PHASE
PREVENT HEART ATTACKS AND STROKES EVERYDAY

PHASE Safety Net Community Benefits
Cholesterol Update 2016

What's New and What's Not

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Objectives

By the end of the course the attendees should be able to:

Target Statin at sufficient intensity, not attainment of a particular LDL target, to confer maximal cardiovascular protection

Cultural and Linguistic Competency

Race and gender based cardiovascular risk assessment to determine statin treatment will be discussed

‘New” ACC/AHA Cholesterol Guidelines

On November 12, 2013, the American College of Cardiology and the American Heart Association (ACC/AHA) released a new Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults

The new guideline no longer advises LDL control targets as the optimal way to reduce cardiac risk

48 Recommendations- 6 New Recs

A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines

Endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation, American Pharmacists Association, American Society for Preventive Cardiology, Association of Black Cardiologists, Preventive Cardiovascular Nurses Association, and WomenHeart: The National Coalition for Women with Heart Disease

4 Treatment Benefit Groups
LDL Goals no longer advised
Statin Intensity endorsed
New Risk Calculator
Safety Section

Q and A - Cholesterol

The AHC/ACC Guideline is…

a) a new guideline based on new data

b) a new guideline based on old data

c) a new guideline based on no data

d) an new guideline based on fake data

4 Treatment Benefit Groups

1. **Clinical ASCVD**
2. **Diabetes age 40-75 w LDL 70-189**
3. **LDL > 190 age >/= 21**
4. **10 year CV risk over 7.5%**

Clinical ASCVD

Defined by the inclusion criteria for the secondary prevention statin RCTs

- **acute coronary syndromes, history of MI**
- **stable or unstable angina**
- **coronary or other arterial revascularization**
- **stroke or TIA**
- **clinically significant peripheral arterial disease presumed to be of atherosclerotic origin (such as claudication or revascularization)**

Diabetes age 40-75 w LDL 70-189

Moderate-intensity statin should be initiated or continued for age 40 to 75 w DM w LDL 70-189

High-intensity statin is reasonable for age 40 to 75 w DM, w LDL 70-189 w ≥7.5% estimated 10-year ASCVD risk

Statin optional for age < 40 and >75 w LDL 70-189 after evaluating the potential for ASCVD benefits and for adverse effects, for drug-drug interactions, and to consider patient preferences.

LDL > 190 age >/= 21

LDL–C ≥190 mg/dL or TG ≥500 mg/dL should be evaluated for secondary causes of hyperlipidemia

Drugs	**Alcohol Most Common**
A1C	**Diabetes**
Alk Phos	**Cholestatic Liver Disease**
TSH	**Hypothyroidism**
Albumin	**Nephrotic Syndrome (or urinalysis)**

LDL > 190 age >/= 21

LDL–C ≥190 mg/dL or TG ≥500 mg/dL should be evaluated for secondary causes of hyperlipidemia

≥21 years w LDL–C ≥190 should be treated w high intensity statin
(10-year ASCVD risk estimation is not required)

If unable to tolerate high-intensity statin therapy, use the maximum tolerated statin intensity.

LDL > 190 age >/= 21

It is reasonable to intensify statin therapy to achieve at least a 50% LDL–C reduction.

After max statin, consider add on medication

Consider

- **potential for ASCVD risk reduction**
- **adverse effects**
- **drug-drug interactions**
- **patient preferences**

10 year ASCVD risk 7.5 – 14.9%

For 40-75 yr use ASCVD Calculator if LDL 70-189

if 10 yr ASCVD risk 7.5-14.9%
consider moderate-high-intensity statin

after discussion which considers…

- **potential for ASCVD risk reduction benefits**
- **adverse effects**
- **drug-drug interactions**
- **patient preferences**

10 year ASCVD risk ≥15%

For 40-75 yr use ASCVD Calculator if LDL 70-189

if 10 yr ASCVD risk ≥15%
treat with moderate-high-intensity statin

10 year ASCVD risk 5 – 7.4%

For 40-75 yr use ASCVD Calculator if LDL 70-189

if 10 yr ASCVD risk 5 – 7.4%

It is reasonable to offer treatment with a moderate intensity statin

after discussion which considers…

- **potential for ASCVD risk reduction benefits**
- **adverse effects**
- **drug-drug interactions**
- **patient preferences**

