Hypertension Guidelines: JNC-“Late”, JNC-“8”, or JNC-“Fake”? 

Brian G. Choi, MD, MBA, FACC 
Associate Professor of Medicine 
Co-Director, Advanced Cardiac Imaging 

November 14, 2014 
Washington, DC
Disclosures

None Relevant to This Presentation
The Timeline

- 1997: NHLBI released its first clinical practice guideline for hypertension (“JNC-1”)
- 2003: JNC-7
- 2008: JNC-8 panel appointed
- June 2012: internal review at NIH finds that NHLBI is the lone NIH institute that continues to be engaged in clinical guideline development
- June 19, 2013: NHLBI requests ACC/AHA to assume governance and management of guideline development
- “We are inviting all chairs and members of the current writing panels to continue to work together with us to finalize the guidelines.”

Imagine You Are on The JNC-8 Panel
The Aftermath

- 2 senior NHLBI representatives on JNC-8 panel withdrew
- 1 senior scientist from NIDDK withdrew
- 2 other members withdrew “because of new job commitments”
- 17 panel members continued on, to complete their work in January 2013 and then submitted their manuscript for external peer review to 20 “experts” and 16 federal agencies
- June 2013: revised manuscript sent to JAMA without review by ACC or AHA

HC Sox. JAMA 2014;311:472.
Kim Williams: “Because the JNC 8 panel chose not to be part of the AHA-ACC structure, we felt we needed to go forward to make sure that we had guidance that reflected the evidence. We felt the need to have risk covered as best we could, and have some hypertension guidance out there, even if it is not a guideline.”

Hypertension 2014;63:878.
Hypertension 2014;63:878.

### Systolic 140–159 or diastolic 90–99
- **Stage 1 hypertension**
- Lifestyle modifications as a trial
- Consider adding thiazide

#### Recheck and review readings in 3 months*^4^

**BP at goal?**
- Thiazide for most patients or ACEI, ARB, CCB, or combo
- If currently on BP med(s), titrate and/or add drug from different class

#### Recheck and review readings in 2–4 weeks*^2^

**BP at goal?**
- Yes
  - Encourage self-monitoring and adherence to meds
  - Advise patient to alert office if he/she notes BP elevation or side effects
  - Continue office visits as clinically appropriate

- No
  - Optimize dosage(s) or add medications
  - Address adherence, advise on self-monitoring, and request readings from home and other settings
  - Consider secondary causes

Consider referral to HTN specialist

### Systolic >160 or diastolic >100
- **Stage 2 hypertension**
- Two drugs preferred:
  - Lifestyle modifications and
  - Thiazide and ACEI, ARB, or CCB
  - Or consider ACEI and CCB

#### Recheck and review readings in 2–4 weeks*^2^

**BP at goal?**
- Yes
  - Encourage self-monitoring and adherence to meds
  - Advise patient to alert office if he/she notes BP elevation or side effects
  - Continue office visits as clinically appropriate

- No
  - Optimize dosage(s) or add medications
  - Address adherence, advise on self-monitoring, and request readings from home and other settings
  - Consider secondary causes

Consider referral to HTN specialist

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*Recheck interval should be based on patient’s risk of adverse outcomes

This algorithm should not be used to counter the treating healthcare provider’s best clinical judgment.
William White: “ASH leaders had discussions with the JNC 8 panel last summer, but the two groups could not reach an agreement on how to use the panel’s work for management recommendations.”
Blood Pressure >140/90 in Adults Aged >18 years
(For age >80 years, pressure >150/90 or >140/90 if high risk [diabetes, kidney disease])

Start Lifestyle Changes
(Lose weight, reduce dietary salt and alcohol, stop smoking)

Drug Therapy
(Consider a delay in uncomplicated Stage 1 patients)*

Stage 1
140-159/90-99

Black Patients
CCB or Thiazide
If Needed, Add ...
ACE-i or ARB OR combine CCB+Thiazide
If Needed ...

non-Black Patients

Age <60 Years
ACE-i or ARB
If Needed, Add ...
CCB or Thiazide
If Needed ...

