Hypertension and Hyperlipidemia

Guideline Directed Medical Therapy

Paul Zellers, DO, FACC
University Hospitals - LHPG/ Northeast Ohio Heart Associates
January 28, 2022

Hypertension

Objectives

- Hypertension and CVD risk
- Classification of BP
- Patient evaluation, proper BP measuring technique
- Causes of Hypertension
- Non-pharmacologic therapies
- Medical Therapy
- HTN in patients with comorbidities / Special Considerations

Hypertension and CVD Risk

Observational Studies and Meta-analyses

- Increase in systolic and diastolic blood pressure increase risk of CV events in log-linear fashion
  - Angina
  - Stroke
  - MI
  - CV death
  - PAD
  - Abdominal Aortic Aneurysm (AAA)

Blood pressure and incidence of twelve cardiovascular diseases: lifetime risks, healthy life-years lost, and age-specific associations in 1·25 million people

Eleni Rapsomaniki, Adam Timmis, Julie George, Mar Pujades-Rodriguez, Anoop D Shah, Spiros Denaxas, Ian R White, Mark J Caulfield, John E Deanfield, Liam Smeeth, Bryan Williams, Aroon Hingorani, Harry Hemingway

Lancet 2014; 383: 1899–911

- Hazard Ratio associated with an increase in SBP/DBP of 20/10 in blood pressures ranging from 115/75 to 180/105
- After consideration of SBP through adjustment/stratification, DBP alone not associated with elevated risk

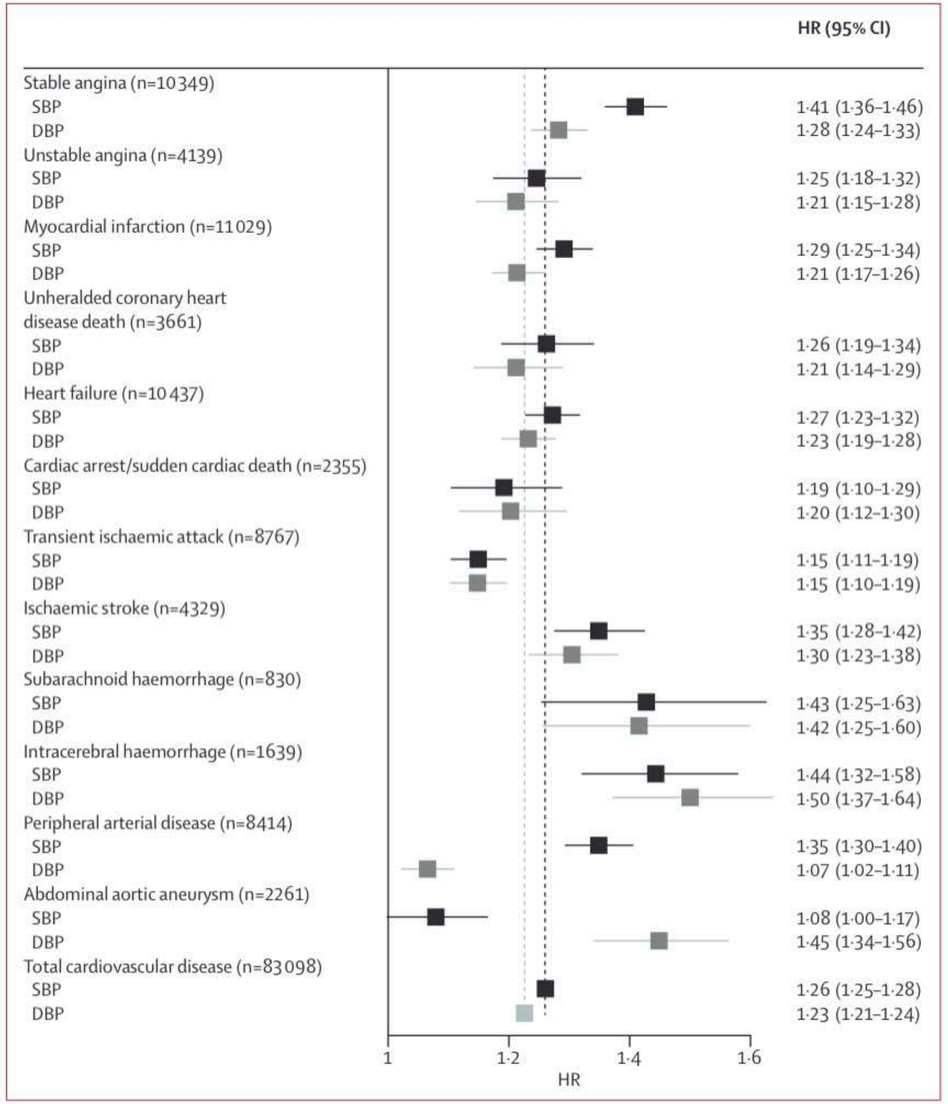


Figure 1: **Forest plot of HRs (95% CIs) per 20/10 mm Hg increase in systolic (black) or diastolic (grey) blood pressure, adjusted for age and sex**

The vertical dashed lines correspond to the associations of SBP (black) or DBP (grey) with total cardiovascular disease. Adjustments include age, quadratic age, and stratification by sex and primary care practice. CIs are Bonferroni corrected (13 endpoints × 2 variables=26 tests). HR=hazard ratio. SBP=systolic blood pressure. DBP=diastolic blood pressure.

Hypertension

Population Risk

- HTN accounts for more CV deaths than any other modifiable risk factor
- Second only to smoking for preventable cause of death for any reason

Hypertension

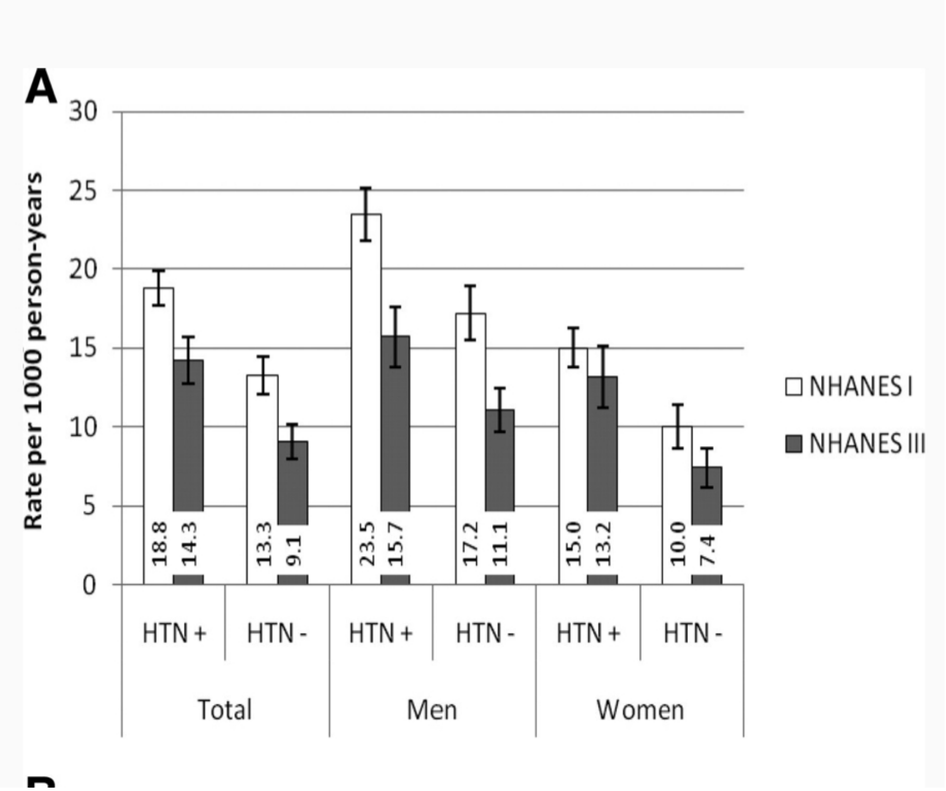
Population Risk

- 23,272 US NHANES participants
- >50% deaths from coronary heart disease and stroke occurred in patients with HTN

Trends in Mortality From All Causes and Cardiovascular Disease Among Hypertensive and Nonhypertensive Adults in the United States

Earl S. FordMD, MPH

Originally published 26 Apr 2011 | https://doi.org/10.1161/CIRCULATIONAHA.110.005645 | Circulation. 2011;123:1737–1744



Hypertension

Population Risk

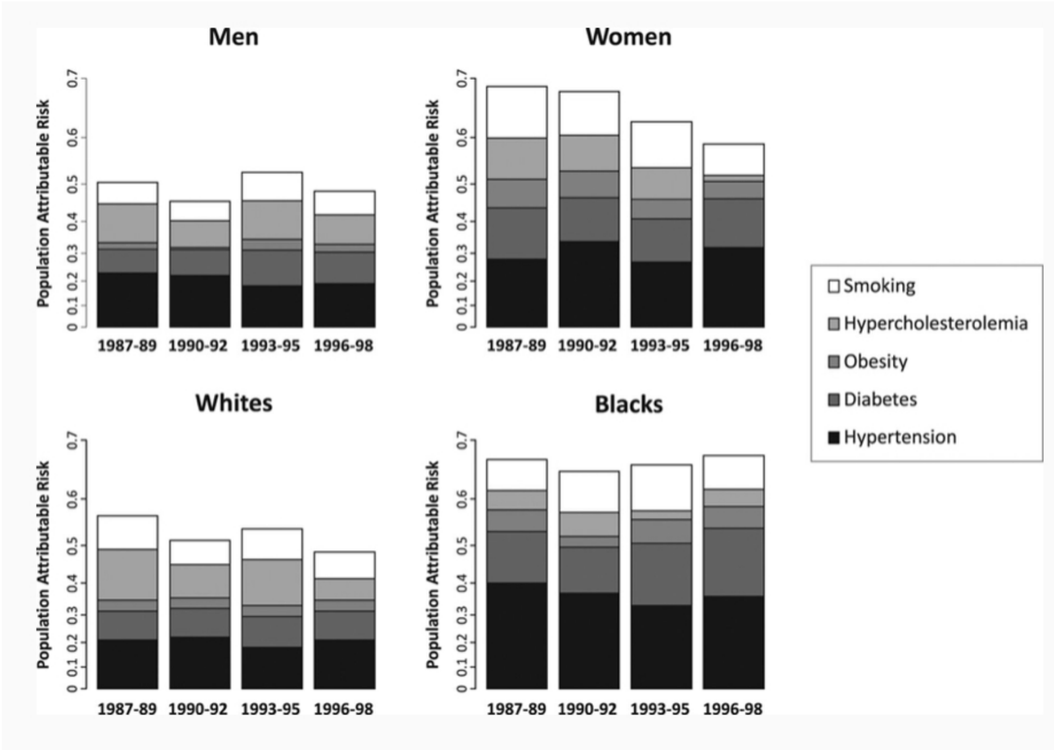
- Population based ARIC study, 25% of CV events (CHD, coronary revascularization, stroke, heart failure) associated with HTN
- HTN was single largest contributor to population CVD risk over time

Temporal Trends in the Population Attributable Risk for Cardiovascular Disease

The Atherosclerosis Risk in Communities Study

Susan Cheng, MD, MPH Brian Claggett, PhD
Andrew W. Correia, PhD Amil M. Shah, MD, MPH
Deepak K. Gupta, MD Hicham Skali, MD, MSc Hanyu Ni, PhD, MPH Wayne D. Rosamond, PhD, MS
Gerardo Heiss, MD, MSc, PhD Aaron R. Folsom, MD, MPH Josef Coresh, and MD, PhD Scott D. SolomonMD

Originally published 11 Aug 2014 |
https://doi.org/10.1161/CIRCULATIONAHA.113.008506 |
Circulation. 2014;130:820–828



Hypertension and CVD Risk

- Among adults with HTN (2009-2012)
  - 15.5% smokers
  - 49.5% obese
  - 63.2% with hyperlipidemia
  - 27.2% Diabetic
  - 15.8% Chronic kidney disease

TABLE 5 CVD Risk Factors Common in Patients With Hypertension

Modifiable Risk Factors*	Relatively Fixed Risk Factors†
■ Current cigarette smoking, secondhand smoking	■ CKD
■ Diabetes mellitus	■ Family history
■ Dyslipidemia/hypercholesterolemia	■ Increased age
■ Overweight/obesity	■ Low socioeconomic/ educational status
■ Physical inactivity/low fitness	■ Male sex
■ Unhealthy diet	■ Obstructive sleep apnea
	■ Psychosocial stress

Whelton *et al.*
2017 High Blood Pressure Clinical Practice Guideline

JACC VOL. 71, NO. 19, 2018
MAY 15, 2018:e127-248

Hypertension

Classification

- Useful to categorize for clinical decision making
- Based on average BPs measured in a healthcare setting
- Stage 1 HTN is normal/ pre-HTN per JNC-8
- Stage 2 HTN corresponds with stage 1&2 in JNC-8

TABLE 6 Categories of BP in Adults*

BP Category	SBP		DBP
Normal	<120 mm Hg	and	<80 mm Hg
Elevated	120-129 mm Hg	and	<80 mm Hg
Hypertension			
Stage 1	130-139 mm Hg	or	80-89 mm Hg
Stage 2	≥140 mm Hg	or	≥90 mm Hg

Whelton *et al.*
2017 High Blood Pressure Clinical Practice Guideline

JACC VOL. 71, NO. 19, 2018
MAY 15, 2018:e127-248

Accurate BP Measurement

In Office

COR	LOE	RECOMMENDATION
I	C-EO	1. For diagnosis and management of high BP, proper methods are recommended for accurate measurement and documentation of BP (Table 8).

TABLE 8 Checklist for Accurate Measurement of BP (S4.1-3,S4.1-4)

Key Steps for Proper BP Measurements	Specific Instructions
Step 1: Properly prepare the patient	1. Have the patient relax, sitting in a chair (feet on floor, back supported) for >5 min. 2. The patient should avoid caffeine, exercise, and smoking for at least 30 min before measurement. 3. Ensure patient has emptied his/her bladder. 4. Neither the patient nor the observer should talk during the rest period or during the measurement. 5. Remove all clothing covering the location of cuff placement. 6. Measurements made while the patient is sitting or lying on an examining table do not fulfill these criteria.
Step 2: Use proper technique for BP measurements	1. Use a BP measurement device that has been validated, and ensure that the device is calibrated periodically.* 2. Support the patient's arm (e.g., resting on a desk). 3. Position the middle of the cuff on the patient's upper arm at the level of the right atrium (the midpoint of the sternum). 4. Use the correct cuff size, such that the bladder encircles 80% of the arm, and note if a larger- or smaller-than-normal cuff size is used (Table 9). 5. Either the stethoscope diaphragm or bell may be used for auscultatory readings (S4.1-5,S4.1-6).
Step 3: Take the proper measurements needed for diagnosis and treatment of elevated BP/hypertension	1. At the first visit, record BP in both arms. Use the arm that gives the higher reading for subsequent readings. 2. Separate repeated measurements by 1-2 min. 3. For auscultatory determinations, use a palpated estimate of radial pulse obliteration pressure to estimate SBP Inflate the cuff 20-30 mm Hg above this level for an auscultatory determination of the BP level. 4. For auscultatory readings, deflate the cuff pressure 2 mm Hg per second, and listen for Korotkoff sounds.
Step 4: Properly document accurate BP readings	1. Record SBP and DBP. If using the auscultatory technique, record SBP and DBP as onset of the first Korotkoff sound and disappearance of all Korotkoff sounds, respectively, using the nearest even number. 2. Note the time of most recent BP medication taken before measurements.
Step 5: Average the readings	Use an average of ≥2 readings obtained on ≥2 occasions to estimate the individual's level of BP.
Step 6: Provide BP readings to patient	Provide patients the SBP/DBP readings both verbally and in writing.

*See Section 4.2 for additional guidance. Adapted with permission from Mancia et al. (S4.1-3) (Oxford University Press), Pickering et al. (S4.1-2) (American Heart Association, Inc.), and Weir et al. (S4.1-4) (American College of Physicians, Inc.).

BP indicates blood pressure; DBP, diastolic blood pressure; and SBP, systolic blood pressure.

TABLE 9 Selection Criteria for BP Cuff Size for Measurement of BP in Adults

Arm Circumference	Usual Cuff Size
22-26 cm	Small adult
27-34 cm	Adult
35-44 cm	Large adult
45-52 cm	Adult thigh

Adapted with permission from Pickering et al. (S4.1-2) (American Heart Association, Inc.).

BP indicates blood pressure.

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
VOL. 71, NO. 19, 2018

CLINICAL PRACTICE GUIDELINE

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

A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines

COR	LOE	RECOMMENDATION
I	B-NR	1. Screening for and management of other modifiable CVD risk factors are recommended in adults with hypertension (S2.4-1,S2.4-2).

Hypertension

Basic Testing

- Facilitate CVD risk factor profiling
- Establish baselines for treatment selection
- Screen for secondary causes
- Identify target organ damage
  - Ex: LVH is a long term consequence of HTN and is an independent predictor of CV events.

TABLE 17 Basic and Optional Laboratory Tests for Primary Hypertension

Basic testing	Fasting blood glucose*
	Complete blood count
	Lipid profile
	Serum creatinine with eGFR*
	Serum sodium, potassium, calcium*
	Thyroid-stimulating hormone
	Urinalysis
	Electrocardiogram
Optional testing	Echocardiogram
	Uric acid
	Urinary albumin to creatinine ratio

*May be included in a comprehensive metabolic panel.
eGFR indicates estimated glomerular filtration rate.

Whelton *et al.*
2017 High Blood Pressure Clinical Practice Guideline

JACC VOL. 71, NO. 19, 2018
MAY 15, 2018:e127-248

Out-of-office and Self-monitoring

- Ambulatory blood pressure (ABP) monitoring is more reliable
- Home blood pressure (HBP) monitoring is more practical

COR	LOE	RECOMMENDATION
I	A^{SR}	1. Out-of-office BP measurements are recommended to confirm the diagnosis of hypertension (Table 11) and for titration of BP-lowering medication, in conjunction with telehealth counseling or clinical interventions (S4.2-1–S4.2-4).

SR indicates systematic review.

TABLE 10 Procedures for Use of HBPM (S4.2-8–S4.2-10)

Patient training should occur under medical supervision, including:

- Information about hypertension
- Selection of equipment
- Acknowledgment that individual BP readings may vary substantially
- Interpretation of results

Devices:

- Verify use of automated validated devices. Use of auscultatory devices (mercury, aneroid, or other) is not generally useful for HBPM because patients rarely master the technique required for measurement of BP with auscultatory devices.
- Monitors with provision for storage of readings in memory are preferred.
- Verify use of appropriate cuff size to fit the arm (Table 9).
- Verify that left/right inter-arm differences are insignificant. If differences are significant, instruct patient to measure BPs in the arm with higher readings.

