

**PREVENTION OF  
CARDIOVASCULAR DISEASE IN  
WOMEN:  
Implications of the New Guidelines  
for Hypertension and Lipids**

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**Disclosure**

No relevant financial  
relationships

**EXPLAINING THE DECREASE IN  
DEATHS FROM CVD**

1980 to 2000: death rate fell by approximately  
50% in both men and women

2000 to 2010: Death still falling: down 31%

- About 1/2 from acute treatments, 1/2 from  
risk factor modification:
- **Predominantly cholesterol (1/4), BP,  
smoking**

Go, Circulation, 2014

**New Lipid Guidelines**

ACC/AHA December 2013

### Prevention Of CVD in Women

- Overwhelming majority of recommendations are the same for women and for men
- But...there are gender differences in the *magnitude of the absolute potential benefits*

Mosca, Circulation 2011

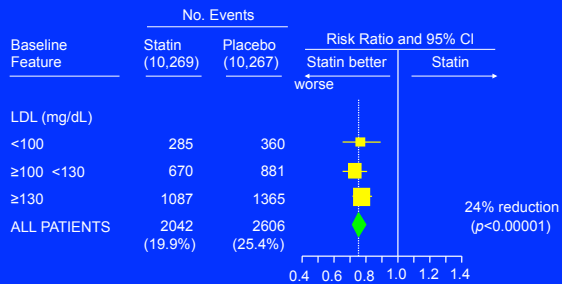
### 2013 ACC/AHA Guidelines

What is New?

- 4 groups of patients who benefit from statins
- Identifies high and moderate intensity statins
- No LDL treatment targets
- Non-statin therapies no not provide acceptable risk reduction
- Estimate 10-year ASCVD risk with new equation

Stone, Circulation 2013

### Heart Protection Study: Vascular Events by Baseline LDL-C



### 2013 ACC/AHA Guidelines

Four Groups of Patients Who Benefit From Statins

- Individuals with clinical ASCVD
- Individuals with primary elevations of LDL ≥190
- Individuals age 40-75 with diabetes and LDL ≥ 70
- Individuals without ASCVD or diabetes, age 40-75, with LDL ≥ 70, and 10 year risk 7.5% or higher

Stone, Circulation 2013

**2013 ACC/AHA Guidelines**  
**Importance of Lifestyle Recommendations**

- Heart healthy diet
- Regular aerobic exercise
- Desirable body weight
- Avoidance of tobacco

Stone, Circulation 2013

**2013 ACC/AHA Guidelines**  
**What Statin for Each Group?**

- **Individuals with clinical ASCVD:**
  - Treat with: high intensity statin, or moderate intensity statin if > age 75
- **Individuals with primary elevations of LDL  $\geq$ 190:**
  - Treat with: high intensity statin

Stone, Circulation 2013

**2013 ACC/AHA Guidelines**  
**What Statin for Each Group?**

- **Individuals 40-75 with diabetes and LDL  $\geq$  70:**
  - Treat with: moderate intensity statin, or high intensity statin if risk over 7.5%
- **Individuals without ASCVD or diabetes, 40-75, with LDL  $\geq$  70, and 10 year risk 7.5% or higher:**
  - Treat with: moderate-to-high intensity statin

Stone, Circulation 2013

**2013 ACC/AHA Guidelines**  
**High Intensity vs. Moderate Intensity Statin**

- **High Intensity: lowers LDL by >50%**
  - Atorvastatin 40 - 80
  - Rosuvastatin 20 - 40
- **Moderate Intensity: lowers LDL by 30-50%**
  - Atorvastatin 10 - 20
  - Rosuvastatin 5 - 10
  - Simvastatin 20 - 40
  - Pravastatin 40 - 80
  - Lovastatin 40

Stone, Circulation 2013

## How Best To Calculate 10 Year Risk?

### Old Issues

- Hard vs. hard + soft CHD end points (angina)
- CHD or CVD
- Include diabetes or not
- Include peripheral vascular disease or not
- Race/ethnicity (usually not)
- Include family history and hs-CRP (Reynolds)
- Ranges vs. exact numbers
- Paper vs. computer vs. phone

