

ACC/AHA Guidelines Bulls-eyes and Misses

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October 18, 2014



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ACC/AHA Prevention Guideline

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

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Key Words:

OPEN ACCESS ARTICLE

This Article

Circulation.
2014;129:51–545
Published online before print
November 2013.
doi:
10.1161/01.cir.0000437738.63853.
7a

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Risk Calculator for Cholesterol Appears Flawed

By GINA KOLATA

Published: November 17, 2013 | 794 Comments

Lipid panel co-chair Neil Stone said that 7.5% is not “an absolute cutoff. This is not the end of the discussion it’s the start of the discussion.”

THE LANCET

Statins: new American guidelines for prevention of cardiovascular disease

[Paul M Ridker](#), [Nancy R Cook](#)

Guidelines released on Nov 13, 2013, by the American Heart Association (AHA) and the American College of Cardiology (ACC) for the management of cholesterol are a major step in the right direction. [1](#) These new guidelines emphasise prevention of stroke as well as heart disease, focus appropriately on statin therapy rather than alternative unproven therapeutic agents, and recognise that more intensive treatment is superior to less intensive treatment for many patients. Furthermore, the new ACC/AHA gu ...



Larry Husten
Contributor

PHARMA & HEALTHCARE 11/18/2013 @ 1:39PM | 6,454 views

Controversy Erupts Over Accuracy Of Cardiovascular Risk Calculator For Guidelines

Level of Evidence

- The systematic review was limited to Randomized Control Trials (RCT) with ASCVD outcomes and systematic reviews and meta-analyses of RCTs with ASCVD outcomes.
- Did not use “lower quality RCTs,” observational studies, understanding pathophysiology of atherosclerosis, expert recommendations, case reports

Targets of Statin Rx

- Secondary Prevention (ASCVD)
- LDL > 190 mg/dl
- DM
- Primary prevention patients (without DM), but at higher risk

ASCVD Risk Calculator

Pooled Cohort Equations

| Risk Factor | Units | Value | Acceptable range of values | Optimal values |
|-----------------------------------|----------|------------|----------------------------|----------------|
| Sex | M or F | F | M or F | |
| Age | years | 55 | 20-79 | |
| Race | AA or WH | AA | AA or WH | |
| Total Cholesterol | mg/dL | 210 | 130-320 | 170 |
| HDL-Cholesterol | mg/dL | 56 | 20-100 | 50 |
| Systolic Blood Pressure | mm Hg | 145 | 90-200 | 110 |
| Treatment for High Blood Pressure | Y or N | Y | Y or N | N |
| Diabetes | Y or N | N | Y or N | N |
| Smoker | Y or N | N | Y or N | N |

