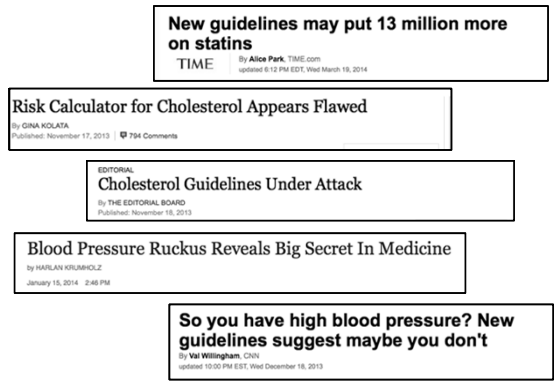
Guidelines for the Management of Cardiovascular Risk

CONSENSUS OR CONTROVERSY?

Brent N. Reed, PharmD, BCPS-AQ Cardiology, FAHA
Assistant Professor, Department of Pharmacy Practice and Science
University of Maryland School of Pharmacy



Headlines from NPR, *The New York Times*, and *Time*

WHY THE CONTROVERSY?

- Significant departure from previous editions
- Discrepancies between experts
- Evidence-based, but unanswered questions

> "… not a substitute for clinical judgment, and decisions about care must carefully consider… each individual patient."
>
> **- JNC8 Guidelines**

Parachute use to prevent death and major trauma related to gravitational challenge: systematic review of randomised controlled trials

BMJ

Gordon C S Smith, Jill P Pell

"Parachutes reduce the risk of injury after gravitational challenge, but their effectiveness has not been proved with randomized controlled trials"

BMJ 2003;327:1459-1461.

LEARNING OBJECTIVES

- Describe pharmacologic management of blood cholesterol and blood pressure
- Summarize evidence responsible for major changes in updated practice guidelines
- Recognize where important questions remain

GUIDELINES FOR BLOOD CHOLESTEROL

Stone NJ, et al. *Circulation*. 2013.

TRIAL DATA

Statin vs. Control

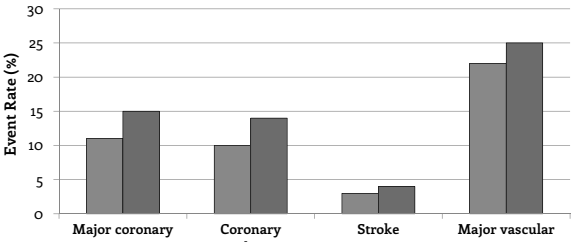
- SSSS
- HPS
- ALLIANCE
- CARDS
- JUPITER
- ASCOT-LLA
- Post-CABG
- WOSCOPS
- PROSPER
- CARE
- LIPID
- ASPEN
- AURORA
- AFCAPS/ TexCAPS
- LIPS
- GISSI-HF
- 4D
- ALERT
- MEGA
- ALLHAT-LLT
- GISSI-P

More vs. Less Statin

- PROVE-IT
- TNT
- IDEAL
- SEARCH
- A to Z

SECONDARY PREVENTION

5-year absolute benefits per mg/dL LDL-C reduction

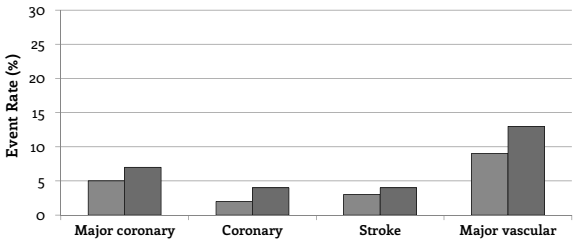


Outcomes avoided per 1000 (95% CI)	Major coronary events	Coronary revascularization	Stroke	Major vascular events
	30 (24-37)	27 (20-34)	8 (4-12)	48 (39-57)

Adapted from Lancet 2005; 366(9493):1267-78.