Instructions on HBPM procedures:

- **Remain still:**
  - Avoid smoking, caffeinated beverages, or exercise within 30 min before BP measurements.
  - Ensure ≥5 min of quiet rest before BP measurements.
- **Sit correctly:**
  - Sit with back straight and supported (on a straight-backed dining chair, for example, rather than a sofa).
  - Sit with feet flat on the floor and legs uncrossed.
  - Keep arm supported on a flat surface (such as a table), with the upper arm at heart level.
- Bottom of the cuff should be placed directly above the antecubital fossa (bend of the elbow).
- **Take multiple readings:**
  - Take at least 2 readings 1 min apart in morning before taking medications and in evening before supper. Optimally, measure and record BP daily. Ideally, obtain weekly BP readings beginning 2 weeks after a change in the treatment regimen and during the week before a clinic visit.
- **Record all readings accurately:**
  - Monitors with built-in memory should be brought to all clinic appointments.
  - BP should be based on an average of readings on ≥2 occasions for clinical decision making.

The information above may be reinforced with videos available online.

Whelton *et al.*
2017 High Blood Pressure Clinical Practice Guideline

JACC VOL. 71, NO. 19, 2018
MAY 15, 2018:e127-248

BP Patterns

TABLE 12 **BP Patterns Based on Office and Out-of-Office Measurements**

	Office/Clinic/ Healthcare Setting	Home/Nonhealthcare/ ABPM Setting
Normotensive	No hypertension	No hypertension
Sustained hypertension	Hypertension	Hypertension
Masked hypertension	No hypertension	Hypertension
White coat hypertension	Hypertension	No hypertension

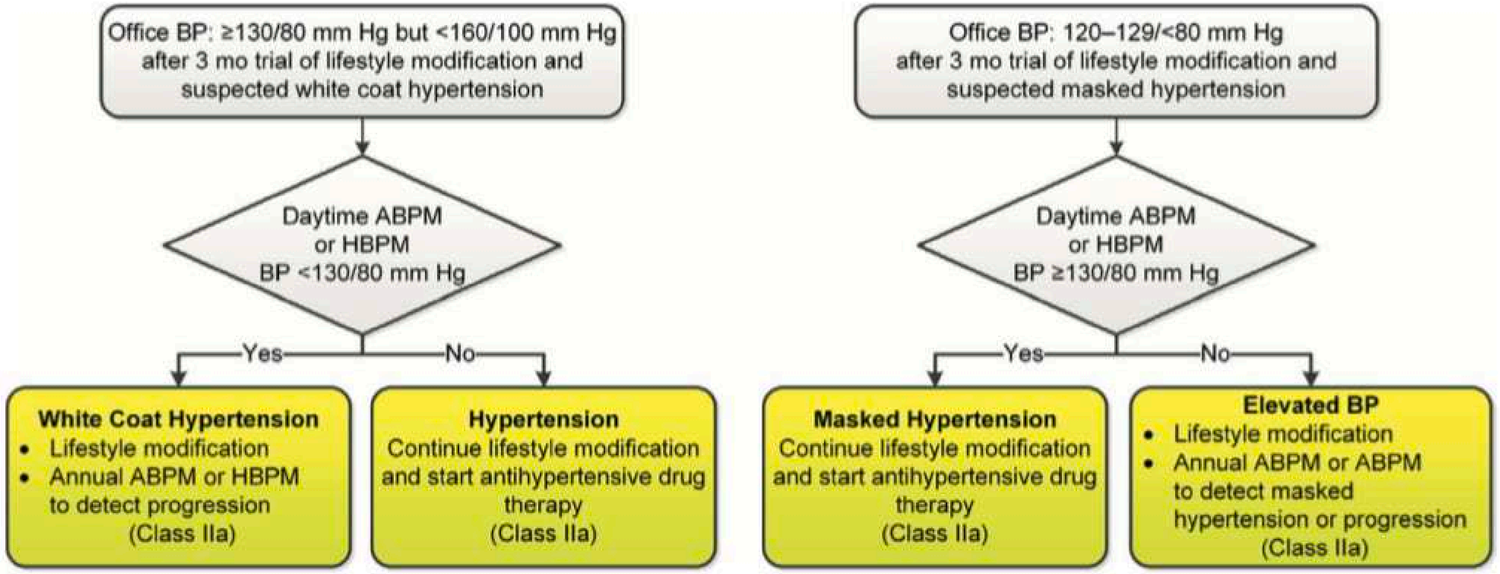
Whelton *et al.*
2017 High Blood Pressure Clinical Practice Guideline

JACC VOL. 71, NO. 19, 2018
MAY 15, 2018:e127–248

White Coat Hypertension/Masked Hypertension

Not on medical therapy

FIGURE 1 Detection of White Coat Hypertension or Masked Hypertension in Patients Not on Drug Therapy



Colors correspond to Class of Recommendation in Table 1. ABPM indicates ambulatory blood pressure monitoring; BP, blood pressure; and HBPM, home blood pressure monitoring.

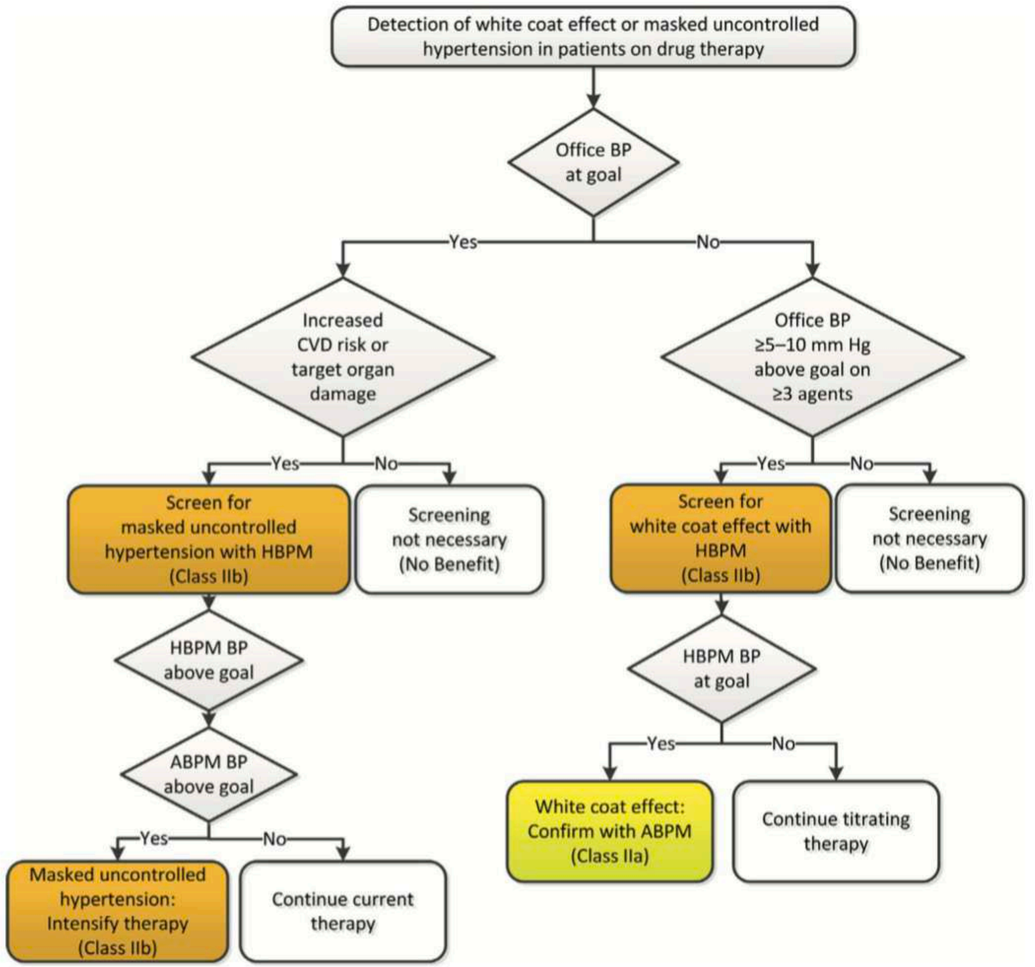
Whelton *et al.*
2017 High Blood Pressure Clinical Practice Guideline

JACC VOL. 71, NO. 19, 2018
MAY 15, 2018:e127-248

White coat hypertension/ Masked Hypertension

On Medical Therapy

FIGURE 2 Detection of White Coat Effect or Masked Uncontrolled Hypertension in Patients on Drug Therapy



Colors correspond to Class of Recommendation in Table 1. See Section 8 for treatment options. ABPM indicates ambulatory blood pressure monitoring; BP, blood pressure; CVD, cardiovascular disease; and HBPM, home blood pressure monitoring.

Whelton *et al.*
2017 High Blood Pressure Clinical Practice Guideline

JACC VOL. 71, NO. 19, 2018
MAY 15, 2018:e127-248

White Coat HTN

- Prevalence ranges from 15-35%
- ABP and HBP measurements better predictors of CVD risk than office measurements.
  - ABP preferred, better predictor. Cumbersome and inconvenient for the pt (BPs every 15-30 minutes)
  - HBP more practical
- Vascular risk of pts with uncontrolled HTN in the office and a white coat effect is similar to those with controlled HTN

Whelton *et al.*
2017 High Blood Pressure Clinical Practice Guideline

JACC VOL. 71, NO. 19, 2018
MAY 15, 2018:e127–248

HTN

Causes

- Genetic:
  - Multiple single-nucleotide polymorphisms influencing BP control
  - Rare, accounting for approximately 3.5% of total BP variability
- Environmental: diet, physical inactivity, alcohol consumption
  - Excess sodium, insufficient calcium, potassium, magnesium, vegetable protein, fiber, fish fats
  - Excess Alcohol intake (10% of HTN burden in US)
  - Obesity
  - Lack of regular physical exercise (150min/week)

Whelton *et al.*
2017 High Blood Pressure Clinical Practice Guideline

JACC VOL. 71, NO. 19, 2018
MAY 15, 2018:e127-248

Secondary HTN

Causes

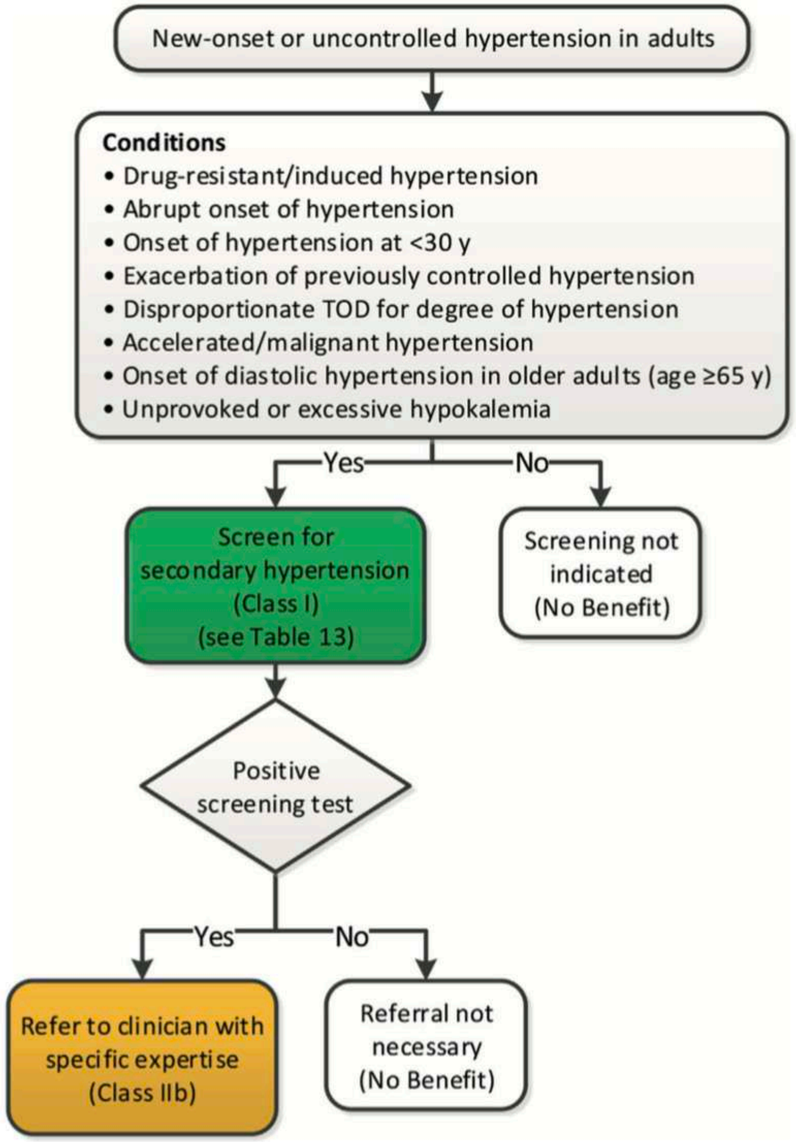
TABLE 13 Causes of Secondary Hypertension With Clinical Indications and Diagnostic Screening Tests

	Prevalence	Clinical Indications	Physical Examination	Screening Tests	Additional/ Confirmatory Tests
Common causes					
Renal parenchymal disease (S5.4-1, S5.4-3)	1%-2%	Urinary tract infections; obstruction, hematuria; urinary frequency and nocturia; analgesic abuse; family history of polycystic kidney disease; elevated serum creatinine; abnormal urinalysis	Abdominal mass (polycystic kidney disease); skin pallor	Renal ultrasound	Tests to evaluate cause of renal disease
Renovascular disease (S5.4-4)	5%-34%*	Resistant hypertension; hypertension of abrupt onset or worsening or increasingly difficult to control; flash pulmonary edema (atherosclerotic); early-onset hypertension, especially in women (fibromuscular hyperplasia)	Abdominal systolic-diastolic bruit; bruits over other arteries (carotid – atherosclerotic or fibromuscular dysplasia), femoral	Renal Duplex Doppler ultrasound; MRA; abdominal CT	Bilateral selective renal intra-arterial angiography
Primary aldosteronism (S5.4-5,S5.4-6)	8%-20%†	Resistant hypertension; hypertension with hypokalemia (spontaneous or diuretic induced); hypertension and muscle cramps or weakness; hypertension and incidentally discovered adrenal mass; hypertension and obstructive sleep apnea; hypertension and family history of early-onset hypertension or stroke	Arrhythmias (with hypokalemia); especially atrial fibrillation	Plasma aldosterone/ renin ratio under standardized conditions (correction of hypokalemia and withdrawal of aldosterone antagonists for 4-6 wk)	Oral sodium loading test (with 24-h urine aldosterone) or IV saline infusion test with plasma aldosterone at 4 h of infusion Adrenal CT scan, adrenal vein sampling.
Obstructive sleep apnea (S5.4-7)‡	25%-50%	Resistant hypertension; snoring; fitful sleep; breathing pauses during sleep; daytime sleepiness	Obesity, Mallampati class III-IV; loss of normal nocturnal BP fall	Berlin Questionnaire (S5.4-8); Epworth Sleepiness Score (S5.4-9); overnight oximetry	Polysomnography

Whelton *et al.*
2017 High Blood Pressure Clinical Practice Guideline

JACC VOL. 71, NO. 19, 2018
MAY 15, 2018:e127-248

FIGURE 3 Screening for Secondary Hypertension



Colors correspond to Class of Recommendation in Table 1. TOD indicates target organ damage (e.g., cerebrovascular disease, hypertensive retinopathy, left ventricular hypertrophy, left ventricular dysfunction, heart failure, coronary artery disease, chronic kidney disease, albuminuria, peripheral artery disease).

Medication-induced HTN

TABLE 14 Frequently Used Medications and Other Substances That May Cause Elevated BP*

Agent	Possible Management Strategy
Alcohol	■ Limit alcohol to ≤1 drink daily for women and ≤2 drinks for men (S5.4.1-7)
Amphetamines (e.g., amphetamine, methylphenidate dexmethylphenidate, dextroamphetamine)	■ Discontinue or decrease dose (S5.4.1-8) ■ Consider behavioral therapies for ADHD (S5.4.1-9)
Antidepressants (e.g., MAOIs, SNRIs, TCAs)	■ Consider alternative agents (e.g., SSRIs) depending on indication ■ Avoid tyramine-containing foods with MAOIs
Atypical antipsychotics (e.g., clozapine, olanzapine)	■ Discontinue or limit use when possible ■ Consider behavior therapy where appropriate ■ Recommend lifestyle modification (see Section 6.2) ■ Consider alternative agents associated with lower risk of weight gain, diabetes mellitus, and dyslipidemia (e.g., aripiprazole, ziprasidone) (S5.4.1-10,S5.4.1-11)
Caffeine	■ Generally limit caffeine intake to <300 mg/d ■ Avoid use in patients with uncontrolled hypertension ■ Coffee use in patients with hypertension is associated with acute increases in BP; long-term use is not associated with increased BP or CVD (S5.4.1-12)
Decongestants (e.g., phenylephrine, pseudoephedrine)	■ Use for shortest duration possible, and avoid in severe or uncontrolled hypertension ■ Consider alternative therapies (e.g., nasal saline, intranasal corticosteroids, antihistamines) as appropriate
Herbal supplements (e.g., Ma Huang [ephedra], St. John's wort [with MAO inhibitors, yohimbine])	■ Avoid use
Immunosuppressants (e.g., cyclosporine)	■ Consider converting to tacrolimus, which may be associated with fewer effects on BP (S5.4.1-13–S5.4.1-15)
Oral contraceptives	■ Use low-dose (e.g., 20-30 mcg ethinyl estradiol) agents (S5.4.1-16) or a progestin-only form of contraception, or consider alternative forms of birth control where appropriate (e.g., barrier, abstinence, IUD) ■ Avoid use in women with uncontrolled hypertension (S5.4.1-16)
NSAIDs	■ Avoid systemic NSAIDs when possible ■ Consider alternative analgesics (e.g., acetaminophen, tramadol, topical NSAIDs), depending on indication and risk
Recreational drugs (e.g., "bath salts" [MDPV], cocaine, methamphetamine, etc.)	■ Discontinue or avoid use
Systemic corticosteroids (e.g., dexamethasone, fludrocortisone, methylprednisolone, prednisone, prednisolone)	■ Avoid or limit use when possible ■ Consider alternative modes of administration (e.g., inhaled, topical) when feasible
Angiogenesis inhibitor (e.g., bevacizumab) and tyrosine kinase inhibitors (e.g., sunitinib, sorafenib)	■ Initiate or intensify antihypertensive therapy

Whelton *et al.*
2017 High Blood Pressure Clinical Practice Guideline

JACC VOL. 71, NO. 19, 2018
MAY 15, 2018:e127–248

Secondary HTN

ACC/AHA Screening Recommendations

Recommendations for Primary Aldosteronism

COR	LOE	RECOMMENDATIONS
I	C-EO	1. In adults with hypertension, screening for primary aldosteronism is recommended in the presence of any of the following concurrent conditions: resistant hypertension, hypokalemia (spontaneous or substantial, if diuretic induced), incidentally discovered adrenal mass, family history of early-onset hypertension, or stroke at a young age (<40 years).
I	C-LD	2. Use of the plasma aldosterone: renin activity ratio is recommended when adults are screened for primary aldosteronism (S5.4.2-1).
I	C-EO	3. In adults with hypertension and a positive screening test for primary aldosteronism, referral to a hypertension specialist or endocrinologist is recommended for further evaluation and treatment.

Recommendations for Renal Artery Stenosis
References that support recommendations are summarized in Online Data Supplements 7 and 24.

