Using the New Lipid and Blood Pressure Guidelines in Your Clinical Practice

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New lipid guidelines

- 2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults
- Statins beneficial across broad range of LDLs and patient populations
  - Except CHF II-IV and hemodialysis?
- No RCTs titrated lipid therapy to goal
- Treat based on presence of certain high-risk features or calculation of overall risk

Stone NJ, et al. 2013 ACC/AHA Blood Cholesterol Guideline

Question #1

- Which of the following groups does NOT have at least moderate or strong evidence supporting use of statin therapy?

A) Age ≤ 75 with clinical atherosclerotic cardiovascular disease (ASCVD)
B) Age ≥ 21 with LDL ≥ 190
C) Age 40-75 with diabetes mellitus (DM)
D) Age 40-75 (without ASCVD or DM) and estimated 10-year ASCVD risk ≥ 7.5%
E) Age >75 with ASCVD and/or DM

4 “statin benefit” groups

1) Age ≤ 75 with clinical atherosclerotic cardiovascular disease (ASCVD)
  - High-intensity statin
  - Grade: A / I / A

2) Age ≥ 21 with LDL ≥ 190
  - High-intensity statin
  - B / I / B

Stone NJ, et al. 2013 ACC/AHA Blood Cholesterol Guideline

4 “statin benefit” groups

3) Age 40-75 with diabetes mellitus
- Moderate-intensity statin (A / I / A)
- High-intensity if 10-year ASCVD risk ≥ 7.5%
  - E / IIa / B

4) Age 40-75 (without ASCVD or DM) and estimated 10-year ASCVD risk ≥ 7.5%
- Moderate- to High-intensity statin
- A / I / A

Stone NJ, et al. 2013 ACC/AHA Blood Cholesterol Guideline

Statin intensity?

Rosuva Atorva Simva Lova/Prava Fluva

(Rosuva 5mg ≈ Atorva 10mg ≈ Simva 20mg ≈ Lova/Prava 40mg ≈ Fluva 80mg)

- High-intensity: atorva 40-80mg
- Medium-intensity: atorva 10-20mg

Answer: E

Stone NJ, et al. 2013 ACC/AHA Blood Cholesterol Guideline

Question #2

- 56yo woman with total cholesterol of 302, HDL 68, TGs 71, and LDL 220. No history of hypertension, no family history of cardiovascular disease, no medications, BP 126/70.
- What is the most appropriate next step?

A) Recommend high-intensity statin / intensive lifestyle changes
B) Recommend intensive lifestyle changes alone
C) Estimate her 10-year ASCVD risk
D) Check a TSH, liver metabolic panel, urinalysis
E) Recheck a lipid panel in 1 year

Really high LDL (≥190)

ACC/AHA 2013 recommendations:

- High-intensity statin without estimation of 10-year risk (B / I / B)
  - Based on high lifetime risk of ASCVD
- Target ≥ 50% LDL reduction (E / IIa / B)

Stone NJ, et al. 2013 ACC/AHA Blood Cholesterol Guideline
Lancet 2010;376:1670–81

Really high LDL (≥190)

- Eval for 2º cause if LDL ≥190 or TG ≥500

Secondary Cause	Elevated LDL–C	Elevated Triglycerides
Diet	Saturated or *trans* fats, weight gain, anorexia	Weight gain, very low-fat diets, high intake of refined carbohydrates, excessive alcohol intake
Drugs	Diuretics, cyclosporine, glucocorticoids, amiodarone	Oral estrogens, glucocorticoids, bile acid sequestrants, protease inhibitors, retinoic acid,
		anabolic steroids, sirolimus, raloxifene, tamoxifen, beta blockers (not carvedilol), thiazides
Diseases	Biliary obstruction, nephrotic syndrome	Nephrotic syndrome, chronic renal failure, lipodystrophies
Disorders and altered states of metabolism	Hypothyroidism, obesity, pregnancy*	Diabetes (poorly controlled), hypothyroidism, obesity; pregnancy*

- Excess EtOH, uncontrolled DM, albuminuria, hypothyroidism, meds

Stone NJ, et al. 2013 ACC/AHA Blood Cholesterol Guideline

Really high LDL (≥190)

- By the way, her 10-year ASCVD risk?