## How Best To Calculate 10 Year Risk?

### Old Issues

- Insufficient shared decision making

## How Best To Calculate 10 Year Risk?

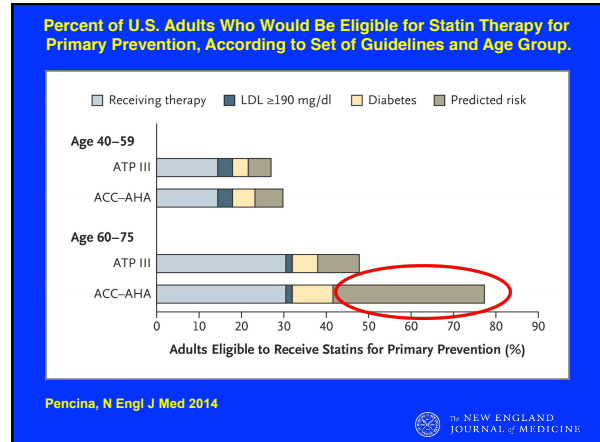
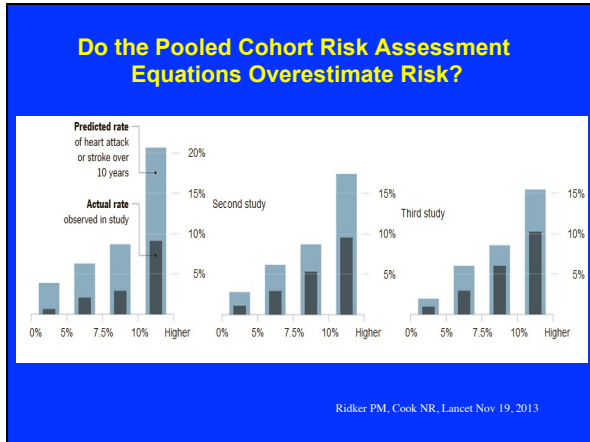
### New

### Pooled Cohort Risk Assessment Equations: hard CHD events and stroke

- [http://my.americanheart.org/professional/StatementsGuidelines/PreventionGuidelines/Prevention-Guidelines\\_UCM\\_457698\\_SubHomePage.jsp](http://my.americanheart.org/professional/StatementsGuidelines/PreventionGuidelines/Prevention-Guidelines_UCM_457698_SubHomePage.jsp)
- <http://www.cardiosource.org/en/Science-And-Quality/Practice-Guidelines-and-Quality-Standards/2013-Prevention-Guideline-Tools.aspx>
- <http://clincalc.com/Cardiology/ASCVD/PooledCohort.aspx>

## Pooled Cohort Risk Assessment Equations

- Age
- Gender
- Race (White/African American)
- Total cholesterol (170 mg/dl)
- HDL cholesterol (50 mg/dl)
- Systolic BP (110 mmHg)
- Yes/no meds for BP
- Yes/no DM
- Yes/no cigs
- Outcome: 10-year risk of total CVD (fatal and non-fatal MI and stroke)



### How Best To Calculate 10 Year Risk? Baron Approach December 2014

- Use both CHD (hard end points) calculator and new CV risk calculator
- Include both in shared decision-making discussion

### Summary Lipid-Lowering Drugs

- Statins are treatment of choice based on RCT to decrease risk
- No evidence to support adding niacin or fibrates to statins
- If completely statin-intolerant, niacin may reduce CVD risk (weak evidence)
- Fibrates appear to lower MI risk, but no other CVD endpoints

### Summary Lipid-Lowering Drugs

• Ezetimibe: new study (IMPROVE-IT) presented as abstract November 2014

18,000 ACS patients (40% from North America)

RCT: Simvastatin vs simvastatin + ezetimibe.  
Took 7 years. Death, MI, Stroke

Simvastatin: 34.7% vs Simva/ezetimibe 32.7%  
(270 fewer events over 7 years)

63 yo woman, no traditional risk factors

LDL 155  
HDL 55  
TG 160  
SBP 120  
No BP meds  
No DM  
Nonsmoker

### The best next step in lipid management is to calculate 10 year risk and:

1. Continue current therapy (no meds)
2. Begin atorvastatin 40
3. Begin atorvastatin 10
4. Begin simvastatin 20
5. Begin sustained release niacin
6. Begin red yeast rice

### 2013 ACC/AHA Guidelines What Statin for Each Group?

- Individuals without ASCVD or diabetes, 40-75, with LDL  $\geq$  70, and 10 year risk 7.5% or higher:
  - Treat with: moderate-to-high intensity statin

Stone, Circulation 2013

**63 yo woman, no risks**

LDL 155, HDL 55, TG 160  
SBP 120, No BP meds  
Nonsmoker, No DM

10 yr CHD risk (old calculator): 2%...  
10 yr CV risk (new calculator): 4.5%...