COR	LOE	RECOMMENDATIONS
I	A	1. Medical therapy is recommended for adults with atherosclerotic renal artery stenosis (S5.4.3-1,S5.4.3-2).
IIb	C-EO	2. In adults with renal artery stenosis for whom medical management has failed (refractory hypertension, worsening renal function, and/or intractable HF) and those with nonatherosclerotic disease, including fibromuscular dysplasia, it may be reasonable to refer the patient for consideration of revascularization (percutaneous renal artery angioplasty and/or stent placement).

Recommendation for Obstructive Sleep Apnea
References that support the recommendation are summarized in Online Data Supplement 8.

COR	LOE	RECOMMENDATION
IIb	B-R	1. In adults with hypertension and obstructive sleep apnea, the effectiveness of continuous positive airway pressure (CPAP) to reduce BP is not well established (S5.4.4-1–S5.4.4-5).

Whelton *et al.*
2017 High Blood Pressure Clinical Practice Guideline

JACC VOL. 71, NO. 19, 2018
MAY 15, 2018:e127-248

Non-pharmacological Therapies

Evidence-based

- Weight loss
- DASH Diet
  - Sodium restriction
  - Increased dietary potassium and magnesium
  - High in fruits, vegetables, low fat dairy products
    - 3510-4700mg K+ daily recommended (4-5 servings of fruits and vegetables)
- Reduced Alcohol consumption

Whelton *et al.*
2017 High Blood Pressure Clinical Practice Guideline

JACC VOL. 71, NO. 19, 2018
MAY 15, 2018:e127-248

Non-pharmacological Therapies

Less Supported

- Probiotics
- Increased intake of protein, flax seed, fiber
- Low carb diets
- Garlic
- Dark chocolate
- Yoga/meditation/biofeedback

Whelton *et al.*
2017 High Blood Pressure Clinical Practice Guideline

JACC VOL. 71, NO. 19, 2018
MAY 15, 2018:e127-248

Non-pharmacological Therapies

Impact

TABLE 15 Best Proven Nonpharmacological Interventions for Prevention and Treatment of Hypertension*

	Nonpharmacological Intervention	Dose	Approximate Impact on SBP		
			Hypertension	Normotension	Reference
Weight loss	Weight/body fat	Best goal is ideal body weight, but aim for at least a 1-kg reduction in body weight for most adults who are overweight. Expect about 1 mm Hg for every 1-kg reduction in body weight.	−5 mm Hg	−2/3 mm Hg	(S6.2-1)
Healthy diet	DASH dietary pattern	Consume a diet rich in fruits, vegetables, whole grains, and low-fat dairy products, with reduced content of saturated and total fat.	−11 mm Hg	−3 mm Hg	(S6.2-6,S6.2-7)
Reduced intake of dietary sodium	Dietary sodium	Optimal goal is <1500 mg/d, but aim for at least a 1000-mg/d reduction in most adults.	−5/6 mm Hg	−2/3 mm Hg	(S6.2-9,S6.2-10)
Enhanced intake of dietary potassium	Dietary potassium	Aim for 3500-5000 mg/d, preferably by consumption of a diet rich in potassium.	−4/5 mm Hg	−2 mm Hg	(S6.2-13)
Physical activity	Aerobic	■ 90-150 min/wk ■ 65%-75% heart rate reserve	−5/8 mm Hg	−2/4 mm Hg	(S6.2-18,S6.2-22)
	Dynamic resistance	■ 90-150 min/wk ■ 50%-80% 1 rep maximum ■ 6 exercises, 3 sets/exercise, 10 repetitions/set	−4 mm Hg	−2 mm Hg	(S6.2-18)
	Isometric resistance	■ 4 × 2 min (hand grip), 1 min rest between exercises, 30%-40% maximum voluntary contraction, 3 sessions/wk ■ 8-10 wk	−5 mm Hg	−4 mm Hg	(S6.2-19,S6.2-31)
Moderation in alcohol intake	Alcohol consumption	In individuals who drink alcohol, reduce alcohol† to: ■ Men: ≤2 drinks daily ■ Women: ≤1 drink daily	−4 mm Hg	−3 mm Hg	(S6.2-22–S6.2-24)

Resources: Your Guide to Lowering Your Blood Pressure With DASH—How Do I Make the DASH? Available at: https://www.nhlbi.nih.gov/health/resources/heart/hbp-dash-how-to. Accessed September 15, 2017. (S6.2-72) Top 10 Dash Diet Tips. Available at: http://dashdiet.org/dash_diet_tips.asp. Accessed September 15, 2017. (S6.2-73) *Type, dose, and expected impact on BP in adults with a normal BP and with hypertension. †In the United States, one "standard" drink contains roughly 14 g of pure alcohol, which is typically found in 12 oz of regular beer (usually about 5% alcohol), 5 oz of wine (usually about 12% alcohol), and 1.5 oz of distilled spirits (usually about 40% alcohol) (S6.2-29).

DASH indicates Dietary Approaches to Stop Hypertension; and SBP, systolic blood pressure.

Whelton *et al.*
2017 High Blood Pressure Clinical Practice Guideline

JACC VOL. 71, NO. 19, 2018
MAY 15, 2018:e127-248

Non-Pharmacological Therapies

Guidelines

Recommendations for Nonpharmacological Interventions
References that support recommendations are summarized in Online Data Supplements 9-21.

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 (S6.2-1–S6.2-4).
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 (S6.2-5–S6.2-7).
I	A	3. Sodium reduction is recommended for adults with elevated BP or hypertension (S6.2-8–S6.2-12).
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 (S6.2-13–S6.2-17).
I	A	5. Increased physical activity with a structured exercise program is recommended for adults with elevated BP or hypertension (S6.2-3,S6.2-4,S6.2-12,S6.2-18–S6.2-22).
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 (S6.2-23–S6.2-28).

*In the United States, 1 "standard" drink contains roughly 14 g of pure alcohol, which is typically found in 12 oz of regular beer (usually about 5% alcohol), 5 oz of wine (usually about 12% alcohol), and 1.5 oz of distilled spirits (usually about 40% alcohol) (S6.2-29).

Whelton *et al.*
2017 High Blood Pressure Clinical Practice Guideline

JACC VOL. 71, NO. 19, 2018
MAY 15, 2018:e127-248

Hypertension

Medical Therapy

- Clinical cardiovascular disease (CVD) = coronary heart disease (CHD), congestive heat failure (CHF) and stroke
- Clinicians should focus on overall health with emphasis on reduction of cardiovascular events
- For any specific difference in BP, the relative risk of CVD events is constant across groups that differ in absolute risk of atherosclerotic CVD events.
- Some evidence of lesser relative risk but greater absolute risk in older vs younger patients.
- **Potentially more preventable CVD events attributable to elevated BP in higher vs lower risk patients, and en older vs younger patients.**
- **Use of the combination of BP level and absolute CVD risk rather than BP level alone is more cost efficient and effective at reducing risk of CVD events.**

ACC/AHA Guidelines

Medical Therapy

Recommendations for BP Treatment Threshold and Use of Risk Estimation* to Guide Drug Treatment of Hypertension
References that support recommendations are summarized in Online Data Supplement 23.

COR	LOE	RECOMMENDATIONS
I	SBP: A DBP: C-EO	1. 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 (S8.1.2-1–S8.1.2-9).
I	C-LD	2. 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 (S8.1.2-3,S8.1.2-10–S8.1.2-13).

*ACC/AHA Pooled Cohort Equations (http://tools.acc.org/ASCVD-Risk-Estimator/) (S8.1.2-13a) to estimate 10-year risk of atherosclerotic CVD. ASCVD was defined as a first CHD death, non-fatal MI or fatal or non-fatal stroke.

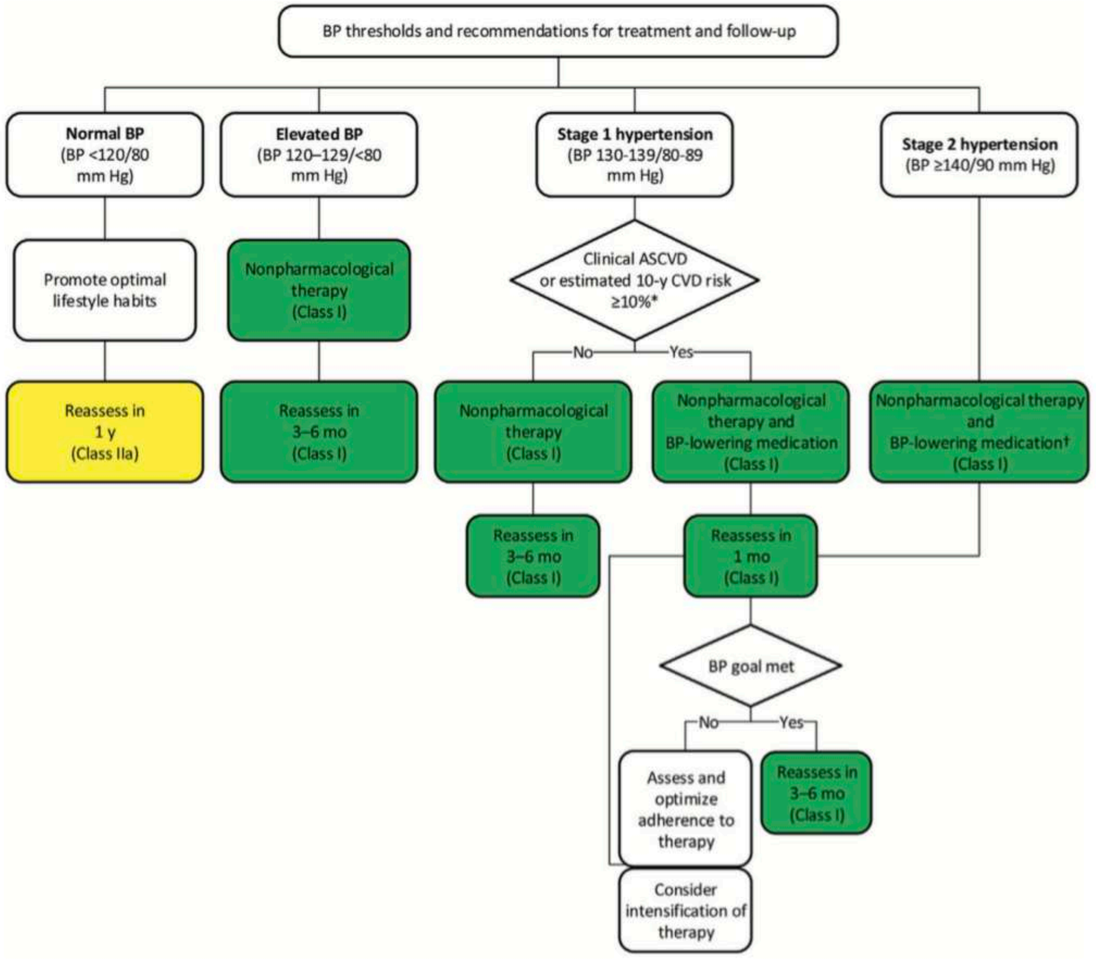
COR	LOE	RECOMMENDATIONS
I	SBP: B-R[SR] DBP: C-EO	1. For adults with confirmed hypertension and known CVD or 10-year ASCVD event risk of 10% or higher (see Section 8.1.2), a BP target of less than 130/80 mm Hg is recommended (S8.1.5-1–S8.1.5-5).
IIb	SBP: B-NR DBP: C-EO	2. For adults with confirmed hypertension, without additional markers of increased CVD risk, a BP target of less than 130/80 mm Hg may be reasonable (S8.1.5-6–S8.1.5-9).

SR indicates systematic review.

Whelton *et al.*
2017 High Blood Pressure Clinical Practice Guideline

JACC VOL. 71, NO. 19, 2018
MAY 15, 2018:e127-248

FIGURE 4 Blood Pressure (BP) Thresholds and Recommendations for Treatment and Follow-Up



Colors correspond to Class of Recommendation in **Table 1**. *Using the ACC/AHA Pooled Cohort Equations (S8.1.2-56,S8.1.2-57). Note that patients with DM or CKD are automatically placed in the high-risk category. For initiation of RAS inhibitor or diuretic therapy, assess blood tests for electrolytes and renal function 2 to 4 weeks after initiating therapy. †Consider initiation of pharmacological therapy for stage 2 hypertension with 2 antihypertensive agents of different classes. Patients with stage 2 hypertension and BP ≥160/100 mm Hg should be promptly treated, carefully monitored, and subject to upward medication dose adjustment as necessary to control BP. Reassessment includes BP measurement, detection of orthostatic hypotension in selected patients (e.g., older or with postural symptoms), identification of white coat hypertension or a white coat effect, documentation of adherence, monitoring of the response to therapy, reinforcement of the importance of adherence, reinforcement of the importance of treatment, and assistance with treatment to achieve BP target. ACC indicates American College of Cardiology; AHA, American Heart Association; ASCVD, atherosclerotic cardiovascular disease; BP, blood pressure; CKD, chronic kidney disease; DM, diabetes mellitus; and RAS, renin-angiotensin system.

HTN

Follow-up

Recommendations for Follow-Up After Initial BP Evaluation
References that support recommendations are summarized in Online Data Supplement 24.

COR	LOE	RECOMMENDATIONS
I	B-R	1. Adults with an elevated BP or stage 1 hypertension who have an estimated 10-year ASCVD risk less than 10% should be managed with nonpharmacological therapy and have a repeat BP evaluation within 3 to 6 months (S8.1.3-1,S8.1.3-2).
I	B-R	2. Adults with stage 1 hypertension who have an estimated 10-year ASCVD risk of 10% or higher should be managed initially with a combination of nonpharmacological and antihypertensive drug therapy and have a repeat BP evaluation in 1 month (S8.1.3-1,S8.1.3-2).
I	B-R	3. Adults with stage 2 hypertension should be evaluated by or referred to a primary care provider within 1 month of the initial diagnosis, have a combination of nonpharmacological and antihypertensive drug therapy (with 2 agents of different classes) initiated, and have a repeat BP evaluation in 1 month (S8.1.3-1,S8.1.3-2).
I	B-R	4. For adults with a very high average BP (e.g., SBP ≥180 mm Hg or DBP ≥110 mm Hg), evaluation followed by prompt antihypertensive drug treatment is recommended (S8.1.3-1,S8.1.3-2).
IIa	C-EO	5. For adults with a normal BP, repeat evaluation every year is reasonable.

Whelton *et al.*
2017 High Blood Pressure Clinical Practice Guideline

JACC VOL. 71, NO. 19, 2018
MAY 15, 2018:e127-248

Medications

First Line

Class	Drug	Usual Dose, Range (mg/d)*	Daily Frequency	Comments
Primary agents				
Thiazide or thiazide-type diuretics	Chlorthalidone	12.5–25	1	■ Chlorthalidone is preferred on the basis of prolonged half-life and proven trial reduction of CVD. ■ Monitor for hyponatremia and hypokalemia, uric acid and calcium levels. ■ Use with caution in patients with history of acute gout unless patient is on uric acid–lowering therapy.
	Hydrochlorothiazide	25–50	1	
	Indapamide	1.25–2.5	1	
	Metolazone	2.5–5	1	
ACE inhibitors	Benazepril	10–40	1 or 2	■ Do not use in combination with ARBs or direct renin inhibitor. ■ There is an increased risk of hyperkalemia, especially in patients with CKD or in those on K^+ supplements or K^+-sparing drugs. ■ There is a risk of acute renal failure in patients with severe bilateral renal artery stenosis. ■ Do not use if patient has history of angioedema with ACE inhibitors. ■ Avoid in pregnancy.
	Captopril	12.5–150	2 or 3	
	Enalapril	5–40	1 or 2	
	Fosinopril	10–40	1	
	Lisinopril	10–40	1	
	Moexipril	7.5–30	1 or 2	
	Perindopril	4–16	1	
	Quinapril	10–80	1 or 2	
	Ramipril	2.5–20	1 or 2	
	Trandolapril	1–4	1	
ARBs	Azilsartan	40–80	1	■ Do not use in combination with ACE inhibitors or direct renin inhibitor. ■ There is an increased risk of hyperkalemia in CKD or in those on K^+ supplements or K^+-sparing drugs. ■ There is a risk of acute renal failure in patients with severe bilateral renal artery stenosis. ■ Do not use if patient has history of angioedema with ARBs. Patients with a history of angioedema with an ACE inhibitor can receive an ARB beginning 6 weeks after ACE inhibitor is discontinued. ■ Avoid in pregnancy.
	Candesartan	8–32	1	
	Eprosartan	600–800	1 or 2	
	Irbesartan	150–300	1	
	Losartan	50–100	1 or 2	
	Olmesartan	20–40	1	
	Telmisartan	20–80	1	
	Valsartan	80–320	1	
CCB—dihydropyridines	Amlodipine	2.5–10	1	■ Avoid use in patients with HF*r*EF; amlodipine or felodipine may be used if required. ■ They are associated with dose-related pedal edema, which is more common in women than men.
	Felodipine	2.5–10	1	
	Isradipine	5–10	2	
	Nicardipine SR	60–120	2	
	Nifedipine LA	30–90	1	
	Nisoldipine	17–34	1	
CCB—nondihydropyridines	Diltiazem ER	120–360	1	■ Avoid routine use with beta blockers because of increased risk of bradycardia and heart block. ■ Do not use in patients with HF*r*EF. ■ There are drug interactions with diltiazem and verapamil (*CYP3A4* major substrate and moderate inhibitor).
	Verapamil IR	120–360	3	
	Verapamil SR	120–360	1 or 2	
	Verapamil-delayed onset ER	100–300	1 (in the evening)	

