, however, standards vary by study and laboratory.<sup>91</sup> Reproducibility standards in clinical trials also have been described.<sup>86,92</sup> **Sonographers and readers should have appropriate training to perform and understand the findings on ultrasound examinations (Table 9). Sonographers and readers should complete a formal educational program covering the content areas in Table 9 with hands-on training and follow-up.** Recommendations for the number of hours dedicated to training are not based on educational outcomes research, but are a consensus recommendation regarding the minimum time it typically takes to achieve the recommendations in this document. They also reflect the minimum amount of time invested by attendees at currently available CIMT training programs that have tracked training outcomes. Recommendations for maintenance of certification also are in Table 9. Quality assurance measures should be documented with plans for remedial training and possible disqualification, if needed. Ideally, a national certification and registry for carotid ultrasound scanning for CVD risk assessment, as described in this document, would be developed. Laboratories with significant CIMT expertise should determine and document their measurement accuracy and reproducibility, to assure that it is similar to that reported in the literature.<sup>86-88,91-94</sup>

#### **CONCLUSIONS**

Ultrasonic detection of carotid plaque and CIMT measurements can be useful for refining CVD risk assessment in some asymptomatic patients. This noninvasive approach can detect subclinical vascular disease and help identify patients at increased risk of CVD. Strict attention to quality control in image acquisition, measurement, interpretation, and reporting are necessary for implementation of this technique in clinical practice.

#### **REFERENCES**

1. McGill HC Jr, McMahan CA, Herderick EE, Tracy RE, Malcom GT, Zieske AW, et al. Effects of coronary heart disease risk factors on atherosclerosis of selected regions of the aorta and right coronary artery: PDAY research group, Pathobiological Determinants of Atherosclerosis in Youth. *Arterioscler Thromb Vasc Biol* 2000;20:836-45.
2. Virmani R, Burke AP, Farb A, Kolodgie FD. Pathology of the vulnerable plaque. *J Am Coll Cardiol* 2006;47:C13-8.
3. Greenland P, Abrams J, Aurigemma GP, Bond MG, Clark LT, Criqui MH, et al. Prevention conference V: beyond secondary prevention, identifying the high-risk patient for primary prevention, noninvasive tests of atherosclerotic burden, writing group III. *Circulation* 2000;101:E16-22.
4. Taylor AJ, Merz CN, Udelson JE. 34th Bethesda conference: executive summary—can atherosclerosis imaging techniques improve the detection of patients at risk for ischemic heart disease? *J Am Coll Cardiol* 2003;41:1860-2.
5. Chambless LE, Heiss G, Folsom AR, Rosamond W, Szklo M, Sharrett AR, 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. *Am J Epidemiol* 1997;146:483-94.
6. O'Leary DH, Polak JF, Kronmal RA, Manolio TA, Burke GL, Wolfson SK Jr. Carotid-artery intima and media thickness as a risk factor for myocardial infarction and stroke in older adults: Cardiovascular Health Study Collaborative Research Group. *N Engl J Med* 1999;340:14-22.
7. Greenland P, LaBree L, Azen SP, Doherty TM, Detrano RC. Coronary artery calcium score combined with Framingham score for risk prediction in asymptomatic individuals. *JAMA* 2004;291:210-5.
8. Stein JH, Fraizer MC, Aeschlimann SE, Nelson-Worel J, McBride PE, Douglas PS. Individualizing coronary risk assessment using carotid intima media thickness measurements to estimate vascular age. *Clin Cardiol* 2004;27:388-92.
9. Gepner AD, Keevil JG, Wyman RA, Korcarz CE, Aeschlimann SE, Busse KL, et al. Use of carotid intima-media thickness and vascular age to modify cardiovascular risk prediction. *J Am Soc Echocardiogr* 2006;19:1170-4.
10. Bard RL, Kalsi H, Rubenfire M, Wakefield T, Fex B, Rajagopalan S, et al. Effect of carotid atherosclerosis screening on risk stratification during primary cardiovascular disease prevention. *Am J Cardiol* 2004;93:1030-2.
11. Rembold KE, Ayers CR, Wills MB, Rembold CM. Usefulness of carotid intimal medial thickness and flow-mediated dilation in a preventive cardiovascular practice. *Am J Cardiol* 2003;91:1475-7.
12. Ali YS, Rembold KE, Weaver B, Wills MB, Tatar S, Ayers CR, et al. Prediction of major adverse cardiovascular events by age-normalized carotid intimal medial thickness. *Atherosclerosis* 2006;187:186-90.
13. Barth JD. An update on carotid ultrasound measurement of intima-media thickness. *Am J Cardiol* 2002;89:32-8B.
14. National Cholesterol Education Program (NCEP) Expert Panel (ATP III). Third report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. *Circulation* 2002;106:3143-421.
15. Roman MJ, Naqvi TZ, Gardin JM, Gerhard-Herman M, Jaff M, Mohler E. Clinical application of noninvasive vascular ultrasound in cardiovascular risk stratification: a report from the American Society of Echocardiography and the Society of Vascular Medicine and Biology. *J Am Soc Echocardiogr* 2006;19:943-54.
16. Pignoli P, Tremoli E, Poli A, Oreste P, Paoletti R. Intimal plus medial thickness of the arterial wall: a direct measurement with ultrasound imaging. *Circulation* 1986;74:1399-406.
17. Persson J, Formgren J, Israelsson B, Berglund G. Ultrasound-determined intima-media thickness and atherosclerosis: direct and indirect validation. *Arterioscler Thromb* 1994;14:261-4.

