2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease

Web Supplement

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Preamble (full version)

Since 1980, the American College of Cardiology (ACC) and American Heart Association (AHA) have translated scientific evidence into clinical practice guidelines with recommendations to improve cardiovascular health. These guidelines, which are based on systematic methods to evaluate and classify evidence, provide a foundation for the delivery of quality cardiovascular care. The ACC and AHA sponsor the development and publication of clinical practice guidelines without commercial support, and members volunteer their time to the writing and review efforts. Guidelines are official policy of the ACC and AHA. For some guidelines, the ACC and AHA partner with other organizations.

Intended Use

Clinical practice guidelines provide recommendations applicable to patients with or at risk of developing cardiovascular disease. The focus is on medical practice in the United States, but these guidelines are relevant to patients throughout the world. Although guidelines may be used to inform regulatory or payer decisions, the intent is to improve quality of care and align with patients' interests. Guidelines are intended to define practices meeting the needs of patients in most, but not all, circumstances, and should not replace clinical judgment.

Clinical Implementation

Management, in accordance with guideline recommendations, is effective only when followed by both practitioners and patients. Adherence to recommendations can be enhanced by shared decision-making between clinicians and patients, with patient engagement in selecting interventions on the basis of individual values, preferences, and associated conditions and comorbidities.

Methodology and Modernization

The ACC/AHA Task Force on Clinical Practice Guidelines (Task Force) continuously reviews, updates, and modifies guideline methodology on the basis of published standards from organizations, including the Institute of Medicine (1, 2), and on the basis of internal reevaluation. Similarly, presentation and delivery of guidelines are reevaluated and modified in response to evolving technologies and other factors to optimally facilitate dissemination of information to healthcare professionals at the point of care.

Beginning in 2017, numerous modifications to the guidelines have been and continue to be implemented to make guidelines shorter and enhance "user friendliness." Guidelines are written and presented in a modular knowledge chunk format, in which each chunk includes a table of recommendations, a brief synopsis, recommendation-specific supportive text and, when appropriate, flow diagrams or additional tables. Hyperlinked references are provided for each modular knowledge chunk to facilitate quick access and review. More structured guidelines—including word limits ("targets") and a web guideline supplement for useful but noncritical tables and figures—are 2 such changes. Also, to promote conciseness, the Preamble is presented in abbreviated form in the executive summary and full-text guideline documents.

In recognition of the importance of cost–value considerations in certain guidelines, when appropriate and feasible, an analysis of value for a drug, device, or intervention may be performed in accordance with the ACC/AHA methodology (3).

To ensure that guideline recommendations remain current, new data are reviewed on an ongoing basis, with full guideline revisions commissioned ideally in approximate 6-year cycles. Publication of potentially practice-changing new study results relevant to an existing or new drug, device, or management strategy prompts evaluation by the Task Force, in consultation with the relevant guideline writing committee, to determine whether a focused update should be commissioned. For additional information and policies on guideline development, we encourage readers to consult the ACC/AHA guideline methodology manual (4) and other methodology articles (5-8).

Selection of Writing Committee Members

The Task Force strives to ensure that the guideline writing committee both contains requisite expertise and is representative of the broader medical community by selecting experts from a broad array of backgrounds, representing different geographic regions, sexes, races, ethnicities, intellectual perspectives/biases, and scopes of clinical practice, and by inviting organizations and professional societies with related interests and expertise to participate as partners or collaborators.

Relationships With Industry and Other Entities

The ACC and AHA have rigorous policies and methods to ensure that documents are developed without bias or improper influence. The complete policy on relationships with industry and other entities (RWI) can be found at http://www.acc.org/guidelines/about-guidelines-and-clinical-documents/relationships-with-industry-policy. Appendix 2 of the guideline lists writing committee members' relevant RWI; for the purposes of full transparency, their comprehensive disclosure information is available online (●●●●●●●●●●). Comprehensive disclosure information for the Task Force is also available at http://www.acc.org/guidelines/about-guidelines-and-clinical-documents/guidelines-and-documents-task-forces.

Guideline-Directed Management and Therapy

The term *guideline-directed management and therapy* encompasses clinical evaluation, diagnostic testing, and both pharmacological and procedural treatments. For these and all recommended drug treatment regimens, the reader should confirm dosage with product insert material and evaluate for contraindications and interactions. Recommendations are limited to drugs, devices, and treatments approved for clinical use in the United States.

Class of Recommendation and Level of Evidence

The Class of Recommendation (COR) indicates the strength of recommendation, encompassing the estimated magnitude and certainty of benefit in proportion to risk. The Level of Evidence (LOE) rates the quality of scientific evidence supporting the intervention on the basis of the type, quantity, and consistency of data from clinical trials and other sources (see Table 2 in the guideline) (5).

Patrick T. O'Gara, MD, MACC, FAHA

Chair, ACC/AHA Task Force on Clinical Practice Guidelines

Supplemental Tables

Table S1. Associated Guidelines and Statements

Title	Organization	Publication Year (Reference)
Guidelines		
Guideline on the Management of Blood Cholesterol	ACC/AHA/AACVPR/AAPA/ABC/ACPM/ ADA/AGS/APhA/ASPC/NLA/PCNA	2018 (9)
Use of Risk Assessment Tools to Guide Decision-Making in the Primary Prevention of Atherosclerotic Cardiovascular Disease	AHA/ACC	2018 (10)
2018 Physical Activity Guidelines for Americans	U.S. HHS	2018 (11)
Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults	ACC/AHA/AAPA/ABC/ACPM/AGS/ APhA/ASH/ASPC/NMA/PCNA	2017 (12)
Healthful Diet and Physical Activity for Cardiovascular Disease Prevention in Adults Without Known Risk Factors: Behavioral Counseling	U.S. Preventive Services Task Force	2017 (13)
Guideline on the Management of Patients With Lower-Extremity Peripheral Artery Disease	ACC/AHA	2016 (14)
Focused Update of the Guideline for the Diagnosis and Management of Patients With Stable Ischemic Heart Disease	ACC/AHA/AATS/PCNA/SCAI/STS	2014 (15)
Behavioral Counseling to Promote a Healthful Diet and Physical Activity for Cardiovascular Disease Prevention in Adults With Cardiovascular Risk Factors: U.S. Preventive	U.S. Preventive Services Task Force	2014 (16)

Services Task Force Recommendation Statement		
Guideline for the Management of Overweight and Obesity in Adults	AHA/ACC/TOS	2013 (17)
Guideline on Lifestyle Management to Reduce Cardiovascular Risk	AHA/ACC	2013 (18)
Guideline on the Assessment of Cardiovascular Risk	ACC/AHA	2013 (19)
Secondary Prevention and Risk Reduction Therapy for Patients With Coronary and Other Atherosclerotic Vascular Disease: 2011 Update	AHA/ACCF	2011 (20)
Guidelines for Primary Prevention of Cardiovascular Disease and Stroke: 2002 Update: Consensus Panel Guide to Comprehensive Risk Reduction for Adult Patients Without Coronary or Other Atherosclerotic Vascular Diseases	AHA	2002 (21)
Statements		
Spontaneous Coronary Artery Dissection: Current State of the Science	AHA	2018 (22)
Health Policy Statement on Cardiovascular Team-Based Care and the Role of Advanced Practice Providers	ACC	2015 (23)
Eligibility and Disqualification Recommendations for Competitive Athletes With Cardiovascular Abnormalities: Preamble, Principles, and General Considerations	ACC/AHA	2015 (24)

Update on Prevention of Cardiovascular Disease in Adults With Type 2 Diabetes Mellitus in Light of Recent Evidence	AHA/ADA	2015 (25)
The Agenda for Familial Hypercholesterolemia	AHA	2015 (26)
Social Determinants of Risk and Outcomes for Cardiovascular Disease	AHA	2015 (27)
Electronic Cigarettes	AHA	2014 (28)
Statement on Cost/Value Methodology in Clinical Practice Guidelines and Performance Measures	ACC/AHA	2014 (3)
Primary Prevention of Cardiovascular Diseases in People With Diabetes Mellitus	AHA/ADA	2007 (29)

AACVPR indicates American Association of Cardiovascular and Pulmonary Rehabilitation; AAPA, American Academy of Physician Assistants; AATS, American Association for Thoracic Surgery; ABC, Association of Black Cardiologists; ACC, American College of Cardiology; ACCF, American College of Cardiology Foundation; ACPM, American College of Preventive Medicine; ADA, American Diabetes Association; AGS, American Geriatrics Society; AHA, American Heart Association; APhA, American Pharmacists Association; ASH, American Society of Hematology; ASPC, Association of Surgeons in Primary Care; HHS, U.S. Department of Health and Human Services; NLA, National Lipid Association; NMA, National Medical Association; PCNA, Preventive Cardiovascular Nurses Association; SCAI, Society for Cardiovascular Angiography and Interventions; STS, Society of Thoracic Surgeons; and TOS, The Obesity Society.