Whelton *et al.*
2017 High Blood Pressure Clinical Practice Guideline

JACC VOL. 71, NO. 19, 2018
MAY 15, 2018:e127–248

Medications

Secondary agents

Diuretics—loop	Bumetanide	0.5-2	2	■ These are preferred diuretics in patients with symptomatic HF. They are preferred over thiazides in patients with moderate-to-severe CKD (e.g., GFR <30 mL/min).
	Furosemide	20-80	2	
	Torsemide	5-10	1	
Diuretics—potassium sparing	Amiloride	5-10	1 or 2	■ These are monotherapy agents and minimally effective antihypertensive agents. ■ Combination therapy of potassium-sparing diuretic with a thiazide can be considered in patients with hypokalemia on thiazide monotherapy. ■ Avoid in patients with significant CKD (e.g., GFR <45 mL/min).
	Triamterene	50-100	1 or 2	
Diuretics—aldosterone antagonists	Eplerenone	50-100	1 or 2	■ These are preferred agents in primary aldosteronism and resistant hypertension. ■ Spironolactone is associated with greater risk of gynecomastia and impotence as compared with eplerenone. ■ This is common add-on therapy in resistant hypertension. ■ Avoid use with K^+ supplements, other K^+-sparing diuretics, or significant renal dysfunction. ■ Eplerenone often requires twice-daily dosing for adequate BP lowering.
	Spironolactone	25-100	1	
Beta blockers—cardioselective	Atenolol	25-100	2	■ Beta blockers are not recommended as first-line agents unless the patient has IHD or HF. ■ These are preferred in patients with bronchospastic airway disease requiring a beta blocker. ■ Bisoprolol and metoprolol succinate are preferred in patients with HFrEF. ■ Avoid abrupt cessation.
	Betaxolol	5-20	1	
	Bisoprolol	2.5-10	1	
	Metoprolol tartrate	100-200	2	
	Metoprolol succinate	50-200	1	
Beta blockers—cardioselective and vasodilatory	Nebivolol	5-40	1	■ Nebivolol induces nitric oxide-induced vasodilation. ■ Avoid abrupt cessation.
Beta blockers—noncardioselective	Nadolol	40-120	1	■ Avoid in patients with reactive airways disease. ■ Avoid abrupt cessation.
	Propranolol IR	80-160	2	
	Propranolol LA	80-160	1	
Beta blockers—intrinsic sympathomimetic activity	Acebutolol	200-800	2	■ Generally avoid, especially in patients with IHD or HF. ■ Avoid abrupt cessation.
	Penbutolol	10-40	1	
	Pindolol	10-60	2	
Beta blockers—combined alpha- and beta-receptor	Carvedilol	12.5-50	2	■ Carvedilol is preferred in patients with HFrEF. ■ Avoid abrupt cessation.
	Carvedilol phosphate	20-80	1	
	Labetalol	200-800	2	
Direct renin inhibitor	Aliskiren	150-300	1	■ Do not use in combination with ACE inhibitors or ARBs. ■ Aliskiren is very long acting. ■ There is an increased risk of hyperkalemia in CKD or in those on K^+ supplements or K^+-sparing drugs. ■ Aliskiren may cause acute renal failure in patients with severe bilateral renal artery stenosis. ■ Avoid in pregnancy.
Alpha-1 blockers	Doxazosin	1-16	1	■ These are associated with orthostatic hypotension, especially in older adults. ■ They may be considered as second-line agent in patients with concomitant BPH.
	Prazosin	2-20	2 or 3	
	Terazosin	1-20	1 or 2	
Central alpha$_2$-agonist and other centrally acting drugs	Clonidine oral	0.1-0.8	2	■ These are generally reserved as last-line because of significant CNS adverse effects, especially in older adults. ■ Avoid abrupt discontinuation of clonidine, which may induce hypertensive crisis; clonidine must be tapered to avoid rebound hypertension.
	Clonidine patch	0.1-0.3	1 weekly	
	Methyldopa	250-1000	2	
	Guanfacine	0.5-2	1	
Direct vasodilators	Hydralazine	100-200	2 or 3	■ These are associated with sodium and water retention and reflex tachycardia; use with a diuretic and beta blocker. ■ Hydralazine is associated with drug-induced lupus-like syndrome at higher doses. ■ Minoxidil is associated with hirsutism and requires a loop diuretic. Minoxidil can induce pericardial effusion.
	Minoxidil	5-100	1 -3	

Whelton *et al.*
2017 High Blood Pressure Clinical Practice Guideline

JACC VOL. 71, NO. 19, 2018
MAY 15, 2018:e127-248

Hypertension

Stable Ischemic Heart Disease (SIHD)

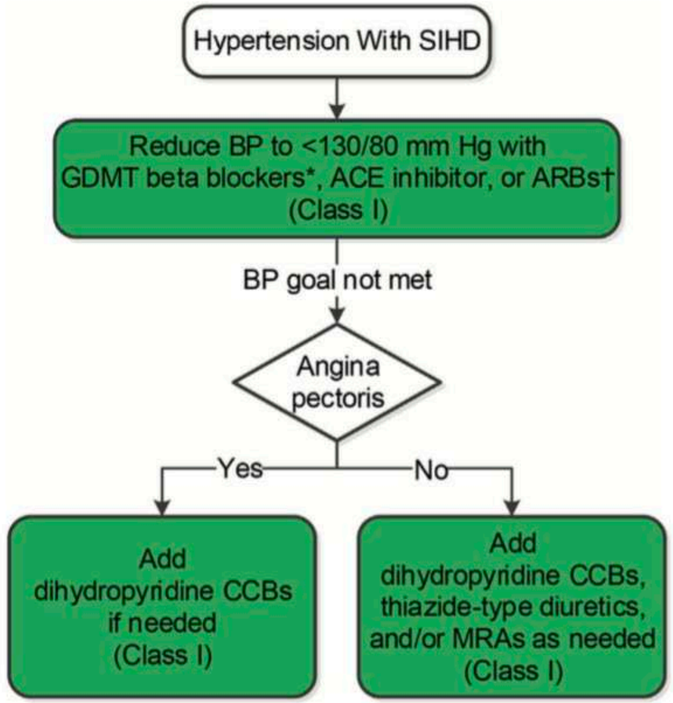
- In patients with increased cardiovascular risk, BP reduction to <130/80 translates to 25% CVD event risk reduction, 27% decrease in all-cause mortality.

- RCT evidence that beta blocker use after MI shows 23% reduction in all-cause mortality

Whelton *et al.*
2017 High Blood Pressure Clinical Practice Guideline

JACC VOL. 71, NO. 19, 2018
MAY 15, 2018:e127–248

FIGURE 5 Management of Hypertension in Patients With SIHD



Colors correspond to Class of Recommendation in Table 1. *GDMT beta blockers for BP control or relief of angina include carvedilol, metoprolol tartrate, metoprolol succinate, nadolol, bisoprolol, propranolol, and timolol. Avoid beta blockers with intrinsic sympathomimetic activity. The beta blocker atenolol should not be used because it is less effective than placebo in reducing cardiovascular events. †If needed for BP control. ACE indicates angiotensin-converting enzyme; ARB, angiotensin receptor blocker; BP, blood pressure; CCB, calcium channel blocker; GDMT, guideline-directed management and therapy; and SIHD, stable ischemic heart disease.

ACC/AHA Guidelines

HTN with SIHD

Recommendations for Treatment of Hypertension in Patients With Stable Ischemic Heart Disease (SIHD)
References that support recommendations are summarized in Online Data Supplements 30-32.

COR	LOE	RECOMMENDATIONS
I	SBP: B-R DBP: C-EO	1. In adults with SIHD and hypertension, a BP target of less than 130/80 mm Hg is recommended (S9.1-1–S9.1-5).
I	SBP: B-R DBP: C-EO	2. Adults with SIHD and hypertension (BP ≥130/80 mm Hg) should be treated with medications (e.g., GDMT (S9.1-6) beta blockers, ACE inhibitors, or ARBs) for compelling indications (e.g., previous MI, stable angina) as first-line therapy, with the addition of other drugs (e.g., dihydropyridine CCBs, thiazide diuretics, and/or mineralocorticoid receptor antagonists) as needed to further control hypertension (S9.1-7–S9.1-10).
I	B-NR	3. In adults with SIHD with angina and persistent uncontrolled hypertension, the addition of dihydropyridine CCBs to GDMT (S9.1-6) beta blockers is recommended (S9.1-8,S9.1-11,S9.1-12).
IIa	B-NR	4. In adults who have had a MI or acute coronary syndrome, it is reasonable to continue GDMT (S9.1-6) beta blockers beyond 3 years as long-term therapy for hypertension (S9.1-13,S9.1-14).
IIb	C-EO	5. Beta blockers and/or CCBs might be considered to control hypertension in patients with CAD (without HF*r*EF) who had an MI more than 3 years ago and have angina.

Whelton *et al.*
2017 High Blood Pressure Clinical Practice Guideline

JACC VOL. 71, NO. 19, 2018
MAY 15, 2018:e127–248

β Blockade after myocardial infarction: systematic review and meta regression analysis

Nick Freemantle, John Cleland, Philip Young, James Mason, Jane Harrison

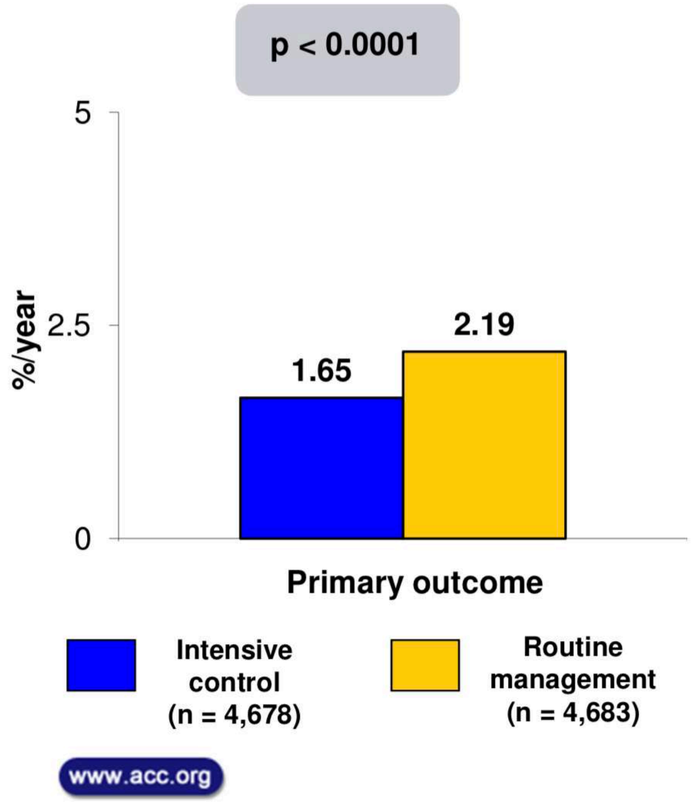
BMJ VOLUME 318 26 JUNE 1999 www.bmj.com

Hypertension

Congestive Heart Failure (CHF)

SPRINT

Trial design: Patients with systolic BP ≥130 mm Hg and at least one risk factor were randomized in a 1:1 fashion to either intensive SBP lowering (target <120 mm Hg) or routine SBP management (target <140 mm Hg). Patients were followed for 5 years.



Results

- Primary outcome, MI/ACS/stroke/CHF/CV death: intensive vs. routine: 1.65%/year vs. 2.19%/year, HR 0.75, 95% CI 0.64-0.89; p < 0.0001; stroke: 1.3% vs. 1.5%, p = 0.5; CHF: 1.3% vs. 2.1%, p = 0.002
- Mortality: 3.3% vs. 4.5%, p = 0.0003; CV death: 0.8% vs. 1.4%, p = 0.0005; worsening renal function among patients without CKD: 3.8% vs. 1.1%, p < 0.001
- Hypotension: 2.4% vs. 1.4%, p = 0.001

Conclusions

- Landmark trial; indicates that intensive BP lowering to a target <120 mm Hg is superior to routine management with a target of <140 mm Hg in non-diabetic patients with HTN, including in elderly patients. Reductions were also noted in CV and all-cause mortality, accompanied by a reduction in CHF
- Likely to impact clinical practice and guidelines

SPRINT Research Group. N Engl J Med 2015;373:2103-16

ACC/AHA Guidelines

CHF

Recommendation for Prevention of HF in Adults With Hypertension
References that support the recommendation are summarized in Online Data Supplement 33.

COR	LOE	RECOMMENDATION
I	SBP: B-R DBP: C-EO	1. In adults at increased risk of HF, the optimal BP in those with hypertension should be less than 130/80 mm Hg (S9.2-1–S9.2-3).

Recommendations for Treatment of Hypertension in Patients With HF*r*EF
References that support recommendations are summarized in Online Data Supplement 34.

COR	LOE	RECOMMENDATIONS
I	C-EO	1. Adults with HF*r*EF and hypertension should be prescribed GDMT (S9.2.1-2) titrated to attain a BP of less than 130/80 mm Hg.
III: No Benefit	B-R	2. Nondihydropyridine CCBs are not recommended in the treatment of hypertension in adults with HF*r*EF (S9.2.1-1).

Recommendations for Treatment of Hypertension in Patients With HF*p*EF
References that support recommendations are summarized in Online Data Supplements 35 and 36.

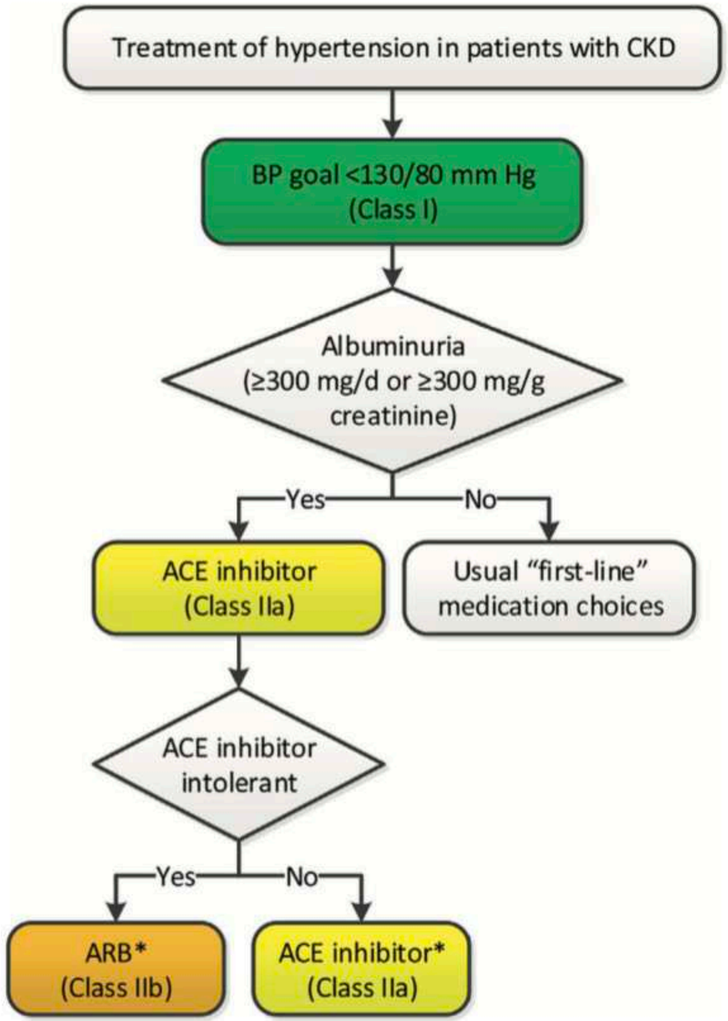
COR	LOE	RECOMMENDATIONS
I	C-EO	1. In adults with HF*p*EF who present with symptoms of volume overload, diuretics should be prescribed to control hypertension.
I	C-LD	2. Adults with HF*p*EF and persistent hypertension after management of volume overload should be prescribed ACE inhibitors or ARBs and beta blockers titrated to attain SBP of less than 130 mm Hg (S9.2.2-1–S9.2.2-6).

Hypertension

Chronic Kidney Disease (CKD)

Stage	GFR (ml/min/1.73m^2)	Terms
1	≥90	Normal or high
2	60-89	Mildly decreased
3a	45-59	Mildly to moderately decreased
3b	30-44	Moderately to severed decreased
4	15-29	Severely decreased
5	<15	Kidney failure

FIGURE 6 Management of Hypertension in Patients With CKD



Colors correspond to Class of Recommendation in Table 1. *CKD stage 3 or higher or stage 1 or 2 with albuminuria ≥300 mg/d or ≥300 mg/g creatinine. ACE indicates angiotensin-converting enzyme; ARB, angiotensin receptor blocker; BP blood pressure; and CKD, chronic kidney disease.

Whelton *et al.*
2017 High Blood Pressure Clinical Practice Guideline

JACC VOL. 71, NO. 19, 2018
MAY 15, 2018:e127-248

Hypertension

Stroke Secondary Prevention

- >750,000 adult patients experience a stroke, 25% are recurrent.
- Annual risk of a subsequent stroke is approximately 4%.
- Among patients with recent TIA/stroke, prevalence of premorbid HTN is approximately 70%.
- Guideline-recommended anti-HTN drug treatment to lower BP linked to reduction in 1-yr recurrence.
    - RCT meta-analyses show 30% reduction

Whelton *et al.*
2017 High Blood Pressure Clinical Practice Guideline

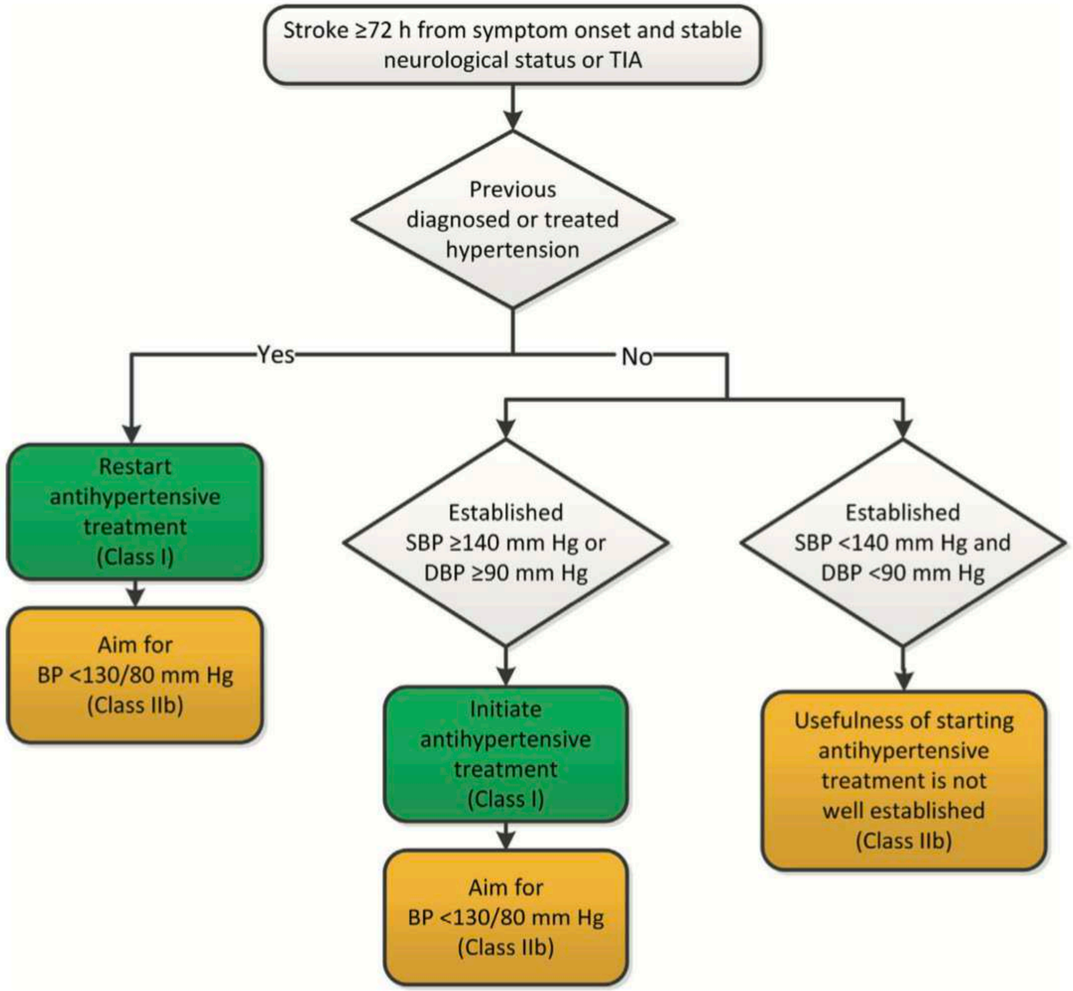
JACC VOL. 71, NO. 19, 2018
MAY 15, 2018:e127-248

Hypertension

Stroke Secondary Prevention

- Specific agents showing benefit in RCTs: diuretics, ARBs, ACE-Is
- Reduction in BP is most important, addition of other 1st line agents is ACE-I/ARB/diuretics do not achieve target.
- RCTs show larger reductions in BP yield greater reductions in recurrent stroke up to 130mmHg.
- <130mmHg less supported

FIGURE 9 Management of Hypertension in Patients With a Previous History of Stroke (Secondary Stroke Prevention)



Colors correspond to Class of Recommendation in Table 1. DBP indicates diastolic blood pressure; SBP, systolic blood pressure; and TIA, transient ischemic attack.