18. Wong M, Edelstein J, Wollman J, Bond MG. Ultrasonic-pathological comparison of the human arterial wall: verification of intima-media thickness. *Arterioscler Thromb* 1993;13:482-6.
19. Chambless LE, Folsom AR, Clegg LX, Sharrett AR, Shahar E, Nieto FJ, et al. Carotid wall thickness is predictive of incident clinical stroke: the Atherosclerosis Risk in Communities (ARIC) study. *Am J Epidemiol* 2000;151:478-87.
20. Lorenz MW, von Kegler S, Steinmetz H, Markus HS, Sitzer M. Carotid intima-media thickening indicates a higher vascular risk across a wide age range: prospective data from the Carotid Atherosclerosis Progression Study (CAPS). *Stroke* 2006;37:87-92.
21. Salonen JT, Salonen R. Ultrasound B-mode imaging in observational studies of atherosclerotic progression. *Circulation* 1993;87:1156-65.
22. Kitamura A, Iso H, Imano H, Ohira T, Okada T, Sato S, et al. Carotid intima-media thickness and plaque characteristics as a risk factor for stroke in Japanese elderly men. *Stroke* 2004;35:2788-94.
23. Rosvall M, Janzon L, Berglund G, Engstrom G, Hedblad B. Incident coronary events and case fatality in relation to common carotid intima-media thickness. *J Intern Med* 2005;257:430-7.
24. van der Meer I, Bots ML, Hofman A, del Sol AI, van der Kuip DA, Witteman JC. Predictive value of noninvasive measures of atherosclerosis for incident myocardial infarction: the Rotterdam study. *Circulation* 2004;109:1089-94.
25. Lorenz MW, Markus HS, Bots ML, Rosvall M, Sitzer M. Prediction of clinical cardiovascular events with carotid intima-media thickness: a systematic review and meta-analysis. *Circulation* 2007;115:459-67.
26. Belcaro G, Nicolaides AN, Ramaswami G, Cesarone MR, De Sanctis M, Incandela L, et al. Carotid and femoral ultrasound morphology screening and cardiovascular events in low risk subjects: a 10-year follow-up study (the CAFES-CAVE study(1)). *Atherosclerosis* 2001;156:379-87.
27. Craven TE, Ryu JE, Espeland MA, Kahl FR, McKinney WM, Toole JF, et al. Evaluation of the associations between carotid artery atherosclerosis and coronary artery stenosis: a case-control study. *Circulation* 1990;82:1230-42.
28. Chambless LE, Folsom AR, Sharrett AR, Sorlie P, Couper D, Szklo M, et al. Coronary heart disease risk prediction in the Atherosclerosis Risk in Communities (ARIC) study. *J Clin Epidemiol* 2003;56:880-90.
29. Cao JJ, Arnold AM, Manolio TA, Polak JF, Psaty BM, Hirsch CH, et al. Association of carotid artery intima-media thickness, plaques, and C-reactive protein with future cardiovascular disease and all-cause mortality: the cardiovascular health study. *Circulation* 2007;116:32-8.
30. Urbina EM, Srinivasan SR, Tang R, Bond MG, Kielyka L, Berenson GS. Impact of multiple coronary risk factors on the intima-media thickness of different segments of carotid artery in healthy young adults (the Bogalusa heart study). *Am J Cardiol* 2002;90:953-8.
31. Li S, Chen W, Srinivasan SR, Bond MG, Tang R, Urbina EM, et al. Childhood cardiovascular risk factors and carotid vascular changes in adulthood: the Bogalusa heart study. *JAMA* 2003;290:2271-6.
32. Tzou WS, Douglas PS, Srinivasan SR, Bond MG, Tang R, Chen W, et al. Increased subclinical atherosclerosis in young adults with metabolic syndrome: the Bogalusa Heart Study. *J Am Coll Cardiol* 2005;46:457-63.
33. Davis PH, Dawson JD, Mahoney LT, Lauer RM. Increased carotid intimal-medial thickness and coronary calcification are related in young and middle-aged adults: the Muscatine study. *Circulation* 1999;100:838-42.
34. Davis PH, Dawson JD, Riley WA, Lauer RM. Carotid intimal-medial thickness is related to cardiovascular risk factors measured from childhood through middle age: the Muscatine study. *Circulation* 2001;104:2815-9.
35. Oren A, Vos LE, Uiterwaal CS, Grobbee DE, Bots ML. Cardiovascular risk factors and increased carotid intima-media thickness in healthy young adults: the Atherosclerosis Risk in Young Adults (ARYA) study. *Arch Intern Med* 2003;163:1787-92.