Age >60 Years
CCB or Thiazide
If Needed, Add ...
ACE-i or ARB
If Needed ...

Stage 2
>160/100

All Patients
Start With 2 Drugs
CCB or Thiazide + ACE-i or ARB
If Needed ...

Special Cases
- Kidney disease
- Diabetes
- Coronary disease
- Stroke history
- Heart failure [see table of recommended drugs for these conditions]

* In stage 1 patients without other cardiovascular risk factors or abnormal findings, some months of regularly monitored lifestyle management without drugs can be considered.

If Needed, Refer to a Hypertension Specialist
One Day Later…
Special Communication

2014 Evidence-Based Guideline for the Management of High Blood Pressure in Adults
Report From the Panel Members Appointed to the Eighth Joint National Committee (JNC 8)

Paul A. James, MD; Suzanne Oparil, MD; Barry L. Carter, PharmD; William C. Cushman, MD;
Cheryl Dennison-Himmelfarb, RN, ANP, PhD; Joel Handler, MD; Daniel T. Lackland, DrPH;
Michael L. LeFevre, MD, MSPH; Thomas D. MacKenzie, MD, MSPH; Olugbenga Ogedegbe, MD, MPH, MS;
Sidney C. Smith Jr, MD; Laura P. Svetkey, MD, MHS; Sandra J. Taler, MD; Raymond R. Townsend, MD;
Jackson T. Wright Jr, MD, PhD; Andrew S. Narva, MD; Eduardo Ortiz, MD, MPH

2014 Evidence-Based Guideline for the Management of High Blood Pressure in Adults
Report From the Panel Members Appointed to the Eighth Joint National Committee (JNC 8)

• 17 authors, 13 pages, 45 references, no endorsements
• JNC-7: 74 contributors, 104 pages, 386 references, 46 endorsements

<table>
<thead>
<tr>
<th>Topic</th>
<th>JNC 7</th>
<th>2014 Hypertension Guideline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methodology</td>
<td>Non-systematic literature review by expert committee including a range of study designs</td>
<td>Critical questions and review criteria defined by expert panel with input from methodology team</td>
</tr>
<tr>
<td></td>
<td>Recommendations based on consensus</td>
<td>Initial systematic review by methodologists restricted to RCT evidence</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Subsequent review of RCT evidence and recommendations by the panel according to a standardized protocol</td>
</tr>
<tr>
<td>Definitions</td>
<td>Defined hypertension and prehypertension</td>
<td>Definitions of hypertension and prehypertension not addressed, but thresholds for pharmacologic treatment were defined</td>
</tr>
<tr>
<td>Treatment goals</td>
<td>Separate treatment goals defined for “uncomplicated” hypertension and for subsets with various comorbid conditions (diabetes and CKD)</td>
<td>Similar treatment goals defined for all hypertensive populations except when evidence review supports different goals for a particular subpopulation</td>
</tr>
<tr>
<td>Lifestyle recommendations</td>
<td>Recommended lifestyle modifications based on literature review and expert opinion</td>
<td>Lifestyle modifications recommended by endorsing the evidence-based Recommendations of the Lifestyle Work Group</td>
</tr>
<tr>
<td>Drug therapy</td>
<td>Recommended 5 classes to be considered as initial therapy but recommended thiazide-type diuretics as initial therapy for most patients without compelling indication for another class Specified particular antihypertensive medication classes for patients with compelling indications, i.e., diabetes, CKD, heart failure, myocardial infarction, stroke, and high CVD risk Included a comprehensive table of oral antihypertensive drugs including names and usual dose ranges</td>
<td>Recommended selection among 4 specific medication classes (ACEI or ARB, CCB or diuretics) and doses based on RCT evidence Recommended specific medication classes based on evidence review for racial, CKD, and diabetic subgroups Panel created a table of drugs and doses used in the outcome trials</td>
</tr>
<tr>
<td>Scope of topics</td>
<td>Addressed multiple issues (blood pressure measurement methods, patient evaluation components, secondary hypertension, adherence to regimens, resistant hypertension, and hypertension in special populations) based on literature review and expert opinion</td>
<td>Evidence review of RCTs addressed a limited number of questions, those judged by the panel to be of highest priority.</td>
</tr>
<tr>
<td>Review process prior to publication</td>
<td>Reviewed by the National High Blood Pressure Education Program Coordinating Committee, a coalition of 39 major professional, public, and voluntary organizations and 7 federal agencies</td>
<td>Reviewed by experts including those affiliated with professional and public organizations and federal agencies; no official sponsorship by any organization should be inferred</td>
</tr>
</tbody>
</table>

Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCB, calcium channel blocker; CKD, chronic kidney disease; CVD, cardiovascular disease; JNC, Joint National Committee; RCT, randomized controlled trial

Set blood pressure goal and initiate blood pressure lowering—medication based on age, diabetes, and chronic kidney disease (CKD).

General population (no diabetes or CKD) vs Diabetes or CKD present:

- Age ≥60 years
  - Blood pressure goal: SBP < 150 mm Hg, DBP < 90 mm Hg

- Age <60 years
  - Blood pressure goal: SBP < 140 mm Hg, DBP < 90 mm Hg

- All ages
  - Diabetes present
    - Blood pressure goal: SBP < 140 mm Hg, DBP < 90 mm Hg
  - No CKD
    - Blood pressure goal: SBP < 140 mm Hg, DBP < 90 mm Hg

- All ages
  - CKD present with or without diabetes
    - Blood pressure goal: SBP < 140 mm Hg, DBP < 90 mm Hg

Nonblack vs Black:

- Initiate thiazide-type diuretic or ACEI or ARB or CCB, alone or in combination.⁸

Select a drug treatment titration strategy:
A. Maximize first medication before adding second or
B. Add second medication before reaching maximum dose of first medication or
C. Start with 2 medication classes separately or as fixed-dose combination.

At goal blood pressure?

Yes

Reinforce medication and lifestyle adherence.
For strategies A and B, add and titrate thiazide-type diuretic or ACEI or ARB or CCB (use medication class not previously selected and avoid combined use of ACEI and ARB).
For strategy C, titrate doses of initial medications to maximum.

No

At goal blood pressure?

Yes

Reinforce medication and lifestyle adherence.
Add and titrate thiazide-type diuretic or ACEI or ARB or CCB (use medication class not previously selected and avoid combined use of ACEI and ARB).

No

Reinforce medication and lifestyle adherence.
Add additional medication class (e.g., β-blocker, aldosterone antagonist, or others) and/or refer to physician with expertise in hypertension management.

Yes

Continue current treatment and monitoring.b

No

At goal blood pressure?
The Reaction

• Elliot Antman (AHA president-elect): “We are concerned that relaxing the recommendations may expose more persons to the problem of inadequately controlled blood pressure.”

• Gary Gibbons (NHLBI director): “JNC-8” is not sanctioned by NHLBI

• ACC/AHA press release: “Until…the revised hypertension guidelines are formally published, the ACC/AHA recognize the most recent hypertension guidelines, published in 2004 by the JNC-7, as the national standard.”

• AHA Statement to NCQA: “we would strongly urge NCQA not to adopt a SBP of less than 150 in those > age 60 at this time.”

“We, the panel minority, believed the evidence was insufficient to increase the SBP goal from its current level of <140 mmHg because of the concern that increasing the goal may cause harm…in Americans older than 60 years…A target of <140 mmHg for patients younger than 80 years would also be in line with guidelines from Europe, Canada, the UK, the ACC, the AHA and ASH/ISH.”