Whelton *et al.*
2017 High Blood Pressure Clinical Practice Guideline

JACC VOL. 71, NO. 19, 2018
MAY 15, 2018:e127-248

ACC/AHA Guidelines

HTN - Stroke Secondary Prevention

COR	LOE	RECOMMENDATIONS
I	A	1. Adults with previously treated hypertension who experience a stroke or transient ischemic attack (TIA) should be restarted on antihypertensive treatment after the first few days of the index event to reduce the risk of recurrent stroke and other vascular events (S9.4.3-1–S9.4.3-3).
I	A	2. For adults who experience a stroke or TIA, treatment with a thiazide diuretic, ACE inhibitor, or ARB, or combination treatment consisting of a thiazide diuretic plus ACE inhibitor, is useful (S9.4.3-1,S9.4.3-3–S9.4.3-5).
I	B-R	3. Adults not previously treated for hypertension who experience a stroke or TIA and have an established BP of 140/90 mm Hg or higher should be prescribed antihypertensive treatment a few days after the index event to reduce the risk of recurrent stroke and other vascular events (S9.4.3-1–S9.4.3-3).
I	B-NR	4. For adults who experience a stroke or TIA, selection of specific drugs should be individualized on the basis of patient comorbidities and agent pharmacological class (S9.4.3-6).
IIb	B-R	5. For adults who experience a stroke or TIA, a BP goal of less than 130/80 mm Hg may be reasonable (S9.4.3-6,S9.4.3-7).
IIb	B-R	6. For adults with a lacunar stroke, a target SBP goal of less than 130 mm Hg may be reasonable (S9.4.3-8).
IIb	C-LD	7. In adults previously untreated for hypertension who experience an ischemic stroke or TIA and have a SBP less than 140 mm Hg and a DBP less than 90 mm Hg, the usefulness of initiating antihypertensive treatment is not well established (S9.4.3-9).

Whelton *et al.*
2017 High Blood Pressure Clinical Practice Guideline

JACC VOL. 71, NO. 19, 2018
MAY 15, 2018:e127-248

ACC/AHA Guidelines

HTN - Diabetes Mellitus

Recommendations for Treatment of Hypertension in Patients With DM
References that support recommendations are summarized in Online Data Supplements 46 and 47 and Systematic Review Report.

COR	LOE	RECOMMENDATIONS
I	SBP: B-R[SR] DBP: C-EO	1. 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 (S9.6-1–S9.6-8).
I	A[SR]	2. In adults with DM and hypertension, all first-line classes of antihypertensive agents (i.e., diuretics, ACE inhibitors, ARBs, and CCBs) are useful and effective (S9.6-1,S9.6-9,S9.6-10).
IIb	B-NR	3. In adults with DM and hypertension, ACE inhibitors or ARBs may be considered in the presence of albuminuria (S9.6-11,S9.6-12).

Whelton *et al.*
2017 High Blood Pressure Clinical Practice Guideline

JACC VOL. 71, NO. 19, 2018
MAY 15, 2018:e127-248

ACC/AHA Guidelines

HTN - Atrial Fibrillation, Valvular Heart Disease

Recommendation for Treatment of Hypertension in Patients With AF
References that support the recommendation are summarized in Online Data Supplement 48.

COR	LOE	RECOMMENDATION
IIa	B-R	1. Treatment of hypertension with an ARB can be useful for prevention of recurrence of AF (S9.8-1,S9.8-2).

Recommendations for Treatment of Hypertension in Patients With Valvular Heart Disease
References that support recommendations are summarized in Online Data Supplements 49 and 50.

COR	LOE	RECOMMENDATIONS
I	B-NR	1. In adults with asymptomatic aortic stenosis, hypertension should be treated with pharmacotherapy, starting at a low dose and gradually titrating upward as needed (S9.9-1–S9.9-4).
IIa	C-LD	2. In patients with chronic aortic insufficiency, treatment of systolic hypertension with agents that do not slow the heart rate (i.e., avoid beta blockers) is reasonable (S9.9-5,S9.9-6).

Whelton *et al.*
2017 High Blood Pressure Clinical Practice Guideline

JACC VOL. 71, NO. 19, 2018
MAY 15, 2018:e127-248

ACC/AHA Guidelines

HTN - Aortic disease

- Aortic wall stress is effected most by the velocity of ventricular contraction (dP/dT)

Recommendation for Management of Hypertension in Patients With Aortic Disease

COR	LOE	RECOMMENDATION
I	C-EO	1. Beta blockers are recommended as the preferred antihypertensive agents in patients with hypertension and thoracic aortic disease (S9.10-1,S9.10-2).

Whelton *et al.*
2017 High Blood Pressure Clinical Practice Guideline

JACC VOL. 71, NO. 19, 2018
MAY 15, 2018:e127-248

ACC/AHA Guidelines

HTN

Recommendations for Race and Ethnicity
References that support recommendations are summarized in Online Data Supplement 51.

COR	LOE	RECOMMENDATIONS
I	B-R	1. In black adults with hypertension but without HF or CKD, including those with DM, initial antihypertensive treatment should include a thiazide-type diuretic or CCB (S10.1.1-1–S10.1.1-4).
I	C-LD	2. Two or more antihypertensive medications are recommended to achieve a BP target of less than 130/80 mm Hg in most adults with hypertension, especially in black adults with hypertension (S10.1.1-5–S10.1.1-7).

Recommendations for Treatment of Hypertension in Pregnancy
References that support recommendations are summarized in Online Data Supplement 53.

COR	LOE	RECOMMENDATIONS
I	C-LD	1. Women with hypertension who become pregnant, or are planning to become pregnant, should be transitioned to methyldopa, nifedipine, and/or labetalol (S10.2.2-1) during pregnancy (S10.2.2-2–S10.2.2-6).
III: Harm	C-LD	2. Women with hypertension who become pregnant should not be treated with ACE inhibitors, ARBs, or direct renin inhibitors (S10.2.2-4–S10.2.2-6).

Whelton *et al.*
2017 High Blood Pressure Clinical Practice Guideline

JACC VOL. 71, NO. 19, 2018
MAY 15, 2018:e127–248

ACC/AHA Guidelines

HTN - Elderly

- Vast majority of older adults have a 10-yr ASCVD risk >10%
- HTN is a leading cause of preventable morbidity and mortality in this population.
  - Under-recognized as major contributor to premature disability and institutionalization
- RCTs over the last 3 decades have included the elderly population, varying levels of frailty (SPRINT, HYVET)
  - BP goals for patients >65yrs (>80 yrs included) should not differ from those <65yrs
  - Those not living independently not represented in RCTs

ACC/AHA Guidelines

HTN - Elderly

Recommendations for Treatment of Hypertension in Older Persons
References that support recommendations are summarized in Online Data Supplement 54.

COR	LOE	RECOMMENDATIONS
I	A	1. Treatment of hypertension with a SBP treatment goal of less than 130 mm Hg is recommended for noninstitutionalized ambulatory community-dwelling adults (≥65 years of age) with an average SBP of 130 mm Hg or higher (S10.3.1-1).
IIa	C-EO	2. For older adults (≥65 years of age) with hypertension and a high burden of comorbidity and limited life expectancy, clinical judgment, patient preference, and a team-based approach to assess risk/benefit is reasonable for decisions regarding intensity of BP lowering and choice of antihypertensive drugs.

Whelton *et al.*
2017 High Blood Pressure Clinical Practice Guideline

JACC VOL. 71, NO. 19, 2018
MAY 15, 2018:e127-248

ACC/AHA Guidelines

Resistant HTN

Whelton *et al.*
2017 High Blood Pressure Clinical Practice Guideline

JACC VOL. 71, NO. 19, 2018
MAY 15, 2018:e127-248

Hypertensive Urgency vs Emergency

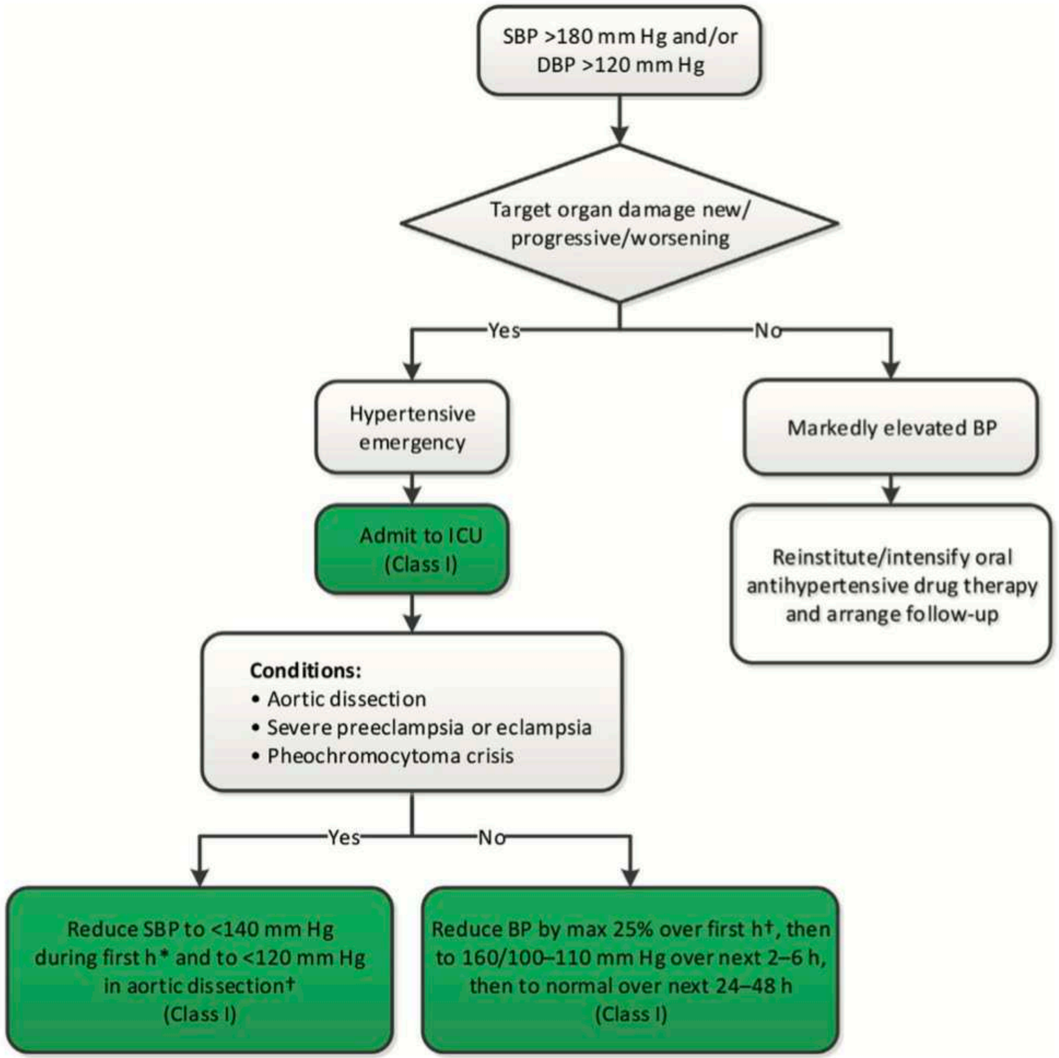
- Emergency - severe elevations in BP (>180/120mmHg) with new/worsening target organ damage.
  - Encephalopathy, ICH, acute ischemic stroke, acute MI, acute LV failure with pulmonary edema, aortic dissection, renal failure, eclampsia.
  - 1-yr death rate of hypertensive emergency >79%, median survival 10.4 months untreated
- Urgency - severe BP elevation in otherwise stable patients.
  - Many withdrawn from or are non compliant with therapy
  - Treated by reinstitution or intensification of therapy.
  - **No indication for referral to the ED, immediate reduction in BP in the ED, or hospitalization.**

Whelton *et al.*
2017 High Blood Pressure Clinical Practice Guideline

JACC VOL. 71, NO. 19, 2018
MAY 15, 2018:e127-248

Hypertensive Urgency vs Emergency

FIGURE 11 Diagnosis and Management of a Hypertensive Crisis



Colors correspond to Class of Recommendation in Table 1. *Use drug(s) specified in Table 19. †If other comorbidities are present, select a drug specified in Table 20. BP indicates blood pressure; DBP, diastolic blood pressure; ICU, intensive care unit; and SBP, systolic blood pressure.

Whelton *et al.*
2017 High Blood Pressure Clinical Practice Guideline

JACC VOL. 71, NO. 19, 2018
MAY 15, 2018:e127-248

ACC/AHA Guidelines

HTN - Perioperative Management

Recommendations for Treatment of Hypertension in Patients Undergoing Surgical Procedures
References that support recommendations are summarized in Online Data Supplements 57 and 58.

Preoperative

COR	LOE	RECOMMENDATIONS
I	B-NR	1. In patients with hypertension undergoing major surgery who have been on beta blockers chronically, beta blockers should be continued (S11.5-1–S11.5-7).
IIa	C-EO	2. In patients with hypertension undergoing planned elective major surgery, it is reasonable to continue medical therapy for hypertension until surgery.
IIb	B-NR	3. In patients with hypertension undergoing major surgery, discontinuation of ACE inhibitors or ARBs perioperatively may be considered (S11.5-8–S11.5-10).
IIb	C-LD	4. In patients with planned elective major surgery and SBP of 180 mm Hg or higher or DBP of 110 mm Hg or higher, deferring surgery may be considered (S11.5-11,S11.5-12).
III: Harm	B-NR	5. For patients undergoing surgery, abrupt preoperative discontinuation of beta blockers or clonidine is potentially harmful (S11.5-2,S11.5-13).
III: Harm	B-NR	6. Beta blockers should not be started on the day of surgery in beta blocker-naïve patients (S11.5-14).

Whelton *et al.*
2017 High Blood Pressure Clinical Practice Guideline

JACC VOL. 71, NO. 19, 2018
MAY 15, 2018:e127-248

HTN Management

Summary - thresholds and goals

TABLE 23 BP Thresholds for and Goals of Pharmacological Therapy in Patients With Hypertension According to Clinical Conditions

Clinical Condition(s)	BP Threshold, mm Hg	BP Goal, mm Hg
General		
Clinical CVD or 10-year ASCVD risk ≥10%	≥130/80	<130/80
No clinical CVD and 10-year ASCVD risk <10%	≥140/90	<130/80
Older persons (≥65 years of age; noninstitutionalized, ambulatory, community-living adults)	≥130 (SBP)	<130 (SBP)
Specific comorbidities		
Diabetes mellitus	≥130/80	<130/80
Chronic kidney disease	≥130/80	<130/80
Chronic kidney disease after renal transplantation	≥130/80	<130/80
Heart failure	≥130/80	<130/80
Stable ischemic heart disease	≥130/80	<130/80
Secondary stroke prevention	≥140/90	<130/80
Peripheral artery disease	≥130/80	<130/80

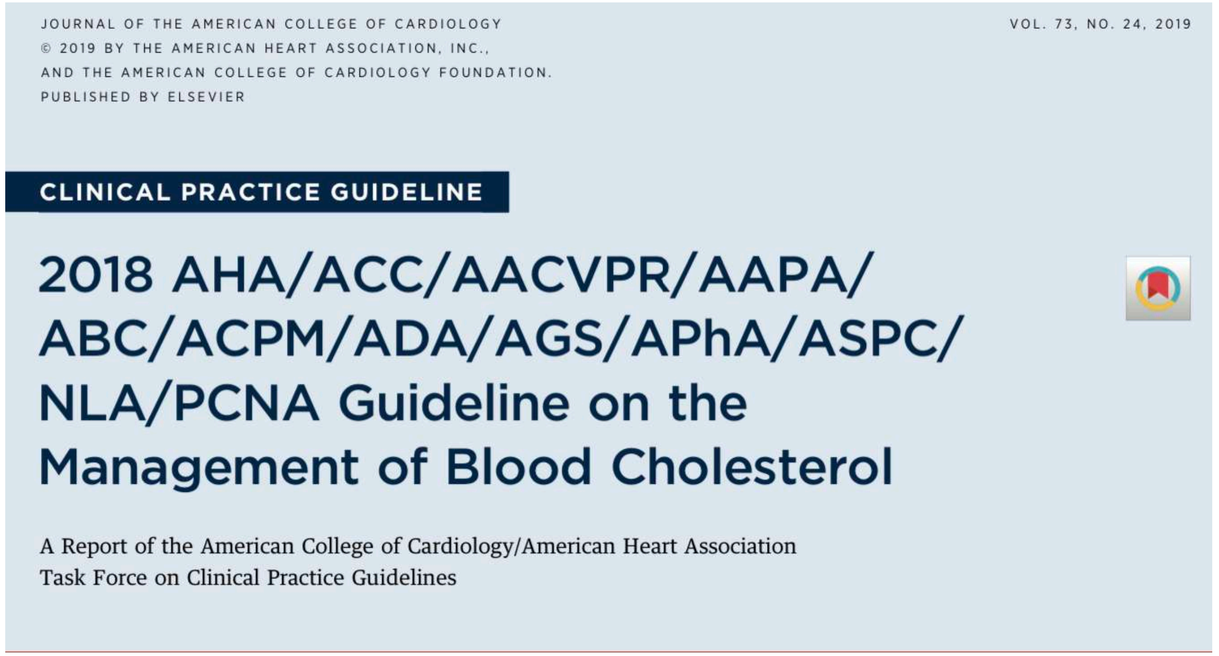
Whelton *et al.*
2017 High Blood Pressure Clinical Practice Guideline

JACC VOL. 71, NO. 19, 2018
MAY 15, 2018:e127-248

Hyperlipidemia Management

Overview

- Hyperlipidemia and ASCVD
- Lifestyle management
- Lipid lowering pharmacological therapies
- Patient management groups (elderly)
- Statin-associated side effects (SAS)


JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
VOL. 73, NO. 24, 2019

PUBLISHED BY ELSEVIER

CLINICAL PRACTICE GUIDELINE

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

Grundy *et al.*
2018 Cholesterol Clinical Practice Guideline

JACC VOL. 73, NO. 24, 2019
JUNE 25, 2019:e285-350

Hyperlipidemia

High blood cholesterol and ASCVD

- Serum cholesterol and its lipoprotein carriers (LDL, VLDL, HDL) associate with ASCVD
- LDL is the dominant form of atherogenic cholesterol.
- VLDL is atherogenic, HDL seemingly not
- LDL and VLDL are considered non-HDL cholesterol which is more atherogenic than LDL alone
- ApoB is major protein imbedded in LDL and VLDL, also strong atherogenic indicator

ACC/AHA Guidelines

LDL-C and nonHDL-C measurement and followup

Recommendations for Measurements of LDL-C and Non-HDL-C
Referenced studies that support recommendations are summarized in Online Data Supplement 1.

