Emerging Challenges in Primary Care: 2016

Cardiovascular Prevention Guidelines (Hypertension, Lipids, Obesity) 2016

Faculty

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  Director, UCLA Barbra Streisand Women’s Heart Health Program
  Los Angeles, CA

Disclosures

- Karol E. Watson, MD, PhD serves as a consultant for Amgen, GSK, Merck and Quest.
Learning Objectives

• To review recent guidelines initiated by NHLBI on hypertension, lipids and obesity
• To discuss controversies and complexities in the recent guidelines
• To review areas of consensus in cardiovascular prevention

Case

• A 61 year-old man with hypertension presents as a new patient. He hasn’t seen a doctor regularly, but is now worried because his “best friend just dropped dead of a heart attack.” He feels well and has begun drinking wine because he heard it’s “good for your heart,” but he wonders what else he should be doing to protect his heart.

Current medications:
Lisinopril 10 mg daily

Pertinent physical exam findings:
BP-149/82, BMI-34.9

Pertinent lab findings:
LDL-115, HbA1c-6.1

History of NHLBI CVD Adult Clinical Prevention Guidelines

In 2013 the NHLBI decided to get out of the guidelines writing business, so turned all guidelines over to the professional organizations:
ACC / AHA and Obesity Society
HYPERTENSION

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)

JAMA. Published online December 18, 2013. doi:10.1001/jama.2013.284427

Important to Note...

- JNC 7 was “The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure”
- JNC 8 is the “2014 Evidence-Based Guideline for the Management of High Blood Pressure”
- In JNC 8 they give 9 Evidence-based Recommendations
- “… these recommendations are not a substitute for clinical judgment, and decisions about care must carefully consider and incorporate the clinical characteristics and circumstances of each individual patient.”
What was different in JNC 8:
Treatment Goals

<table>
<thead>
<tr>
<th></th>
<th>JNC 7</th>
<th>2014 Hypertension Guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults (&lt;60 years)</td>
<td>&lt;140 / 90 mmHg</td>
<td>&lt;140 / 90 mmHg</td>
</tr>
<tr>
<td>Adults (≥60 years)</td>
<td>&lt;140 / 90 mmHg</td>
<td><strong>&lt;150 / 90 mmHg</strong></td>
</tr>
<tr>
<td>Diabetes/Chronic Kidney Disease</td>
<td>&lt;130 / 80 mmHg</td>
<td>&lt;140 / 90 mmHg</td>
</tr>
</tbody>
</table>

What was different in JNC 8:
Medication Recommendations

<table>
<thead>
<tr>
<th>Initial treatment</th>
<th>2014 Hypertension Guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thiazide-diuretics</td>
<td>Thiazide-diuretics, CCB, ACEI, ARB</td>
</tr>
<tr>
<td>CCB, ACEI, ARB, BE</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Subpopulations</th>
<th>JNC 7</th>
<th>2014 Hypertension Guidelines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonblack hypertensive population (including DM)</td>
<td>ACE, ARB, CCB, or thiazide-type diuretic</td>
<td></td>
</tr>
<tr>
<td>Black hypertensive population (including DM)</td>
<td>CCB or thiazide-type diuretic</td>
<td></td>
</tr>
<tr>
<td>CKD</td>
<td>ACE or ARB</td>
<td>ACE or ARB</td>
</tr>
</tbody>
</table>

Adapted from James et al. JAMA. 311(23):2124-2129, 2014
CASE

- A 61 year-old man with hypertension presents as a new patient. He hasn’t seen a doctor regularly, but is now worried because his “best friend just dropped dead from a heart attack.” He feels well and has begun drinking wine because he heard it is “good for your heart,” but he wonders what else he should be doing to protect his heart.

Current medications:
Lisinopril 10 mg daily

Pertinent physical exam findings:
BP 149/82, BMI 34.9

Pertinent lab findings:
LDL 115, HbA1c 6.1

<table>
<thead>
<tr>
<th>How the Guidelines Compare…</th>
<th>2014 HTN (JNC 8)</th>
<th>2014 AHSH/ISH</th>
<th>2013 CHEP</th>
<th>2013 ESH/ESC</th>
<th>2013 ADA</th>
</tr>
</thead>
<tbody>
<tr>
<td>General BP goal</td>
<td>140/90</td>
<td>140/90</td>
<td>140/90</td>
<td>140/90</td>
<td>140/90</td>
</tr>
<tr>
<td>BP goal (elderly)</td>
<td>150/90</td>
<td>150/90</td>
<td>150/90</td>
<td>150/90</td>
<td>150/90</td>
</tr>
<tr>
<td>BP goal CKD</td>
<td>140/90</td>
<td>140/90</td>
<td>140/90</td>
<td>140/90</td>
<td>140/90</td>
</tr>
<tr>
<td>BP goal DM</td>
<td>140/90</td>
<td>140/90</td>
<td>140/90</td>
<td>140/90</td>
<td>140/90</td>
</tr>
</tbody>
</table>