Ann Internal Medicine 2014;160:499.
<table>
<thead>
<tr>
<th>Name</th>
<th>JNC-8</th>
<th>ASH/ISH</th>
<th>Minority Report</th>
</tr>
</thead>
<tbody>
<tr>
<td>PA James</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>S Oparil</td>
<td>X</td>
<td></td>
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<tr>
<td>BL Carter</td>
<td>X</td>
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<td>WC Cushman</td>
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<td>C Dennison-Himmelfarb</td>
<td>X</td>
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<td>X</td>
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<tr>
<td>J Handler</td>
<td>X</td>
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<td>DT Lackland</td>
<td>X</td>
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<td>ML LeFevre</td>
<td>X</td>
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<td>TD MacKenzie</td>
<td>X</td>
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<td>O Ogedegbe</td>
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<td></td>
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<td>SC Smith Jr</td>
<td>X</td>
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<td>LP Svetsky</td>
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<tr>
<td>SJ Taler</td>
<td>X</td>
<td>X</td>
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<td>RR Townsend</td>
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<td>JT Wright Jr</td>
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<td>AS Narva</td>
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<tr>
<td>E Ortiz</td>
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</tbody>
</table>
Table 2. Trials Comparing Different Systolic Blood Pressure Thresholds

<table>
<thead>
<tr>
<th>Trial (Reference)</th>
<th>Participants, n</th>
<th>Duration, y</th>
<th>Total End Points, n</th>
<th>Primary Outcome</th>
<th>Coronary Heart Disease</th>
<th>Composite CVD</th>
<th>Strokes</th>
<th>Heart Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;150 mm Hg vs. higher goal</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HYVET (16)*</td>
<td>3845</td>
<td>2.1</td>
<td>Any CVD: 331 Strokes: 120 Deaths: 431</td>
<td>HR: 0.61 ( P = 0.046 )</td>
<td>HR: 0.72 (95% CI, 0.30–1.70) ( P = 0.45 )</td>
<td>–</td>
<td>HR: 0.61 ( P = 0.046 )</td>
<td>HR: 0.36 ( P &lt; 0.001 )</td>
</tr>
<tr>
<td>SHEP (15)</td>
<td>4736</td>
<td>4.5</td>
<td>Any CVD: 703 Strokes: 245 Deaths: 455</td>
<td>RR: 0.64 (CI, 0.50–0.82) ( P = 0.0003 )</td>
<td>RR: 0.73 (CI, 0.57–0.94) ( P &lt; 0.001 )</td>
<td>–</td>
<td>RR: 0.64 (CI, 0.50–0.82) ( P = 0.0003 )</td>
<td>RR: 0.51 (CI, 0.37–0.71) ( P &lt; 0.001 )</td>
</tr>
<tr>
<td>&lt;140 mm Hg vs. higher goal</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>JATOS (17)</td>
<td>4418</td>
<td>2</td>
<td>CVD or renal event: 172 Deaths: 17</td>
<td>Rate per 1000 PYs: 22.6 vs. 22.7 ( P = 0.99 )</td>
<td>Rate per 1000 PYs: 6.8 vs. 7.4 ( P = 0.78 )</td>
<td>Rate per 1000 PYs: 22.6 vs. 22.7 ( P = 0.99 )</td>
<td>Rate per 1000 PYs: 13.7 vs. 12.9 ( P = 0.77 )</td>
<td>8 vs. 7 events</td>
</tr>
<tr>
<td>VALISH (18)</td>
<td>3260</td>
<td>2.85</td>
<td>CVD or renal event: 99 Deaths: 54</td>
<td>HR: 0.89 (CI, 0.60–1.31) ( P = 0.383 )</td>
<td>HR: 1.23 (CI, 0.33–4.56) ( P = 0.761 )</td>
<td>HR: 0.89 (CI, 0.60–1.31) ( P = 0.383 )</td>
<td>HR: 0.68 (CI, 0.36–1.29) ( P = 0.237 )</td>
<td>–</td>
</tr>
<tr>
<td>FEVER (19)</td>
<td>9711</td>
<td>3.3</td>
<td>Any CVD: 575 Strokes: 428 Deaths: 263</td>
<td>HR: 0.73 ( P = 0.0019 )</td>
<td>HR: 0.68 ( P = 0.0153 )</td>
<td>HR: 0.73 ( P = 0.0002 )</td>
<td>HR: 0.73 ( P = 0.0019 )</td>
<td>HR: 0.70 ( P = 0.26 )</td>
</tr>
</tbody>
</table>