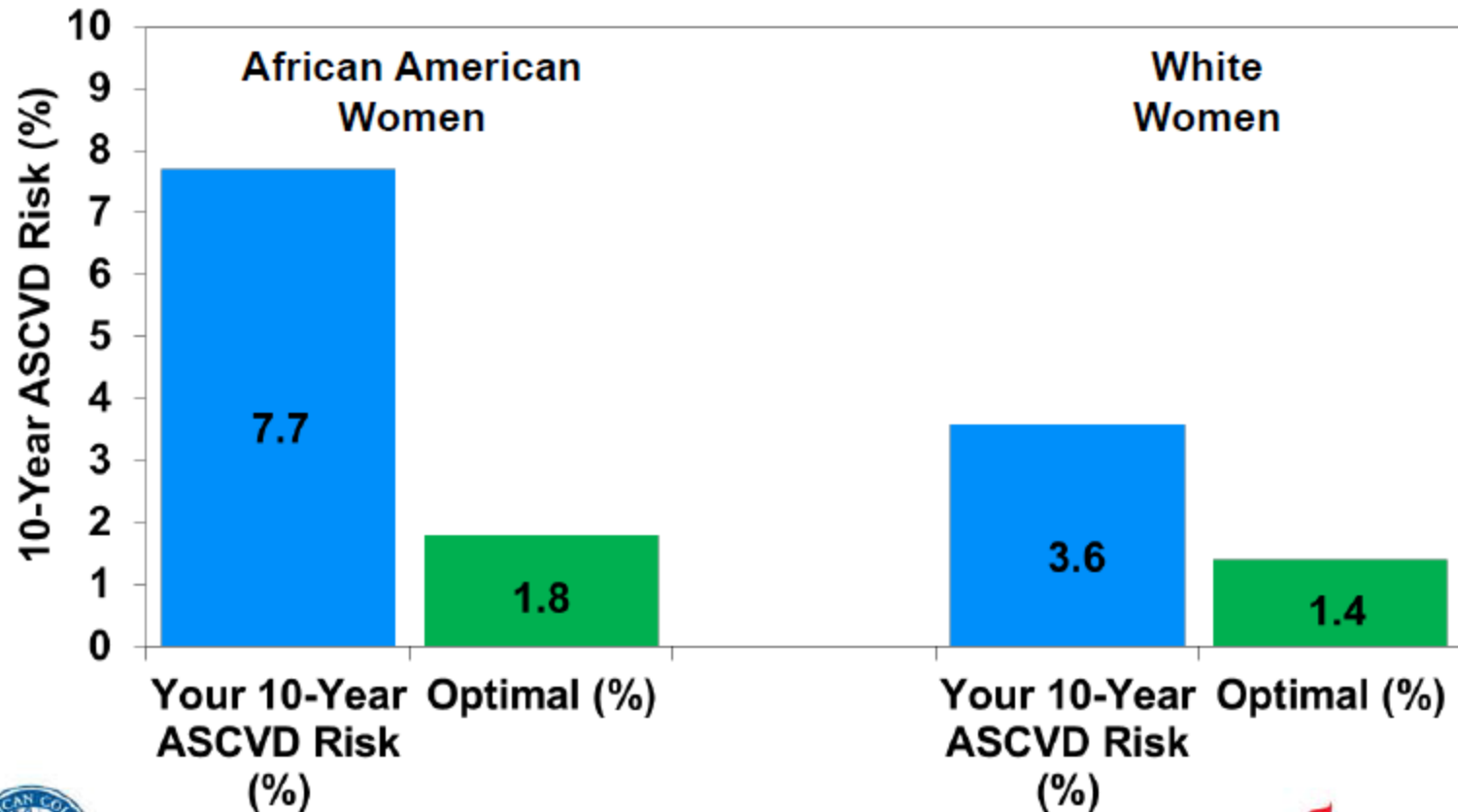


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ASCVD Risk Calculator

55 yo AA and White Women



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Calculator Recommendations

- Every white male >62 yr (with no other risk factors) = high risk
- Every white female >70 yr (with no other risk factors) = high risk
- Every African American male >66 yr (with no other risk factors) = high risk
- Every African American male >70 yr (with no other risk factors) = high risk

Other CV Risk Calculators

- FRS (ATP III)
- FRS (2008)
- Reynolds Risk Score
- International risk scores

High Intensity Statin Rx Recommended Patients

- ASCVD
- LDL>190
- DM with CV risk > 7.5% 10 year CV risk (optional high intensity Rx)

Moderate Intensity Statin Rx Recommended Patients

- ASCVD patients > 75 yrs
- DM patients with risk < 7.5% 10 year CVD risk
- Non-DM patients with < 7.5% 10 year CVD risk

Statin Intensity Categories*

High-intensity statin therapy

(daily dose lowers LDL-C, on average, by approximately $\geq 50\%$)

Atorvastatin (40)-80 mg
Rosuvastatin 20 (40) mg

Moderate-intensity statin therapy

(daily dose lowers LDL-C, on average, by approximately 30% to $< 50\%$)

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

*Individual responses may vary in clinical practice.

Statins and doses that are approved by the US FDA but were not tested in the RCTs reviewed are listed in *italics*.

See full publication for details.

Treatment of > 75 years

- RCT evidence does support the continuation of statins beyond 75 years of age in persons who are already taking and tolerating these drugs.
- Accordingly, a discussion of the potential ASCVD risk-reduction benefits, risk of adverse effects, drug–drug interactions, and consideration of patient preferences should precede the initiation of statin therapy for primary prevention in older individuals.