Initial drug choice for most
- Thiazide
  - ACE / ARB
  - CCB
- ACE / ARB
  - If < 60
  - CCB or thiazide if > 60
- Thiazide / ACE / ARB
  - BB

* With proteinuria

Not even all JNC 8 Authors Agreed with easing up at age 60

14 January 2014
Evidence Supporting a Systolic Blood Pressure Goal of Less Than 150 mm Hg in Patients Aged 60 Years or Older: The Minority View

Jackson T. Wright Jr., MD, PhD; Lawrence J. Fine, MD, DrPH; Daniel T. Lackland, PhD; Gbenga Ogedegbe, MD, MPH, MS; and Cheryl R. Dennison Himmelfarb, PhD, RN, ANP

Hypertension Guidelines
Members of the JNC 8 panel who voted against increasing the target systolic blood pressure in people over age 60 explain why they think the increased target is a bad idea.
But I have a feeling that things are about to change again

Systolic Blood Pressure Intervention Trial (SPRINT)

- A randomized controlled trial examining the effect of a BP goal of <140 mm Hg vs. a goal of < 120 mm Hg
- Primary Outcome = Composite of
  - MI
  - Stroke
  - Heart failure
  - Acute coronary syndrome
  - Cardiovascular death

SPRINT Trial

- At least 50 years old
- Systolic blood pressure 130 – 180 mm Hg
  - Treated or untreated
- Higher Risk patients (one or more of the following)
  - Clinical or subclinical CVD (not stroke)
  - Chronic Kidney Disease (eGFR 20 – 59)
  - Framingham Risk Score ≥ 15% over 10 years
  - Age ≥ 75 years
- Randomized to the intensive BP arm (<120 mm Hg) or the standard BP arm (< 140 mm Hg)
- Agents from all major antihypertensive drug classes available free of charge
**Major Exclusion Criteria**

- Stroke
- Diabetes
- Congestive heart failure (symptoms or EF < 35%)
- Proteinuria >1g/d
- CKD with eGFR < 20 mL/min/1.73m² (MDRD)
- Adherence flags

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**Sprint Trial achieved BP**

- 1.9 drugs per patient in standard arm
- 3.0 drugs per patient in intensive arm

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**Primary Outcome**

- 25 % reduction

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**Total Mortality**

- 27 % reduction
SPRINT Pre-specified Subgroup Analysis

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>HR</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>0.79</td>
<td>0.16</td>
</tr>
<tr>
<td>No Prior CVD</td>
<td>0.79</td>
<td>0.14</td>
</tr>
<tr>
<td>Prior CVD</td>
<td>0.90</td>
<td>0.52</td>
</tr>
<tr>
<td>Age ≥ 75</td>
<td>0.87</td>
<td>0.96</td>
</tr>
<tr>
<td>Female</td>
<td>0.94</td>
<td>0.85</td>
</tr>
<tr>
<td>Male</td>
<td>0.72</td>
<td>0.09</td>
</tr>
<tr>
<td>African-American</td>
<td>0.77</td>
<td>0.60</td>
</tr>
<tr>
<td>Non African-American</td>
<td>0.74</td>
<td>0.05</td>
</tr>
<tr>
<td>No Prior CVD</td>
<td>0.71</td>
<td>0.63</td>
</tr>
<tr>
<td>Prior CVD</td>
<td>0.90</td>
<td>0.17</td>
</tr>
<tr>
<td>SBP ≥ 132</td>
<td>0.70</td>
<td>0.77</td>
</tr>
<tr>
<td>132 ≤ SBP &lt; 145</td>
<td>0.77</td>
<td>0.77</td>
</tr>
<tr>
<td>SBP ≥ 145</td>
<td>0.83</td>
<td>0.09</td>
</tr>
</tbody>
</table>

*Evaluated for mortality

SPRINT. N Engl J Med 2015 November 9

CASE

We added HCTZ to treat his hypertension

Current medications:
Lisinopril 10 mg daily

Pertinent physical exam findings:
BP-149/82 BMI-34.9

Pertinent lab findings:
LDL-115, HbA1c-6.1

CHOLESTEROL
A 61 year-old man with hypertension presents as a new patient. He hasn't seen a doctor regularly, but is now worried because his "best friend just dropped dead from a heart attack." He feels well and has begun drinking wine because he heard it is "good for your heart," but he wonders what else he should be doing to protect his heart.