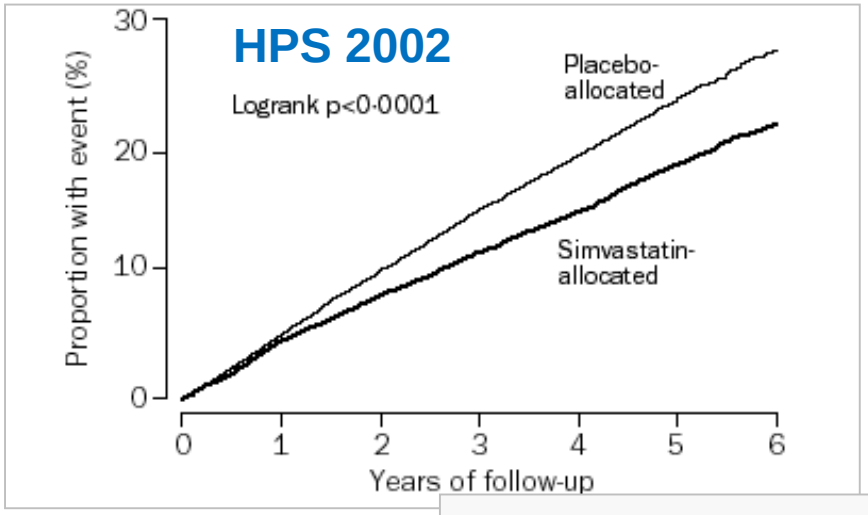
LDL Goals no longer advised

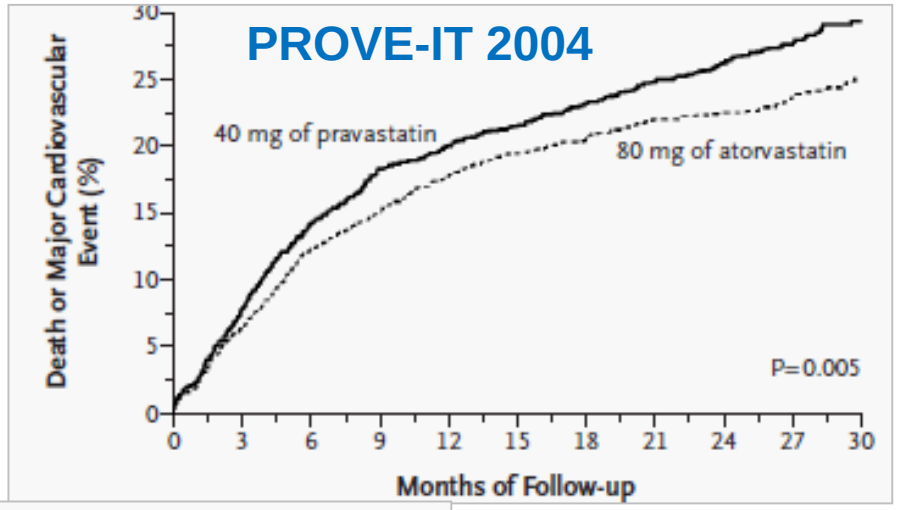
New!

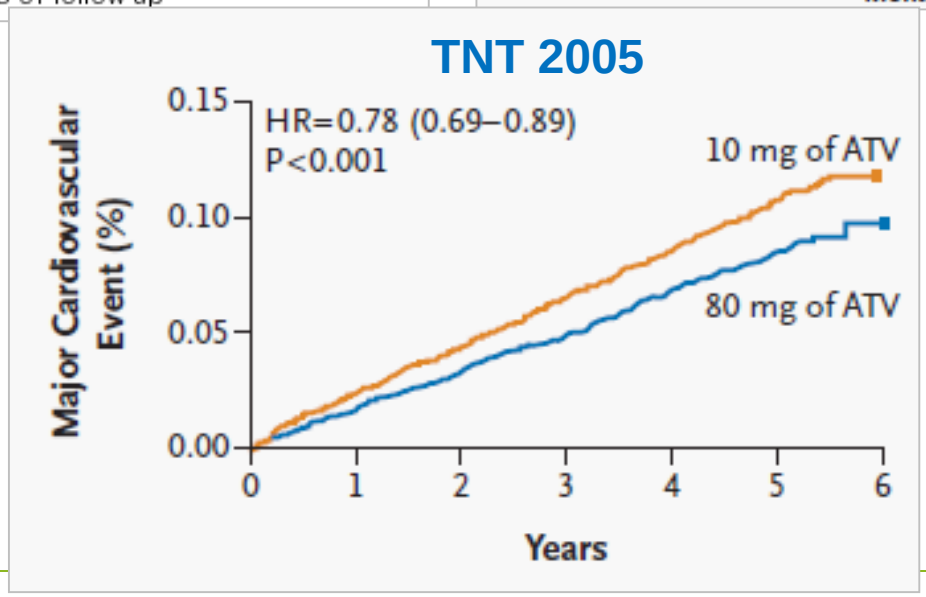
The Expert Panel was unable to find RCT evidence to support continued use of specific LDL and/or non-HDL treatment targets…