→ 2.7% (Lifetime risk: 39%)

- Would you recommend high-intensity statin?

- Consider: family history, hs-CRP, coronary artery calcium score, ABIs. (E / IIb / B)
  - Don't use CIMT
  - ?ApoB, CKD, Ualb, fitness level – no rec

Answer: D

Goff DC Jr, et al. 2013 ACC/AHA Cardiovascular Risk Guideline

Question #3

- 40 yo man with total cholesterol 170, HDL 50, LDL 90. African American, smokes 1/2 PPD, HTN on 2 meds but often forgets to take his pills. BP 160/90. 10-year ASCVD risk is 12.5%.
- Which of the following would NOT be an appropriate next step?

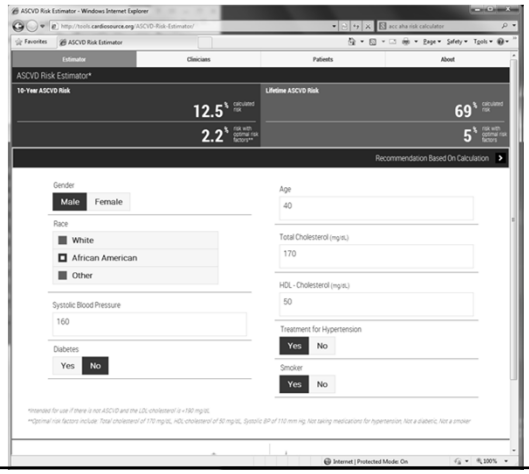
A) Recommend a moderate-intensity statin
B) Recommend diet / activity changes
C) Explore barriers to medication adherence
D) Assess motivation & confidence to quit smoking
E) They are all appropriate

Low cholesterol, high CV risk

- Don't forget about other modifiable risks
  - Smoking cessation
  - Blood pressure control
  - Aspirin

- Have some fun with the risk calculator…

Answer: E



Question #4

- 59 yo woman with total cholesterol 280, HDL 25, TGs 560 (fasting), LDL 85. HTN on lisinopril, no other meds, no smoking or alcohol. BP is 140/80. A1c is 5.9%, TSH, CMR, UA all normal. 10-year ASCVD risk is 11%.
- In addition to intensive lifestyle counseling, what else would you recommend?

A) Statin
B) Fibrate
C) Niacin
D) Statin + fibrate
E) Statin + niacin

High TGs, Low LDL

- ATP III: fibrate or niacin (before statin) if TGs > 500 (to prevent pancreatitis)
- 2012 Endocrine Society guidelines and 2011 AHA scientific statement: Risk for pancreatitis is only if TGs >> 1000
  - Link between TGs and CVD also questionable

ATP III Executive Summary 2001
Circulation 2011;123:2292-2333
J Clin Endocrinol Metab 2012;97: 2969–2989

Fibrates and niacin

- No effect on all-cause or CV mortality
  - ↓ non-fatal MI in monotherapy only
- ACCORD Lipid -- Adding fibrate to statin
  - No CV benefit (except maybe if ↑TG + ↓HDL)
- AIM-HIGH, HPS2-THRIVE -- Adding niacin
  - No CV benefit (despite ↑HDL, ↓TG, ↓LDL)

BMJ 2014;349:g4379 doi: 10.1136/bmj.g4379
NEJM 2010;362:1563-74
NEJM 2011;365:2255-67
NEJM 2014;371:203-12

Niacin concerns

- HPS2-THRIVE, AIM-HIGH (niacin)
  - ↑ flushing / GI side effects / glucose levels (no surprise)
  - Also ↑ infections (surprise)
- Also strong trend towards ↑mortality(!)
  - 0.5% ARI = NNH 200 (9% RRI)
  - p-value nearly significant (p=0.08)

→ AVOID Niacin due to harms (+no benefit)

NEJM 2014;371:203-12
NEJM 2014;371:271-3
NEJM2014;371:288-90

Answer: A

Question #5

- 63yo man with total cholesterol of 170, HDL 50, LDL 95. BP 110/70, not on any medications. Caucasian, no history of diabetes, lifelong non-smoker.
- What is his 10-year ASCVD risk based on the ACC/AHA calculator?