Current medications: Lisinopril 10 mg daily

Pertinent physical exam findings: BP-149/82, BMI-34.9

Pertinent lab findings:
- LDL-115
- HbA1c-6.1
- Total cholesterol – 186 mg/dL
- HDL – 41mg/dL
- Triglycerides – 200 mg/dL

2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults

Neil J. Stone, MD, MACP, FAHA, FACC, Chair
Jennifer Robinson, D, MPH, FAHA, Vice Chair
Alice H. Lichtenstein, DSc, FAHA, Vice Chair

Donald M. Lloyd-Jones, MD, ScM, FACC, FAHA
Sidney C. Smith, Jr, MD, FACC, FAHA
Karol Watson, MD, PhD, FACC, FAHA
Susan T. Shera, MS, RN*
Peter W.F. Wilson, MD, FAHA

ACC/AHA Statin Benefit Groups

- **Secondary Prevention**
  - Clinical ASCVD
  - Age < 75: High-intensity statin
  - Age ≥ 75: Moderate-intensity statin

- **Primary Prevention**
  - LDL-C ≥ 190 mg/dL
  - High-intensity statin

- **Diabetes Mellitus**
  - Type 1 and 2
  - Age 40–75 with diabetes and LDL 70–189 mg/dL
  - Low risk (10-yr risk < 7.5%): Moderate-intensity statin
  - High risk (10-yr risk ≥ 7.5%): High-intensity statin

- **Primary Prevention**
  - Age 40–75, ≥ 7.5%
  - Consider moderate or high intensity statin

ASCVD Risk Estimator

- Gender
- Age
- Race
- Total Cholesterol
- HDL Cholesterol
- Systolic BP
- Treatment for BP?
- Diabetes
- Smoking

http://www.apple.com/itunes/affiliates/download/?id=808875968

Or just google: "ASCVD risk calculator"

Statins for primary prevention of CVD
NNT to prevent one major CVD event compared to NNH over 5 years

- **High intensity statin**
  - (RRR 45%)

- **Low to moderate intensity statin**
  - (RRR 25% & 35%)
### Intensity of Statin Therapy

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

### Understanding the numbers....

You’re fifty-seven years old. I’d like to get that down a bit.

### Age provides an integrated estimate of lifetime exposure to risk factors

“Evidence”

Risk Calculator for Cholesterol Appears Flawed

Last week, the nation’s leading heart organizations released a new, more conservative set of guidelines for lowering cholesterol, along with an online calculator meant to help doctors assess risks and treatment options. But, in a major development in the health community, the guidelines serve to highlight the potential for missing many people who are candidates for statin therapy.

“Higher sociodemographics

Healthier than average

Many were taking statins

External Validation

Ridker. The Lancet, Volume 382, Issue 9907, Pages 1762 - 1765
Rotterdam: Poor Calibration (Unadjusted)

...But who cares how the equations perform in Rotterdam?

Kavousi, JAMA 2014

EPIC-Norfolk: Excellent Calibration (Unadjusted)

...But who cares how the equations perform in Norfolk?

Ray, EHJ 2014

REGARDS

In a validation study involving nearly 11,000 participants in REGARDS Trial (a population-based of 30,000 U.S. black and white patients) the ASCVD risk estimator performed well

Muntner et al JAMA March 29, 2014
Common Misconceptions About the Cholesterol Guidelines

- All patients with a 10-year CVD risk of ≥ 7.5% must be treated with a statin
- Guidelines emphasize patient-provider discussion
- There is no longer a role for rechecking lipids
  - Lipids should be re-checked at 3-12 weeks to verify therapeutic response and monitor adherence; Re-checks should occur q 3-12 months
- There is no role for non-statin therapy
- There remains a role for add-on therapy at provider’s discretion in higher risk patients
- The new risk estimator abandons Framingham
  - The new risk estimator includes Framingham along with 3 other cohorts that add power and diversity