CVD = cardiovascular disease; FEVER = Felodipine Event Reduction; HR = hazard ratio; HYVET = Hypertension in the Very Elderly Trial; JATOS = Japanese Trial to Assess Optimal Systolic Blood Pressure in Elderly Hypertensive Patients; PY = person-year; RR = relative risk; SHEP = Systolic Hypertension in the Elderly Program; VALISH =Valsartan in Elderly Isolated Systolic Hypertension.
* Stopped by data and safety monitoring board because of mortality benefit.

Ann Internal Medicine 2014;160:499.
The Counter-Reaction

• Suzanne Oparil (JNC-8 Co-Chair): “It is very annoying that the AHA and ACC accept this paper in the *Annals*, which is not evidence based.”

• Drs. Taler, Townsend & Carter: “The ASH/ISH document was intended as an international primer with general information, especially in countries with low resources. The ASH/ISH document is ‘clearly’ not evidenced based and should be considered more as ‘an opinion piece.’”

Conclusion
Summary

• In a span of less than 3 months, 4 separate guidelines for the management of hypertension released

• “JNC-8” is not JNC-8 (and there will not be a JNC-8)

• Guideline development for hypertension will be in the hands of a joint ACC/AHA committee

• Until that guideline is released, JNC-7 remains the national standard

• Expect the new ACC/AHA guidelines late 2014/early 2015
My Personal Predictions for the New Guidelines

• Because of ACCORD, targeting more aggressive blood pressure goals for diabetic patients will not be recommended.

• Similarly aggressive goals for CKD patients will not be recommended because of a lack of non-kidney related outcomes in clinical trials.

• A <150/<90 mmHg goal may be adopted for those over 80 years old, but the <140/<90 mmHg standard will remain for the 60-80 year old population.
Cholesterol Guidelines Update:
“Treat-to-Target” to “Set-It-&-Forget-It”

Brian G. Choi, MD, MBA, FACC
Associate Professor of Medicine
Co-Director, Advanced Cardiac Imaging

November 14, 2014
Washington, DC
The 2013 ACC/AHA Cholesterol Guidelines

• Unlike the hypertension guidelines, the ACC/AHA expert panel included all 16 members of NHLBI’s NCEP-ATP IV and was completed under NHLBI’s auspices

• Endorsed by ACC, AHA, AAPA, AACPR, APA, ASPC, ABC, PCNA and WomenHeart

• Similar to hypertension guidelines, only randomized controlled trials, systematic reviews and meta-analyses of RCTs taken into consideration, “genetic and biochemical studies, observational epidemiological and ecological studies, and in vitro and animal experiments” were not included
Four Groups Identified to Benefit from Statins

- Individuals with clinical ASCVD (acute coronary syndromes, or a history of MI, stable or unstable angina, coronary or other arterial revascularization, stroke, TIA, or peripheral arterial disease presumed to be of atherosclerotic origin) without New York Heart Association (NYHA) class II-IV heart failure or receiving hemodialysis.
- Individuals with primary elevations of low-density lipoprotein cholesterol (LDL-C) ≥190 mg/dl.
- Individuals 40-75 years of age with diabetes, and LDL-C 70-189 mg/dl without clinical ASCVD.
- Individuals without clinical ASCVD or diabetes, who are 40-75 years of age with LDL-C 70-189 mg/dl, and have an estimated 10-year ASCVD risk of 7.5% or higher.
Heart healthy lifestyle habits are the foundation of ASCVD prevention. In individuals not receiving cholesterol-lowering drug therapy, recalculate estimated 10-y ASCVD risk every 4-6 y in individuals aged 40-75 y without clinical ASCVD or diabetes and with LDL–C 70-189 mg/dL.