After a comprehensive review, no RCTs were identified that titrated drug therapy to specific LDL–C or non-HDL–C goals to improve ASCVD outcomes…

What's Unchanged? Statins Lower CV Risk







What's New? The Guideline, not Evidence…

No strong evidence supporting LDL targets

Annals of Internal Medicine | Review

Narrative Review: Lack of Evidence for Recommended Low-Density Lipoprotein Treatment Targets: A Solvable Problem

Rodney A. Hayward, MD; Timothy P. Hofer, MD, MSc; and Sandeep Vijan, MD, MSc

"No high-quality evidence could be found that suggests that titrating lipid therapy to LDL targets is superior to empirically prescribing doses of statins used in clinical trials for all patients at high cardiovascular risk."

Lack of Evidence for Recommended LDL Treatment Targets: A Solvable Problem. Hayward RA. *Intern Med* 2006; 520-530.

What's New? The Guideline, not Evidence…

No strong evidence supports statin + combo meds

REVIEW | Annals of Internal Medicine

Systematic Review: Comparative Effectiveness and Harms of Combination Therapy and Monotherapy for Dyslipidemia

Mukul Sharma, MD, MSc; Mohammed T. Ansari, MBBS, MMedSc, MPhil; Ahmed M. Abou-Setta, MD, PhD; Karla Soares-Weiser, MD, PhD; Teik Chye Ooi, MBBS; Margaret Sears, PhD; Fatemeh Yazdi, MSc; Alexander Tsertsvadze, MD, MSc; and David Moher, PhD

"No firm evidence showed that combining a statin with another agent (bile-acid sequestrant, fibrate, ezetimibe, niacin, or O-3 fatty acids) improved clinical outcomes (MI, stroke, or mortality) more than high-dose statin monotherapy."

Sharma M. Comparative Effectiveness and Harms of Combination Therapy and Monotherapy for Dyslipidemia *Ann Intern Med Nov 3, 2009*

New Perspective: LDL &/or Non-HDL Goals

The Expert Panel was unable to find evidence to support use of LDL and/or non-HDL targets

"…the RCT evidence clearly shows that ASCVD events are reduced by using maximum tolerated statin intensity in those groups shown to benefit.

No RCTs were identified that titrated drug therapy to specific LDL–C or non-HDL–C goals to improve ASCVD outcomes."

Stone et al., 2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines.

IMPROVE-IT Trial: Simva 40 +/- Ezetimibe

Does this new trial change the "new" guidelines?

Simva 40 + Ezetimibe slightly better than Simva 40 after Acute Coronary Event

However…

- **We don't give Simva 40 after MIs (A80 or A40)**
- **Studied only for Acute MI, not old MIs, CVA,**
- **New guidelines due out in 2016 and may reintroduce LDL goals**

Cannon CP. Ezetimibe added to statin therapy after acute coronary syndromes. N Engl J Med 2015;372:2387-2397

PCSK9 Inhibitors In the News

Proprotein convertase subtilisin/kexin type 9 inhibitors (PCSK9-i, e.g., evolocumab and alirocumab),

50-70% LDL-C reduction
CV outcome trials still underway
Currently limited role, for example…

- **FH w LDL-C ≥ 200 mg/dL despite max tx**
- **ASCVD w very high LDL despite max med**

PCSK9 Inhibitors In the News

PCSK9-i trials showed LDL reductions

Earlier studies using LDL endpoints have failed to demonstrate reduced CV risk

- **ILLUMINATE (Torcetrapib NEJM 2007)**
- **AIM-HIGH (Niacin NEJM 2011)**
- **ACCORD-Lipid (Fenofibrate NEJM 2010)**
- **HPS2-THRIVE (Niacin NEJM 2014)**

What Does This Mean?