Adapted from Blaha and Wong. FEBRUARY 05, 2014 Cardiosource

CASE

We added Atorvastatin 40 mg daily to manage his cardiovascular risk

Current medications:
- Lisinopril 10 mg daily

Pertinent physical exam findings:
- BP-149/82, BMI-34.9

Pertinent lab findings:
- LDL-115, HbA1c-6.1

Association between statins and development of diabetes

<table>
<thead>
<tr>
<th>Statin</th>
<th>Odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall (n=91 140)</td>
<td>1.09 (1.02–1.17)</td>
</tr>
<tr>
<td>Rosuvasatin only (n=24 714)</td>
<td>1.18 (1.04–1.33)</td>
</tr>
<tr>
<td>Atorvastatin only (n=7773)</td>
<td>1.14 (0.89–1.46)</td>
</tr>
<tr>
<td>Simvastatin only (n=18 815)</td>
<td>1.11 (0.97–1.26)</td>
</tr>
<tr>
<td>Pravastatin (n=33 627)</td>
<td>1.03 (0.90–1.19)</td>
</tr>
<tr>
<td>Lovastatin (n=6211)</td>
<td>0.98 (0.70–1.38)</td>
</tr>
</tbody>
</table>

**Jupiter Trial: Statins and Diabetes,**

*No major risk factors for diabetes*

- 86 deaths or vascular events prevented
- 0 excess cases of diabetes

*Major risk factors for diabetes.*

- Metabolic syndrome, IFG, HbA1c >6%, or BMI ≥30 kg/m²
- HR 1.28 (1.07-1.54) p=0.01
- 134 deaths or vascular events prevented
- 54 excess cases of diabetes

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**FDA reports on the Risk of Diabetes with statins**

*February 2012*

- A small increased risk of elevated blood sugar levels and the development of Type 2 diabetes have been reported with the use of statins.

- “Clearly we think that the heart benefit of statins outweighs this small increased risk” But blood-sugar levels may need to be assessed after instituting statin therapy.

[www.fda.gov/ForConsumers/ConsumerUpdates](http://www.fda.gov/ForConsumers/ConsumerUpdates)

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**OBESITY**
A 61 year-old man with hypertension presents as a new patient. He hasn’t seen a doctor regularly, but is now worried because his “best friend just dropped dead from a heart attack.” He feels well and has begun drinking wine because he heard it is “good for your heart,” but he wonders what else he should be doing to protect his heart.

Current medications: Lisinopril 10 mg daily

Pertinent physical exam findings:
BP-149/82, BMI-34.9

Pertinent lab findings:
LDL-115, HbA1c-6.1

US Obesity trends 2010

Worldwide Obesity trends
(Percentage overweight + Obese)
For Weight Loss

- **Assess**
  - Weight, BMI, Waist circumference

- **Advise**
  - Sustained weight loss of even 3%–5% is likely to result in clinically meaningful benefit

- **Assist**
  a. Prescribe 1,200–1,500 kcal/d for women; 1,500–1,800 kcal/d for men
  b. Prescribe one of the evidence-based diets (such as low-carbohydrate, high-fiber, or low-fat)
  c. A comprehensive lifestyle program including physical activity

For Weight Maintenance

- **Assess**
  - Monitor body weight regularly (at least weekly)
  - Regular contact (at least monthly)

- **Advise**
  - Regular physical activity (i.e., 200–300 min/wk),
  - Consume a reduced-calorie diet (needed to maintain lower body weight).

- **Assist**
  - Trained interventionist
Obesity guidelines Diet Recommendation

Prescribe a diet to achieve reduced calorie intake for obese or overweight individuals who would benefit from weight loss, as part of a comprehensive lifestyle intervention. Any one of the following methods can be used to reduce food and calorie intake:

a. Prescribe 1,200–1,500 kcal/d for women and 1,500–1,800 kcal/d for men (kilocalorie levels are usually adjusted for the individual’s body weight);
b. Prescribe a 500-kcal/d or 750-kcal/d energy deficit; or
c. Prescribe one of the evidence-based diets that restrict certain food types (such as high-carbohydrate foods, low-fiber foods, or high-fat foods) in order to create an energy deficit by reduced food intake.

What about medications?