**ASCVD Statin Benefit Groups**

- **Clinical ASCVD**
  - Yes
  - Age <75 y
  - High-intensity statin
    - Moderate-intensity statin if not candidate for high-intensity statin

- **LDL–C ≥190 mg/dL**
  - Yes
  - Age >75 y OR if not candidate for high-intensity statin
    - Moderate-intensity statin
  - No
    - High-intensity statin
      - Moderate-intensity statin if not candidate for high-intensity statin

- **Diabetes**
  - Type 1 or 2
  - Age 40-75 y
  - Yes
  - Estimated 10-y ASCVD risk ≥7.5%*
    - High-intensity statin
  - No
    - Moderate-intensity statin

- **Estimate 10-y ASCVD Risk with Pooled Cohort Equations**
  - Yes
    - ≥7.5% estimated 10-y ASCVD risk and age 40-75 y
      - Moderate-to-high intensity statin
  - No

*ASCVD prevention benefit of statin therapy may be less clear in other groups. In selected individuals, consider additional factors influencing ASCVD risk and potential ASCVD risk benefits and adverse effects, drug-drug interactions, and patient preferences for statin treatment.

**Definitions of High- and Moderate-Intensity Statin Therapy**

- **High**
  - Daily dose lowers LDL–C by approx. ≥50%

- **Moderate**
  - Daily dose lowers LDL–C by approx. 30% to <50%

---

*See Table 5*
Pooled Cohort Equations for ASCVD Risk Prediction

Web Version Available at www.americanheart.org
### Pooled Cohort Equations for ASCVD Risk Prediction

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Units</th>
<th>Enter patient values in this column</th>
<th>Acceptable range of values</th>
<th>Optimal values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>M (for males) or F (for females)</td>
<td>m</td>
<td>M or F</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>years</td>
<td>41</td>
<td>20-79</td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td>AA (for African Americans) or WH (for whites or others)</td>
<td>wh</td>
<td>AA or WH</td>
<td></td>
</tr>
<tr>
<td>Total Cholesterol</td>
<td>mg/dL</td>
<td>199</td>
<td>130-320</td>
<td>170</td>
</tr>
<tr>
<td>HDL Cholesterol</td>
<td>mg/dL</td>
<td>65</td>
<td>20-100</td>
<td>60</td>
</tr>
<tr>
<td>Systolic Blood Pressure</td>
<td>mm Hg</td>
<td>130</td>
<td>90-200</td>
<td>110</td>
</tr>
<tr>
<td>Treatment for High Blood Pressure (if SBP &gt;120)</td>
<td>Y (for yes) or N (for no)</td>
<td>n</td>
<td>Y or N</td>
<td>N</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Y (for yes) or N (for no)</td>
<td>n</td>
<td>Y or N</td>
<td>N</td>
</tr>
<tr>
<td>Smoker</td>
<td>Y (for yes) or N (for no)</td>
<td>n</td>
<td>Y or N</td>
<td>N</td>
</tr>
</tbody>
</table>

#### Your 10-Year ASCVD Risk (%)
0.9

#### 10-Year ASCVD Risk (%) for Someone Your Age with Optimal Risk Factor Levels (shown above in column E)
0.7

#### Your Lifetime ASCVD Risk* (%)
36.0

#### Lifetime ASCVD Risk (%) for Someone at Age 50 with Optimal Risk Factor Levels (shown above in column E)
5.0

*This is the Lifetime ASCVD risk for an individual at age 50 years with your risk factor levels. In rare cases, 10-year risks may exceed lifetime risks given that the estimates come from the models and may not fully capture long-term risk.