Departure from Agreement

- Limited scope of guidelines
- Special populations excluded
- Goals of therapy removed
- Poor communication
 - Absence of data & recommendations does not mean prohibition
- Unintended consequences
- Use of ancillary studies / laboratories to evaluate intermediate risk patients
- RCT limitations

RCT Limitations

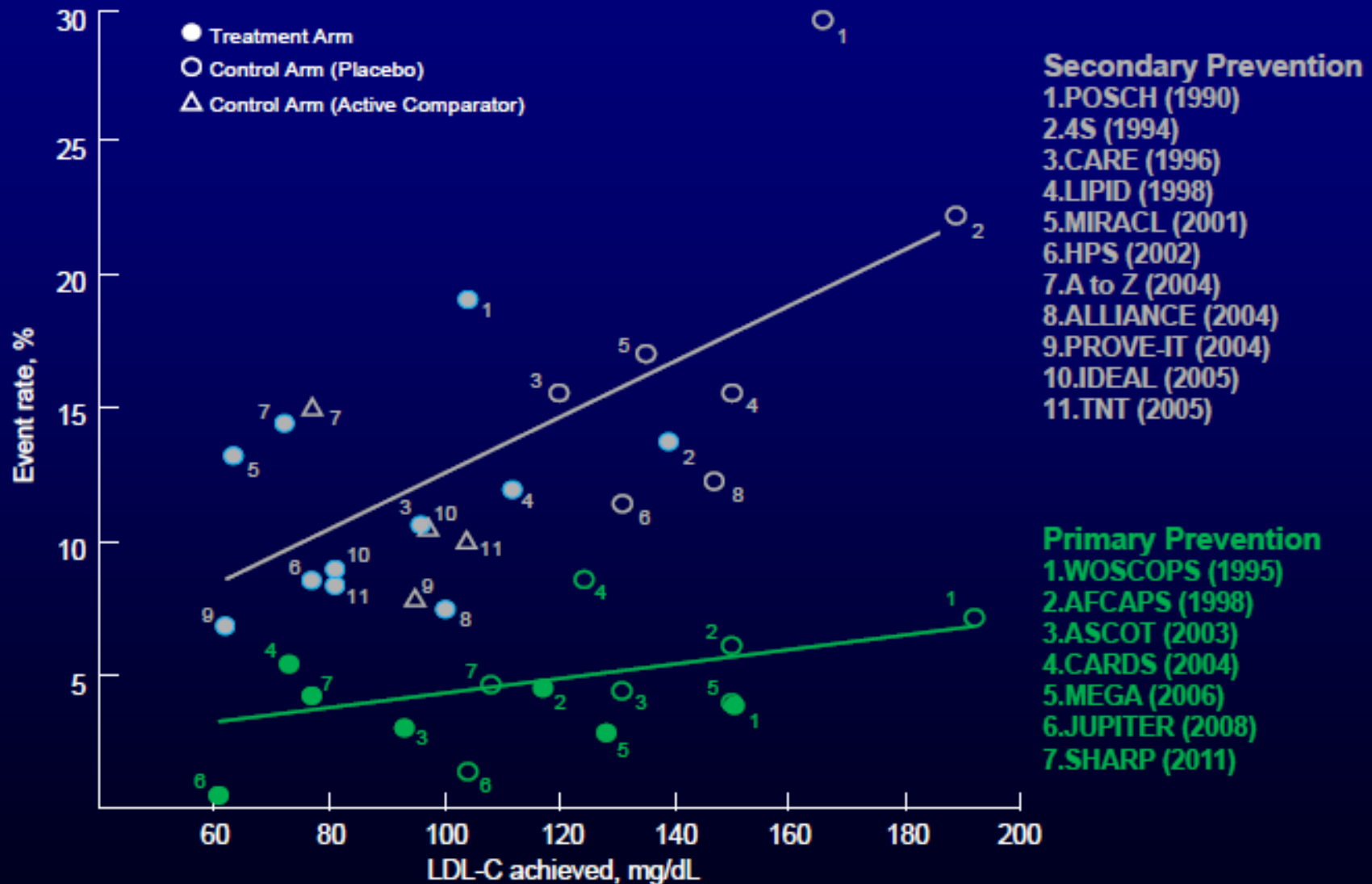
- Trials limited in time, scope, variables, demographics, patient numbers (power) and applicability to real world practice
- Cost; Industry sponsored
- Statistical errors: Type 1 ($p < .05$) & 2 (insuff n)
- Cultural effects