36. Knoflach M, Kiechl S, Kind M, Said M, Sief R, Gisinger M, et al. Cardiovascular risk factors and atherosclerosis in young males: ARMY study (Atherosclerosis Risk factors in Male Youngsters). *Circulation* 2003;108:1064-9.
37. Raitakari OT, Juonala M, Kahonen M, Taittonen L, Laitinen T, Maki-Torkko N, et al. Cardiovascular risk factors in childhood and carotid artery intima-media thickness in adulthood: the Cardiovascular Risk in Young Finns Study. *JAMA* 2003;290:2277-83.
38. Hunt KJ, Sharrett AR, Chambless LE, Folsom AR, Evans GW, Heiss G. Acoustic shadowing on B-mode ultrasound of the carotid artery predicts CHD. *Ultrasound Med Biol* 2001;27:357-65.
39. Salonen JT, Salonen R. Ultrasonographically assessed carotid morphology and the risk of coronary heart disease. *Arterioscler Thromb* 1991;11:1245-9.
40. Prabhakaran S, Rundek T, Ramas R, Elkind MS, Paik MC, Boden-Albala B, et al. Carotid plaque surface irregularity predicts ischemic stroke: the Northern Manhattan Study. *Stroke* 2006;37:2696-701.
41. Stork S, van den Beld AW, von Schacky C, Angermann CE, Lamberts SW, Grobbee DE, et al. Carotid artery plaque burden, stiffness, and mortality risk in elderly men: a prospective, population-based cohort study. *Circulation* 2004;110:344-8.
42. Spence JD, Eliasziw M, DiCicco M, Hackam DG, Galil R, Lohmann T. Carotid plaque area: a tool for targeting and evaluating vascular preventive therapy. *Stroke* 2002;33:2916-22.
43. Wyman RA, Mays ME, McBride ME, Stein JH. Ultrasound-detected carotid plaque as a predictor of cardiovascular events. *Vasc Med* 2006;31:123-30.
44. Touboul PJ, Hennerici MG, Meairs S, Adams H, Amarencio P, Desvarieux M, et al. Mannheim Intima-media Thickness Consensus. *Cerebrovasc Dis* 2004;18:346-9.
45. Touboul PJ, Hennerici MG, Meairs S, Adams H, Amarencio P, Bornstein N, et al. Mannheim Carotid Intima-media Thickness Consensus (2004-2006): an update on behalf of the advisory board of the 3rd and 4th watching the risk symposium 13th and 15th European stroke conferences, Mannheim, Germany, 2004, and Brussels, Belgium, 2006. *Cerebrovasc Dis* 2007;23:75-80.
46. Young W, Gofman J, Tandy R, Malamud N, Waters E. The quantitation of atherosclerosis III: the extent of correlation of degrees of atherosclerosis with and between the coronary and cerebral vascular beds. *Am J Cardiol* 1960;8:300-8.
47. Burke G, Evans G, Riley W, Sharrett A, Howard G, Barnes R, et al. Arterial wall thickness is associated with prevalent cardiovascular disease in middle-aged adults: the Atherosclerosis Risk in Communities (ARIC) study. *Stroke* 1995;26:386-91.
48. Espeland MA, O'Leary DH, Terry JG, Morgan T, Evans G, Mudra H. Carotid intimal-media thickness as a surrogate for cardiovascular disease events in trials of HMG-CoA reductase inhibitors. *Curr Control Trials Cardiovasc Med* 2005;6:3.
49. Hodis H, Mack W, LaBree L, Selzer R, Liu C, Liu C, et al. The role of carotid arterial intima-medial thickness in predicting clinical coronary events. *Ann Intern Med* 1998;128:262-9.
50. Bots ML, Hofman A, Grobbee DE. Increased common carotid intima-media thickness: adaptive response or a reflection of atherosclerosis? Findings from the Rotterdam study. *Stroke* 1997;28:2442-7.
51. Vaudo G, Schillaci G, Evangelista F, Pasqualini L, Verdecchia P, Mannarino E. Arterial wall thickening at different sites and its association with left ventricular hypertrophy in newly diagnosed essential hypertension. *Am J Hypertens* 2000;13:324-31.
52. Nagai Y, Metter EJ, Earley CJ, Kemper MK, Becker LC, Lakatta EG, et al. Increased carotid artery intimal-medial thickness in asymptomatic older subjects with exercise-induced myocardial ischemia. *Circulation* 1998;98:1504-9.
53. Virmani R, Avolio AP, Mergner WJ, Robinowitz M, Herderick EE, Cornhill JF, et al. Effect of aging on aortic morphology in populations with high and low prevalence of hypertension and atherosclerosis: comparison between occidental and Chinese communities. *Am J Pathol* 1991;139:1119-29.