Table S2. Relative Risk Association Between Risk-Enhancing Factors and ASCVD

Risk-Modifying Factor	Risks for ASCVD—Illustrative Examples	References
Parental CVD	Multivariable adjustment gave ORs for premature CVD: – Men: 2.0 (95% CI: 1.2–3.1) – Women: 1.7 (95% CI: 0.9–3.1) Comments: In the Framingham Offspring Study, participants with no parental CVD were compared with those with at least 1 parent with premature CVD with onset at <55 y of age in father and <65 y of age in mother.	(30)
Family history of stroke	Comments: For family history of stroke, multivariable adjustment gave ORs of: – All stroke: OR: 2.79 (95% CI: 1.68–4.66; *P*<0.001) – Ischemic stroke: HR: 3.15 (95% CI: 1.69–5.88; *P*<0.001) This was true for both maternal and paternal stroke.	(31)
Metabolic syndrome with and without DM	RR for patients with metabolic syndrome, including DM: RR for CVD: 2.35 (95% CI: 2.02–2.73) – Men: 2.14 (95% CI: 1.62–2.83) – Women: 2.87 (95% CI: 2.40–3.43) – CVD mortality: 2.40 (95% CI: 1.87–3.08) RR for patients with metabolic syndrome but not with DM: – CVD mortality: 1.75 (95% CI: 1.19–2.58) RR for cardiovascular events and death: 1.78 RR for patients including DM versus those without DM: 1.51 versus 1.69 RR for patients with CHD versus those without CHD: 2.68 versus 1.94	(32, 33)

CKD	HR for cardiovascular mortality (if dipstick proteinuria ≥ ++) – eGFR 45-59: 1.38 (2.67) – eGFR 30-44: 2.42 (3.06) – eGFR 15-29: 3.29	(34)
Inflammatory disorders	RR of cardiometabolic diseases (CHD, stroke, T2DM, venous thromboembolism, and peripheral artery disease) Comment: Magnitude of association with inflammatory disease and cardiometabolic disease was higher among those prescribed nonsteroidal anti-inflammatory or corticosteroid drugs. RR by specific inflammatory conditions	(35)
Rheumatoid arthritis	1.70 (95% CI: 1.59–1.83)	
Ankylosing spondylitis	1.28 (95% CI: 1.09–1.52)	
Psoriasis (most common)	1.25 (95% CI: 1.16–1.35)	
Systematic lupus erythematosus (least common)	6.36 (95% CI: 4.37–9.25)	
Vasculitis	1.64 (95% CI: 1.42–1.90)	
HIV HCV HIV/HCV coinfection	MI rates per 1,000 person-years: – Black men: 6.9 – Black women: 7.2 – White men: 4.4 – White women: 3.3 HR: 2.91 (95% CI: 1.19–7.12) Comments: Note higher RR in black versus white patients and in black women especially. Also, HIV/HCV-coinfected patients had a higher incidence of CVD events and/or death than did HIV-monoinfected adults (36, 37)(4% versus 1.2%, *P*=0.004).	(36, 38)

Conditions specific to women: early menopause and preeclampsia	Early age at menopause (age <40 y versus age 50 to <55 y) associated with higher multivariable-adjusted CVD risk: 1.32 (95% CI: 1.16–1.51), *P* trend <0.0001, with excess risk for both natural and surgical menopause In women with a history of preeclampsia or eclampsia, the following were demonstrated: – An increased risk of CVD (leading to either a clinical diagnosis or a fatal outcome) (HR: 2.28; 95% CI: 1.87–2.78), – cerebrovascular disease (HR: 1.76; 95% CI: 1.43–2.21) – developing hypertension (HR: 3.13; 95% CI: 2.51–3.89) Comments: 1. Prospective cohort study data from Nurses' Health Study. Furthermore, a shorter reproductive life span was associated with higher risk of incident CVD after multivariable adjustment (RR: 1.32 [95% CI: 1.16–1.49] comparing duration in years <30 with ≥42; *P* trend <0.0001). 2. Outcomes for menopausal women <45 y of age relative to women >45 y of age. For overall CHD, relative risks were 1.50 (95% CI: 1.28–1.76). – 1.11 (95% CI: 1.03–1.20) for fatal CHD – 1.23 (95% CI: 0.98–1.53) for overall stroke – 0.99 (95% CI: 0.92–1.07) for stroke mortality – 1.19 (95% CI: 1.08–1.31) for CVD mortality – 1.12 (95% CI: 1.03–1.21) for all-cause mortality 3. A meta-analysis of 43 studies of women with a history of preeclampsia or eclampsia demonstrated increased risk of CVD (leading to either a clinical diagnosis or a fatal outcome). (HR: 2.28; 95% CI: 1.87–2.78), cerebrovascular disease (HR: 1.76; 95% CI: 1.43–2.21), and of developing hypertension (HR: 3.13; 95% CI: 2.51–3.89).	(39-42)

High-risk races/ethnicities (e.g., South Asian)	Proportionate mortality ratios are highest in Asian Indian men (1.43) and women (1.12), followed by Filipino men (1.15). Comments: Examined 10,442,034 U.S. records from 2003 to 2010 using U.S. Census and death records from the National Center for Health Statistics by Asian subgroup. Although non-Hispanic men and women had the highest overall mortality rates, Asian Indian men and women and Filipino men had greater proportionate mortality burden from ischemic heart disease. The proportionate mortality burden of hypertensive heart disease and cerebrovascular disease, especially hemorrhagic stroke, was higher in every Asian-American subgroup than in non-Hispanic whites.	(43, 44)
ABI	ABI <0.9 supports revising risk assessment by PCE upward. Comments: The ABI is to be used when risk-based decisions about initiation of LDL-C–lowering therapy remain uncertain after quantitative risk assessment by PCE. Same analysis also noted this to be true of family history of premature ASCVD and hsCRP (see above).	(19)
Biomarkers		
Hypertriglyceridemia	HR: 1.37 (95% CI: 0.99) Comments: HRs were at least as strong in those who did not fast as in those who were fasting. HR for CHD after adjustment for nonlipid risk factors was 1.37, but HR was only 0.99 (95% CI: 0.91–1.03) after further adjustment for HDL-C and non–HDL-C. For incident fatal and nonfatal cardiovascular relative risks: Men: Univariate RR for TG: 1.32 (95% CI: 1.26–1.39; *P*<0.05) Adjustment for HDL-C: 1.14 (95% CI: 1.05–1.28; *P*<0.05) Women: Univariate RR for TG:	(45, 46)

	1.76 (95% CI: 1.50–2.07; *P*<0.05) Adjustment for HDL-C: Univariate RR for TG: 1.37 (95% CI: 1.13–1.66; *P*<0.05)	
hsCRP	HR: 1.63 (95% CI: 1.37) Comments: When adjusted for age and sex, HR was 1.63, but HR was only 1.37 when adjusted further for CHD risk factors.	(47)
Lipoprotein(a)	1. Lp(a) and CHD relationships. In 24 cohort studies: – RR: 1.16 (95% CI: 1.11–1.22) adjusted for age and sex only – RR: 1.13 (95% CI: 1.09–1.18) further adjustment for lipids and conventional risk factors – RR: 1.10 for ischemic stroke (95% CI: 0.98–1.05) 2. Individuals with Lp(a) ≥80th percentile show increased CVD risk with higher LDL-C values than those with LDL-C <96.8 mg/dL (2.5 mmol/L). 3. Quintile analyses showed that risk for incident CVD was graded but statistically significant only for the highest compared with the lowest quintile for Lp(a): – HR: 1.35 (95% CI: 1.06–1.74) for blacks; – HR: 1.27 (95% CI: 1.10–1.47) for whites 4. In Women's Health Study, a curvilinear association with increased CVD risk was reported if Lp(a) was >50 mg/dL, but only among women with total cholesterol >220 mg/dL. In contrast, authors reported a strong association of Lp(a) with CHD among men with low total cholesterol levels in the JUPITER RCT.	(48-51)

Apolipoprotein B	In large multicenter prospective follow-up of patients without CVD: a) TC /HDL-C ratio or apoprotein ratios illustrated no improved risk prediction over TC and HDL-C. b) Adding apoB to TC and HDL-C was associated with slight improvement in CVD risk prediction. Meta-analysis prospective observational studies show apoB > non–HDL-C > LDL-C: – ApoB: RRR 1.43 (95% CI: 1.35–1.51) – Non–HDL-C: RRR 1.34 (95% CI: 1.24–1.44) – LDL-C: RRR 1.25 (95% CI: 1.18–1.33) In frequentist meta-analyses, the mean CHD risk reduction (95% CI) per standard deviation decrease in LDL-C, non–HDL-C and apoB across 7 placebo-controlled statin trials were: – LDL-C: 20.1% (95% CI: 15.6%–24.3%) – Non–HDL-C: 20.0% (95% CI: 15.2%–24.7%) – Apo B: 24.4% (95% CI: 19.2%–29.2%)	(52-54)

ABI indicates ankle-brachial index; apoB, apolipoprotein B; ASCVD, atherosclerotic cardiovascular disease; CHD, coronary heart disease; CI, confidence interval; CKD, chronic kidney disease; CVD, cardiovascular disease; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; HCV, hepatitis C virus; HDL-C, high-density lipoprotein cholesterol; HIV, human immunodeficiency virus; HR, hazard ratio; hsCRP, high-sensitivity C-reactive protein; JUPITER, Justification for the Use of Statins in Prevention: an Intervention Trial Evaluating Rosuvastatin; LDL-C, low-density lipoprotein cholesterol; Lp(a), lipoprotein (a); MI, myocardial infarction; OR, odds ratio; PCE, pooled cohort equations; RR, risk ratio; RRR, relative risk reduction; TC, total cholesterol; T2DM, type 2 diabetes mellitus; and TG, triglyceride.

*Family history age-adjusted ORs for CVD: 2.6 for men and 2.3 for women. Multivariable-adjusted OR: 2.0 for men and 1.7 for women. Family history of premature CVD was defined as cardiovascular event in first-degree relative <55 y of age in men and <65 y of age in women (4, 30).