**Therefore no medication recommended**

**63 yo man, no risks**

LDL 155, HDL 55, TG 160  
SBP 120, No BP meds  
Nonsmoker, No DM

10 yr CHD risk (old calculator): 10%...  
10 yr CV risk (new calculator): 10.8%...

**“Toss-up.” Shared decision making. If start statin (per new guidelines), can start with moderate intensity statin**

**The Good and The Controversial of the New Cholesterol Guidelines**

- Focus on healthy lifestyle is **good**
- Focus to use statins (and not other agents) is **good**
- Focus to treat patients at high risk is **good**
- Focus to treat all patients with LDL <190 mg/dl and treat patients with DM/existing CV disease is **good**
- Not having target LDL is **controversial**
- Adults with no DM or heart disease and 10-year calculated risk >7.5% (using new risk calculator) to be treated – **controversial**

**NSAIDs and CVD: Meta-analysis**  
31 RCTs, 116,429 patients

MI: No increase naproxen, diclofenac  
Ibuprofen 1.61; celecoxib 1.35

Stroke: All drugs increased  
Naproxen 1.76, Ibuprofen 3.36, Diclofenac 2.86

CV death: No increase naproxen  
Ibuprofen 2.39, diclofenac 3.98, celecoxib 2.07

Total death: All drugs increased  
Naproxen 1.23, Ibuprofen 1.77, Diclofenac 2.31, celecoxib 1.50

Trelle S. BMJ 2011

### Competing Risks

- Example: women with 10-year risk 10%
- Reduce risk by 30% with statins. Risk now 7%.
- Add NSAID. Increase risk by 50%
- Total risk now back to 10%.

### Lipid Conclusions I

- Statins are effective and cost effective in selected groups of patients
- Screen most patients (shared decision-making) at age 21 (to identify those > LDL 190, other genetic lipid disorders)

### Lipid Conclusions II

- Use statins in women with ASCVD, LDL  $\geq$ 190 and diabetes
- For those without ASCVD and diabetes, calculate 10 year risk (how best uncertain), and treat those with risk greater than 7.5% (maybe 10%). Use shared decision making.
- Use appropriate intensity statin (high and moderate)

### Lipid Conclusions III

- Monitor adherence, but do not treat to specific LDL goal
- Do not treat those over age 75 (unless ASCVD), on dialysis or moderate/severe CHF
- Do not treat with other lipid-modifying drugs in addition to statins (but may need if truly statin intolerant)
- Avoid other factors that raise risk as much as statins lower it (i.e. NSAIDS)



## New Hypertension Guidelines

Joint National Committee  
(JNC) 8  
February, 2014

## Current Status of Hypertension

Prevalence 29%; Blacks 33.5%

About 72.5% treated; 53.5% uncontrolled (>140/90)

Risk for poor control: Latinos, Blacks, age 18-44 and ≥80, <300% poverty, < college degree

Better control: Any insurance, ≥2 visits, and a usual source of care

MMWR 2012;61: 703-709

## Accurate BP Measurement

- 1) Seated for 5 minutes in chair
- 2) Arms bared and supported
- 3) No cigs, coffee; no talking
- 4) Correct fitting cuff for arm (small cuff results in elevated BP)
- 5) First appearance of sound is SBP; disappearance is DBP
- 6) Two or more reading in 2 minutes averaged
- 7) Two visits to define HTN

## Joint National Commission 8 (JNC 8)

### Three questions:

- 1) Does Rx at specific BP thresholds improve outcomes?
- 2) Does Rx to a specific BP goal improve outcomes?
- 3) Do various meds differ on outcomes?