COR	LOE	RECOMMENDATIONS
I	B-NR	1. In adults who are 20 years of age or older and not on lipid-lowering therapy, measurement of either a fasting or a nonfasting plasma lipid profile is effective in estimating ASCVD risk and documenting baseline LDL-C (S2.2-1–S2.2-6).
I	B-NR	2. In adults who are 20 years of age or older and in whom an initial nonfasting lipid profile reveals a triglycerides level of 400 mg/dL or higher (≥4.5 mmol/L), a repeat lipid profile in the fasting state should be performed for assessment of fasting triglyceride levels and baseline LDL-C (S2.2-1–S2.2-4).
IIa	C-LD	3. For adults with an LDL-C level less than 70 mg/dL (<1.8 mmol/L), measurement of direct LDL-C or modified LDL-C estimate is reasonable to improve accuracy over the Friedewald formula (S2.2-7–S2.2-9).
IIa	C-LD	4. In adults who are 20 years of age or older and without a personal history of ASCVD, but with a family history of premature ASCVD or genetic hyperlipidemia, measurement of a fasting plasma lipid profile is reasonable as part of an initial evaluation to aid in the understanding and identification of familial lipid disorders.

Recommendation for Monitoring
Referenced studies that support the recommendation are summarized in Online Data Supplement 17.

COR	LOE	RECOMMENDATION
I	A	1. Adherence to changes in lifestyle and effects of LDL-C–lowering medication should be assessed by measurement of fasting lipids and appropriate safety indicators 4 to 12 weeks after statin initiation or dose adjustment and every 3 to 12 months thereafter based on need to assess adherence or safety (S4.4.3-1–S4.4.3-3).

Grundy *et al.*
2018 Cholesterol Clinical Practice Guideline

JACC VOL. 73, NO. 24, 2019
JUNE 25, 2019:e285-350

Hyperlipidemia

Lifestyle management

- Patients should consume a dietary pattern that emphasizes the consumption vegetables, fruits, whole grains, legumes, healthy protein sources, vegetable oils
- Limit intake of saturated fats/oils, refines starches/sugars, red meats
- Diets such as the Mediterranean, vegan/plant-based, vegetarian, flexitarian all enforce these recommendations
- Physical exercise: 150 minutes per week, 3-4 sessions of 40 minutes moderate to vigorous aerobic exercise

Beyond Cholesterol

Inflammatory potential and risk of cardiovascular disease

- Chronic inflammation is a critical mechanism of initiation and progression of atherothrombosis
- Findings from 3 Harvard prospective cohorts of 200,000 individuals with 24-30 years follow up. Related inflammatory potential of diet to incident CVD
- Higher inflammatory index was associated with higher incident CVD.
  - 28% for stroke
  - 46% for ischemic heart disease
- Empirical dietary inflammatory pattern (EDIP) score used based on levels of 3 systemic inflammatory biomarkers

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. 76, NO. 19, 2020

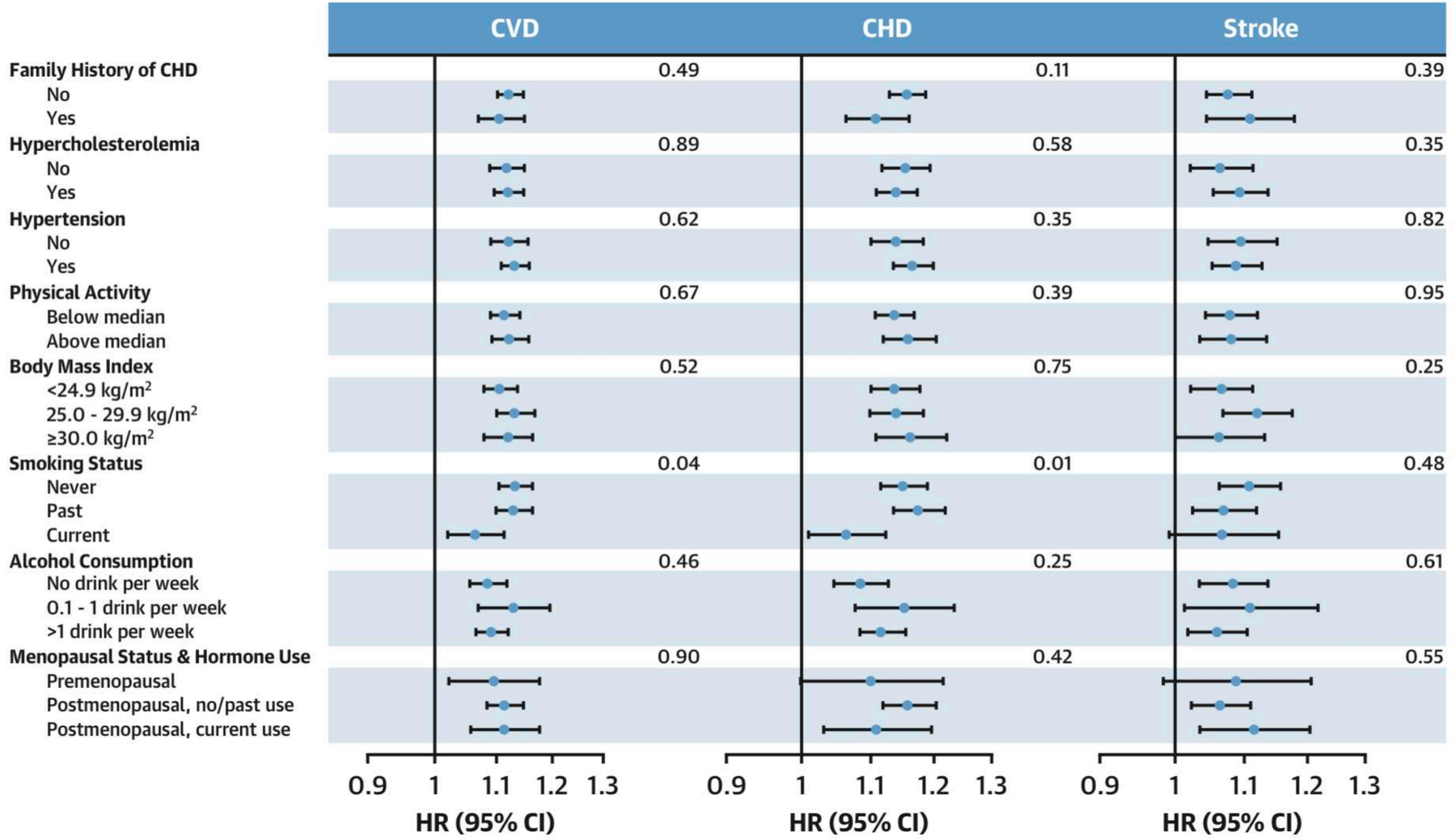
PUBLISHED BY ELSEVIER

ORIGINAL INVESTIGATIONS

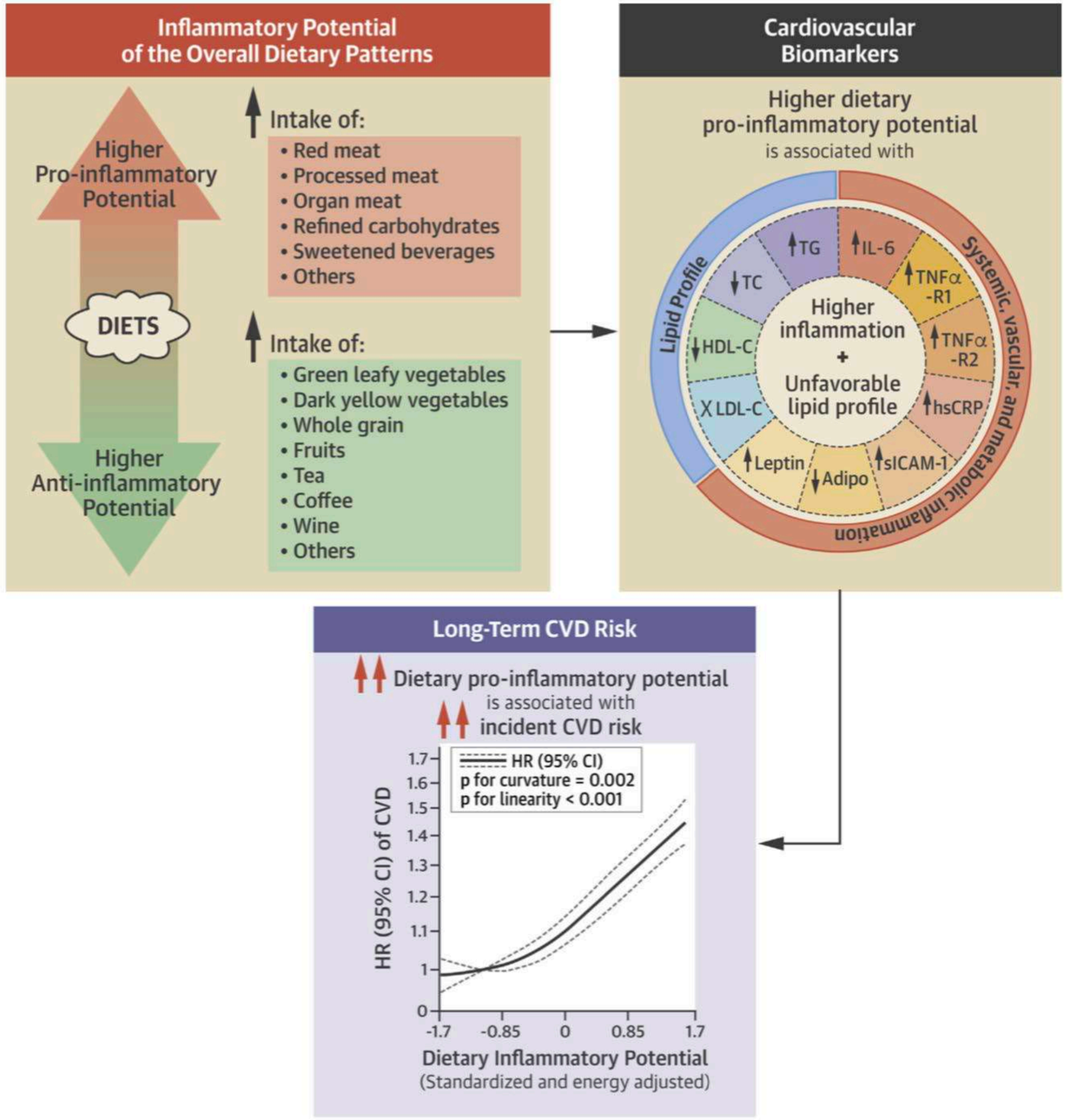
Dietary Inflammatory Potential and Risk of Cardiovascular Disease Among Men and Women in the U.S.

Jun Li, MD, PhD,[a,b,*] Dong Hoon Lee, ScD,[a,*] Jie Hu, MD, PhD,[c] Fred K. Tabung, PhD,[a,d] Yanping Li, MD, PhD,[a] Shilpa N. Bhupathiraju, PhD,[a,e] Eric B. Rimm, ScD,[a,b,e] Kathryn M. Rexrode, MD, MPH,[c] JoAnn E. Manson, MD, DrPH,[b,f,g] Walter C. Willett, MD, DrPH,[a] Edward L. Giovannucci, MD, ScD,[a] Frank B. Hu, MD, PhD[a,b,e]

FIGURE 2 HR (95% CI) for CVD, CHD, and Stroke Associated With a 1-SD Increase in EDIP Scores, Stratified by Pre-Selected Cardiovascular Risk Factors



CENTRAL ILLUSTRATION Adherence to Proinflammatory Dietary Patterns and Cardiovascular Disease Incidence



Li, J. et al. J Am Coll Cardiol. 2020;76(19):2181–93.

Hyperlipidemia

Medication and lipid-lowering effect

- Statins
  - Low intensity: <30% lowering LDL-C
  - Moderate intensity: 30-49% lowering LDL-C
  - High: >/= 50% lowering LDL-C
- Bile Sequestrants: 15-30% LDL-C lowering. GI complaints, can raise triglycerides
- Ezetimibe: 13-20% LDL-C lowering
- PCSK9 Inhibitors: when added to statin therapy, additional 40-60% reduction in LDL-C

Hyperlipidemia

Statins

TABLE 3 High-, Moderate-, and Low-Intensity Statin Therapy*

	High Intensity	Moderate Intensity	Low Intensity
LDL-C lowering†	≥50%	30%–49%	<30%
Statins	**Atorvastatin (40 mg‡) 80 mg** **Rosuvastatin 20 mg (40 mg)**	**Atorvastatin 10 mg** (20 mg) **Rosuvastatin** (5 mg) **10 mg** **Simvastatin 20–40 mg§**	Simvastatin 10 mg
	…	**Pravastatin 40 mg** (80 mg) **Lovastatin 40 mg** (80 mg) Fluvastatin XL 80 mg **Fluvastatin 40 mg BID** Pitavastatin 1–4 mg	**Pravastatin 10–20 mg** **Lovastatin 20 mg** Fluvastatin 20–40 mg

Grundy *et al.*
2018 Cholesterol Clinical Practice Guideline

JACC VOL. 73, NO. 24, 2019
JUNE 25, 2019:e285-350

ACC/AHA Guidelines

HLD- Primary Prevention

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).

Grundy *et al.*
2018 Cholesterol Clinical Practice Guideline

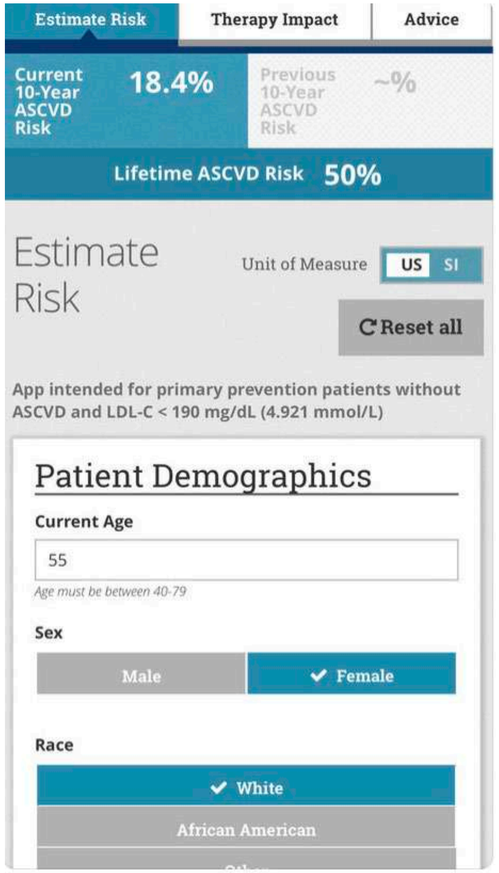
JACC VOL. 73, NO. 24, 2019
JUNE 25, 2019:e285-350

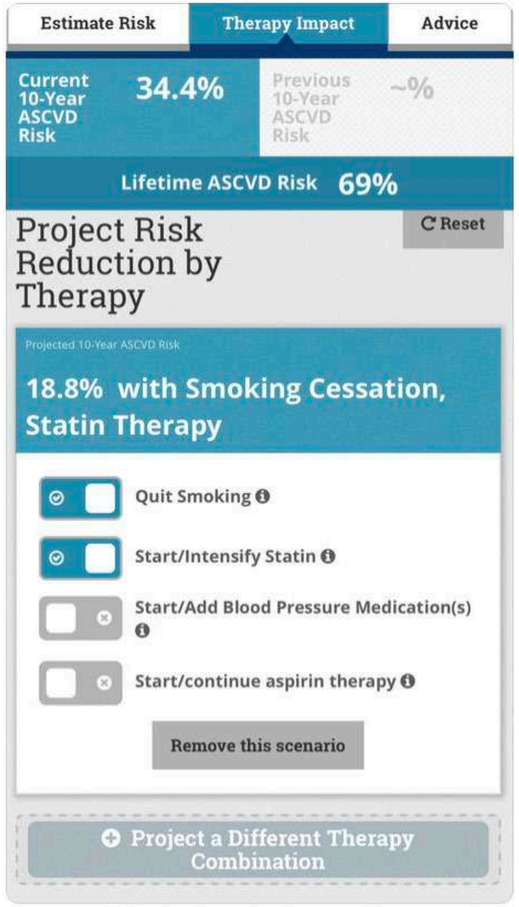
ASCVD Risk Estimator Plus 17+

American College of Cardiology

★★★½☆ 3.3, 11 Ratings

Free





10-year ASCVD Risk:

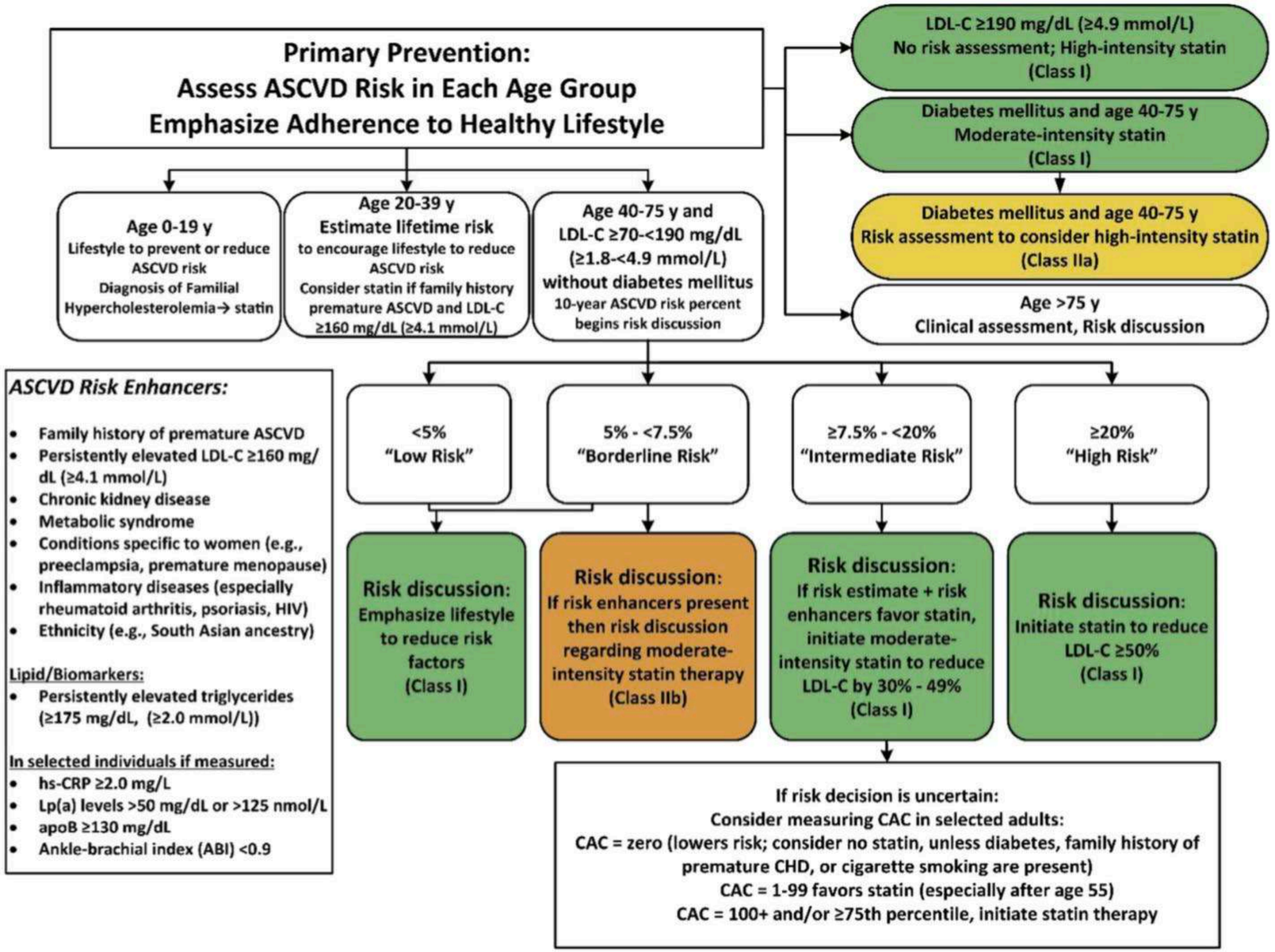
- High >20%
- Intermediate 7.5-19%
- Borderline 5-7.5%
- Low <5%