Table S3. Strategies to Improve Guideline Implementation by Setting and Target Audience (19, 55-57)

Patient	Clinician	Office/Health System	Health Plan	Retail Pharmacy
• Simplify medication regimens • Provide clear instructions (what the medications is for, how to take it, what to expect) • Encourage the use of telephone alarms, prompts, and other tools to help patient remember to take medication • Encourage support of family and peers • Lower barriers to getting medication (cost, delivery method) • Provide consistent messaging • Remind patients about appointments and follow up on missed appointments • Ask patients to bring	• Initiate clinician–patient risk discussions • Provide brief, simple messages • Assess adherence at every encounter • Maintain contact with patient (follow-up laboratory tests and follow-up visits) • Use shared decision-making aids, motivational interviewing, decision coaching, and question prompt lists (60) • Incorporate discussion about lifestyle into every encounter • Provide prescriptions for diet and exercise recommendations • Teach clinicians to implement ASCVD risk reduction guidelines (61, 62) • Use apps (e.g., ASCVD Risk Estimator Plus	• Leverage decision-support tools imbedded in electronic medical records to promote formulary-based prescribing, minimal out-of-pocket expenses, and implementation of guidelines (72) • Use technology to identify high-risk patients who are not receiving GDMT • Collaborate with other team members to provide patient care (pharmacists, including retail-based; nurses; NP; PA) (23, 73, 74) • Structure care by developing standard treatment plans and pathways • Use peer-to-peer feedback	• Reduce the out-of-pocket cost of GDMT/prescriptions (72, 75-77) • Provide greater transparency to allow the patient and clinician determine which medications are included in the patient's drug formulary, the tier level, and the out-of-pocket cost to the patient • Increase access to care • Promote and reimburse for team-based collaborative care (pharmacists, including retail based; nurses, NP, PA) (23, 73, 74)	• Encourage enrollment in automatic refill programs (78) • Encourage 90-d refills versus 30-d refills (79, 80) • Encourage packaging that promotes adherence (81-83) • Encourage use of medication synchronization programs (84, 85)

prescription and nonprescription medication bottles to each office visit • Provide education with behavior support, case management, or telehealth counseling • Increase empowerment through peer-to-peer and social support moderated by clinician • Consider clinician–patient shared accountability for performance measures (58, 59)	(63), CardioSmart Explorer (64), LDL-C Manager (65), Statin Intolerance (66), Mayo Clinic Statin Choice Decision Aid) (67) and other resources (American Heart Association Life's Simple 7 (68), National Lipid Association Patient Tear Sheets (69), Clinicians' Lifestyle Modification Toolbox (70), Preventive Cardiovascular Nurses Association Heart Healthy Toolbox (71), cholesterol tear sheets, and patient education booklets)	from past performance with guideline implementation to promote change in future care • Participate in registries to improve care • Use academic detailing (61, 62) • Identify stakeholders and make use of audit and feedback on clinical performance (61, 62)		

ASCVD indicates atherosclerotic cardiovascular disease; GDMT, guideline-directed medical therapy; LDL-C, low-density lipoprotein cholesterol; NP, nurse practitioner; and PA, physician assistant.

Table S4. Clinician–Patient Risk Discussion: Useful Checklist

Individualize decision for patient with regard to prevention of ASCVD
1. Importance of addressing other risk factors • Cigarette smoking • Hypertension • DM • Metabolic syndrome, obesity, sedentary behaviors • Other risk-modifying factors (9) **2. Importance of adherence to optimal lifestyle** • Lifestyle improves all metabolic risk factors • Lifestyle still important even in presence of genetic disease or if patient is on statin therapy **3. Understand current risk status with PCE risk estimation** • If age 20–39 y, estimate lifetime ASCVD risk • If age 40–75 y, use 10-y ASCVD risk estimator (63) o Risk estimator estimates to age 79 y if of interest o Reliability of PCEs; need to adjust for ethnic and other factors (use ACC/AHA risk estimator) (9, 86); see Section 7 (9) • Understand that risk estimates are not precise; they start the risk discussion **4. Resolving uncertainty about risk estimation** • If uncertain, consider benefit of CAC scoring (see Section 6 (9)), as a CAC score of zero may indicate that benefits of statin therapy do not outweigh risks. • Understand that, especially in younger patients, a CAC score of zero does not provide information on noncalcified plaques **5. Potential benefit of statin therapy** • Multiple meta-analyses show statins to be effective and safe. In those at risk, statins have been shown to reduce all-cause and cardiovascular mortality rate in primary and as well as in secondary prevention. • Concept of reversal of unstable plaques for high risk • Concept of “the lower, the better” for LDL-C, especially in those at highest risk (favors higher intensity) • Expected risk reduction from prescribed dose (see section on pharmacotherapy (9)) **6. Potential for adverse effects of statins (See Section 5 (9))** • Lack of specificity of common musculoskeletal symptoms and other symptoms falsely attributed to statin therapy. • Consider genetic reasons (SLC01B1) for side effects on simvastatin • Dose versus side effect relationship (See Section 5 (9)) • Potential for drug–drug interaction (see section on pharmacotherapy (9)) • Guidelines encourage pharmacist input to check for drug–drug interactions • In those with DM risk factors, progression to DM more likely with statins, but this is not seen in those with 0–1 DM risk factors. Another reason to stick with heart-healthy lifestyle if placed on a statin. **7. Potential adherence issues of lifetime statin therapy (See Section 6 (9))** • Studies show increased risk in those assigned to statin therapy who did not persist in finding a tolerated statin or dose

- Discuss that benefits from statin therapy are greater in year 3 than in year 1; benefits increase with duration of therapy
- Discuss several studies with long-term follow-up showing benefit

8. **Patient preference and expectations**
   - Patients values, goals, and attitudes toward using medication should be shared so a joint decision can be made
   - Important to inquire about prior experiences with drugs and/or statins
   - Communicate the essential nature of a risk decision involving the evidence, patient characteristics, clinician judgment and after hearing about benefits, risks, and options, the inclusion of patient preference in shared decision-making
   - Use best practices for discussing numeric risk, including teaching aides
   - Ongoing reassessment of patient status and measurements of adherence and percent lowering of LDL-C on statin therapy, along with patient preference, which may change
   - Special considerations for women, various racial/ethnic groups, and those >75 y of age, including cessation of statin therapy in the elderly (see Section 4.4.4.1, 4.4.5.1, and 4.4.5.4 (9))
9. **Consider knowledgeable staff and consider materials for patients who wish to think about this decision (see Section 6 (9)). The decision may, in some cases, require a repeat visit to review issues important to the patient.**

ACC indicates American College of Cardiology; AHA, American Heart Association; ASCVD, atherosclerotic cardiovascular disease; CAC, coronary artery calcium; DM, diabetes mellitus; LDL-C, low-density lipoprotein cholesterol; and PCE, pooled cohort equations.

Table S5. High Blood Pressure or Hypertension: 2017 and 2019 Guideline Recommendations

2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease

Recommendations from the 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults (12) are adapted below.

<table>
<tr><th colspan="3">Section 4.4. Recommendations for Lowering High Blood Pressure
Referenced studies that support recommendations are summarized in Data Supplements 13 and 14.</th></tr>
<tr><th>COR</th><th>LOE</th><th>Recommendations</th></tr>
<tr><td>I</td><td>A</td><td>1. In adults with elevated blood pressure (BP) or hypertension, including those requiring antihypertensive medications, nonpharmacological interventions are recommended to reduce BP. These include:
weight loss (87-90),
a heart-healthy dietary pattern (91-93),
sodium reduction (94-98),
dietary potassium supplementation (99-103),
increased physical activity with a structured exercise program (88, 90, 96, 104-108); and
limited alcohol (109-114).
Adapted from recommendations in the 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults (12).</td></tr>
<tr><td rowspan="2">I</td><td>SBP: A</td><td rowspan="2">2. In adults with an estimated 10-year ASCVD risk* of 10% or higher and an average systolic BP (SBP) of 130 mm Hg or higher or an average diastolic BP (DBP) of 80 mm Hg or higher, use of BP-lowering medications is recommended for primary prevention of CVD (115-123).
Adapted from recommendations in the 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults (12).</td></tr>
<tr><td>DBP: C-EO</td></tr>
<tr><td rowspan="2">I</td><td>SBP: B-R^{SR}</td><td rowspan="2">3. In adults with confirmed hypertension and 10-year ASCVD event risk of 10% or higher, a BP target of less than 130/80 mm Hg is recommended (118, 124-127).
Adapted from recommendations in the 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults (12).</td></tr>
<tr><td>DBP: C-EO</td></tr>
</table>

I	SBP: B-R[SR] DBP: C-EO	**4. In adults with hypertension and chronic kidney disease, treatment to a BP goal of less than 130/80 mm Hg is recommended (128-133).** Adapted from recommendations in the 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults (12).
I	SBP: B-R[SR] DBP: C-EO	**5. In adults with T2DM and hypertension, antihypertensive drug treatment should be initiated at a BP of 130/80 mm Hg or higher with a treatment goal of less than 130/80 mm Hg (118, 132, 134-139).** Adapted from recommendations in the 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults (12).
I	C-LD	**6. In adults with an estimated 10-year ASCVD risk <10% and an SBP of 140 mm Hg or higher or a DBP of 90 mm Hg or higher, initiation and use of BP-lowering medication is recommended (121, 140-143).** Adapted from recommendations in the 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults (12).
IIb	SBP: B-NR DBP: C-EO	**7. In adults with confirmed hypertension without additional markers of increased ASCVD risk, a BP target of less than 130/80 mm Hg may be reasonable (144-147).** Adapted from recommendations in the 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults (12).

2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults (12).