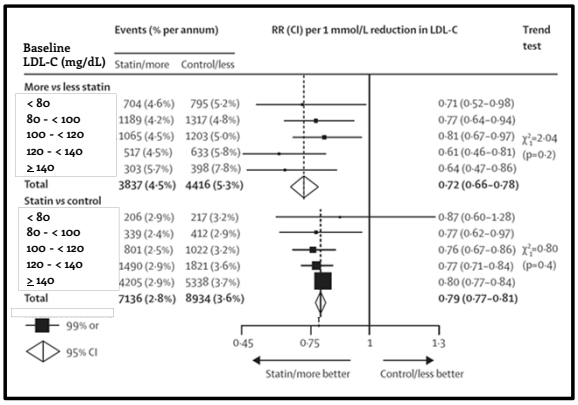
PRIMARY PREVENTION

5-year absolute benefits per mg/dL LDL-C reduction



Outcomes avoided per 1000 (95% CI)	Major coronary events	Coronary revascularization	Stroke	Major vascular events
	18 (14-23)	12 (9-16)	5 (1-8)	25 (19-31)

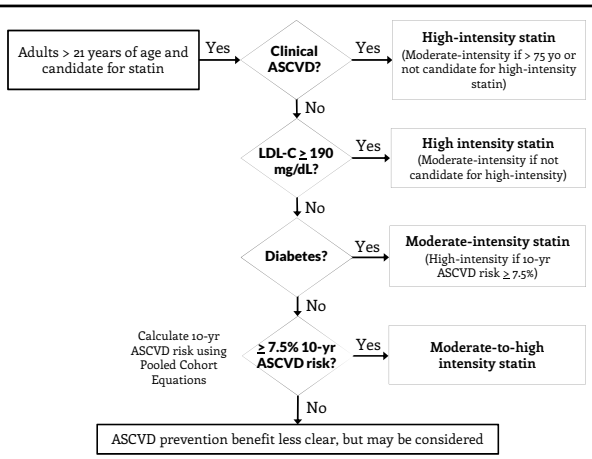
Adapted from Lancet 2005; 366(9493):1267-78.



Reduction of vascular events by baseline LDL-C. Adapted from Lancet. 2010 Nov 13;376(9753):1670-81. LDL-C values converted to non-SI units, and rounded to nearest 20 mg/dL.

AREAS OF INADEQUATE EVIDENCE

- Titration of statin therapy to LDL-C or non-HDL-C targets, or "lower is better" strategy
- Adjunct use of non-statin therapies
- Symptomatic heart failure (NYHA Class II-IV) or hemodialysis-dependent kidney disease
- Age < 40 or > 75 years



STATIN INTENSITY

High Intensity (Lowers LDL-C by ≥ 50%)	**Moderate-Intensity** (Lowers LDL-C by 30-50%)	**Low-Intensity** (Lowers LDL-C by < 30%)
Atorvastatin 40-80 mg Rosuvastatin 20-*40* mg	Atorvastatin 10-*20* mg Rosuvastatin *5*-10 mg Simvastatin 20-40 mg Pravastatin 40-*80* mg Lovastatin 40 mg Fluvastatin 40 mg BID *Pitavastatin 2-4 mg*	*Simvastatin 10 mg* Pravastatin 10-20 mg Lovastatin 20 mg *Fluvastatin 20-40 mg* *Pitavastatin 1 mg*

Statins and doses listed in italics are approved for use but have not been studied in randomized controlled trials. Adapted from Stone NJ, et al. 2013 ACC/AHA Blood Cholesterol Guideline.

RISK FACTORS FOR ADVERSE EVENTS

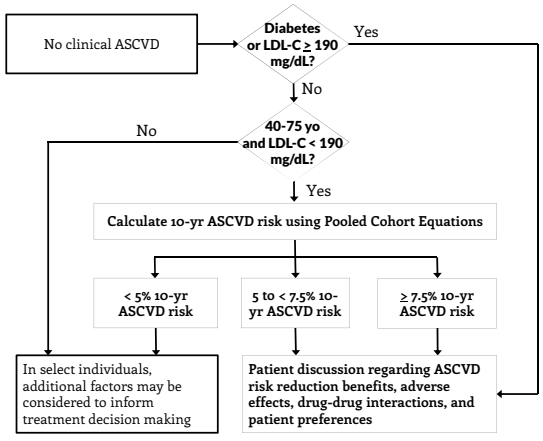
- Multiple or serious comorbidities
- History or statin intolerance, muscle disorders
- Unexplained ALT elevations > 3 times ULN
- Patient characteristics and/or concomitant medications affecting statin metabolism
- Age > 75 years

STATINS IN PRIMARY PREVENTION

- Absolute benefit proportional to baseline risk
- Risk reduction proportional to LDL-C lowering
- Risk for adverse events must be weighed against risk of catastrophic CVD event
- Clear net benefit at 10-year ASCVD risk ≥ 7.5%; less clear at 5 to < 7.5%