## Nine recommendations

73 yo woman. BP=148/88. No DM. Creat  
1.1. Otherwise well. On non-drug therapy.  
The next best step is:

1. Continue current therapy
2. Begin hydrochlorothiazide
3. Begin Ace Inhibitor
4. Begin Calcium Channel Blocker
5. Begin beta blocker

Recommendations for Management of Hypertension

Recommendation 1

≥60 years:

❖ Lower BP at SBP ≥150 mm Hg or DBP ≥90 mm Hg

❖ Treat to a goal SBP <150 mm Hg and goal DBP <90 mm Hg.

**Strong Recommendation – Grade A (but not unanimous)**

JAMA 2014;311(5):507-520.

**Recommendation 1**

Evidence from 6 studies of patients over age 60, treated to goal ≤150/90: HYVET, Syst-Eur, SHEP, JATOS, VALISH, CARDIO-SIS

Some evidence (lower quality) comparing ≤160 to ≤140 and ≤150 to ≤140 showing no additional benefit

**Hypertension in the Very Elderly Trial (HYVET)**

3845 patients ≥ 80 y, 2 years

>160 mm Hg – goal of 150/80 mm Hg  
BP=173/91

Indapamide SR 1.5 mg vs. placebo  
Added perindopril if needed

Beckett NS, NEJM 2008; 358: 1887-1898

## HYVET Study Results

End Point	Meds	Placebo	HR (95% CI)
Stroke	12.4	17.7	0.64 (0.46 -0.95)
CVA Death	6.5	10.7	0.55 (0.33 -0.93)
CHF	5.3	14.8	0.28 (0.17 -0.48)
CV Death	23.9	30.7	0.73 (0.55 -0.97)
Any Death	47.2	59.6	0.72 (0.59-0.88)

Beckett NS. NEJM 2008; 358: 1887-1898

## HYVET Conclusions and Implications

Benefits appear at 1 year of Rx

NNT = 20 to prevent one stroke

NNT = 10 to prevent one CHF

Never too old to treat SBP > 160

Goal does not have to be < 140

73 yo woman. BP=148/88. No DM. Creat  
 1.1. Otherwise well. On non-drug therapy.  
 The next best step is:

1. Continue current therapy
2. Begin hydrochlorothiazide
3. Begin Ace Inhibitor
4. Begin Calcium Channel Blocker
5. Begin beta blocker

### Recommendations for Management of Hypertension

#### Corollary Recommendation

≥60 years:

✧ If treatment results in lower SBP (eg, <140 mm Hg) and is well tolerated treatment does not need to be adjusted.

Expert Opinion – Grade E

JAMA.2014;311(5):507-520.

### Recommendations for Management of Hypertension

#### Recommendation 2

<60 years:

- ❖ Treat to lower BP at DBP  $\geq$ 90 mm Hg
- ❖ Treat to a goal DBP <90 mm Hg.

**30-59 years, Strong Recommendation – Grade A**  
**18-29 years, Expert Opinion – Grade E**

JAMA.2014;311(5):507-520.

### Recommendations for Management of Hypertension

#### Recommendation 3

<60 years:

- ❖ Treat to lower BP at SBP  $\geq$ 140 mm Hg
- ❖ Treat to a goal SBP <140 mm Hg.

(Expert Opinion – Grade E)

JAMA.2014;311(5):507-520.

### Recommendations for Management of Hypertension

#### Recommendation 4

$\geq$ 18 years with chronic kidney disease (CKD)  
(GFR < 60 or proteinuria >30 mg alb/g creat):

- ❖ Treat to lower SBP  $\geq$ 140 mm Hg or DBP  $\geq$ 90 mm Hg
- ❖ Treat to goal SBP <140 mm Hg and goal DBP <90 mm Hg.

JAMA.2014;311(5):507-520.

**Expert Opinion – Grade E**

### Recommendations for Management of Hypertension

#### Recommendation 5

❖  $\geq$ 18 years with diabetes, treat to lower BP at SBP  $\geq$ 140 mm Hg or DBP  $\geq$ 90 mm Hg

❖ Treat to a goal SBP <140 mm Hg and goal DBP <90 mm Hg.