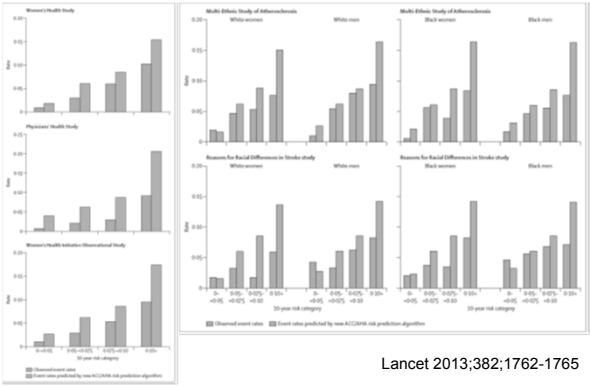
A) 1%
B) 2.5%
C) 5%
D) 7.5%
E) 10%

New ASCVD risk calculator

- Age at which 10-year ASCVD risk exceeds 7.5% despite "optimal" lipids, BP, etc?
  - Caucasian men: 63yo+
  - African American men: 66yo+
  - Women: 70-71yo+
- Uses cohort data from previous risk scores
  - e.g. Framingham, Reynolds, QRISK

Goff DC Jr, et al. 2013 ACC/AHA Cardiovascular Risk Guideline
Lancet 2013;382;1762-1765

Overestimates CV risk?



Lancet 2013;382;1762-1765

Outcome assessment issues?

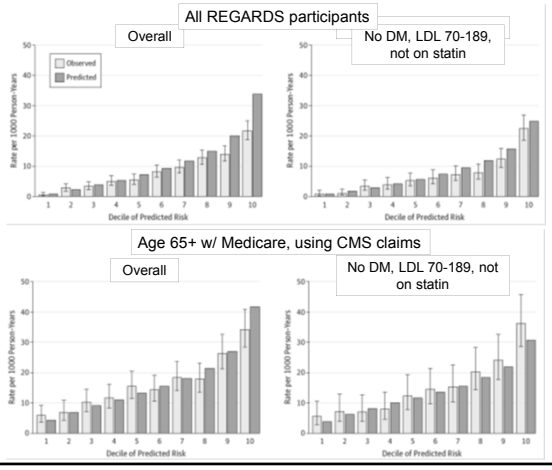
- Women's Health Initiative
  - WHI criteria: review of medical records
  - Medicare data: hospital discharge coding
- Outcome assessments
  - WHI criteria: 1345 MIs
  - Medicare criteria: 1501 MIs
  - WHI or Medicare: 1784 MIs

Circ Cardiovasc Qual Outcomes. 2014;7:157-162

Recent validation studies

- REGARDS cohort
  - 18,498 adults, 45+ yo, 48 US states + D.C.
    - 42% Black, 58% Women
  - Outcome assessment:
    - q6mo telephone f/u
    - Also used Medicare claims data when possible

JAMA. 2014;311(14):1406-1415



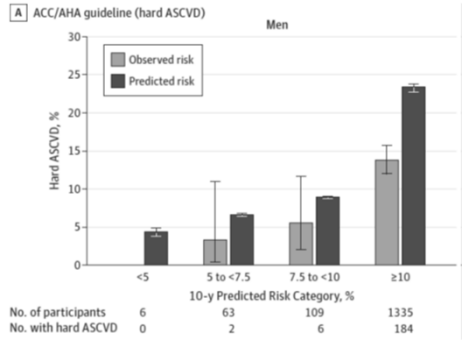
JAMA. 2014;311(14):1406-1415

Recent validation studies

- Rotterdam Study
  - 4209 participants, 55+ yo, single Rotterdam suburb, not on statin
  - Outcomes via automated f/u system + manual review of pt records + hospital records + f/u interviews