Use of a statin alone at sufficient intensity, not attainment of a particular LDL target, confers maximal cardiovascular protection.

Statin Intensity endorsed

New!

What does moderate and high intensity look like?

Population	Recommended Treatment	Qualifying Statin Medication Examples
Highest risk: **ASCVD** **DM > 7.5% Risk** **LDL >/=190**	**High intensity statin**	• **Atorva 40 – 80 mg** • **Rosuva 20 – 40 mg**
High risk: **DM 40 – 75 yrs** **>7.5% risk**	**Mod or High intensity statin**	**Above +** • **Atorva 10 – 20 mg** • **Simva 20 – 40 mg** • **Prava 40 – 80 mg** • **Lova 40 – 80 mg**

Statin Safety- How can LDL go?

New!

Decreasing the statin dose may be considered when 2 consecutive values of LDL–C levels are <40 mg/dL

What About CAC Testing?

"The lack of a randomized screening trial demonstrating the efficacy, utility (including potential adverse events), cost-effectiveness, and net clinical benefit of CAC screening, particularly in intermediate-risk patients when there is uncertainty regarding decisions, is a substantial barrier to widespread adoption," writes Lloyd-Jones. "Without these data, current clinical practice guidelines cannot provide strong evidence-based recommendations to guide practice.“

Absence of Coronary Calcium Reclassifies Nearly 50% of Statin-Eligible Patients: MESA Analysis. Medscape. Oct 06, 2015

What About CAC Testing?

Consider other factors if treatment is uncertain

- **LDL-C ≥160 or genetic hyperlipidemias**
- **Elevated lifetime risk of ASCVD**
- **FHx early ASCVD (m<55 or f<55)**
- **hsCRP**
- **Ankle-Brachial Index (ABI),**
- **Coronary Artery Calcium (CAC)**

Order only if result would change decision

Use shared decision making to discuss significant differences in convenience, cost, invasiveness, and radiation exposure.

Case 1

56 year old female with diabetes, LDL 85

10 year CV risk 6.8%

A) Atovastatin 80 mg

B) Lovastatin 10 mg

C) Simvastatin 40 mg

D) Niacin 2,000 mg tid

Moderate Intensity Statin if DM and age >40

Case 2

62 year old man with TIA, LDL 165

No statin

A) Atovastatin 80 mg

B) Atorvastain 40 mg

C) Simvastatin 40 mg

D) Ezetimibe 10 mg

Atrovastatin 80 mg for ASCVD (40 is acceptable…)

Case 3

72 year old female with PAD, LDL 35, 38

On Atorvastatin 80 mg statin

A) Stop Atorvastatin

B) Reduce to Atorvastain 40 mg

C) Switch to Simvastatin 40 mg

D) Add isotretinoin

For LDL < 40 x 2, reduce dose

Case 4

45 year old male with LDL 215

A) start Atorvastatin 80 mg

B) calculate 10 yr CV risk using the calculator

C) start simvastatin 40 mg

D) diet and exercise without medications

For LDL > 190, high intensity statin

Case 5

45 year old female w DM, LDL 165
10 year CV risk 6%

A) start Atorvastatin 40 mg

B) start Atorvastatin 80 mg

C) start Simvastatin 40 mg

D) Only start statin AFTER determining her risk of pregnancy, and AFTER a reliable form of contraception is confirmed

Statins are category X in pregnancy

Case 6

62 year old female w stroke, LDL 110,

On atorvastatin 80 mg daily

A) Increase to atorvastatin 160 mg

B) Switch to rosuvastatin 40 mg

C) Add ezetimibe 10 mg

D) Continue atorvastatin 80 mg, encourage adherence and lifestyle changes

LDL targets no longer advised for titration

Case 7

52 year old male, LDL 158, HTN, 10 year CV risk 12.5%

A) Start atorvastatin 80 mg

B) Start simvastatin 40 mg

C) Start Lovastatin 20 mg

D) Order probucol from a mail order pharmacy

Start moderate intensity statin for primary prevention

Case 8

52 year old female, LDL 108, 10 year CV risk 2.5%

A) Diet and exercise, and retest in 4-6 years

B) Start simvastatin 40 mg

C) Start Lovastatin 20 mg

D) Start plasmapharesis

Statins not usually advised when 10 yr risk < 5-7.5%