Table 8
Atherosclerotic Cardiovascular Disease Risk Calculators

ASCVD risk calculators (date)	Atherosclerotic cardiovascular disease risk factors											ASCVD end points*
	Age	Sex	Family history	Current tobacco use	T2D	SBP		Lipid profile (mg/dL)			Other CVD RFs	
						mm Hg	Rx	TC	HDL-C	Rx[a]		
Reynolds CVD Risk Score (2007-2008) [290,291]	X	X	X	X	X[b]	X		X	X		hs-CRP	1,2,5,7
Framingham CVD Risk Score (2008-2009) [292,293]	X	X		X	X	X	X	X	X			1,2,3,4,6,7,8,9,10
ACC/AHA Pooled Cohort CVD Risk Calculator (2013) [294,295]	X[c]	X		X	X	X	X	X	X			1,2,7,8
MESA Risk Score (2015) [296]	X[d]	X	X[e]	X	X	X	X	X	X	X	CAC score	1,2,5[f]

Abbreviations: ACC/AHA = American College of Cardiology/American Heart Association; ASCVD = atherosclerotic cardiovascular disease; CAC = coronary artery calcification; CHD = coronary heart disease; CVD = cardiovascular disease; hs-CRP = high-sensitivity C-reactive protein; HDL-C = high-density lipoprotein cholesterol; mm Hg = millimeters mercury; MI = myocardial infarction; RF = risk factor; Rx = treatment; SBP = systolic blood pressure; T2D = type 2 diabetes; TC = total cholesterol

* Endpoints: (1) CHD death, (2) nonfatal MI, (3) unstable angina, (4) stable angina, (5) coronary revascularization, (6) heart failure, (7) nonfatal stroke, (8) fatal stroke, (9) transient ischemic attack, (10) claudication

[a] Use of lipid-lowering therapy.

[b] Assessed by A1C value for women only, not for men.

[c] Validated for adults 40–79 years of age.

[d] Included non-Hispanic White, Hispanic, African American, and Chinese American ethnic groups.

[e] Family history of MI at any age.

[f] Also included resuscitated cardiac arrest.

associated with increased risk of ASCVD events and may be helpful when the lipid management goal is unclear.[276-285] These biomarkers may enhance understanding of an individual's risk and inform decisions of initiating or intensifying pharmacotherapy.[286] However, sequential monitoring of some of these biomarkers is not recommended at this time; high-sensitivity CRP is not mechanistically linked to the pathophysiology of atherosclerosis, coronary artery calcium changes are unlikely to be reversed, and lipoprotein(a) as a targetable marker requires validation by future outcome trials.[287-289] In addition, repeat measures of these biomarkers add to costs and may result in unproven therapeutic strategies.

Where the decision for need to intervene with pharmacotherapy based upon the above risk factor assessments remains unclear, we recommend the use of a risk calculator[290-296] (Table 8). In persons younger than 40 years, initiation of statin therapy for primary prevention of CVD in both men and women needs to be individualized, based on other risk factors and comorbidities.[273] The use of various 10-year or lifetime risk calculators is an option to decide the intensity of treatment (Table 8). By definition, these calculators are based on observational data for risk prediction but have been verified for prediction accuracy using large databases. The use of a statin choice decision aid also may assist in shared decision-making between clinicians and persons considering statin treatment choices.[297-299]

Persons who have T1D with persistent proteinuria are at increased risk of premature atherosclerosis.[300] In addition, the rising prevalence of overweight and obesity may contribute to increased rates of abnormal lipoprotein patterns related to insulin resistance among persons with T1D.[301,302] Despite limited observational and RCT data, we recommend treating persons with T1D and proteinuria and those over the age of 40 in a similar fashion to those with T2D.

Very low-density lipoprotein (VLDL) is secreted by the liver and is strongly influenced by insulin and carbohydrate intake, whereas chylomicrons are derived from the intestine and are secreted in response to dietary fat intake. VLDL remnants (apo B-100) are atherogenic and the primary particles accumulating when triglycerides are between 250 to 500 mg/dL. VLDL and chylomicrons may coexist in hypertriglyceridemia >500 mg/dL, though chylomicron remnants (apo B-48) predominate with significantly increasing triglyceride levels >500 mg/dL.

Multiple disturbances in lipoprotein metabolism in individuals with prediabetes and T2D result from the combined effects of insulin deficiency, insulin resistance, and hyperglycemia.[303-308] T2D dyslipidemia is characterized by increased levels of triglyceride-rich lipoproteins (VLDL), intermediate-density lipoprotein, and remnant particles—all apo B–containing particles—which metabolically lead to low levels of HDL-C and increased levels of small, dense LDL-C.[278,309-311] Hypertriglyceridemia is indirectly linked with changes in HDL-C and LDL-C composition that are conducive to accelerated atherogenesis.[312,313] Accumulating evidence favors the need to assess apo B–containing lipoproteins to account for remnant lipoproteins and small dense lipoproteins responsible for residual ASCVD risk not seen with a standard lipid panel of total cholesterol, LDL-C, and HDL-C.[314-316]

Lipid Targets

Treatment targets for dyslipidemia in persons with DM or prediabetes and without ASCVD or target organ damage are based on the duration of DM and the presence of traditional ASCVD risk factors including advancing age, hypertension, CKD stage 3a, cigarette smoking, family history of premature ASCVD in men <55 years and women <65 years, low HDL-C, or high non-HDL-C (Fig. 1 and Table 9). T2D carries a high lifetime risk for developing ASCVD.[317] In individuals with T2D, ASCVD risk should be assessed and stratified as *high* (persons with T1D <40 years of age or T2D duration <10 years and less than 2 additional ASCVD risk factors), *very high* (persons with T2D >10 years or T1D >20 years and age >40 plus 2 or more traditional ASCVD risk factors), or *extreme risk* (DM or prediabetes plus established ASCVD or target organ damage, including left ventricular systolic or diastolic dysfunction, estimated glomerular filtration rate [eGFR] <45 mL/min/1.73 m^2, and ankle-brachial index <0.9) to help define lipid treatment targets and direct appropriate lipid-lowering therapy.[318] Risk stratification in this manner can guide management strategies as well as laboratory testing to ensure efficacy of therapy. We recommend the use of apo B measurements as this is more accurate than non-HDL-C and predicts ASCVD risk more accurately than LDL-C.[319] In persons at high risk, the lipid targets should be LDL-C <100 mg/dL, apo B <90 mg/dL, and non-HDL-C <130 mg/dL.[314,315,320-325] In persons at very high risk for ASCVD, the lipid targets should be LDL-C <70 mg/dL, apo B <80 mg/dL, and non-HDL-C <100 mg/dL.[306] In persons with DM at extreme risk of ASCVD events, the lipid targets should be LDL-C <55 mg/dL, apo B <70 mg/dL, and non-HDL-C <90 mg/dL.[322-324,326] Note that the risk categories vary in name and definition in the references cited. The choice of statin and other lipid-lowering therapies prescribed should be based upon their relative intensity in lowering LDL-C required for lowering risk of ASCVD (Table 9 and Table 10).