Recommendations for Nonpharmacological Interventions References that support recommendations are summarized in Online Data Supplements 9 through 21.		
COR	**LOE**	**Recommendations**
I	**A**	**1. Weight loss is recommended to reduce BP in adults with elevated BP or hypertension who are overweight or obese (87-90).**
I	**A**	**2. A heart-healthy diet, such as the DASH (Dietary Approaches to Stop Hypertension) diet, that facilitates achieving a desirable weight is recommended for adults with elevated BP or hypertension (91-93).**
I	**A**	**3. Sodium reduction is recommended for adults with elevated BP or hypertension (94-98).**
I	**A**	**4. Potassium supplementation, preferably in dietary modification, is recommended for adults with elevated BP or hypertension, unless contraindicated by the presence of CKD or use of drugs that reduce potassium excretion (99-103).**
I	**A**	**5. Increased physical activity with a structured exercise program is recommended for adults with elevated BP or hypertension (88, 90, 96, 104-108).**
I	**A**	**6. Adult men and women with elevated BP or hypertension who currently consume alcohol should be advised to drink no more than 2 and 1 standard drinks* per day, respectively (109-114).**
I	**SBP: A**	**7. Use of BP-lowering medications is recommended ~~for secondary prevention of recurrent CVD events in patients with clinical CVD and an average SBP of 130 mm Hg or higher or an average DBP of 80 mm Hg or higher, and~~ for primary prevention in adults with an estimated 10-year atherosclerotic cardiovascular disease (ASCVD) risk of 10% or higher and an average SBP 130 mm Hg or higher or an average DBP 80 mm Hg or higher (115-123).**
I	**SBP: B-R^{SR}** **DBP: C-EO**	**8. For adults with confirmed hypertension and known CVD or 10-year ASCVD event risk of 10% or higher (see Section 8.1.2), a BP target of less than 130/80 mm Hg is recommended (118, 124-127).**

I	SBP: B-R[SR] DBP: C-EO	9. Adults with hypertension and CKD should be treated to a BP goal of less than 130/80 mm Hg (128-133).
	SBP: B-R[SR] DBP: C-EO	10. In adults with DM and hypertension, antihypertensive drug treatment should be initiated at a BP of 130/80 mm Hg or higher with a treatment goal of less than 130/80 mm Hg (118, 132, 134-139).
I	C-LD	11. Use of BP-lowering medication is recommended for primary prevention of CVD in adults with no history of CVD and with an estimated 10-year ASCVD risk <10% and an SBP of 140 mm Hg or higher or a DBP of 90 mm Hg or higher (121, 140-143).
IIb	SBP: B-NR	12. For adults with confirmed hypertension, without additional markers of increased CVD risk, a BP target of less than 130/80 mm Hg may be reasonable (144-147).

Table S6. Cholesterol: 2018 and 2019 Guideline Recommendations

2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease

Recommendations from the 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol (9) are adapted below.

Section 4.3. Recommendations for Lowering High Blood Cholesterol Referenced studies that support recommendations are summarized in Data Supplement 11 and 12.		
COR	**LOE**	**Recommendations**
I	**A**	**1. In adults at intermediate-risk (≥7.5% to <20% 10-year ASCVD risk), statin therapy reduces risk of ASCVD, and in the context of a risk discussion, if a decision is made for statin therapy, a moderate-intensity statin should be recommended (148-155).** Adapted from recommendations in the 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol (9).
I	**A**	**2. In intermediate risk (≥7.5% to <20% 10-year ASCVD risk) patients, LDL-C levels should be reduced by 30% or more, and for optimal ASCVD risk reduction, especially in patients at high-risk (≥20% 10-year ASCVD risk), levels should be reduced by 50% or more (148, 151-156).** Adapted from recommendations in the 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol (9).
I	**A**	**3. In adults 40 to 75 years of age with diabetes, regardless of estimated 10-year ASCVD risk, moderate-intensity statin therapy is indicated (157-165).** Included from recommendations in the 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol (9).
I	**B-R**	**4. In patients 20 to 75 years of age with an LDL-C level of 190 mg/dL (≥4.9 mmol/L) or higher, maximally tolerated statin therapy is recommended (148, 166-171).** Included from recommendations in the 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol (9).
IIa	**B-R**	**5. In adults with diabetes mellitus who have multiple ASCVD risk factors, it is reasonable to prescribe high-intensity statin therapy with the aim to reduce LDL-C levels by 50% or more (148, 153).** Included from recommendations in the 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol (9).
IIa	**B-R**	**6. In intermediate-risk (≥7.5 to <20% 10-year ASCVD risk) adults, risk-enhancing factors favor initiation or intensification of statin therapy (53, 153, 172-178).**

		Adapted from recommendations in the 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol (9).
IIa	**B-NR**	**7. In intermediate-risk (≥7.5% to <20% 10-year ASCVD risk) adults or selected borderline-risk (5% to <7.5% 10-year ASCVD risk) adults in whom a coronary artery calcium score is measured for the purpose of making a treatment decision, AND** • **If the coronary calcium score is zero, it is reasonable to withhold statin therapy and reassess in 5 to 10 years, as long as higher risk conditions are absent (e.g., diabetes, family history of premature CHD, cigarette smoking);** • **If coronary artery calcium score is 1 to 99, it is reasonable to initiate statin therapy for patients ≥ 55 years of age;** • **If coronary artery calcium score is 100 or higher or in the 75th percentile or higher, it is reasonable to initiate statin therapy (174, 179).** Adapted from recommendations in the 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol (9).
IIb	**B-R**	**8. In patients at borderline risk (5% to <7.5% 10-year ASCVD risk), in risk discussion, the presence of risk-enhancing factors may justify initiation of moderate-intensity statin therapy (174, 180).** Adapted from recommendations in the 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol (9).

2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol (9)

Primary Prevention Recommendations for Adults 40 to 75 Years of Age With LDL Levels 70 to 189 mg/dL (1.7 to 4.8 mmol/L) Referenced studies that support recommendations are summarized in Online Data Supplement 16.		
COR	**LOE**	**Recommendations**
I	**A**	**1. In adults at intermediate-risk, statin therapy reduces risk of ASCVD, and in the context of a risk discussion, if a decision is made for statin therapy, a moderate-intensity statin should be recommended (S4.4.2-1–S4.4.2-8).**
I	**A**	**2. In intermediate-risk patients, LDL-C levels should be reduced by 30% or more, and for optimal ASCVD risk reduction, especially in high-risk patients, levels should be reduced by 50% or more (S4.4.2-1, S4.4.2-4–S4.4.2-9).**
I	**B-NR**	**3. For the primary prevention of clinical ASCVD* in adults 40 to 75 years of age without diabetes mellitus and with an LDL-C level of 70 to 189 mg/dL (1.7 to 4.8 mmol/L), the 10-year ASCVD risk of a first "hard" ASCVD event (fatal and nonfatal MI or stroke) should be estimated by using the race- and sex-specific PCE, and adults should be categorized as being at low risk (<5%), borderline risk (5% to <7.5%), intermediate-risk (≥7.5% to <20%), and high-risk (≥20%) (S4.4.2-10, S4.4.2-11).**
I	**B-NR**	**4. Clinicians and patients should engage in a risk discussion that considers risk factors, adherence to healthy lifestyle, the potential for ASCVD risk-reduction benefits, and the potential for adverse effects and drug–drug interactions, as well as patient preferences, for an individualized treatment decision (S4.4.2-12-S4.4.2-14).**
IIa	**B-R**	**5. In intermediate-risk adults, risk-enhancing factors favor initiation or intensification of statin therapy (S4.4.2-6, S4.4.2-15–S4.4.2-22).**
IIa	**B-NR**	**6. In intermediate-risk or selected borderline-risk adults, if the decision about statin use remains uncertain, it is reasonable to use a CAC score in the decision to withhold, postpone or initiate statin therapy (S4.4.2-15, S4.4.2-17, S4.4.2-23).**
IIa	**B-NR**	**7. In intermediate-risk adults or selected borderline-risk adults in whom a CAC score is measured for the purpose of making a treatment decision, AND** • **If the coronary calcium score is zero, it is reasonable to withhold statin therapy and reassess in 5 to 10 years, as long as higher risk conditions are absent (diabetes mellitus, family history of premature CHD, cigarette smoking);** • **If CAC score is 1 to 99, it is reasonable to initiate statin therapy for patients ≥55 years of age;** • **If CAC score is 100 or higher or in the 75th percentile or higher, it is reasonable to initiate statin therapy (S4.4.2-17, S4.4.2-23).**

IIb	**B-R**	**8. In intermediate-risk adults who would benefit from more aggressive LDL-C lowering and in whom high-intensity statins are advisable but not acceptable or tolerated, it may be reasonable to add a nonstatin drug (ezetimibe or bile acid sequestrant) to a moderate-intensity statin (S4.4.2-9).**
IIb	**B-R**	**9. In patients at borderline risk, in risk discussion, the presence of risk-enhancing factors may justify initiation of moderate-intensity statin therapy (S4.4.2-17, S4.4.2-24).**