JAMA 2014;311:1416-1423
Eur J Epidemiol 2012;27:173–185

Rotterdam Study



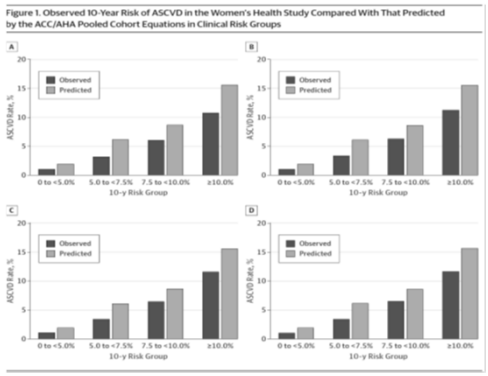
JAMA. 2014;311(14):1416-1423

Recent validation studies

- Women's Health Study cohort
  - 27,542 women, 45-79yo, followed for 10y
  - Adjustments for statins, revascularizations
  - Analysis of under-ascertainment

JAMA Intern Med 2014:174;1910-1971

Women's Health Study



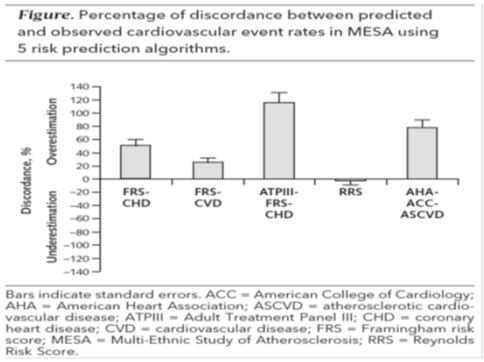
JAMA Intern Med 2014:174;1910-1971

Recent validation studies

- Multi-Ethnic Study of Atherosclerosis (MESA)
  - 4227 people, 50-74yo, no diabetes
  - 42% White, 26% African American, 20% Hispanic, 12% Chinese
  - 54% women
  - Evaluated new risk calculator along with 3 Framingham scores and Reynold Risk Score
  - Adjusted for ASA, lipid/BP meds, revascularizations

Ann Intern Med 2015;162:266-275

MESA



Ann Intern Med 2015;162:313-314

New ASCVD risk calculator

- The new risk calculator may overestimate risk – substantially in some cases
  - Consider calculating risk using multiple different calculators (e.g. Reynolds)
- Strict adherence to the 7.5% cutoff → statin therapy for 80% of 60+ yo adults

→ take calculated risk and 7.5% cutoff with a grain of salt

BMJ 2012;344:e3318doi:10.1136/bmj.e3318
Goff DC Jr, et al. 2013 ACC/AHA Cardiovascular Risk Guideline
J Am Coll Cardiol 2015; doi: 10.1016/j.jacc.2015.02.025.

Age- and sex-specific thresholds?

- 7.5% threshold: may undertreat younger patients and overtreat older patients
- Studied sensitivities and specificities of varying treatment thresholds
- Consider (more study needed):
  - All 40-55yo and women 56-65yo: 5%
  - Men 56-65yo: 7.5%
  - Women 66-75yo: 10%
  - Men 66-75yo: 15-20%

Answer: D

J Am Coll Cardiol 2015; doi: 10.1016/j.jacc.2015.02.025.

Question #6

- 55 yo man with total cholesterol 220, HDL 40, TGs 150, LDL 150. Caucasian, no significant past medical history, no family history of vascular disease or smoking. His BP is 130/75. His 10-year ASCVD risk is 7.8%
- What is the most appropriate next step?

A) Recommend a statin
B) Recommend intensive lifestyle changes
C) A and B
D) Recheck lipids in 3 months
E) Engage in a shared decision making process

Putting it all together…

- Use of global CV risk information:
  - Improves accuracy of risk perception
  - Increases statin Rx's in mod-high risk patients
  - May reduce predicted CV risk over time
- Use of decisions aids improves:
  - Knowledge of options, benefits, and harms
  - Informed values-based choices
  - Patient involvement in decision making
  - Patient-practitioner communication

BMC Health Services Research 2008;8:60-73
Arch Int Med 2010;170:230-9
Cochrane Database of Syst Rev 2011, Issue 11

Statin risks

- Liver failure: *really rare* -- 1 in 1,000,000 pt-years
  - Idiosyncratic; routine monitoring not helpful
  - Liver disease: not contraindication to statin use (except ALF or decompensated cirrhosis)
- Muscle: myalgias -- 5-10%, rhabdo – 1 in 10,000
- Diabetes: 1 extra case per 255 on statin for 4 years
  - 1 fewer CV event per 24 on statin for 5 years