**Expert Opinion – Grade E**

JAMA.2014;311(5):507-520.

### Intensive BP Control in Type 2 DM: ACCORD

- RCT of 4733 patients with type 2 DM
- Compare BP less than 120 mm Hg vs 140

	120	140	P
• BP	119	133	
• CV events plus death	1.87%	2.09%	.20
• Mortality	1.28%	1.19%	.55
• Stroke	0.32%	0.53%	.01
• Adverse events	3.3%	1.3%	.001

In type 2 DM: treating to 120 mm Hg did not reduce the rate of composite fatal and non-fatal CV events

ACCORD, NEJM 2010

### Recommendations for Management of Hypertension

#### Recommendation 6

Nonblack population, including diabetes:

Initial treatment:

- ✓Thiazide-type diuretic
- ✓Calcium channel blocker (CCB)
- ✓Angiotensin-converting enzyme inhibitor (ACEI)
- ✓Angiotensin receptor blocker (ARB).

(Moderate Recommendation – Grade B

JAMA.2014;311(5):507-520.

**53 yo African-American man, BP=148/88. + DM Type 2, Creatinine 1.1. Otherwise well. On non-drug therapy. The next best step is:**

- 1) Continue current therapy
- 2) Begin hydrochlorothiazide
- 3) Begin ace inhibitor
- 4) Begin calcium channel blocker
- 5) Begin angiotensin receptor blocker

### Recommendations for Management of Hypertension

#### Recommendation 7

Black population, including diabetes:

Initial treatment:

- ✓Thiazide-type diuretic
- ✓Calcium Channel Blocker (CCB)

**General black population: Moderate Rec – Grade B**

**Black patients with diabetes: Weak Rec – Grade C**

JAMA.2014;311(5):507-520.

**53 yo African-American man, BP=148/88. + DM Type 2, Creatinine 1.1. Otherwise well. On non-drug therapy. The next best step is:**

- 1) Continue current therapy
- 2) Begin hydrochlorothiazide
- 3) Begin ace inhibitor
- 4) Begin calcium channel blocker
- 5) Begin angiotensin receptor blocker

### Recommendations for Management of Hypertension

#### Recommendation 8

≥18 years with CKD, initial (or add-on) treatment:

- ❖ ACEI or ARB to improve kidney outcomes.
- ❖ For all CKD patients with HTN regardless of race or diabetes

**Moderate Recommendation – Grade B**

JAMA.2014;311(5):507-520.

### Recommendations for Management of Hypertension

#### Recommendation 9

❖ If goal BP not reached within 1 month, increase the dose of the initial drug or add a second drug from one of the classes in recommendation 6 (thiazide-type diuretic, CCB, ACEI, or ARB).

❖ Assess BP and adjust the treatment regimen until goal is reached.

❖ If goal cannot be reached with 2 drugs, add and titrate a third drug from the list provided.

JAMA.2014;311(5):507-520.

### Recommendations for Management of Hypertension

#### Recommendation 9

❖ Do not use and ACE and an ARB in the same patient.

❖ If goal cannot be reached using the drugs in rec 6 drugs from other classes can be used.

❖ Referral to a specialist may be indicated

**❖ Expert Opinion – Grade E**

JAMA.2014;311(5):507-520.

### Evidence-based Medications

#### ACE inhibitors

Captopril  
Enalapril  
Lisinopril

#### Angiotensin receptor blockers

Eprosartan  
Candesartan  
Losartan  
Valsartan  
Irbesartan

### Evidence-based Medications

#### Beta blockers

Atenolol,  
Metoprolol

#### Calcium channel blockers

Amlodipine,  
Diltiazem ER  
Nitrendipine

#### Thiazide-type diuretics

Bendroflumethiazide,  
Chlorthalidone,  
Hydrochlorothiazide,  
Indapamide

### Key Points of JNC 8

- 1)  $\geq 60$  yo: goal  $\leq 150$
- 2) Others  $< 140/90$  (including DM, CKD, race/ethnicity)
- 3) Non blacks: thiazide, CCB, ACEI, ARB
- 4) Blacks: thiazide, CCB
- 5) CKD: ACEI or ARB

### One Other Key Point

Take the BP accurately yourself, and record it in the medical record.