References

1. Committee on Standards for Developing Trustworthy Clinical Practice Guidelines, Institute of Medicine (U.S.). Clinical Practice Guidelines We Can Trust. Washington, DC): The: National Academies Press; 2011.
2. Committee on Standards for Systematic Reviews of Comparative Effectiveness Research, Institute of Medicine (U.S.). Finding What Works in Health Care: Standards for Systematic Reviews. Washington, DC): The: National Academies Press; 2011.
3. Anderson JL, Heidenreich PA, Barnett PG, et al. ACC/AHA statement on cost/value methodology in clinical practice guidelines and performance measures: a report of the American College of Cardiology/American Heart Association Task Force on Performance Measures and Task Force on Practice Guidelines. J Am Coll Cardiol. 2014;63:2304-22.
4. ACCF/AHA Task Force on Practice Guidelines. Methodology Manual and Policies From the ACCF/AHA Task Force on Practice Guidelines. American College of Cardiology and American Heart Association. 2010. Available at: http://assets.cardiosource.com/Methodology_Manual_for_ACC_AHA_Writing_Committees.pdf and http://professional.heart.org/idc/groups/ahamah-public/@wcm/@sop/documents/downloadable/ucm_319826.pdf. Accessed September 23, 2018.
5. Halperin JL, Levine GN, Al-Khatib SM, et al. Further evolution of the ACC/AHA clinical practice guideline recommendation classification system: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol. 2016;67:1572-4.
6. Jacobs AK, Kushner FG, Ettinger SM, et al. ACCF/AHA clinical practice guideline methodology summit report: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2013;61:213-65.
7. Jacobs AK, Anderson JL, Halperin JL. The evolution and future of ACC/AHA clinical practice guidelines: a 30-year journey: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2014;64:1373-84.
8. Arnett DK, Goodman RA, Halperin JL, et al. AHA/ACC/HHS strategies to enhance application of clinical practice guidelines in patients with cardiovascular disease and comorbid conditions: from the American Heart Association, American College of Cardiology, and U.S. Department of Health and Human Services. J Am Coll Cardiol. 2014;64:1851-6.
9. Grundy SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of blood cholesterol: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines [published online ahead of print November 10, 2018]. Circulation doi: 101161/CIR0000000000000625.
10. Lloyd-Jones DM, Braun LT, Ndumele CE, et al. Use of risk assessment tools to guide decision-making in the primary prevention of atherosclerotic cardiovascular disease: a special report from the American Heart Association and American College of Cardiology. J Am Coll Cardiol. 2018. doi:10.1016/j.jacc.2018.11.005.
11. 2018 Physical Activity Guidelines Advisory Committee. 2018 Physical Activity Guidelines Advisory Committee Scientific Report. Washington, DC: U.S. Department of Health and Human

Services; 2018. Available at: https://health.gov/paguidelines/second-edition/report. Accessed January 3, 2019.
12. Whelton PK, Carey RM, Aronow WS, et al. Guideline on the Management of Blood Cholesterol. A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Hypertension. 2018;71:1269-324.
13. US Preventive Services Task Force, Grossman DC, Bibbins-Domingo K, et al. Behavioral counseling to promote a healthful diet and physical activity for cardiovascular disease prevention in adults without cardiovascular risk factors: US Preventive Services Task Force Recommendation Statement. JAMA. 2017;318:167-74.
14. Gerhard-Herman MD, Gornik HL, Barrett C, et al. 2016 AHA/ACC Guideline on the Management of Patients With Lower Extremity Peripheral Artery Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation. 2017;135:e726-e779.
15. Fihn SD, Blankenship JC, Alexander KP, et al. 2014 ACC/AHA/AATS/PCNA/SCAI/STS focused update of the guideline for the diagnosis and management of patients with stable ischemic heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines, and the American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. J Am Coll Cardiol. 2014;64:1929-49.
16. LeFevre ML, U.S. Preventive Services Task Force. Behavioral counseling to promote a healthful diet and physical activity for cardiovascular disease prevention in adults with cardiovascular risk factors: U.S. Preventive Services Task Force Recommendation Statement. Ann Intern Med. 2014;161:587-93.
17. Jensen MD, Ryan DH, Apovian CM, et al. 2013 AHA/ACC/TOS guideline for the management of overweight and obesity in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Obesity Society. J Am Coll Cardiol. 2014;63:2985-3023.
18. Eckel RH, Jakicic JM, Ard JD, et al. 2013 AHA/ACC guideline on lifestyle management to reduce cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2014;63:2960-84.
19. Goff DC Jr, Lloyd-Jones DM, Bennett G, et al. 2013 ACC/AHA guideline on the assessment of cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2014;63:2935-59.
20. Smith SC Jr, Benjamin EJ, Bonow RO, et al. AHA/ACCF secondary prevention and risk reduction therapy for patients with coronary and other atherosclerotic vascular disease: 2011 update: a guideline from the American Heart Association and American College of Cardiology Foundation. Circulation. 2011;124:2458-73.
21. Pearson TA, Blair SN, Daniels SR, et al. AHA guidelines for primary prevention of cardiovascular disease and stroke: 2002 update: consensus panel guide to comprehensive risk reduction for adult patients without coronary or other atherosclerotic vascular diseases. Circulation. 2002;106:388-91.
22. Hayes SN, Kim ESH, Saw J, et al. Spontaneous coronary artery dissection: current state of the science: a scientific statement from the American Heart Association. Circulation. 2018;137:e523-57.

23. Brush JE Jr, Handberg EM, Biga C, et al. 2015 ACC health policy statement on cardiovascular team-based care and the role of advanced practice providers. J Am Coll Cardiol. 2015;65:2118-36.
24. Maron BJ, Zipes DP, Kovacs RJ, et al. Eligibility and disqualification recommendations for competitive athletes with cardiovascular abnormalities: preamble, principles, and general considerations: a scientific statement from the American Heart Association and American College of Cardiology. Circulation. 2015;132:e256-61.
25. Fox CS, Golden SH, Anderson C, et al. Update on prevention of cardiovascular disease in adults with type 2 diabetes mellitus in light of recent evidence: a scientific statement from the American Heart Association and the American Diabetes Association. Circulation. 2015;132:691-718.
26. Gidding SS, Champagne MA, de Ferranti SD, et al. The agenda for familial hypercholesterolemia: a scientific statement from the American Heart Association. Circulation. 2015;132:2167-92.
27. Havranek EP, Mujahid MS, Barr DA, et al. Social determinants of risk and outcomes for cardiovascular disease: a scientific statement from the American Heart Association. Circulation. 2015;132:873-98.
28. Bhatnagar A, Whitsel LP, Ribisl KM, et al. Electronic cigarettes: a policy statement from the American Heart Association. Circulation. 2014;130:1418-36.
29. Buse JB, Ginsberg HN, Bakris GL, et al. Primary prevention of cardiovascular diseases in people with diabetes mellitus: a scientific statement from the American Heart Association and the American Diabetes Association. Circulation. 2007;115:114-26.
30. Lloyd-Jones DM, Nam B-H, D'Agostino RB Sr, et al. Parental cardiovascular disease as a risk factor for cardiovascular disease in middle-aged adults: a prospective study of parents and offspring. JAMA. 2004;291:2204-11.
31. Seshadri S, Beiser A, Pikula A, et al. Parental occurrence of stroke and risk of stroke in their children: the Framingham study. Circulation. 2010;121:1304-12.
32. Mottillo S, Filion KB, Genest J, et al. The metabolic syndrome and cardiovascular risk a systematic review and meta-analysis. J Am Coll Cardiol. 2010;56:1113-32.
33. Gami AS, Witt BJ, Howard DE, et al. Metabolic syndrome and risk of incident cardiovascular events and death: a systematic review and meta-analysis of longitudinal studies. J Am Coll Cardiol. 2007;49:403-14.
34. Chronic Kidney Disease Prognosis Consortium, Matsushita K, van der Velde M, et al. Association of estimated glomerular filtration rate and albuminuria with all-cause and cardiovascular mortality in general population cohorts: a collaborative meta-analysis. Lancet. 2010;375:2073-81.
35. Dregan A, Chowienczyk P, Molokhia M. Cardiovascular and type 2 diabetes morbidity and all-cause mortality among diverse chronic inflammatory disorders. Heart. 2017;103:1867-73.
36. Fernández-Montero JV, Barreiro P, de Mendoza C, et al. Hepatitis C virus coinfection independently increases the risk of cardiovascular disease in HIV-positive patients. J Viral Hepat. 2016;23:47-52.
37. Hiratzka LF, Bakris GL, Beckman JA, et al. 2010 ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM guidelines for the diagnosis and management of patients with Thoracic Aortic Disease: a report of the American College of

Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, American Association for Thoracic Surgery, American College of Radiology, American Stroke Association, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society of Interventional Radiology, Society of Thoracic Surgeons, and Society for Vascular Medicine. Circulation. 2010;121:e266-369.
38. Feinstein MJ, Nance RM, Drozd DR, et al. Assessing and refining myocardial infarction risk estimation among patients with human immunodeficiency virus: a study by the Centers for AIDS Research Network of Integrated Clinical Systems. JAMA Cardiol. 2017;2:155-62.
39. Ley SH, Li Y, Tobias DK, et al. Duration of reproductive life span, age at menarche, and age at menopause are associated with risk of cardiovascular disease in women. J Am Heart Assoc. 2017;6:e006713.
40. Muka T, Oliver-Williams C, Kunutsor S, et al. Association of age at onset of menopause and time since onset of menopause with cardiovascular outcomes, intermediate vascular traits, and all-cause mortality: a systematic review and meta-analysis. JAMA Cardiol. 2016;1:767-76.
41. Brown MC, Best KE, Pearce MS, et al. Cardiovascular disease risk in women with pre-eclampsia: systematic review and meta-analysis. Eur J Epidemiol. 2013;28:1-19.
42. Ahmed R, Dunford J, Mehran R, et al. Pre-eclampsia and future cardiovascular risk among women: a review. J Am Coll Cardiol. 2014;63:1815-22.
43. Jose PO, Frank ATH, Kapphahn KI, et al. Cardiovascular disease mortality in Asian Americans. J Am Coll Cardiol. 2014;64:2486-94.
44. Volgman AS, Palaniappan LS, Aggarwal NT, et al. Atherosclerotic cardiovascular disease in South Asians in the United States: epidemiology, risk factors, and treatments: a scientific statement from the American Heart Association. Circulation. 2018;138:e1-34.
45. Emerging Risk Factors Collaboration, Di Angelantonio E, Sarwar N, et al. Major lipids, apolipoproteins, and risk of vascular disease. JAMA. 2009;302:1993-2000.
46. Hokanson JE, Austin MA. Plasma triglyceride level is a risk factor for cardiovascular disease independent of high-density lipoprotein cholesterol level: a meta-analysis of population-based prospective studies. J Cardiovasc Risk. 1996;3:213-9.
47. Emerging Risk Factors Collaboration, Kaptoge S, Di Angelantonio E, et al. C-reactive protein concentration and risk of coronary heart disease, stroke, and mortality: an individual participant meta-analysis. Lancet. 2010;375:132-40.
48. Emerging Risk Factors Collaboration, Erqou S, Kaptoge S, et al. Lipoprotein(a) concentration and the risk of coronary heart disease, stroke, and nonvascular mortality. JAMA. 2009;302:412-23.
49. Verbeek R, Hoogeveen RM, Langsted A, et al. Cardiovascular disease risk associated with elevated lipoprotein(a) attenuates at low low-density lipoprotein cholesterol levels in a primary prevention setting. Eur Heart J. 2018;39:2589-96.
50. Virani SS, Brautbar A, Davis BC, et al. Associations between lipoprotein(a) levels and cardiovascular outcomes in black and white subjects: the Atherosclerosis Risk in Communities (ARIC) Study. Circulation. 2012;125:241-9.
51. Cook NR, Mora S, Ridker PM. Lipoprotein(a) and cardiovascular risk prediction among women. J Am Coll Cardiol. 2018;72:287-96.
52. Emerging Risk Factors Collaboration, Di Angelantonio E, Gao P, et al. Lipid-related markers and cardiovascular disease prediction. JAMA. 2012;307:2499-506.