Am J Cardiol 2006;97[suppl]:77C–81C
Stone NJ, et al. 2013 ACC/AHA Blood Cholesterol Guideline
Ann Intern Med 2009;150:858-868
Lancet 2010;376:1670–81
Lancet 2012; 380: 581–90

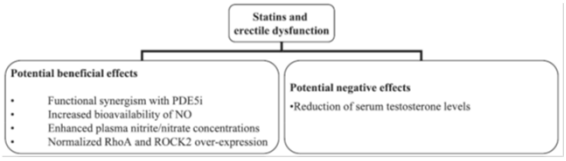
Statin risks -- others(?)

- Statins and memory loss:
  - FDA 2012 label change – rare post-marketing reports of cognitive impairment
  - Onset 1 day to years, generally not serious
  - Reversible (median 3 weeks)
- 3 recent systematic reviews:
  - No adverse effect on cognition; possible reduction in Alzheimer's

http://www.fda.gov/drugs/drugsafety/ucm293101.htm
Ann Intern Med 2013;159:688-697
Mayo Clin Proc 2013;88:1213-1221
J Gen Intern Med 2015;30:348-58

Statin risks -- others(?)

- Statins and Erectile Dysfunction?
  - 2002 review: possible link (case reports)
  - 2012 review: statins may improve erection quality (alone or w/ sildenafil)



→ Probably a little of both

Family Practice 2002;19:95-98
J Androl 2012;33:552–558

Putting it all together…

- Mayo statin decision aid

statindecisionaid.mayoclinic.org/

Answer: E

Question #7

- 67 yo woman w/ PMH of DM II, HTN, and hyperlipidemia, on metformin 1000mg BID, lisinopril 10mg daily, and atorvastatin 20mg daily. Average BP:135/85. HbA1c 7.8%, Cr 0.9, Urine alb/cr ratio 16 mg/g.
- Which of the following is the most appropriate next step in her blood pressure management?

A) Add diltiazem
B) Add amlodipine
C) Add hydrochlorothiazide
D) Increase the dose of lisinopril
E) No change in blood pressure meds

Blood pressure targets in diabetes

JNC 7:

- Goal blood pressure < 140/90
- Exceptions:
  - Diabetes Mellitus
  - Chronic Kidney Disease

  → goal blood pressure < 130/80

JAMA 2003;289:2560-2572

Blood pressure targets in diabetes

- ACCORD BP:
  - 4733 pts w/ high-risk DM, HbA1c ≥ 7.5%
  - SBP goals of <120 vs <140 mmHg
  - SBPs achieved: 119 vs 133.5 mmHg
  - No change in primary CV outcome at 4.7y
    - reduction in CVA: 0.32% vs 0.53%
  - SBP <120: ↑ serious adverse events (ARI 2%)
- No difference for microvascular outcomes

NEJM 2010;362:1575-85
Kidney Int 2012;81:586-594

Blood pressure targets in diabetes

- 2011 meta-analysis (broad inclusion):
  - 13 RCTs, 37,736 pts, BP <135 vs <140
  - No difference in overall macro/microvacular outcomes
  - ↓ mortality by 10% (BP 130-135), ↓ CVA by 17%
  - ↑ serious adverse effects by 20%
- 2012 meta-analysis (strict inclusion):
  - 5 RCTs, 7312 pts, DBP <75-80 vs <90, + ACCORD
  - No difference in mortality or MI
  - ↓ CVA by 35% (1% ARI)

Circulation 2011;123:2799-2810
Arch Intern Med 2012;172:1296-1303

Blood pressure targets in CKD?

- JNC 7 & NKF K/DOQI: < 130/80
- Extrapolated from recommendations for other high-risk groups (e.g. diabetes)
- Annals 2011 systematic review:
  - 3 RCTs, 2272 patients
  - No clear benefit from lower BP targets
  - Possible benefit in proteinuric patients

Am J Kidney Dis 2004;43:S1-S290
Ann Intern Med 2011;154:541-548

What's new in JNC 8?