54. Li Z, Froehlich J, Galis ZS, Lakatta EG. Increased expression of matrix metalloproteinase-2 in the thickened intima of aged rats. *Hypertension* 1999;33:116-23.
55. Asai K, Kudej RK, Shen YT, Yang GP, Takagi G, Kudej AB, et al. Peripheral vascular endothelial dysfunction and apoptosis in old monkeys. *Arterioscler Thromb Vasc Biol* 2000;20:1493-9.
56. Najjar SS, Scuteri A, Lakatta EG. Arterial aging: is it an immutable cardiovascular risk factor? *Hypertension* 2005;46:454-62.
57. Lakatta EG, Levy D. Arterial and cardiac aging—major shareholders in cardiovascular disease enterprises, part I: aging arteries, a “set up” for vascular disease. *Circulation* 2003;107:139-46.
58. Greenland P, Smith SC Jr, Grundy SM. Improving coronary heart disease risk assessment in asymptomatic people: role of traditional risk factors and noninvasive cardiovascular tests. *Circulation* 2001;104:1863-7.
59. Budoff MJ, Achenbach S, Blumenthal RS, Carr JJ, Goldin JG, Greenland P, et al. Assessment of coronary artery disease by cardiac computed tomography: a scientific statement from the American Heart Association Committee on Cardiovascular Imaging and Intervention, Council on Cardiovascular Radiology and Intervention, and Committee on Cardiac Imaging, Council on Clinical Cardiology. *Circulation* 2006;114:1761-91.
60. Lloyd-Jones DM, Leip EP, Larson MG, D’Agostino RB, Beiser A, Wilson PW, et al. Prediction of lifetime risk for cardiovascular disease by risk factor burden at 50 years of age. *Circulation* 2006;113:791-8.
61. Michos ED, Vasamreddy CR, Becker DM, Yanek LR, Moy TF, Fishman EK, et al. Women with a low Framingham risk score and a family history of premature coronary heart disease have a high prevalence of subclinical coronary atherosclerosis. *Am Heart J* 2005;150:1276-81.
62. Michos ED, Nasir K, Braunstein JB, Rumberger JA, Budoff MJ, Post WS, et al. Framingham risk equation underestimates subclinical atherosclerosis risk in asymptomatic women. *Atherosclerosis* 2006;184:201-6.
63. Nasir K, Michos ED, Blumenthal RS, Raggi P. Detection of high-risk young adults and women by coronary calcium and National Cholesterol Education Program Panel III Guidelines. *J Am Coll Cardiol* 2005;46:1931-6.
64. Grundy SM, Pasternak R, Greenland P, Smith SJ, Fuster V. Assessment of cardiovascular risk by use of multiple-risk-factor assessment equations: a statement for healthcare professionals from the American Heart Association and the American College of Cardiology. *Circulation* 1999;100:1481-92.
65. Grundy SM. Coronary plaque as a replacement for age as a risk factor in global risk assessment. *Am J Cardiol* 2001;88:8-11E.
66. Greenland P, Bonow RO, Brundage BH, Budoff MJ, Eisenberg MJ, Grundy SM, et al. ACCF/AHA 2007 clinical expert consensus document on coronary artery calcium scoring by computed tomography in global cardiovascular risk assessment and in evaluation of patients with chest pain: a report of the American College of Cardiology Foundation clinical expert consensus task force (ACCF/AHA writing committee to update the 2000 expert consensus document on electron beam computed tomography). *Circulation* 2007;115:402-26.
67. Coles DR, Smail MA, Negus IS, Wilde P, Oberhoff M, Karsch KR, et al. Comparison of radiation doses from multislice computed tomography coronary angiography and conventional diagnostic angiography. *J Am Coll Cardiol* 2006;47:1840-5.
68. McClelland RL, Chung H, Detrano R, Post W, Kronmal RA. Distribution of coronary artery calcium by race, gender, and age: results from the Multi-Ethnic Study of Atherosclerosis (MESA). *Circulation* 2006;113:30-7.
69. Baldassarre D, Amato M, Bondioli A, Sirtori CR, Tremoli E. Carotid artery intima-media thickness measured by ultrasonography in normal clinical practice correlates well with atherosclerosis risk factors. *Stroke* 2000;31:2426-30.
70. Wyman RA, Fraizer MC, Keevil JG, Busse KL, Aeschlimann SE, Korcarz CE, et al. Ultrasound-detected carotid plaque as a screening tool for advanced subclinical atherosclerosis. *Am Heart J* 2005;150:1081-5.
71. Wyman RA, Gimelli G, McBride PE, Korcarz CE, Stein JH. Does detection of carotid plaque affect physician behavior or motivate patients? *Am Heart J* 2007;154:1072-77.
72. Bovet P, Perret F, Cornuz J, Quilindo J, Paccaud F. Improved smoking cessation in smokers given ultrasound photographs of their own atherosclerotic plaques. *Prev Med* 2002;34:215-20.
73. Barth JD. Which tools are in your cardiac workshop? Carotid ultrasound, endothelial function, and magnetic resonance imaging. *Am J Cardiol* 2001;87:8-14A.
74. Crouse JR III, Raichlen JS, Riley WA, Evans GW, Palmer MK, O’Leary DH, et al. Effect of rosuvastatin on progression of carotid intima-media thickness in low-risk individuals with subclinical atherosclerosis: the METEOR trial. *JAMA* 2007;297:1344-53.
75. Mitchell CK, Aeschlimann SE, Korcarz CE. Carotid intima-media thickness testing: technical considerations. *J Am Soc Echocardiogr* 2004;17:690-2.
76. Howard G, Sharrett A, Heiss G, Evans G, Chambless L, Riley W, et al. Carotid artery intimal-medial thickness distribution in general populations as evaluated by B-mode ultrasound. *Stroke* 1993;24:1297-304.
77. Tzou WS, Douglas PS, Srinivasan SR, Bond MG, Tang R, Chen W, et al. Distribution and predictors of carotid artery intima-media thickness in young adults: the Bogalusa Heart Study. *Prev Cardiol* 2007;10:181-9.
78. Fried LP, Borhani NO, Enright P, Furberg CD, Gardin JM, Kronmal RA, et al. The Cardiovascular Health Study: design and rationale. *Ann Epidemiol* 1991;1:263-76.
79. Simon A, Garipey J, Chironi G, Megnien JL, Levenson J. Intima-media thickness: a new tool for diagnosis and treatment of cardiovascular risk. *J Hypertens* 2002;20:159-69.
80. Denarie N, Garipey J, Chironi G, Massonneau M, Laskri F, Salomon J, et al. Distribution of ultrasonographically-assessed dimensions of common carotid arteries in healthy adults of both sexes. *Atherosclerosis* 2000;148:297-302.
81. Allan PL, Mowbray PI, Lee AJ, Fowkes FG. Relationship between carotid intima-media thickness and symptomatic and asymptomatic peripheral arterial disease: the Edinburgh artery study. *Stroke* 1997;28:348-53.
82. Gepner AD, Wyman RA, Korcarz CE, Aeschlimann SA, Stein JH. An abbreviated carotid intima-media thickness scanning protocol to facilitate clinical screening for subclinical atherosclerosis. *J Am Soc Echocardiogr* 2007;20:1269-75.
83. Bond M, Barnes R, Riley W, Wilmoth S, Chambless L, Howard G, et al. High-resolution B-mode ultrasound scanning methods in the Atherosclerosis Risk in Communities Study (ARIC). *J Neuroimaging* 1991;1:68-73.
84. Bonithon-Kopp C, Scarabin PY, Taquet A, Touboul PJ, Malmejac A, Guize L. Risk factors for early carotid atherosclerosis in middle-aged French women. *Arterioscler Thromb* 1991;11:966-72.
85. Kizer JR, Wiebers DO, Whisnant JP, Galloway JM, Welty TK, Lee ET, et al. Mitral annular calcification, aortic valve sclerosis, and incident stroke in adults free of clinical cardiovascular disease: the Strong Heart Study. *Stroke* 2005;36:2533-7.
86. Bots ML, Evans GW, Riley WA, Grobbee DE. Carotid intima-media thickness measurements in intervention studies: design options, progression rates, and sample size considerations: a point of view. *Stroke* 2003;34:2985-94.
87. Gepner AD, Korcarz CE, Aeschlimann SE, LeCaire TJ, Palta M, Tzou WS, et al. Validation of a carotid intima-media thickness border detection program for use in an office setting. *J Am Soc Echocardiogr* 2006;19:223-8.
88. Stein JH, Korcarz CE, Mays ME, Douglas PS, Palta M, Zhang H, et al. A semi-automated border detection program that facilitates clinical use of ultrasound carotid intima-media thickness measurements. *J Am Soc Echocardiogr* 2005;18:244-51.
89. Wendelhag I, Liang Q, Gustavsson T, Wikstrand J. A new automated computerized analyzing system simplifies readings and reduces the variability in ultrasound measurement of intima-media thickness. *Stroke* 1997;28:2195-200.