53. Sniderman AD, Williams K, Contois JH, et al. A meta-analysis of low-density lipoprotein cholesterol, non-high-density lipoprotein cholesterol, and apolipoprotein B as markers of cardiovascular risk. Circ Cardiovasc Qual Outcomes. 2011;4:337-45.
54. Thanassoulis G, Williams K, Ye K, et al. Relations of change in plasma levels of LDL-C, non-HDL-C and apoB with risk reduction from statin therapy: a meta-analysis of randomized trials. J Am Heart Assoc. 2014;3:e000759.
55. American Heart Association. Identifying Strategies to Address Gaps in Cholesterol Management in the U.S.: Cholesterol Summit Report. Dallas, TX: American Heart Association; 2017. Available at: https://www.heart.org/idc/groups/heart-public/@wcm/@hcm/documents/downloadable/ucm_494491.pdf. Accessed January 3, 2019.
56. Jacobson TA, Maki KC, Orringer CE, et al. National Lipid Association recommendations for patient-centered management of dyslipidemia: part 2. J Clin Lipidol. 2015;9:S1-122.e1.
57. Chobanian AV, Bakris GL, Black HR, et al. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Hypertension. 2003;42:1206-52.
58. Peterson ED, Ho PM, Barton M, et al. ACC/AHA/AACVPR/AAFP/ANA concepts for clinician-patient shared accountability in performance measures: a report of the American College of Cardiology/American Heart Association Task Force on Performance Measures. Circulation. 2014;130:1984-94.
59. Drozda JP Jr, Ferguson TB Jr, Jneid H, et al. 2015 ACC/AHA focused update of secondary prevention lipid performance measures: a report of the American College of Cardiology/American Heart Association Task Force on Performance Measures. J Am Coll Cardiol. 2016;67:558-87.
60. Stacey D, Hill S, McCaffery K, et al. Shared decision making interventions: theoretical and empirical evidence with implications for health literacy. Stud Health Technol Inform. 2017;240:263-83.
61. Chan WV, Pearson TA, Bennett GC, et al. ACC/AHA special report: clinical practice guideline implementation strategies: a summary of systematic reviews by the NHLBI Implementation Science Work Group: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation. 2017;135:e122-37.
62. Fischer F, Lange K, Klose K, et al. Barriers and strategies in guideline implementation—a scoping review. Healthcare (Basel). 2016;4:36. doi:10.3390/healthcare4030036.
63. American College of Cardiology. ASCVD Risk Estimator Plus. Available at: http://tools.acc.org/ASCVD-Risk-Estimator-Plus/#!/calculate/estimate. Accessed January 3, 2019.
64. American College of Cardiology. CardioSmart Heart Explorer App. Available at: https://www.cardiosmart.org/For-Clinicians/CardioSmart-Explorer-App-for-Your-Office. Accessed January 3, 2019.
65. American College of Cardiology. LDL-C Manager. Available at: http://tools.acc.org/ldl. Accessed January 3, 2019.
66. American College of Cardiology. ACC Statin Intolerance App. Available at: https://www.acc.org/statinintoleranceapp. Accessed January 3, 2019.
67. Mayo Foundation for Medical Education and Research. Mayo Clinic Statin Choice Decision Aid. Available at: https://statindecisionaid.mayoclinic.org. Accessed January 3, 2019.

68. American Heart Association Life's Simple 7. Available at: https://www.heart.org/en/professional/workplace-health/lifes-simple-7. Accessed January 3, 2019.
69. National Lipid Association. Patient Tear Sheets. Available at: https://www.lipid.org/practicetools/tools/tearsheets. Accessed January 3, 2019.
70. National Lipid Association. Clinician's Lifestyle Modification Toolbox. Available at: https://www.lipid.org/CLMT. Accessed January 3, 2019.
71. Preventive Cardiovascular Nurses Association. A Heart Healthy Toolbox: Lifestyle Change Tools for Health Care Professionals and Their Patients. Available at: http://pcna.net/clinical-tools/tools-for-healthcare-providers/heart-healthy-toolbox. Accessed January 3, 2019.
72. Michelis KC, Hassouna B, Owlia M, et al. Effect of electronic prescription on attainment of cholesterol goals. Clin Cardiol. 2011;34:254-60.
73. Merenich JA, Olson KL, Delate T, et al. Mortality reduction benefits of a comprehensive cardiac care program for patients with occlusive coronary artery disease. Pharmacotherapy. 2007;27:1370-8.
74. Sandhoff BG, Nies LK, Olson KL, et al. Clinical pharmacy cardiac risk service for managing patients with coronary artery disease in a health maintenance organization. Am J Health Syst Pharm. 2007;64:77-84.
75. Choudhry NK, Avorn J, Glynn RJ, et al. Full coverage for preventive medications after myocardial infarction. N Engl J Med. 2011;365:2088-97.
76. Navar AM, Taylor B, Mulder H, et al. Association of prior authorization and out-of-pocket costs with patient access to PCSK9 inhibitor therapy. JAMA Cardiol. 2017;2:1217-25.
77. Watanabe JH, Kazerooni R, Bounthavong M. Association of copayment with likelihood and level of adherence in new users of statins: a retrospective cohort study. J Manag Care Pharm. 2014;20:43-50.
78. Lester CA, Mott DA, Chui MA. The influence of a community pharmacy automatic prescription refill program on Medicare Part D adherence metrics. J Manag Care Spec Pharm. 2016;22:801-7.
79. Leslie RS, Gilmer T, Natarajan L, et al. A multichannel medication adherence intervention influences patient and prescriber behavior. J Manag Care Spec Pharm. 2016;22:526-38.
80. Taitel M, Fensterheim L, Kirkham H, et al. Medication days' supply, adherence, wastage, and cost among chronic patients in Medicaid. Medicare Medicaid Res Rev. 2012;2. doi:10.5600/mmrr.002.03.a04.
81. Conn VS, Ruppar TM, Chan KC, et al. Packaging interventions to increase medication adherence: systematic review and meta-analysis. Curr Med Res Opin. 2015;31:145-60.
82. Zedler BK, Kakad P, Colilla S, et al. Does packaging with a calendar feature improve adherence to self-administered medication for long-term use? A systematic review. Clin Ther. 2011;33:62-73.
83. Zullig LL, Pathman J, Melnyk SD, et al. A protocol to evaluate the efficacy, perceptions, and cost of a cholesterol packaging approach to improve medication adherence. Contemp Clin Trials. 2014;39:106-12.
84. Doshi JA, Lim R, Li P, et al. Synchronized prescription refills and medication adherence: a retrospective claims analysis. Am J Manag Care. 2017;23:98-104.

85. Holdford D, Saxena K. Impact of appointment-based medication synchronization on existing users of chronic medications. J Manag Care Spec Pharm. 2015;21:662-9.
86. American Heart Association, American College of Cardiology. ASCVD Risk Calculator. Available at: https://professional.heart.org/professional/GuidelinesStatements/PreventionGuidelines/UCM_457698_ASCVD-Risk-Calculator.jsp. Accessed January 3, 2019.
87. Neter JE, Stam BE, Kok FJ, et al. Influence of weight reduction on blood pressure: a meta-analysis of randomized controlled trials. Hypertension. 2003;42:878-84.
88. The effects of nonpharmacologic interventions on blood pressure of persons with high normal levels. Results of the Trials of Hypertension Prevention, Phase I. JAMA. 1992;267:1213-20.
89. Whelton PK, Kumanyika SK, Cook NR, et al. Efficacy of nonpharmacologic interventions in adults with high-normal blood pressure: results from phase 1 of the Trials of Hypertension Prevention. Trials of Hypertension Prevention Collaborative Research Group. Am J Clin Nutr. 1997;65:652S-660S.
90. Effects of weight loss and sodium reduction intervention on blood pressure and hypertension incidence in overweight people with high-normal blood pressure. The Trials of Hypertension Prevention, phase II. The Trials of Hypertension Prevention Collaborative Research Group. Arch Intern Med. 1997;157:657-67.
91. Sacks FM, Svetkey LP, Vollmer WM, et al. Effects on blood pressure of reduced dietary sodium and the Dietary Approaches to Stop Hypertension (DASH) diet. DASH-Sodium Collaborative Research Group. N Engl J Med. 2001;344:3-10.
92. Appel LJ, Moore TJ, Obarzanek E, et al. A clinical trial of the effects of dietary patterns on blood pressure. DASH Collaborative Research Group. N Engl J Med. 1997;336:1117-24.
93. Appel LJ, Champagne CM, Harsha DW, et al. Effects of comprehensive lifestyle modification on blood pressure control: main results of the PREMIER clinical trial. JAMA. 2003;289:2083-93.
94. Mozaffarian D, Fahimi S, Singh GM, et al. Global sodium consumption and death from cardiovascular causes. N Engl J Med. 2014;371:624-34.
95. He FJ, Li J, Macgregor GA. Effect of longer term modest salt reduction on blood pressure: Cochrane systematic review and meta-analysis of randomised trials. BMJ. 2013;346:f1325.
96. Whelton PK, Appel LJ, Espeland MA, et al. Sodium reduction and weight loss in the treatment of hypertension in older persons: a randomized controlled trial of nonpharmacologic interventions in the elderly (TONE). TONE Collaborative Research Group. JAMA. 1998;279:839-46.
97. Aburto NJ, Ziolkovska A, Hooper L, et al. Effect of lower sodium intake on health: systematic review and meta-analyses. BMJ. 2013;346:f1326.
98. Graudal NA, Hubeck-Graudal T, Jürgens G. Effects of low-sodium diet vs. high-sodium diet on blood pressure, renin, aldosterone, catecholamines, cholesterol, and triglyceride (Cochrane Review). Am J Hypertens. 2012;25:1-15.
99. Whelton PK, He J, Cutler JA, et al. Effects of oral potassium on blood pressure: meta-analysis of randomized controlled clinical trials. JAMA. 1997;277:1624-32.
100. Aburto NJ, Hanson S, Gutierrez H, et al. Effect of increased potassium intake on cardiovascular risk factors and disease: systematic review and meta-analyses. BMJ. 2013;346:f1378.