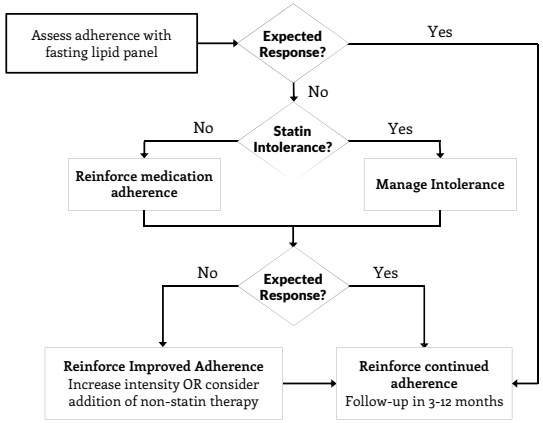
RISK CALCULATOR

Image from ASCVD Risk Calculator App (iTunes).



PRIOR TO STATIN INITIATION

- Emphasize heart-healthy lifestyle
- Obtain baseline laboratories
  - Fasting lipid panel
  - Alanine transaminase (ALT)
  - Creatinine kinase (CK) if indicated
- Exclude secondary causes of dyslipidemia
- Evaluate for risk of drug-related adverse effects



NON-STATIN THERAPIES

Agent	Improved Outcomes†	Monitoring
Niacin	• Mortality (all-cause, CV) • Recurrent CV events	• Hepatic transaminases • Hgb A1C or FBG • Uric acid concentrations • Intolerance (flushing)
Fibrates	• Mortality (CV) • Recurrent CV events	• Renal function • Triglycerides (for potential benefit if added to statin) • Avoid gemfibrozil/statin combination
Bile Acid Sequestrants	• Recurrent CV events	• Triglycerides (adverse effect)
Fish Oil	• CV mortality	• Intolerance (GI disturbances, skin changes, bleeding)
Ezetimibe	• None	• Hepatic transaminases

†In the absence of statin therapy. CV = cardiovascular, FBG = fasting blood glucose, GI = gastrointestinal, Hgb = hemoglobin

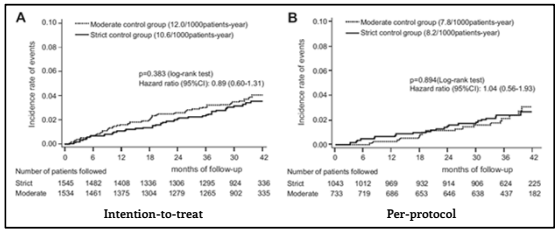
GUIDELINES FOR BLOOD PRESSURE

James PA, et al. *JAMA.* 2014; 311(5):507-520.

MAJOR DIFFERENCES FROM JNC7

Topic	Difference in JNC8
Methodology	• Systematic search and review process • Standardized protocol for recommendations
Definitions	• Hypertension, prehypertension not defined
Treatment goals	• Similar except when trial evidence supported different goals in a specific subgroup
Lifestyle recommendations	• Addressed separately
Drug therapy	• ACEi or ARB, CCB, or thiazide • Specific drug in racial or disease subgroups
Review process	• Expert review from various organizations • No official sponsorship

AGE-STRATIFIED GOALS



Strict vs. Moderate Blood Pressure Control in Older Patients

Showing no differences in the primary composite endpoint when a goal of < 140 mmHg (strict) vs. 140-150 mmHg (moderate) was compared.

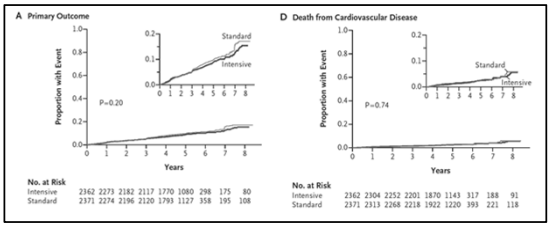
Hypertension. 2010;56:196-202.

CHRONIC KIDNEY DISEASE

- No improvement in cardiovascular outcomes at lower BP goals (i.e., < 130 / 80 mmHg)
- Some improvement in kidney-related outcomes in post-hoc analyses but results inconsistent

Lancet. 2005;365(9463):939-946. JAMA. 2002;288(19):2421-2431. N Engl J Med. 1994;330(13):877-884.