90. Selzer RH, Hodis HN, Kwong-Fu H, Mack WJ, Lee PL, Liu CR, et al. Evaluation of computerized edge tracking for quantifying intima-media thickness of the common carotid artery from B-mode ultrasound images. *Atherosclerosis* 1994;111:1-11.
91. Berglund GL, Riley WA, Barnes RW, Furberg CD. Quality control in ultrasound studies on atherosclerosis. *J Intern Med* 1994;236:581-6.
92. Gottdiener JS, Bednarz J, Devereux RM, Gardin J, Klein A, Kitzman D, et al. Recommendations for use of echocardiography in clinical trials: a report from the American Society of Echocardiography's nomenclature and Standards Committee and the Task Force on Echocardiography in Clinical Trials. *J Am Soc Echocardiogr* 2004;17:1086-119.
93. Kanters SD, Algra A, van Leeuwen MS, Banga JD. Reproducibility of in vivo carotid intima-media thickness measurements: a review. *Stroke* 1997;28:665-71.
94. Tang R, Hennig M, Bond MG, Hollweck R, Mancia G, Zanchetti A. Quality control of B-mode ultrasonic measurement of carotid artery intima-media thickness: the European Lacidipine Study on Atherosclerosis. *J Hypertens* 2005;23:1047-54.
95. Chow S, Liu J. Design and analysis of bioequivalence studies. New York: Marcel Dekker; 1992.
96. Bland JM, Altman DG. Measurement error proportional to the mean. *BMJ* 1996;313:106.