101. Geleijnse JM, Kok FJ, Grobbee DE. Blood pressure response to changes in sodium and potassium intake: a metaregression analysis of randomised trials. J Hum Hypertens. 2003;17:471-80.
102. World Health Organization. Guideline: Potassium Intake for Adults and Children. Geneva, Switzerland: World Health Organization, Department of Nutrition for Health and Development; 2012.
103. Whelton PK, He J. Health effects of sodium and potassium in humans. Curr Opin Lipidol. 2014;25:75-9.
104. Cornelissen VA, Smart NA. Exercise training for blood pressure: a systematic review and meta-analysis. J Am Heart Assoc. 2013;2:e004473.
105. Whelton SP, Chin A, Xin X, et al. Effect of aerobic exercise on blood pressure: a meta-analysis of randomized, controlled trials. Ann Intern Med. 2002;136:493-503.
106. Carlson DJ, Dieberg G, Hess NC, et al. Isometric exercise training for blood pressure management: a systematic review and meta-analysis. Mayo Clin Proc. 2014;89:327-34.
107. García-Hermoso A, Saavedra JM, Escalante Y. Effects of exercise on resting blood pressure in obese children: a meta-analysis of randomized controlled trials. Obes Rev. 2013;14:919-28.
108. Rossi AM, Moullec G, Lavoie KL, et al. The evolution of a Canadian Hypertension Education Program recommendation: the impact of resistance training on resting blood pressure in adults as an example. Can J Cardiol. 2013;29:622-7.
109. Roerecke M, Kaczorowski J, Tobe SW, et al. The effect of a reduction in alcohol consumption on blood pressure: a systematic review and meta-analysis. Lancet Public Health. 2017;2:e108-20.
110. Xin X, He J, Frontini MG, et al. Effects of alcohol reduction on blood pressure: a meta-analysis of randomized controlled trials. Hypertension. 2001;38:1112-7.
111. Stewart SH, Latham PK, Miller PM, et al. Blood pressure reduction during treatment for alcohol dependence: results from the Combining Medications and Behavioral Interventions for Alcoholism (COMBINE) study. Addiction. 2008;103:1622-8.
112. Dickinson HO, Mason JM, Nicolson DJ, et al. Lifestyle interventions to reduce raised blood pressure: a systematic review of randomized controlled trials. J Hypertens. 2006;24:215-33.
113. Wallace P, Cutler S, Haines A. Randomised controlled trial of general practitioner intervention in patients with excessive alcohol consumption. BMJ. 1988;297:663-8.
114. Lang T, Nicaud V, Darné B, et al. Improving hypertension control among excessive alcohol drinkers: a randomised controlled trial in France. The WALPA Group. J Epidemiol Community Health. 1995;49:610-6.
115. Law MR, Morris JK, Wald NJ. Use of blood pressure lowering drugs in the prevention of cardiovascular disease: meta-analysis of 147 randomised trials in the context of expectations from prospective epidemiological studies. BMJ. 2009;338:b1665.
116. Ettehad D, Emdin CA, Kiran A, et al. Blood pressure lowering for prevention of cardiovascular disease and death: a systematic review and meta-analysis. Lancet. 2016;387:957-67.
117. Sundström J, Arima H, Jackson R, et al. Effects of blood pressure reduction in mild hypertension: a systematic review and meta-analysis. Ann Intern Med. 2015;162:184-91.
118. Xie X, Atkins E, Lv J, et al. Effects of intensive blood pressure lowering on cardiovascular and renal outcomes: updated systematic review and meta-analysis. Lancet. 2016;387:435-43.

119. SPRINT Research Group, Wright JT Jr, Williamson JD, et al. A randomized trial of intensive versus standard blood-pressure control. N Engl J Med. 2015;373:2103-16.
120. Czernichow S, Zanchetti A, Turnbull F, et al. The effects of blood pressure reduction and of different blood pressure-lowering regimens on major cardiovascular events according to baseline blood pressure: meta-analysis of randomized trials. J Hypertens. 2011;29:4-16.
121. Blood Pressure Lowering Treatment Trialists' Collaboration. Blood pressure-lowering treatment based on cardiovascular risk: a meta-analysis of individual patient data. Lancet. 2014;384:591-8.
122. Thomopoulos C, Parati G, Zanchetti A. Effects of blood pressure lowering on outcome incidence in hypertension: 2. Effects at different baseline and achieved blood pressure levels—overview and meta-analyses of randomized trials. J Hypertens. 2014;32:2296-304.
123. Thompson AM, Hu T, Eshelbrenner CL, et al. Antihypertensive treatment and secondary prevention of cardiovascular disease events among persons without hypertension: a meta-analysis. JAMA. 2011;305:913-22.
124. Thomopoulos C, Parati G, Zanchetti A. Effects of blood pressure lowering on outcome incidence in hypertension: 7. Effects of more vs. less intensive blood pressure lowering and different achieved blood pressure levels—updated overview and meta-analyses of randomized trials. J Hypertens. 2016;34:613-22.
125. Verdecchia P, Angeli F, Gentile G, et al. More versus less intensive blood pressure-lowering strategy: cumulative evidence and trial sequential analysis. Hypertension. 2016;68:642-53.
126. Bangalore S, Toklu B, Gianos E, et al. Optimal systolic blood pressure target after SPRINT: insights from a network meta-analysis of randomized trials. Am J Med. 2017;130:707-19.e8.
127. Bundy JD, Li C, Stuchlik P, et al. Systolic blood pressure reduction and risk of cardiovascular disease and mortality: a systematic review and network meta-analysis. JAMA Cardiol. 2017;2:775-81.
128. Ruggenenti P, Perna A, Loriga G, et al. Blood-pressure control for renoprotection in patients with non-diabetic chronic renal disease (REIN-2): multicentre, randomised controlled trial. Lancet. 2005;365:939-46.
129. Wright JT Jr, Bakris G, Greene T, et al. Effect of blood pressure lowering and antihypertensive drug class on progression of hypertensive kidney disease: results from the AASK trial. JAMA. 2002;288:2421-31.
130. Upadhyay A, Earley A, Haynes SM, et al. Systematic review: blood pressure target in chronic kidney disease and proteinuria as an effect modifier. Ann Intern Med. 2011;154:541-8.
131. Jafar TH, Stark PC, Schmid CH, et al. Progression of chronic kidney disease: the role of blood pressure control, proteinuria, and angiotensin-converting enzyme inhibition: a patient-level meta-analysis. Ann Intern Med. 2003;139:244-52.
132. Lv J, Ehteshami P, Sarnak MJ, et al. Effects of intensive blood pressure lowering on the progression of chronic kidney disease: a systematic review and meta-analysis. CMAJ. 2013;185:949-57.
133. Klahr S, Levey AS, Beck GJ, et al. The effects of dietary protein restriction and blood-pressure control on the progression of chronic renal disease. Modification of Diet in Renal Disease Study Group. N Engl J Med. 1994;330:877-84.
134. Emdin CA, Rahimi K, Neal B, et al. Blood pressure lowering in type 2 diabetes: a systematic review and meta-analysis. JAMA. 2015;313:603-15.