TABLE 6 Risk-Enhancing Factors for Clinician–Patient Risk Discussion

Risk-Enhancing Factors

- **Family history of premature ASCVD** (males, age <55 y; females, age <65 y)
- **Primary hypercholesterolemia** (LDL-C, 160–189 mg/dL [4.1–4.8 mmol/L); non-HDL-C 190–219 mg/dL [4.9–5.6 mmol/L])*
- **Metabolic syndrome** (increased waist circumference, elevated triglycerides [>150 mg/dL], elevated blood pressure, elevated glucose, and low HDL-C [<40 mg/dL in men; <50 in women mg/dL] are factors; tally of 3 makes the diagnosis)
- **Chronic kidney disease** (eGFR 15–59 mL/min/1.73 m^2 with or without albuminuria; not treated with dialysis or kidney transplantation)
- **Chronic inflammatory conditions** such as psoriasis, RA, or HIV/AIDS
- **History of premature menopause (before age 40 y) and history of pregnancy-associated conditions that increase later ASCVD risk such as preeclampsia**
- **High-risk race/ethnicities** (e.g., South Asian ancestry)
- **Lipid/biomarkers:** Associated with increased ASCVD risk
  - Persistently* elevated, primary hypertriglyceridemia (≥175 mg/dL);
  - If measured:
    1. **Elevated high-sensitivity C-reactive protein** (≥2.0 mg/L)
    2. **Elevated Lp(a):** A relative indication for its measurement is family history of premature ASCVD. An Lp(a) ≥50 mg/dL or ≥125 nmol/L constitutes a risk-enhancing factor especially at higher levels of Lp(a).
    3. **Elevated apoB** ≥130 mg/dL: A relative indication for its measurement would be triglyceride ≥200 mg/dL. A level ≥130 mg/dL corresponds to an LDL-C >160 mg/dL and constitutes a risk-enhancing factor
    4. **ABI** <0.9

FIGURE 2 Primary Prevention



Colors correspond to Class of Recommendation in Table 2. apoB indicates apolipoprotein B; ASCVD, atherosclerotic cardiovascular disease; CAC, coronary artery calcium; human immunodeficiency virus; hsCRP, high-sensitivity C-reactive protein; LDL-C, low-density lipoprotein cholesterol; and Lp(a), lipoprotein (a).

ACC/AHA Guidelines

Diabetes

Recommendations for Patients With Diabetes Mellitus
Referenced studies that support recommendations are summarized in Online Data Supplements 11 and 12.

COR	LOE	RECOMMENDATIONS
I	A	1. In adults 40 to 75 years of age with diabetes mellitus, regardless of estimated 10-year ASCVD risk, moderate-intensity statin therapy is indicated (S4.3-1–S4.3-9).
IIa	B-NR	2. In adults 40 to 75 years of age with diabetes mellitus and an LDL-C level of 70 to 189 mg/dL (1.7 to 4.8 mmol/L), it is reasonable to assess the 10-year risk of a first ASCVD event by using the race and sex-specific PCE to help stratify ASCVD risk (S4.3-10, S4.3-11).
IIa	B-R	3. 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 (S4.3-12, S4.3-13).
IIa	B-NR	4. In adults older than 75 years of age with diabetes mellitus and who are already on statin therapy, it is reasonable to continue statin therapy (S4.3-5, S4.3-8, S4.3-13).
IIb	C-LD	5. In adults with diabetes mellitus and 10-year ASCVD risk of 20% or higher, it may be reasonable to add ezetimibe to maximally tolerated statin therapy to reduce LDL-C levels by 50% or more (S4.3-14, S4.3-15).
IIb	C-LD	6. In adults older than 75 years with diabetes mellitus, it may be reasonable to initiate statin therapy after a clinician-patient discussion of potential benefits and risks (S4.3-5, S4.3-8, S4.3-13).
IIb	C-LD	7. In adults 20 to 39 years of age with diabetes mellitus that is either of long duration (≥10 years of type 2 diabetes mellitus, ≥20 years of type 1 diabetes mellitus), albuminuria (≥30 mcg of albumin/mg creatinine), estimated glomerular filtration rate (eGFR) less than 60 mL/min/1.73 m^2, retinopathy, neuropathy, or ankle-brachial index (ABI; <0.9), it may be reasonable to initiate statin therapy (S4.3-5, S4.3-6, S4.3-8, S4.3-16–S4.3-25).

Grundy *et al.*
2018 Cholesterol Clinical Practice Guideline

JACC VOL. 73, NO. 24, 2019
JUNE 25, 2019:e285-350

ACC/AHA Guidelines

Primary severe hyperlipidemia

Recommendations for Primary Severe Hypercholesterolemia (LDL-C ≥190 mg/dL [≥4.9 mmol/L])
Referenced studies that support recommendations are summarized in Online Data Supplements 9 and 10.

COR	LOE	RECOMMENDATIONS
I	B-R	1. In patients 20 to 75 years of age with an LDL-C level of 190 mg/dL or higher (≥4.9 mmol/L) maximally tolerated statin therapy is recommended (S4.2-1–S4.2-7).
IIa	B-R	2. In patients 20 to 75 years of age with an LDL-C level of 190 mg/dL or higher (≥4.9 mmol/L) who achieve less than a 50% reduction in LDL-C while receiving maximally tolerated statin therapy and/or have an LDL-C level of 100 mg/dL or higher (≥2.6 mmol/L) ezetimibe therapy is reasonable (S4.2-8–S4.2-10).
IIb	B-R	3. In patients 20 to 75 years of age with a baseline LDL-C level 190 mg/dL or higher (≥4.9 mmol/L), who achieve less than a 50% reduction in LDL-C levels and have fasting triglycerides 300 mg/dL or lower (≤3.4 mmol/L). while taking maximally tolerated statin and ezetimibe therapy, the addition of a bile acid sequestrant may be considered (S4.2-11, S4.2-12).
IIb	B-R	4. In patients 30 to 75 years of age with heterozygous FH and with an LDL-C level of 100 mg/dL or higher (≥2.6 mmol/L) while taking maximally tolerated statin and ezetimibe therapy, the addition of a PCSK9 inhibitor may be considered (S4.2-9, S4.2-13–S4.2-15).
IIb	C-LD	5. In patients 40 to 75 years of age with a baseline LDL-C level of 220 mg/dL or higher (≥5.7 mmol/L) and who achieve an on-treatment LDL-C level of 130 mg/dL or higher (≥3.4 mmol/L) while receiving maximally tolerated statin and ezetimibe therapy, the addition of a PCSK9 inhibitor may be considered (S4.2-13–S4.2-17).

Grundy *et al.*
2018 Cholesterol Clinical Practice Guideline

JACC VOL. 73, NO. 24, 2019
JUNE 25, 2019:e285-350

ACC/AHA Guidelines

HLD - Secondary Prevention

COR	LOE	RECOMMENDATIONS
I	A	1. In patients who are 75 years of age or younger with clinical ASCVD,* high-intensity statin therapy should be initiated or continued with the aim of achieving a 50% or greater reduction in LDL-C levels (S4.1-1–S4.1-5).
I	A	2. In patients with clinical ASCVD in whom high-intensity statin therapy is contraindicated or who experience statin-associated side effects, moderate-intensity statin therapy should be initiated or continued with the aim of achieving a 30% to 49% reduction in LDL-C levels (S4.1-3, S4.1-6–S4.1-13).
I	B-NR	3. In patients with clinical ASCVD who are judged to be very high risk and considered for PCSK9 inhibitor therapy, maximally tolerated LDL-C lowering therapy should include maximally tolerated statin therapy and ezetimibe (S4.1-14, S4.1-15).
IIa	A^{SR}	4. In patients with clinical ASCVD who are judged to be very high risk and who are on maximally tolerated LDL-C lowering therapy with LDL-C 70 mg/dL or higher (≥1.8 mmol/L) or a non-HDL-C level of 100 mg/dL or higher (≥2.6 mmol/L) it is reasonable to add a PCSK9 inhibitor following a clinician-patient discussion about the net benefit, safety, and cost (S4.1-15–S4.1-19).
IIa	B-R	5. In patients with clinical ASCVD who are on maximally tolerated statin therapy and are judged to be at very high risk and have an LDL-C level of 70 mg/dL or higher (≥1.8 mmol/L) it is reasonable to add ezetimibe therapy (S4.1-14, S4.1-15).
IIa	B-R	7. In patients older than 75 years of age with clinical ASCVD, it is reasonable to initiate moderate- or high-intensity statin therapy after evaluation of the potential for ASCVD risk reduction, adverse effects, and drug-drug interactions, as well as patient frailty and patient preferences (S4.1-23–S4.1-31).
IIa	C-LD	8. In patients older than 75 years of age who are tolerating high-intensity statin therapy, it is reasonable to continue high-intensity statin therapy after evaluation of the potential for ASCVD risk reduction, adverse effects, and drug-drug interactions, as well as patient frailty and patient preferences (S4.1-3, S4.1-10, S4.1-23, S4.1-26, S4.1-31–S4.1-36).
IIb	B-R	9. In patients with clinical ASCVD who are receiving maximally tolerated statin therapy and whose LDL-C level remains 70 mg/dL or higher (≥1.8 mmol/L) it may be reasonable to add ezetimibe (S4.1-15).
IIb	B-R	10. In patients with heart failure (HF) with reduced ejection fraction attributable to ischemic heart disease who have a reasonable life expectancy (3 to 5 years) and are not already on a statin because of ASCVD, clinicians may consider initiation of moderate-intensity statin therapy to reduce the occurrence of ASCVD events (S4.1-37).

Grundy *et al.*
2018 Cholesterol Clinical Practice Guideline

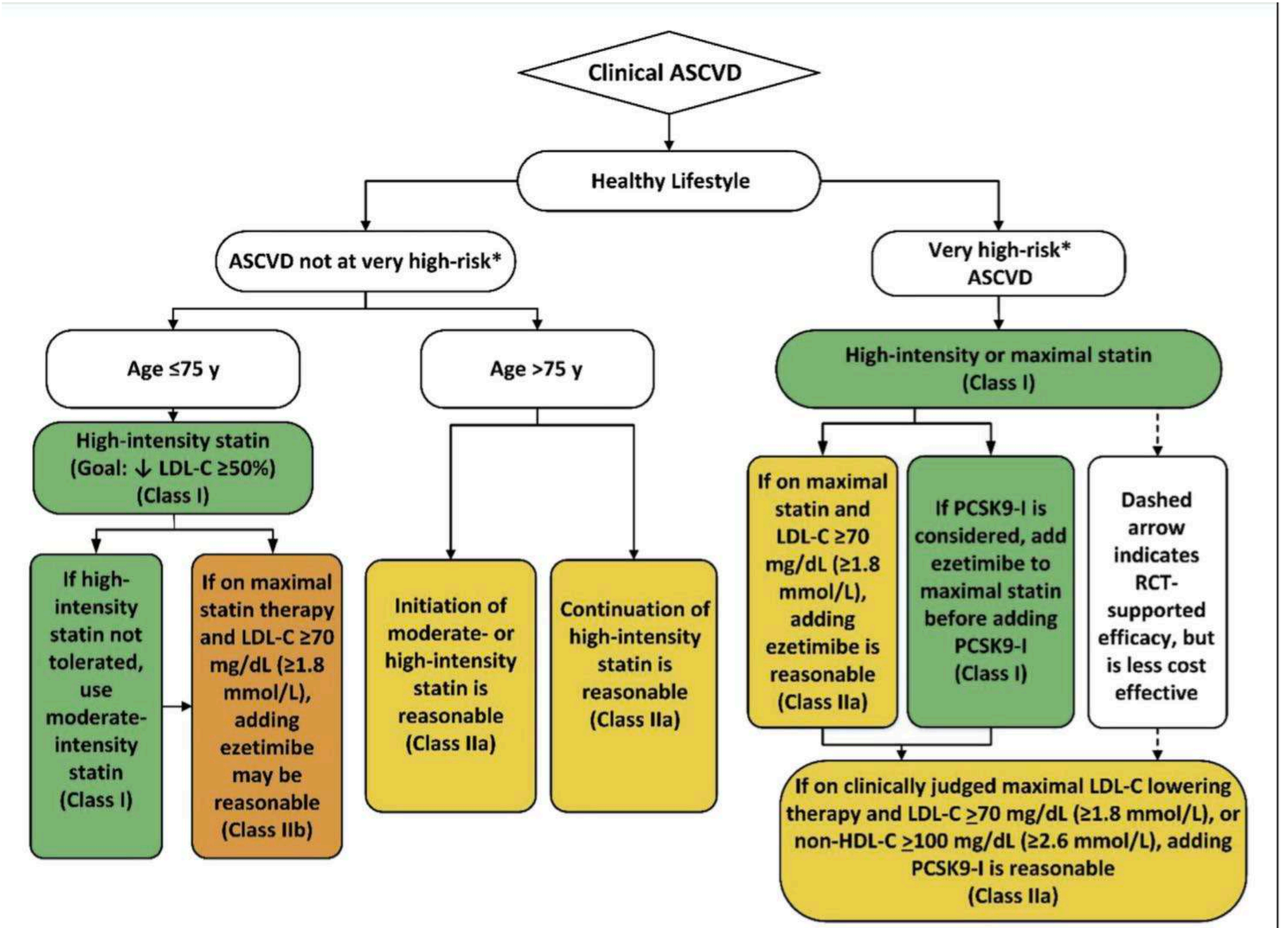
JACC VOL. 73, NO. 24, 2019
JUNE 25, 2019:e285-350

TABLE 4 Very High-Risk* of Future ASCVD Events

Major ASCVD Events
Recent ACS (within the past 12 mo)
History of MI (other than recent ACS event listed above)
History of ischemic stroke
Symptomatic peripheral arterial disease (history of claudication with ABI <0.85, or previous revascularization or amputation [S4.1-40])
High-Risk Conditions
Age ≥65 y
Heterozygous familial hypercholesterolemia
History of prior coronary artery bypass surgery or percutaneous coronary intervention outside of the major ASCVD event(s)
Diabetes mellitus
Hypertension
CKD (eGFR 15-59 mL/min/1.73 m^2) (S4.1-15, S4.1-17)
Current smoking
Persistently elevated LDL-C (LDL-C ≥100 mg/dL [≥2.6 mmol/L]) despite maximally tolerated statin therapy and ezetimibe
History of congestive HF

*Very high risk includes a history of multiple major ASCVD events or 1 major ASCVD event and multiple high-risk conditions.

ABI indicates ankle-brachial index; ACS, acute coronary syndrome; ASCVD, atherosclerotic cardiovascular disease; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; HF, heart failure; LDL, low-density lipoprotein cholesterol; and MI, myocardial infarction.



Colors correspond to Class of Recommendation in Table 2. Clinical ASCVD consists of ACS, those with history of MI, stable or unstable angina or coronary other arterial revascularization, stroke, transient ischemic attack (TIA), or peripheral artery disease (PAD) including aortic aneurysm, all of atherosclerotic origin Very high-risk includes a history of multiple major ASCVD events or 1 major ASCVD event and multiple high-risk conditions (Table 4). ACS indicates acute coronary syndrome; ASCVD, atherosclerotic cardiovascular disease; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; MI, myocardial infarction; and PCSK9-I, PCSK9 inhibitor.

Hyperlipidemia

PCSK9 Inhibitors

The NEW ENGLAND JOURNAL of MEDICINE

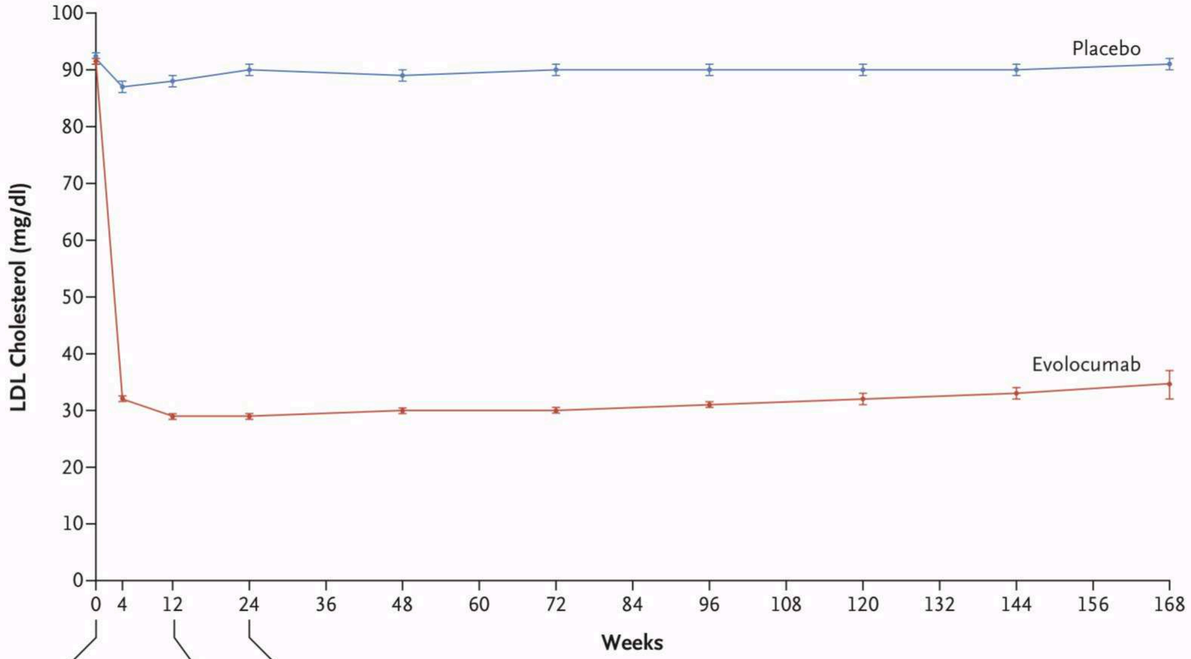
ESTABLISHED IN 1812 MAY 4, 2017 VOL. 376 NO. 18

Evolocumab and Clinical Outcomes in Patients with Cardiovascular Disease

Marc S. Sabatine, M.D., M.P.H., Robert P. Giugliano, M.D., Anthony C. Keech, M.D., Narimon Honarpour, M.D., Ph.D., Stephen D. Wiviott, M.D., Sabina A. Murphy, M.P.H., Julia F. Kuder, M.A., Huei Wang, Ph.D., Thomas Liu, Ph.D., Scott M. Wasserman, M.D., Peter S. Sever, Ph.D., F.R.C.P., and Terje R. Pedersen, M.D., for the FOURIER Steering Committee and Investigators*

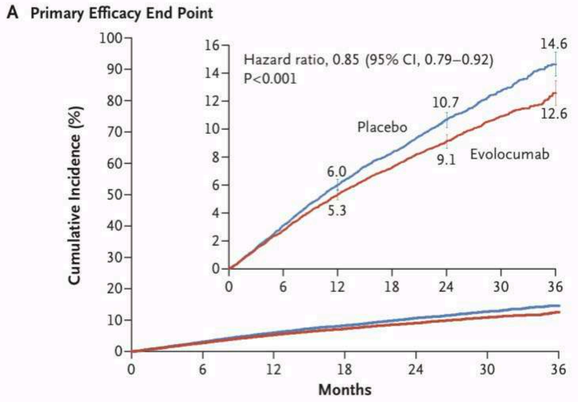
Hyperlipidemia

PCSK9 Inhibitors

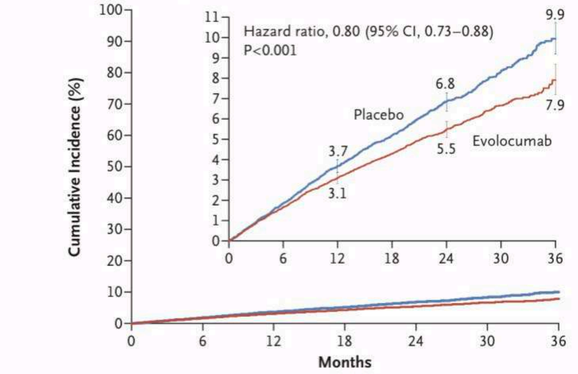


No. at Risk										
Placebo	13,779	13,251	13,151	12,954	12,596	12,311	10,812	6926	3352	790
Evolocumab	13,784	13,288	13,144	12,964	12,645	12,359	10,902	6958	3323	768
Absolute difference (mg/dl)		54	58	57	56	55	54	52	53	50
Percentage difference		57	61	61	59	58	57	55	56	54
P value		<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

N Engl J Med 2017;376:1713-22.
DOI: 10.1056/NEJMoa1615664



No. at Risk							
Placebo	13,780	13,278	12,825	11,871	7610	3690	686
Evolocumab	13,784	13,351	12,939	12,070	7771	3746	689



No. at Risk							
Placebo	13,780	13,449	13,142	12,288	7944	3893	731
Evolocumab	13,784	13,501	13,241	12,456	8094	3935	724

Figure 2. Cumulative Incidence of Cardiovascular Events.