**Appendix 1 Common carotid artery carotid intima-media thickness values and percentiles from large North American cohort studies**

**A. Mean far wall common carotid artery carotid intima-media thickness values from the Atherosclerosis Risk in Communities Study<sup>76</sup>**

Right												
Age, y/percentile	White male			White female			Black male			Black female		
	45	55	65	45	55	65	45	55	65	45	55	65
25th	0.496	0.572	0.648	0.476	0.542	0.608	0.514	0.614	0.714	0.518	0.578	0.638
50th	0.570	0.664	0.758	0.536	0.616	0.696	0.604	0.724	0.844	0.588	0.668	0.748
75th	0.654	0.774	0.894	0.610	0.710	0.810	0.700	0.850	1.000	0.664	0.764	0.864
Left												
Age, y/percentile	White male			White female			Black male			Black female		
	45	55	65	45	55	65	45	55	65	45	55	65
25th	0.524	0.588	0.652	0.472	0.540	0.608	0.530	0.610	0.690	0.494	0.558	0.622
50th	0.598	0.684	0.770	0.538	0.622	0.706	0.614	0.714	0.814	0.566	0.646	0.726
75th	0.690	0.806	0.922	0.610	0.710	0.810	0.704	0.840	0.976	0.644	0.748	0.852

**B. Maximum far wall common carotid artery carotid intima-media thickness values from the Bogalusa Heart Study<sup>77</sup>**

Right																
Age, y/percentile	White male				White female				Black male				Black female			
	25	30	35	40	25	30	35	40	25	30	35	40	25	30	35	40
25th	0.611	0.636	0.662	0.687	0.562	0.586	0.611	0.635	0.637	0.675	0.712	0.750	0.616	0.650	0.685	0.719
50th	0.663	0.702	0.740	0.779	0.633	0.654	0.676	0.697	0.719	0.756	0.793	0.830	0.682	0.718	0.754	0.790
75th	0.768	0.807	0.845	0.884	0.717	0.735	0.754	0.772	0.839	0.884	0.929	0.974	0.750	0.793	0.837	0.880
Left																
Age, y/percentile	White male				White female				Black male				Black female			
	25	30	35	40	25	30	35	40	25	30	35	40	25	30	35	40
25th	0.577	0.617	0.658	0.698	0.554	0.586	0.618	0.650	0.640	0.676	0.713	0.749	0.587	0.629	0.670	0.712
50th	0.655	0.707	0.760	0.812	0.621	0.657	0.693	0.729	0.736	0.774	0.812	0.850	0.646	0.691	0.736	0.781
75th	0.763	0.814	0.864	0.915	0.660	0.713	0.766	0.819	0.794	0.844	0.894	0.944	0.714	0.768	0.822	0.876

**C. Maximum near and far wall common carotid artery carotid intima-media thickness Values from the CHS Study (Alice M. Arnold, PhD, personal communication, December 2006)**

Age, y/percentile	Male					Female				
	65-69	70-74	75-79	80-84	85+	65-69	70-74	75-79	80-84	85+
25th	0.94	0.95	1.00	1.03	1.05	0.87	0.89	0.92	0.96	0.99
50th	1.03	1.07	1.10	1.15	1.18	1.96	0.99	1.03	1.05	1.12
75th	1.16	1.21	1.25	1.30	1.32	1.07	1.10	1.16	1.19	1.28