Option for adding pharmacotherapy as an adjunct to comprehensive lifestyle intervention

Weight Loss Drugs Approved by FDA

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Trade Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liraglutide (injection)</td>
<td>Saxenda</td>
</tr>
<tr>
<td>Phentermine/Topiramate</td>
<td>Qsymia</td>
</tr>
<tr>
<td>Lorcaserin</td>
<td>Belviq</td>
</tr>
<tr>
<td>Orlistat</td>
<td>Xenical, Alli</td>
</tr>
<tr>
<td>Phentermine</td>
<td>Adipex, Fastin, Ionamin</td>
</tr>
<tr>
<td>Diethylpropion</td>
<td>Tenuate, Tenuate, Dospin</td>
</tr>
<tr>
<td>Phendimetrazine</td>
<td>Bontril, Plegine, Preli-2, X-</td>
</tr>
<tr>
<td>Trozine</td>
<td>Methamphetamine, Desoxyn</td>
</tr>
<tr>
<td>Benzphetamine</td>
<td>Didrex</td>
</tr>
<tr>
<td>Mazindol</td>
<td>Sanorex, Mazano</td>
</tr>
</tbody>
</table>
Obesity guidelines- Pharmacotherapy Recommendation

- Conspicuous by its absence from the guidelines, is pharmacotherapy.
- When the obesity guidelines were developed, the only medications that were FDA approved for weight loss were sibutramine and orlistat, with sibutramine having since been taken off the market.
- The writing group included pharmacotherapies for obesity based on expert opinion.
- Pharmacotherapy is recommended for patients who are unable to achieve and sustain weight loss with comprehensive lifestyle alone. If they are not effective in for a given patient’s weight loss, they should not be continued.

Efficacy of Currently Available Weight Loss Medications

<table>
<thead>
<tr>
<th>Drug</th>
<th>Average Weight Loss</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phentermine</td>
<td>3.6% &gt; placebo</td>
</tr>
<tr>
<td>Orlistat</td>
<td>2.75% &gt; placebo</td>
</tr>
<tr>
<td>Lorcaserin</td>
<td>3.3% &gt; placebo</td>
</tr>
<tr>
<td>Phentermine/Topiramate</td>
<td>9% &gt; placebo</td>
</tr>
</tbody>
</table>

Weight Regulating Mechanisms and Effect of Anti-obesity Drugs - It's Complicated!
Advise adults with a BMI ≥40 kg/m² or BMI ≥35 kg/m² with obesity-related comorbid conditions who are motivated to lose weight and who have not responded to behavioral treatment with or without pharmacotherapy with sufficient weight loss to achieve targeted health outcome goals that bariatric surgery may be an appropriate option...


### Obesity guidelines- Surgery Recommendation

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Effectiveness</th>
<th>Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lap Band</td>
<td>Low</td>
<td></td>
</tr>
<tr>
<td>Sleeve Gastrectomy</td>
<td>High</td>
<td></td>
</tr>
<tr>
<td>Gastric Bypass</td>
<td></td>
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</tr>
</tbody>
</table>

**Maestro weight loss system**

- A pacemaker-like device that is implanted in the abdomen in a laparoscopic procedure
- The system delivers intermittent Pulses (5 minutes on / 5 minutes Off) to the vagus nerve during waking hours to induce satiety
- The FDA approved the device for treatment of obese adults (BMI > 40 or >35 with comorbidities)
- Candidates should have failed a supervised weight loss program within the prior 5 years
Weight regulation in Humans

- The human body is hardwired to know how many fat cells are on board and to keep body weight stable.
- At ~ 5% to 10% weight loss the human body responds by:
  - Lowering metabolic rate (more than 5%-10%)
  - Lowering the hormones that signal satiety after eating
  - Increase thoughts and hormones to make humans seek out and eat more food
- All as part of a defense of body weight to survive
  - This does not change with time (always trying to get back to that highest weight)

CASE

We prescribed a diet and exercise plan to manage his obesity

Current medications:
Lisinopril 10 mg daily

Pertinent physical exam findings:
BP-149/82, BMI 34.9

Pertinent lab findings:
LDL-115, HbA1c-6.1

CASE

Recommendations
1. Daily walking for exercise
2. Calorie reduced diet of his choice
3. Referral to our weight loss center
4. Screening for diabetes
5. Increase Lisinopril to 20 mg daily
6. Continue Aspirin 81 mg daily
7. Begin Atorvastatin 40 mg daily
8. Continue to enjoy wine…in moderation