- Diabetes: BP goal < 140/90 (grade: E)
- CKD: BP goal < 140/90 (E)
  - Insufficient evidence for CKD + age >70

Answer: E

2014 Evidence-Based Guideline for the Management of High Blood Pressure in Adults (JNC 8). JAMA 2013

Question #8

- 65 yo woman w/ PMH HTN and chronic stable angina on ASA, metoprolol, and lisinopril. No CP, SOB, edema, HAs, lightheadedness. Healthy diet, regular exercise. Average BP: 145/85. HR 60, nl CV exam, no edema. Cr 0.9, K 4.2, UA neg.
- Which of the following is the most appropriate next step in management?

A) Add a thiazide
B) Add losartan
C) Add amlodipine
D) Increase metoprolol dose
E) No change in blood pressure meds

BP targets in older patients

- SHEP (chlorthalidone +/- atenolol) – age 60+
  - Target SBP: 20 pts lower (or <160)
  - Achieved SBPs of 143 vs 155
  - CVA: 3 fewer per 100 pts (also ↓CV events)
- HYVET (Indapamide +/- perindopril) – age 80+
  - Target SBP: 150/80 (vs placebo)
  - Achieved SBPs of 144 vs 159
  - Death: 12.4 fewer per 1000 pt-yrs

NEJM 2008;358:1887-98

BP targets in older patients

- JATOS (efonidipine) – age 65-85
  - Target SBP < 140 vs SBP 140-160
  - Achieved SBPs of 136 vs 146
  - No change in CV / renal outcome
- VALISH (valsartan) – age 70-84
  - Target SBP <140 vs SBP 140-150
  - Achieved SBPs of 137 vs 142
  - No change in CV / renal outcome

Hypertens Res 2008;31:2115–2127
Hypertension 2010;56:196-202

What's new in JNC 8?

- Age 60+: BP goal < 150/90 (A)
  - But okay if already <140/90 on meds (E)
- Minority dissent on this recommendation:
  - Citing SHEP / HYVET, and safety in JATOS/VALISH
  - JATOS/VALISH – short f/u, Japanese population
  - Many groups use 80+yo as cutoff for SBP < 150

2014 Evidence-Based Guideline for the Management of High Blood Pressure in Adults (JNC 8). JAMA 2013
Ann Intern Med. Published online 14 January 2014 doi:10.7326/M13-2981

Other considerations

- SBP<130 + ≥2 BP meds in ≥80yo= bad
  - HR 1.78 for mortality (nursing home cohort)
- Caution w/ DBP <60 if ≥ 60yo or DM
  - 2015 AHA/ACC/ASH guideline (C level evidence)
- VA CKD cohort study: DBP < 70 associated w/ worse mortality than mod-high SBP (e.g. BP 155/75 better than 130/60)

Answer: E

JAMA Intern Med. doi:10.1001/jamainternmed.2014.8012
J Am Coll Cardiol. 2015. doi:10.1016/j.jacc.2015.02.038
Annals Intern Med 2013;159:233-242

Question #9

- 42 yo man w/ new diagnosis of HTN, average BP 145/90 after intensive lifestyle improvements. Normal serum electrolytes and creatinine, UA negative, EKG wnl. Otherwise healthy.
- Which of the following is the most appropriate next step in management?

A) Lisinopril
B) Chlorthalidone
C) Amlodipine
D) Atenolol
E) No medication, continued monitoring

Initial Therapy in HTN

- BMJ 2009 meta-analysis:
  - All classes similar efficacy for reducing CHD events and CVA
  - Beta-blockers extra protection first few years post-MI
  - CCBs slight advantage for CVA prevention
- Cochrane 2009 meta-analysis:
  - Low-dose thiazides (HCTZ <50mg/day, chlorthalidone <50mg/day): strongest evidence
  - ACE-I: similar benefit, less evidence
  - CCBs: insufficient evidence
  - β-blockers (atenolol) and high-dose thiazides: inferior

BMJ 2009;338:b1665
Cochrane Database of Systematic Reviews 2009

Initial Therapy(?) in HTN

- Cochrane 2012: mild hypertension
  - BP 140-159 / 90-99, primary prevention
  - 4 RCTs, 8912 patients, 4-5y f/u
  - No change in mortality, CHD, CVA, CV events
  - 9% ARI of withdrawals due to adverse effects
- Caveats:
  - Low event rates, mostly driven by a single trial (MRC), half on propranolol-based Rx
  - Wide confidence intervals
  - Long enough follow-up?