DIABETES MELLITUS



Systolic Blood Pressure Goals in Diabetes Mellitus

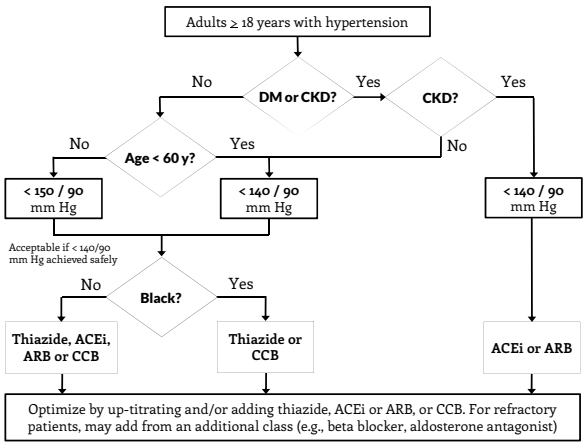
Showing no differences in the primary composite endpoint and cardiovascular death when a goal SBP of < 140 mmHg vs. < 120 mmHg was compared.

N Engl J Med. 2010;362(17):1575-1585.

SELECTION OF INITIAL THERAPY

- Non-blacks: similar improvements with ACEi or ARB, calcium channel blockers, or thiazides
- Blacks: calcium channel blockers or thiazides prior to ACEi or ARB
- Not impacted by presence of diabetes
- ACEi or ARB recommended as initial therapy in chronic kidney disease

JAMA. 1991;265(24):3255-3264. JAMA. 1979;242(23):2562-2571. JAMA. 1970;213(7):1143-1152. JAMA. 2002;288(23):2981-2997. JAMA. 2002;288(19):2421-2431.



ANTIHYPERTENSIVE STRATEGIES

Strategy	Description
A	Start with one drug, titrate to maximum dose, then add a second drug
B	Add second drug before achieving a maximum dose of first drug
C	Begin two drugs at same time either as separate pills or combination pill

- Select ACEi or ARB, CCB, or thiazide first
- Avoid ACEi / ARB combination therapy
- Consider Strategy C if BP > 160/100 or if SBP is > 20 over goal and DBP is > 10 over goal (mm Hg)

Class	Medication	Initial Daily Dose (mg)	Target Daily Dose (mg)	Doses/day
ACEi	Captopril	50	150-200	twice
	Enalapril	5	20	once to twice
	Lisinopril	10	40	once
ARB	Candesartan	4	12-32	once
	Losartan	50	100	once to twice
	Valsartan	40-80	160-320	once
	Irbesartan	75	300	once
CCB	Amlodipine	2.5	10	once
	Diltiazem ER	120-180	360	once
Thiazide diuretic	Chlorthalidone	12.5	12.5-25	once
	Hydrochlorothiazide	12.5-25	25-100	once to twice

ACEi = ACE inhibitor, ARB = angiotensin receptor blocker, CCB = calcium channel blocker. International drugs omitted from table. Adapted from James PA, et al. JAMA 2014;311(5):507-520.

EVIDENCE FOR RECOMMENDATIONS

Group	Recommendation	Grade
Age ≥ 60 y	Goal < 150 / 90 mmHg	A (Strong)
Age < 60 y	Goal < 140 / 90 mmHg	E (Expert opinion) (SBP) A (Strong) (DBP)
CKD	Goal < 140 / 90 mmHg	E (Expert opinion)
DM	Goal < 140 / 90 mmHg	E (Expert opinion)
Non-blacks	Thiazide, ACEi/ARB, or CCB	B (Moderate)
Blacks	Initial: CCB or thiazide	B (Moderate) (non-DM) C (Weak) (DM)
CKD	Initial ACEi or ARB	B (Moderate)
All	Strategies for achieving goal	E (Expert opinion)

REMAINING QUESTIONS

Blood Cholesterol

- Primary prevention in older populations
- Alternate strategies for reducing ASCVD risk
- Non-statin therapies added to low-dose statin
- Diabetes risks
- New therapies vs. statins

Blood Pressure

- Goals for older patients with high-risk features
- Goals in younger patients
- Non-hypertensive populations (e.g., HF)
- Which optimization strategy is best?

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