**D. Common carotid artery carotid intima-media thickness values from the Multi-Ethnic Study of Atherosclerosis Study (Robyn L. McClelland, PhD, personal communication, January 2007)<sup>6</sup>**

Mean far wall-right																
Age, y/percentile	White male				White female				Black male				Black female			
	45-54	55-64	65-74	75-84	45-54	55-64	65-74	75-84	45-54	55-64	65-74	75-84	45-54	55-64	65-74	75-84
25th	0.52	0.57	0.65	0.72	0.51	0.55	0.65	0.72	0.58	0.61	0.71	0.74	0.55	0.60	0.65	0.71
50th	0.62	0.68	0.77	0.83	0.58	0.65	0.75	0.83	0.67	0.74	0.85	0.85	0.64	0.71	0.76	0.83
75th	0.71	0.81	0.92	0.97	0.67	0.76	0.87	0.93	0.80	0.92	0.99	1.02	0.74	0.81	0.92	0.96

## Appendix 1 Continued

Age, y/percentile	Chinese male				Chinese female				Hispanic male				Hispanic female			
	45-54	55-64	65-74	75-84	45-54	55-64	65-74	75-84	45-54	55-64	65-74	75-84	45-54	55-64	65-74	75-84
25th	0.54	0.56	0.62	0.66	0.55	0.54	0.59	0.67	0.53	0.60	0.65	0.71	0.51	0.57	0.65	0.63
50th	0.64	0.70	0.73	0.79	0.60	0.63	0.71	0.77	0.62	0.67	0.78	0.81	0.58	0.69	0.76	0.78
75th	0.73	0.83	0.92	0.98	0.70	0.77	0.84	0.96	0.73	0.82	0.90	0.92	0.67	0.77	0.87	0.92
Mean far wall-left																
Age, y/percentile	Chinese male				Chinese female				Hispanic male				Hispanic female			
	45-54	55-64	65-74	75-84	45-54	55-64	65-74	75-84	45-54	55-64	65-74	75-84	45-54	55-64	65-74	75-84
25th	0.55	0.57	0.62	0.69	0.49	0.52	0.58	0.64	0.55	0.61	0.68	0.72	0.51	0.58	0.62	0.68
50th	0.63	0.70	0.72	0.84	0.58	0.63	0.71	0.76	0.64	0.72	0.80	0.86	0.58	0.68	0.72	0.77
75th	0.73	0.84	0.86	0.97	0.67	0.72	0.87	0.94	0.75	0.85	0.98	0.97	0.68	0.79	0.86	0.91
Age, y/percentile	White male				White female				Black male				Black female			
	45-54	55-64	65-74	75-84	45-54	55-64	65-74	75-84	45-54	55-64	65-74	75-84	45-54	55-64	65-74	75-84
25th	0.54	0.57	0.67	0.71	0.50	0.55	0.63	0.70	0.56	0.63	0.69	0.72	0.54	0.59	0.63	0.68
50th	0.63	0.69	0.81	0.85	0.58	0.64	0.73	0.80	0.69	0.75	0.82	0.85	0.63	0.67	0.76	0.78
75th	0.78	0.82	0.95	1.00	0.67	0.75	0.85	0.94	0.81	0.92	0.99	1.02	0.73	0.80	0.90	0.91
Maximum far wall-right																
Age, y/percentile	White male				White female				Black male				Black female			
	45-54	55-64	65-74	75-84	45-54	55-64	65-74	75-84	45-54	55-64	65-74	75-84	45-54	55-64	65-74	75-84
25th	0.61	0.66	0.73	0.83	0.59	0.66	0.77	0.82	0.66	0.72	0.79	0.83	0.63	0.72	0.72	0.79
50th	0.72	0.79	0.89	0.94	0.67	0.74	0.88	0.94	0.77	0.83	0.94	0.96	0.74	0.83	0.87	0.94
75th	0.87	0.94	1.05	1.11	0.79	0.88	1.00	1.07	0.89	1.05	1.11	1.13	0.87	0.94	1.05	1.10
Age, y/percentile	Chinese male				Chinese female				Hispanic male				Hispanic female			
	45-54	55-64	65-74	75-84	45-54	55-64	65-74	75-84	45-54	55-64	65-74	75-84	45-54	55-64	65-74	75-84
25th	0.66	0.63	0.66	0.72	0.62	0.61	0.66	0.72	0.61	0.67	0.72	0.78	0.61	0.67	0.72	0.72
50th	0.75	0.79	0.83	0.90	0.72	0.72	0.80	0.88	0.74	0.82	0.88	0.89	0.67	0.77	0.87	0.88
75th	0.86	0.94	1.05	1.07	0.83	0.82	0.94	1.05	0.87	0.95	1.05	1.05	0.78	0.91	1.00	1.03
Maximum far wall-left																
Age, y/percentile	White male				White female				Black male				Black female			
	45-54	55-64	65-74	75-84	45-54	55-64	65-74	75-84	45-54	55-64	65-74	75-84	45-54	55-64	65-74	75-84
25th	0.64	0.68	0.77	0.77	0.61	0.66	0.72	0.82	0.66	0.72	0.82	0.83	0.62	0.66	0.72	0.77
50th	0.73	0.79	0.90	0.97	0.67	0.77	0.84	0.94	0.79	0.86	0.93	0.95	0.72	0.78	0.84	0.89
75th	0.89	0.94	1.09	1.12	0.78	0.88	1.00	1.11	0.94	1.04	1.11	1.11	0.86	0.94	1.03	1.00
Age, y/percentile	Chinese male				Chinese female				Hispanic male				Hispanic female			
	45-54	55-64	65-74	75-84	45-54	55-64	65-74	75-84	45-54	55-64	65-74	75-84	45-54	55-64	65-74	75-84
25th	0.65	0.64	0.72	0.77	0.61	0.61	0.66	0.72	0.62	0.72	0.77	0.77	0.61	0.66	0.72	0.77
50th	0.75	0.79	0.81	0.94	0.72	0.73	0.82	0.83	0.72	0.83	0.94	0.94	0.66	0.77	0.83	0.88
75th	0.88	0.95	1.00	1.06	0.80	0.83	0.96	1.05	0.88	0.97	1.11	1.11	0.78	0.89	0.97	1.02