135. Arguedas JA, Leiva V, Wright JM. Blood pressure targets for hypertension in people with diabetes mellitus. Cochrane Database Syst Rev. 2013;CD008277.
136. Margolis KL, O'Connor PJ, Morgan TM, et al. Outcomes of combined cardiovascular risk factor management strategies in type 2 diabetes: the ACCORD randomized trial. Diabetes Care. 2014;37:1721-8.
137. Bress AP, Bellows BK, King JB, et al. Cost-effectiveness of intensive versus standard blood-pressure control. N Engl J Med. 2017;377:745-55.
138. Soliman EZ, Byington RP, Bigger JT, et al. Effect of intensive blood pressure lowering on left ventricular hypertrophy in patients with diabetes mellitus: Action to Control Cardiovascular Risk in Diabetes blood pressure trial. Hypertension. 2015;66:1123-9.
139. ACCORD Study Group, Cushman WC, Evans GW, et al. Effects of intensive blood-pressure control in type 2 diabetes mellitus. N Engl J Med. 2010;362:1575-85.
140. Lewington S, Clarke R, Qizilbash N, et al. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. Lancet. 2002;360:1903-13.
141. Kassaï B, Boissel J-P, Cucherat M, et al. Treatment of high blood pressure and gain in event-free life expectancy. Vasc Health Risk Manag. 2005;1:163-9.
142. van Dieren S, Kengne AP, Chalmers J, et al. Effects of blood pressure lowering on cardiovascular outcomes in different cardiovascular risk groups among participants with type 2 diabetes. Diabetes Res Clin Pract. 2012;98:83-90.
143. Montgomery AA, Fahey T, Ben-Shlomo Y, et al. The influence of absolute cardiovascular risk, patient utilities, and costs on the decision to treat hypertension: a Markov decision analysis. J Hypertens. 2003;21:1753-9.
144. Lonn EM, Bosch J, López-Jaramillo P, et al. Blood-pressure lowering in intermediate-risk persons without cardiovascular disease. N Engl J Med. 2016;374:2009-20.
145. Neaton JD, Grimm RH Jr, Prineas RJ, et al. Treatment of Mild Hypertension Study: final results. Treatment of Mild Hypertension Study Research Group. JAMA. 1993;270:713-24.
146. Julius S, Nesbitt SD, Egan BM, et al. Feasibility of treating prehypertension with an angiotensin-receptor blocker. N Engl J Med. 2006;354:1685-97.
147. Lawes CMM, Bennett DA, Lewington S, et al. Blood pressure and coronary heart disease: a review of the evidence. Semin Vasc Med. 2002;2:355-68.
148. Cholesterol Treatment Trialists' (CTT) Collaboration, Baigent C, Blackwell L, et al. Efficacy and safety of more intensive lowering of LDL cholesterol: a meta-analysis of data from 170,000 participants in 26 randomised trials. Lancet. 2010;376:1670-81.
149. Baigent C, Landray MJ, Reith C, et al. The effects of lowering LDL cholesterol with simvastatin plus ezetimibe in patients with chronic kidney disease (Study of Heart and Renal Protection): a randomised placebo-controlled trial. Lancet. 2011;377:2181-92.
150. Cholesterol Treatment Trialists' (CTT) Collaboration, Herrington W, Emberson J, et al. Impact of renal function on the effects of LDL cholesterol lowering with statin-based regimens: a meta-analysis of individual participant data from 28 randomised trials. Lancet Diabetes Endocrinol. 2016;4:829-39.
151. Chou R, Dana T, Blazina I, et al. Statin use for the prevention of cardiovascular disease in adults: a systematic review for the U.S. Preventive Services Task Force. Report No. 14-05206-

EF-2. Rockville, MD: U.S. Agency for Healthcare Research and Quality; 2016. Available at: http://www.ncbi.nlm.nih.gov/books/NBK396415. Accessed January 3, 2019.
152. Downs JR, Clearfield M, Weis S, et al. Primary prevention of acute coronary events with lovastatin in men and women with average cholesterol levels: results of AFCAPS/TexCAPS. Air Force/Texas Coronary Atherosclerosis Prevention Study. JAMA. 1998;279:1615-22.
153. Ridker PM, Danielson E, Fonseca FAH, et al. Rosuvastatin to prevent vascular events in men and women with elevated C-reactive protein. N Engl J Med. 2008;359:2195-207.
154. Taylor F, Huffman MD, Macedo AF, et al. Statins for the primary prevention of cardiovascular disease. Cochrane Database Syst Rev. 2013;CD004816.
155. Yusuf S, Bosch J, Dagenais G, et al. Cholesterol lowering in intermediate-risk persons without cardiovascular disease. N Engl J Med. 2016;374:2021-31.
156. Silverman MG, Ference BA, Im K, et al. Association between lowering LDL-C and cardiovascular risk reduction among different therapeutic interventions: a systematic review and meta-analysis. JAMA. 2016;316:1289-97.
157. Colhoun HM, Betteridge DJ, Durrington PN, et al. Primary prevention of cardiovascular disease with atorvastatin in type 2 diabetes in the Collaborative Atorvastatin Diabetes Study (CARDS): multicentre randomised placebo-controlled trial. Lancet. 2004;364:685-96.
158. Collins R, Armitage J, Parish S, et al. MRC/BHF Heart Protection Study of cholesterol-lowering with simvastatin in 5963 people with diabetes: a randomised placebo-controlled trial. Lancet. 2003;361:2005-16.
159. de Vries FM, Denig P, Pouwels KB, et al. Primary prevention of major cardiovascular and cerebrovascular events with statins in diabetic patients: a meta-analysis. Drugs. 2012;72:2365-73.
160. Knopp RH, d'Emden M, Smilde JG, et al. Efficacy and safety of atorvastatin in the prevention of cardiovascular end points in subjects with type 2 diabetes: the Atorvastatin Study for Prevention of Coronary Heart Disease Endpoints in non-insulin-dependent diabetes mellitus (ASPEN). Diabetes Care. 2006;29:1478-85.
161. Mulnier HE, Seaman HE, Raleigh VS, et al. Risk of myocardial infarction in men and women with type 2 diabetes in the UK: a cohort study using the General Practice Research Database. Diabetologia. 2008;51:1639-45.
162. Rana JS, Liu JY, Moffet HH, et al. Diabetes and prior coronary heart disease are not necessarily risk equivalent for future coronary heart disease events. J Gen Intern Med. 2016;31:387-93.
163. Sever PS, Poulter NR, Dahlöf B, et al. Reduction in cardiovascular events with atorvastatin in 2,532 patients with type 2 diabetes: Anglo-Scandinavian Cardiac Outcomes Trial—lipid-lowering arm (ASCOT-LLA). Diabetes Care. 2005;28:1151-7.
164. Soedamah-Muthu SS, Fuller JH, Mulnier HE, et al. High risk of cardiovascular disease in patients with type 1 diabetes in the U.K.: a cohort study using the general practice research database. Diabetes Care. 2006;29:798-804.
165. Wong ND, Glovaci D, Wong K, et al. Global cardiovascular disease risk assessment in United States adults with diabetes. Diab Vasc Dis Res. 2012;9:146-52.
166. Besseling J, Hovingh GK, Huijgen R, et al. Statins in familial hypercholesterolemia: consequences for coronary artery disease and all-cause mortality. J Am Coll Cardiol. 2016;68:252-60.

167. Khera AV, Won H-H, Peloso GM, et al. Diagnostic yield and clinical utility of sequencing familial hypercholesterolemia genes in patients with severe hypercholesterolemia. J Am Coll Cardiol. 2016;67:2578-89.
168. Nanchen D, Gencer B, Muller O, et al. Prognosis of patients with familial hypercholesterolemia after acute coronary syndromes. Circulation. 2016;134:698-709.
169. Perak AM, Ning H, de Ferranti SD, et al. Long-term risk of atherosclerotic cardiovascular disease in US adults with the familial hypercholesterolemia phenotype. Circulation. 2016;134:9-19.
170. Shepherd J, Cobbe SM, Ford I, et al. Prevention of coronary heart disease with pravastatin in men with hypercholesterolemia. West of Scotland Coronary Prevention Study Group. N Engl J Med. 1995;333:1301-7.
171. Versmissen J, Oosterveer DM, Yazdanpanah M, et al. Efficacy of statins in familial hypercholesterolaemia: a long term cohort study. BMJ. 2008;337:a2423.
172. Mortensen MB, Fuster V, Muntendam P, et al. A simple disease-guided approach to personalize ACC/AHA-recommended statin allocation in elderly people: the BioImage Study. J Am Coll Cardiol. 2016;68:881-91.
173. Willeit P, Kiechl S, Kronenberg F, et al. Discrimination and net reclassification of cardiovascular risk with lipoprotein(a): prospective 15-year outcomes in the Bruneck Study. J Am Coll Cardiol. 2014;64:851-60.
174. Nasir K, Bittencourt MS, Blaha MJ, et al. Implications of coronary artery calcium testing among statin candidates according to American College of Cardiology/American Heart Association cholesterol management guidelines: MESA (Multi-Ethnic Study of Atherosclerosis). J Am Coll Cardiol. 2015;66:1657-68.
175. Ridker PM, Mora S, Rose L, et al. Percent reduction in LDL cholesterol following high-intensity statin therapy: potential implications for guidelines and for the prescription of emerging lipid-lowering agents. Eur Heart J. 2016;37:1373-9.
176. Yano Y, O'Donnell CJ, Kuller L, et al. Association of coronary artery calcium score vs age with cardiovascular risk in older adults: an analysis of pooled population-based studies. JAMA Cardiol. 2017;2:986-94.
177. Malik S, Zhao Y, Budoff M, et al. Coronary artery calcium score for long-term risk classification in individuals with type 2 diabetes and metabolic syndrome from the Multi-Ethnic Study of Atherosclerosis. JAMA Cardiol. 2017;2:1332-40.
178. Sniderman AD, Tsimikas S, Fazio S. The severe hypercholesterolemia phenotype: clinical diagnosis, management, and emerging therapies. J Am Coll Cardiol. 2014;63:1935-47.
179. Budoff MJ, Young R, Burke G, et al. Ten-year association of coronary artery calcium with atherosclerotic cardiovascular disease (ASCVD) events: the multi-ethnic study of atherosclerosis (MESA). Eur Heart J. 2018;39:2401-8.
180. Cholesterol Treatment Trialists' (CTT) Collaborators, Mihaylova B, Emberson J, et al. The effects of lowering LDL cholesterol with statin therapy in people at low risk of vascular disease: meta-analysis of individual data from 27 randomised trials. Lancet. 2012;380:581-90.