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**10-Year and Lifetime ASCVD Risks**

![Graph showing 10-Year and Lifetime ASCVD Risks](chart.png)
Pooled Cohort Equations for ASCVD Risk Prediction

Percentage of 40-75 year old non-pregnant White (Wh) and African American (AA) Men and Women (Wom) free of ASCVD in US population with ≥7.5% 10-year hard CVD risk

(NHANES 2007-2010)
Additional Key Points

• Lifestyle modification is still recommended
• Evidence lacking to continue recommending LDL-C or non-HDL-C-based targets
• Non-statin therapies, alone or in conjunction with statins, are not recommended
Clinical Judgment Recommended for the Following Individuals with 10-year Risk <7.5%

- Family history of premature ASCVD
- LDL-C >160 mg/dl
- High-sensitivity C-reactive protein ≥2 mg/dl
- Coronary calcium score ≥300 Agatston units or ≥75th percentile for age, sex, ethnicity
- Ankle-brachial index <0.9
- Elevated lifetime risk of ASCVD ≥39%
Relative Risk Reduction Appears Consistent Across Groups That May Benefit From Statin Therapy

<table>
<thead>
<tr>
<th>Previous vascular disease</th>
<th>Events (% per annum)</th>
<th>RR (CI) per 1 mmol/L reduction in LDL-C</th>
<th>Heterogeneity/trend test</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Statin/more</td>
<td>Control/less</td>
<td></td>
</tr>
<tr>
<td>CHD</td>
<td>8,395 (4.5%)</td>
<td>10,123 (5.6%)</td>
<td>0.79 (0.76–0.82)</td>
</tr>
<tr>
<td>Non-CHD vascular</td>
<td>674 (3.1%)</td>
<td>802 (3.7%)</td>
<td>0.81 (0.71–0.92)</td>
</tr>
<tr>
<td>None</td>
<td>1,904 (1.4%)</td>
<td>2,425 (1.8%)</td>
<td>0.75 (0.69–0.82)</td>
</tr>
<tr>
<td>Total</td>
<td>10,973 (3.2%)</td>
<td>13,350 (4.0%)</td>
<td>0.78 (0.76–0.80)</td>
</tr>
</tbody>
</table>

99% or 95% CI
Risk vs. Benefit of **Moderate-Intensity Statin Therapy**

**MODERATE INTENSITY STATIN TREATMENT**
Assumes a 35% relative risk reduction in ASCVD from moderate intensity statin treatment.
NNT to prevent 1 ASCVD event varies by baseline estimated 10-year ASCVD risk.
NNH based on 1 excess case of incident diabetes per 100 individuals* treated with statins for 10 years.

*The Richard B. and Lynne V. Cheney Cardiovascular Institute at the George Washington University
Assumes a 45% relative risk reduction in ASCVD from high intensity statin treatment. NNT to prevent 1 ASCVD event varies by baseline estimated 10-year ASCVD risk. NNH based on 3 excess cases of incident diabetes* per 100 individuals treated with statins for 10 years.

**HIGH INTENSITY STATIN TREATMENT**

- NNT to prevent 1 ASCVD event varies by baseline estimated 10-year ASCVD risk.
- NNH based on 3 excess cases of incident diabetes* per 100 individuals treated with statins for 10 years.

**Risk vs. Benefit of High-Intensity Statin Therapy**

![Graph showing the relation between NNT to prevent 1 ASCVD event and 10-year ASCVD risk.](image)

- **NNH=33**
### High- vs. Moderate- vs. Low-Intensity Statin Therapy

<table>
<thead>
<tr>
<th>High-Intensity Statin Therapy</th>
<th>Moderate-Intensity Statin Therapy</th>
<th>Low-Intensity Statin Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily dose lowers LDL–C by approximately ≥50%</td>
<td>Daily dose lowers LDL–C by approximately 30% to &lt;50%</td>
<td>Daily dose lowers LDL–C by &lt;30%</td>
</tr>
<tr>
<td>Atorvastatin (40†)–80 mg Rosuvastatin 20 (40) mg</td>
<td>Atorvastatin 10 (20) mg Rosuvastatin (5) 10 mg Simvastatin 20–40 mg‡ Pravastatin 40 (80) mg Lovastatin 40 mg Fluvastatin XL 80 mg Fluvastatin 40 mg bid Pitavastatin 2–4 mg</td>
<td>Simvastatin 10 mg Pravastatin 10–20 mg Lovastatin 20 mg Fluvastatin 20–40 mg Pitavastatin 1 mg</td>
</tr>
</tbody>
</table>