Y, years. All values are in mm.

**Appendix 2 Common carotid artery carotid intima-media thickness values and percentiles from large European cohort studies**

**A. Mean far wall common carotid artery carotid intima-media thickness values from the AXA Study<sup>79,80</sup>**

Right common carotid artery								
Age, y/percentile	Male				Female			
	≤30	31-40	41-50	>50	≤30	31-40	41-50	>50
25th	0.39	0.42	0.46	0.46	0.39	0.42	0.44	0.50
50th	0.43	0.46	0.50	0.52	0.40	0.45	0.48	0.54
75th	0.48	0.50	0.57	0.62	0.43	0.49	0.53	0.59

Left common carotid artery								
Age, y/percentile	Male				Female			
	≤30	31-40	41-50	>50	≤30	31-40	41-50	>50
25th	0.42	0.44	0.50	0.53	0.30	0.44	0.46	0.52
50th	0.44	0.47	0.55	0.61	0.44	0.47	0.51	0.59
75th	0.49	0.57	0.61	0.70	0.47	0.51	0.57	0.64

**B. Mean far wall common carotid artery carotid intima-media thickness values from the Carotid Atherosclerosis Progression Study (Matthias W. Lorenz, MD, personal communication, December 6)<sup>20</sup>**

Age, y/percentile	Male							Female						
	25	35	45	55	65	75	85	25	35	45	55	65	75	85
25th	0.515	0.585	0.634	0.68	0.745	0.814	0.83	0.524	0.575	0.619	0.665	0.718	0.771	0.807
50th	0.567	0.633	0.686	0.746	0.83	0.914	0.937	0.567	0.615	0.665	0.719	0.778	0.837	0.880
75th	0.633	0.682	0.756	0.837	0.921	1.028	1.208	0.612	0.66	0.713	0.776	0.852	0.921	0.935

**C. Maximum\* far wall common carotid artery carotid intima-media thickness values from the Edinburgh Artery Study (F. Gerald R. Fowkes, MBChB, PhD, personal communication, November 2006)<sup>81</sup>**

Age, y/percentile	Male					Female				
	60-64	65-69	70-74	75-79	>80	60-64	65-69	70-74	75-79	>80
25th	0.60	0.70	0.70	0.70	0.80	0.60	0.60	0.70	0.70	0.72
50th	0.80	0.80	0.80	0.90	1.00	0.70	0.80	0.80	0.90	0.90
75th	0.90	1.00	1.00	1.20	1.20	0.80	0.90	0.90	1.00	1.40

Y, years. All values are in mm.

\*Maximum of right or left common carotid artery.

**D. Mean far wall common carotid artery carotid intima-media thickness values from the Malmö Diet and Cancer Study (Maria Rosvall, MD, PhD, Bo Hedblad, MD, PhD, and Goran Berglund, MD, PhD, personal communication, December 2006)<sup>23</sup>**

Age, y/percentile	Men		Women	
	55	65	55	65
25th	0.66	0.73	0.64	0.73
50th	0.75	0.81	0.71	0.81
75th	0.86	0.94	0.78	0.88

Y, years. All values are in mm.