Cochrane Database Syst Rev 2012;8 :CD006742

Initial Therapy(!) in HTN

- 2015 update w/ individual patient-data from BPLTTC database
- More power: 6391 additional pts (96% w/ DM, 61% w/ previous anti-HTsives)
  → 2x total # of pts, 4x # of CV events
- Mostly ACE-I trials, a few CCB trials
- Results: ↓CVA, ↓CV deaths, ↓mortality
  - Similar RRRs in BPLTTC and non-BPLTTC trials

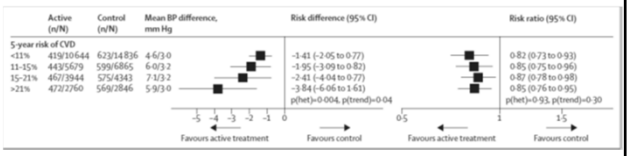
Ann Intern Med 2015;162:184-191.

Anti-HTsives in normotension

- JAMA 2011 meta-analysis:
  - Anti-HTsives in normotensive patients w/ CVD
  - 25 RCTs, 64,000 patients
  - ↓ mortality, CVA, MI, CHF, total CVD events
- Eur Heart J 2012 meta-analysis:
  - ACE-I or ARB in normotensive patients w/ CVD or CVD risk factors
  - 13 RCTs, 80,000 patients
  - ↓ composite CV endpoint, CV mortality

JAMA 2011;305:913-922
Eur Heart J 2012;33:505-514

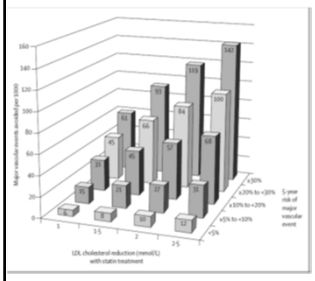
Risk-based HTN treatment?



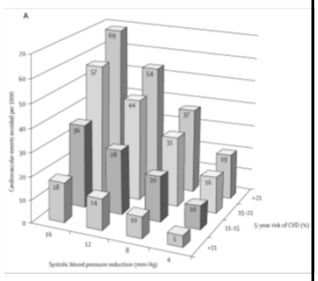
- Relative risk reductions (right):
  - Not affected by baseline risk (~15%)
- Absolute risk reductions (left):
  - ↑ baseline risk → ↑ absolute benefit
  - 5y NNT: 71 (if low risk) → 26 (if high risk)

Lancet 2014;384:591-8

Sound familiar?



CV events prevented:
Lipid reduction w/ statin



CV events prevented:
Blood pressure reduction

Lancet 2014;384:591-8

What's new in JNC 8?

- Age < 60: DBP goal < 90 (A)
- Age < 60: SBP goal < 140 (E)
- First-line therapy: thiazide, CCB, ACE, or ARB (B)
  - African Americans: thiazide or CCB (B)
- Consider overall CV risk when managing HTN
- Really push lifestyle changes

Answer: A, B, C, E

2014 Evidence-Based Guideline for the Management of High Blood Pressure in Adults (JNC 8). JAMA 2013

Take home points

- No more LDL "goals" – focus on CV risk
- Remember non-lipid risk factors
- Consider statin if:
  - Age ≤ 75 with ASCVD
  - Age ≥ 21 with LDL ≥ 190
  - Age 40-75 with diabetes mellitus (DM)
  - Age 40-75 (without ASCVD or DM) and estimated 10-year ASCVD risk ≥ 7.5%

Take home points – lipids

- Minimize use of fibrates, avoid niacin
- New risk calculator may overestimate risk – substantially, in some cases
- Use the "guide"-lines as a guide for shared decision making

Take home points – BP

- Age 60+: goal BP < 150/90
  - Maybe age 80+?
- Age <60: goal BP < 140/90
  - 140 may be a soft goal if low-risk
- DM or CKD: goal BP < 140/90
  - Across ages (not sure for CKD and age 70+)
- 1st line: thiazide, CCB, ACE, ARB
  - Thiazide or CCB if African American
- Consider overall CV risk and med burden