†Evidence from 1 RCT only: down-titration if unable to tolerate atorvastatin 80 mg in IDEAL.
‡Although simvastatin 80 mg was evaluated in RCTs, initiation of simvastatin 80 mg or titration to 80 mg is not recommended by the FDA due to the increased risk of myopathy, including rhabdomyolysis.
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>RCT Exclusion Criteria and Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women of childbearing potential</td>
<td>Few trials enrolled premenopausal women; those that did excluded women who did not use effective birth-control methods or who were pregnant or breastfeeding(18,19,27,59,73,80,146).</td>
</tr>
<tr>
<td>Advanced age</td>
<td>Few trials enrolled individuals age &gt;75(19,59,82).</td>
</tr>
<tr>
<td>Race and ethnicity†</td>
<td>Only one trial reported Black (South African) participants(82).</td>
</tr>
<tr>
<td>Multiple or serious comorbidities</td>
<td>Individuals with heart failure,(18,28,75,77,80,81,147,148) and renal failure(19,73,77,79-81) were excluded from clinical trials(152). Benefit of initiation of statins in individuals with classes II–IV systolic or ischemic heart failure has not been demonstrated(76). Benefit of initiating statins in individuals undergoing maintenance hemodialysis has not been demonstrated(70,74,146).</td>
</tr>
<tr>
<td>Reduced renal function, renal failure, or nephrotic syndrome</td>
<td>Patients with renal failure and nephrotic syndrome were excluded from most clinical trials(18,19,28,73,75,77,81,148) except for SHARP (simvastatin coadministered with ezetimibe)(146). Patients with creatinine &gt;2.0 mg/dL (or &gt;130 μmol/L) or 1.5 times ULN(20,22,59,82,89,106,147) were excluded from many clinical trials. No CVD or other benefit was observed in RCTs including maintenance hemodialysis patients(70,74,146).</td>
</tr>
<tr>
<td>Poorly controlled or uncontrolled hypertension</td>
<td>Individuals were excluded from clinical trials if they had systolic blood pressure &gt;160 mmHg or diastolic blood pressure &gt;100 mmHg(18,27,73,78,79,82,149).</td>
</tr>
<tr>
<td>Uncontrolled diabetes</td>
<td>Individuals with uncontrolled diabetes were excluded from clinical trials(18-20,27,69,73,78,89,147,148).</td>
</tr>
</tbody>
</table>
RCTs Demonstrate No Benefit for the Following Groups

- NYHA Class II-IV ischemic systolic heart failure (CORONA)
- Patients on maintenance hemodialysis (4D, AURORA, SHARP)

The guidelines provide no recommendations for initiating or discontinuing statins in NYHA class II-IV ischemic systolic heart failure patients or those on maintenance hemodialysis
Conclusion
What I Do In My Clinic

The following patients should be on a statin (and TLC):
1. Has ASCVD: if age 21-75, atorva 80 (atorva 40 or rosuva 20 if intolerant); if age >75, atorva 20 (simva 40, prava 40, Lescol XL or low-dose rosuva as alternatives)
2. LDL ≥190: atorva 80 (atorva 40 or rosuva 20 if intolerant)
3. Age 40-75 with DM: if 10-year risk ≥7.5%, atorva 80 (atorva 40 or rosuva 20 if intolerant); otherwise, atorva 20 (simva 40, prava 40, Lescol XL or low-dose rosuva as alternatives)
4. Age 40-75 with 10-year risk ≥7.5% and LDL>70: atorva 40
5. For patients desiring "fine tuning" of risk and not in the above categories, we will recommend statin therapy if LDL ≥160, first-degree male relative with ASCVD<55 years or female <65 years, CRP>2, CACS ≥ 300 or ≥ 75th percentile by MESA calculator, ABI<0.9 or lifetime ASCVD risk ≥39%
What I Do In My Clinic

• No initiation of statins on patients with NYHA Class II-IV CHF or patients on HD (but we will not stop it if they are already on it)
• Baseline ALT prior to statin initiation
• Consider lowering statin dose if LDL<40 two times in a row