Panel A shows the cumulative event rates for the primary efficacy end point (the composite of cardiovascular death, myocardial infarction, stroke, hospitalization for unstable angina, or coronary revascularization), and Panel B shows the rates for the key secondary efficacy end point (the composite of cardiovascular death, myocardial infarction, or stroke). I bars indicate 95% confidence intervals. The Kaplan–Meier rates for the primary end point in the evolocumab group versus the placebo group were as follows: at 1 year, 5.3% (95% confidence interval [CI], 4.9 to 5.7) versus 6.0% (95% CI, 5.6 to 6.4); at 2 years, 9.1% (95% CI, 8.6 to 9.6) versus 10.7% (95% CI, 10.1 to 11.2); and at 3 years, 12.6% (95% CI, 11.7 to 13.5) versus 14.6% (95% CI, 13.8 to 15.5). The Kaplan–Meier rates for the key secondary end point in the evolocumab group versus the placebo group were as follows: at 1 year, 3.1% (95% CI, 2.8 to 3.4) versus 3.7% (95% CI, 3.4 to 4.0); at 2 years, 5.5% (95% CI, 5.1 to 5.9) versus 6.8% (95% CI, 6.4 to 7.3); and at 3 years, 7.9% (95% CI, 7.2 to 8.7) versus 9.9% (95% CI, 9.2 to 10.7). P values were calculated with the use of log-rank tests. The insets show the same data on an enlarged y axis.

Statins for Primary Prevention: Age 66-75

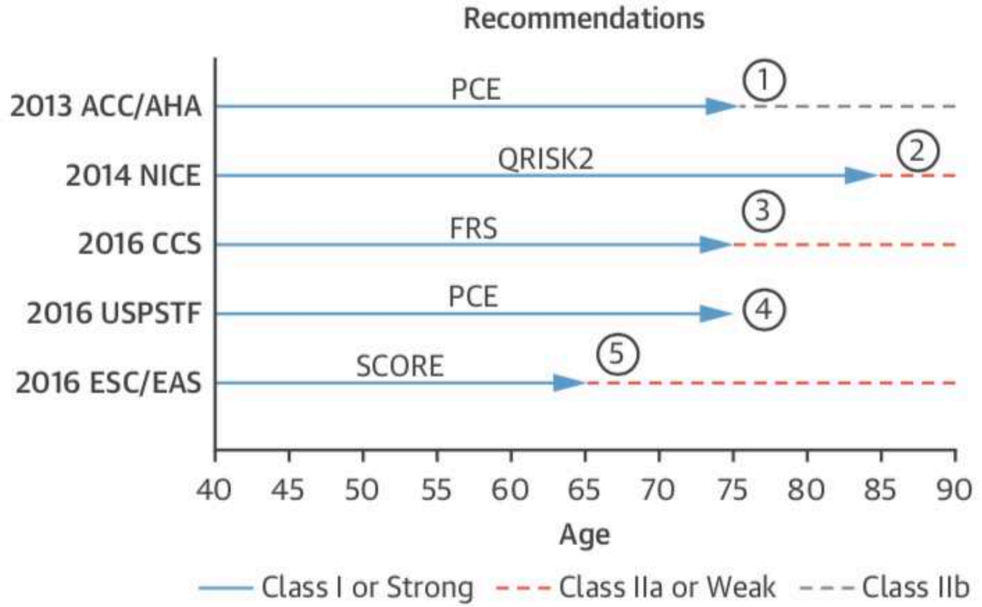
- 4/5 Guidelines give Class I recommendations for statin therapy in individuals at risk (extrapolation of ASCVD and NICE risk assessment tools)
- ESC/EAS does not as these risk assessment tools have an age cutoff of 65yrs
- ACC/AHA, CCS, USPSTF guidelines provide the same risk-based indication for statin therapy.
  - All elderly individuals with optimal risk factors exceed 7.5% threshold by 65yrs in men, 71 yrs in women thus qualifying for statin therapy.
  - Clinical trial evidence supports the use of statins for primary prevention in this cohort (MEGA, CARDS, JUPITER, HOPE-3)

Statins for Primary Prevention: Age >75

- The Dilemma: Although at high risk of near-term ASCVD by age alone, evidence for efficacy in this population is sparse due to under-representation in RCTs.
  - Post Hoc and subgroup analyses from RCTs
  - Meta-analysis
- Must weigh the benefit against the side-effects and impact on quality of life, etc
- Efficacy for secondary prevention in this age group is well documented (PROSPER trial).

Disparity despite same body of evidence

FIGURE 1 Recommendations for Primary Prevention With Statins in Apparently Healthy People



Guideline Recommendations in Elderly

1. "Statin therapy may be considered in selected individuals" (age >75, Class IIb)
2. "For people 85 years or older consider atorvastatin 20 mg as statins may be of benefit in reducing the risk of non-fatal myocardial infarction"
3. FRS is not well validated beyond age 75, and indications for statins are less well defined in this age group
4. There is no recommendation for statins in people >75 years old
5. SCORE is not applicable beyond age 65, but "statin therapy should be considered in older adults, particularly in the presence of hypertension, smoking, diabetes and dyslipidemia" (Class IIa)

Handling of individuals >65 years of age differs substantially among contemporary European and North American guidelines, partly because of the performance (applicability) of the risk model used. ACC/AHA = American College of Cardiology/American Heart Association; CCS = Canadian Cardiovascular Society; ESC/EAS = European Society of Cardiology/European Atherosclerosis Society; FRS = Framingham Risk Score for general cardiovascular disease; NICE = National Institute for Health and Care Excellence; PCE = pooled cohort equation; SCORE = Systematic COronary Risk Evaluation; USPSTF = U.S. Preventive Services Task Force.

JAMA Cardiology | Original Investigation

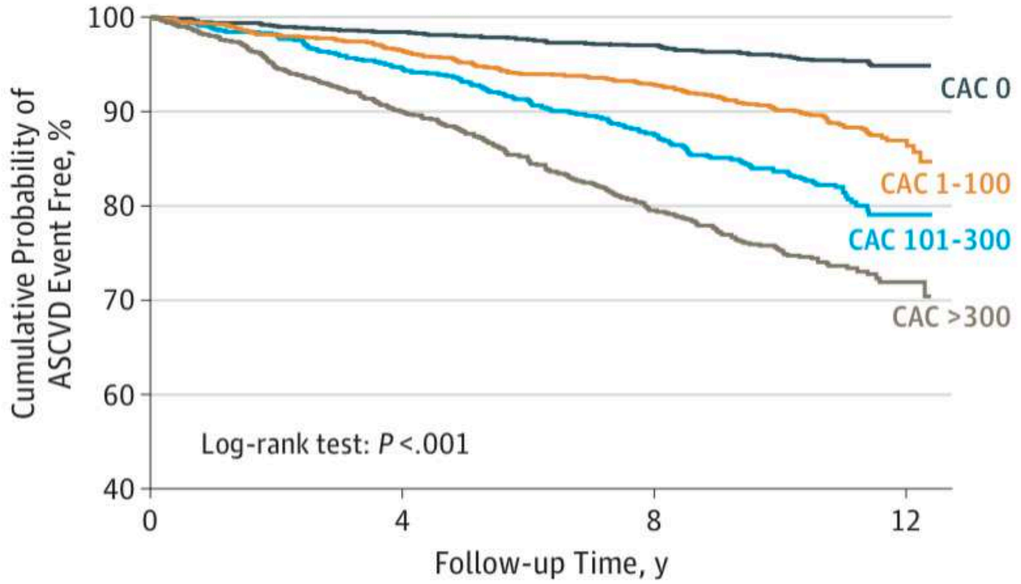
Association of Coronary Artery Calcium Score vs Age With Cardiovascular Risk in Older Adults

An Analysis of Pooled Population-Based Studies

Yuichiro Yano, MD, PhD; Christopher J. O'Donnell, MD, MPH; Lewis Kuller, MD, DrPh; Maryam Kavousi, MD, PhD; Raimund Erbel, MD; Hongyan Ning, MD, MS; Ralph D'Agostino, PhD; Anne B. Newman, MD, MPH; Khurram Nasir, MD; Albert Hofman, MD, PhD; Nils Lehmann, PhD; Klodian Dhana, MD, PhD; Ron Blankstein, MD; Udo Hoffmann, MD, MPH; Stefan Möhlenkamp, MD; Joseph M. Massaro, PhD; Amir-Abbas Mahabadi, MD; Joao A. C. Lima, MD; M. Arfan Ikram, MD, PhD; Karl-Heinz Jöckel, PhD; Oscar H. Franco, MD, PhD; Kiang Liu, PhD; Donald Lloyd-Jones, MD, ScM; Philip Greenland, MD

- Objective: to examine predictability of coronary artery calcium score (CACS) over age in initial ASCVD events.
- Pooled Cohort Analysis (Framingham, MESA, CHS, Rotterdam Study, Heinz Nixdorf Recall Study) 4778 pts
- Minimum age 60, mean age 70
- CACS had a greater association with incident CHD (not stroke) than age
- CACS can help guide statin initiation or discontinuation

Figure 1. Kaplan-Meier Curves of the Cumulative Probability of Atherosclerotic Cardiovascular Disease (ASCVD) Event-Free by Coronary Artery Calcium (CAC) Categories in Original Cohorts



No. at risk				
CAC 0	1470	1379	1228	148
CAC 1-100	1471	1306	1056	145
CAC 101-300	1472	693	525	61
CAC >300	1077	888	618	84

The cumulative probability of free of ASCVD events by CAC categories is shown; ASCVD included coronary heart disease and stroke. The log-rank was used to calculate *P* values. CHD indicates coronary heart disease.

Guidelines-Primary Prevention

Recommendations for Older Adults Referenced studies that support recommendations are summarized in Online Data Supplements 18 and 19.		
COR	**LOE**	**Recommendations**
IIb	**B-R**	**1. In adults 75 years of age or older with an LDL-C level of 70 to 189 mg/dL (1.7 to 4.8 mmol/L), initiating a moderate-intensity statin may be reasonable (S4.4.4.1-1–S4.4.4.1-8)**
IIb	**B-R**	**2. In adults 75 years of age or older, it may be reasonable to stop statin therapy when functional decline (physical or cognitive), multimorbidity, frailty, or reduced life-expectancy limits the potential benefits of statin therapy (S4.4.4.1-9).**
IIb	**B-R**	**3. In adults 76 to 80 years of age with an LDL-C level of 70 to 189 mg/dL (1.7 to 4.8 mmol/L), it may be reasonable to measure CAC to reclassify those with a CAC score of zero to avoid statin therapy (S4.4.4.1-10, S4.4.4.1-11).**

Statins for Primary Prevention >75yrs

Ongoing trials

- PREVENTABLE:
  - RCT
  - 20,000 patients >75 yrs of age
  - Atorvastatin 40mg vs placebo’
  - Primary Outcome includes dementia and physical disability at 4 yrs
- STAREE:
  - Australian community-based RCT
  - 18,000 pts >70 yrs of age
  - Atorvastatin 40mg vs placebo
  - Overall survival, disability-free survival

Statin-associated symptoms (SAS)

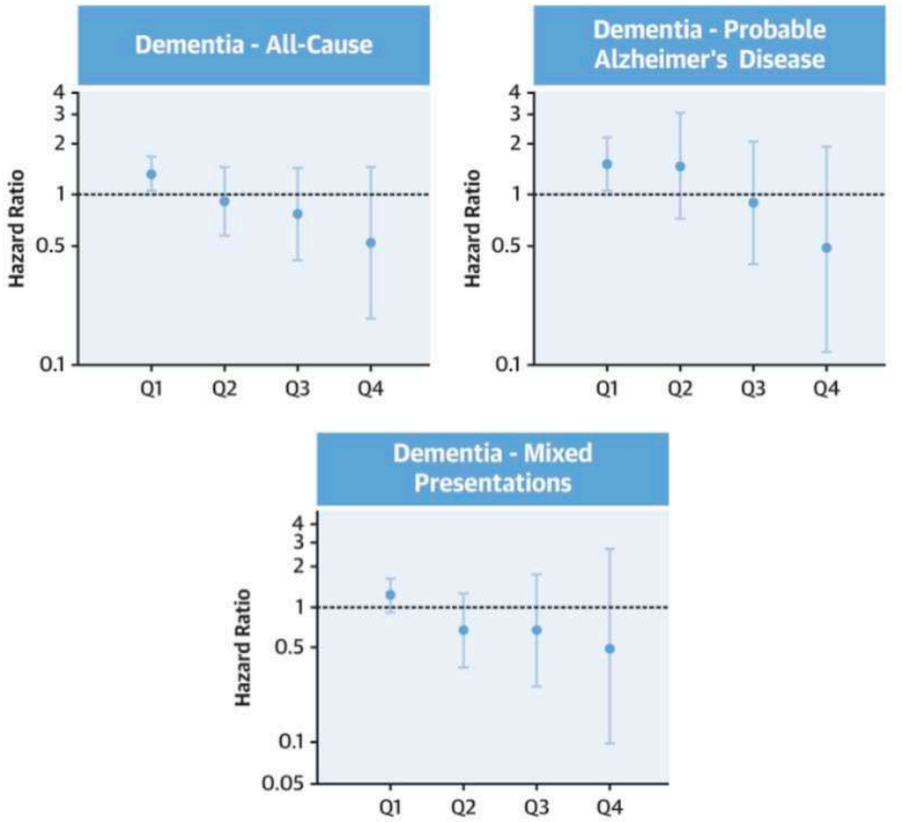
- Muscle symptoms are more often mistaken for true myopathy
- Modest increase in statin-induced diabetes more commonly occurs in those already predisposed (metabolic syndrome)
- Potential benefit not as well described in pts >75 yrs of age must be weighed against life expectancy and potential for SAS.
- Evidence does not currently support the suspicion that statins cause memory loss, cognitive impairment, or dementia.

Effect of Statin Therapy on Cognitive Decline and Incident Dementia in Older Adults

Zhen Zhou, PhD,[a] Joanne Ryan, PhD,[b] Michael E. Ernst, PharmD,[c,d] Sophia Zoungas, MBBS, PhD,[b] Andrew M. Tonkin, PhD,[b] Robyn L. Woods, PhD,[b] John J. McNeil, MBBS, PhD,[b] Christopher M. Reid, PhD,[e] Andrea J. Curtis, PhD,[b] Rory Wolfe, PhD,[b] Jo Wrigglesworth, BSc(Hons),[b] Raj C. Shah, MD,[f] Elsdon Storey, MBBS, DPhil,[b] Anne Murray, MD, MS,[c,g,h] Suzanne G. Orchard, PhD,[b] Mark R. Nelson, MBBS, PhD,[a] on behalf of the ASPREE Investigator Group

- Observational study from the ASPREE database
- 18,846 patients >65yrs old.
- Follow up 4.6 yrs
- Outcome measures: composite z score for all 4 cognitive tests used
  - Incident dementia and subclassifications
  - Mild cognitive impairment (MCI) and subclassifications
  - Domain specific cognition: memory, language and executive function, psychomotor speed, composite.

CENTRAL ILLUSTRATION: Statin Use, Dementia, and Its Subclassifications, by Baseline Composite Cognition



Quartiles of Composite Cognitive z Score (Range)	Dementia HR (95% CI)*	Dementia-Probable AD HR (95% CI)*	Dementia-Mixed Presentations HR (95% CI)*
1st quartile (−2.68 to −0.48)	1.34 (1.07-1.68)	1.53 (1.07-2.18)	1.23 (0.92-1.64)
2nd quartile (−0.48 to 0.04)	0.92 (0.58-1.47)	1.50 (0.73-3.07)	0.67 (0.36-1.26)
3rd quartile (0.04 to 0.51)	0.78 (0.42-1.46)	0.90 (0.39-2.07)	0.67 (0.26-1.75)
4th quartile (0.51 to 2.51)	0.53 (0.19-1.49)	0.49 (0.12-1.94)	0.50 (0.10-2.69)
p interaction between statin use and baseline composite cognition (treated as a continuous variable)			
	<0.001	*0.01*	*0.007*

Zhou, Z. et al. J Am Coll Cardiol. 2021;77(25):3145-56.

Statins and Cognitive Decline

Summary

- Over 4.5 yrs statins not associated with incident dementia, mild cognitive impairment or cognitive change
- No difference between lipophilic or hydrophilic statins
- If anything, patients in lower cognitive quartile at baseline had higher hazards for dementia and change in episodic memory (component in testing most associated with AD).
- 2 ongoing randomized trials to assess effects on cognition of statins in pts with pre-existing mild cognitive impairment.


Thank You