LDL hypothesis

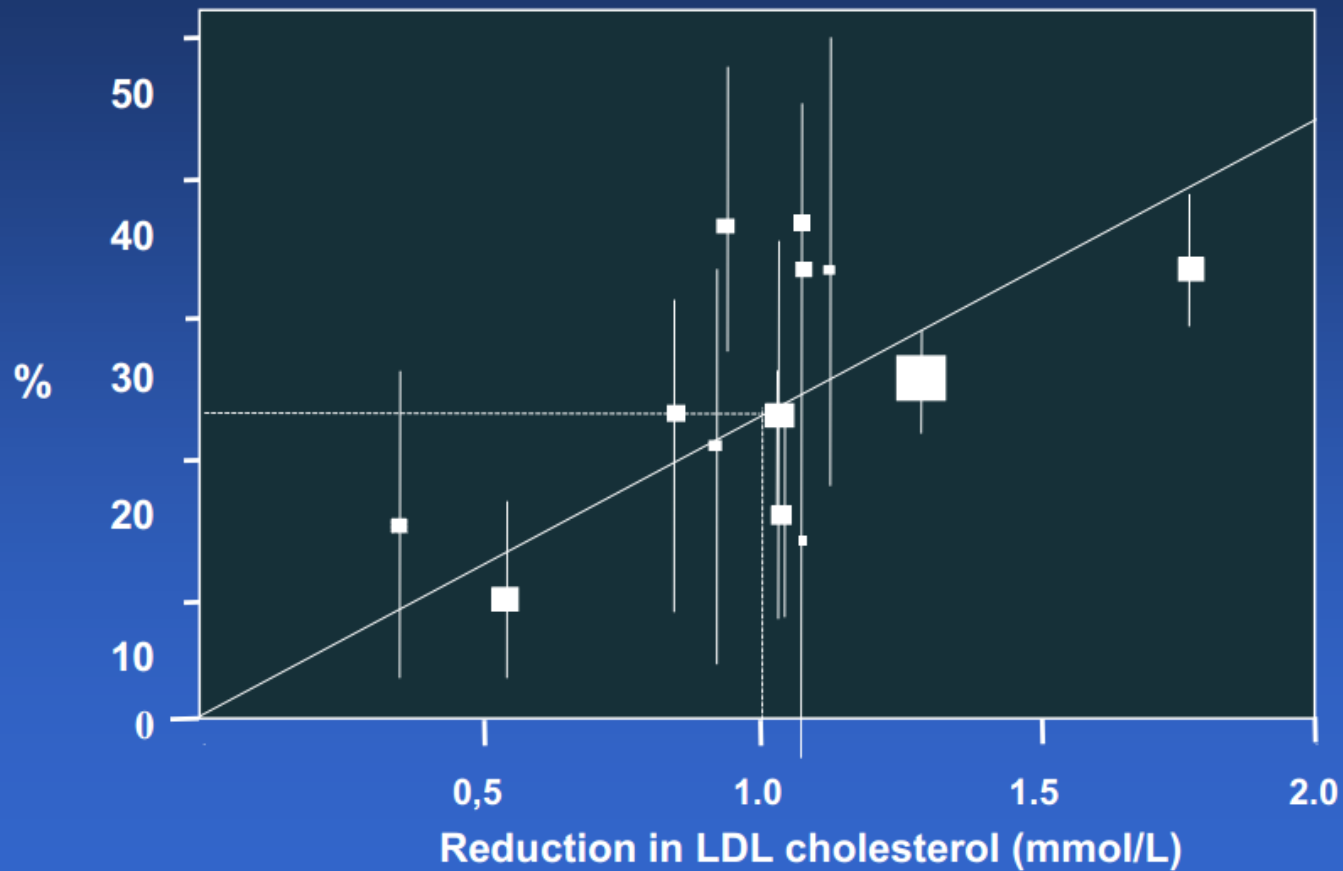
- “Lower is better”
- Multiple confirmatory corroborating studies using multiple technologies or outcomes
- Ancillary treatment not supported by recent RCTs (with low baseline LDLs on statin Rx)
 - Accord, Field, AIM High, HPS-Thrive, Omega
- Clinically practiced for 4 decades

Major Lipid Trials

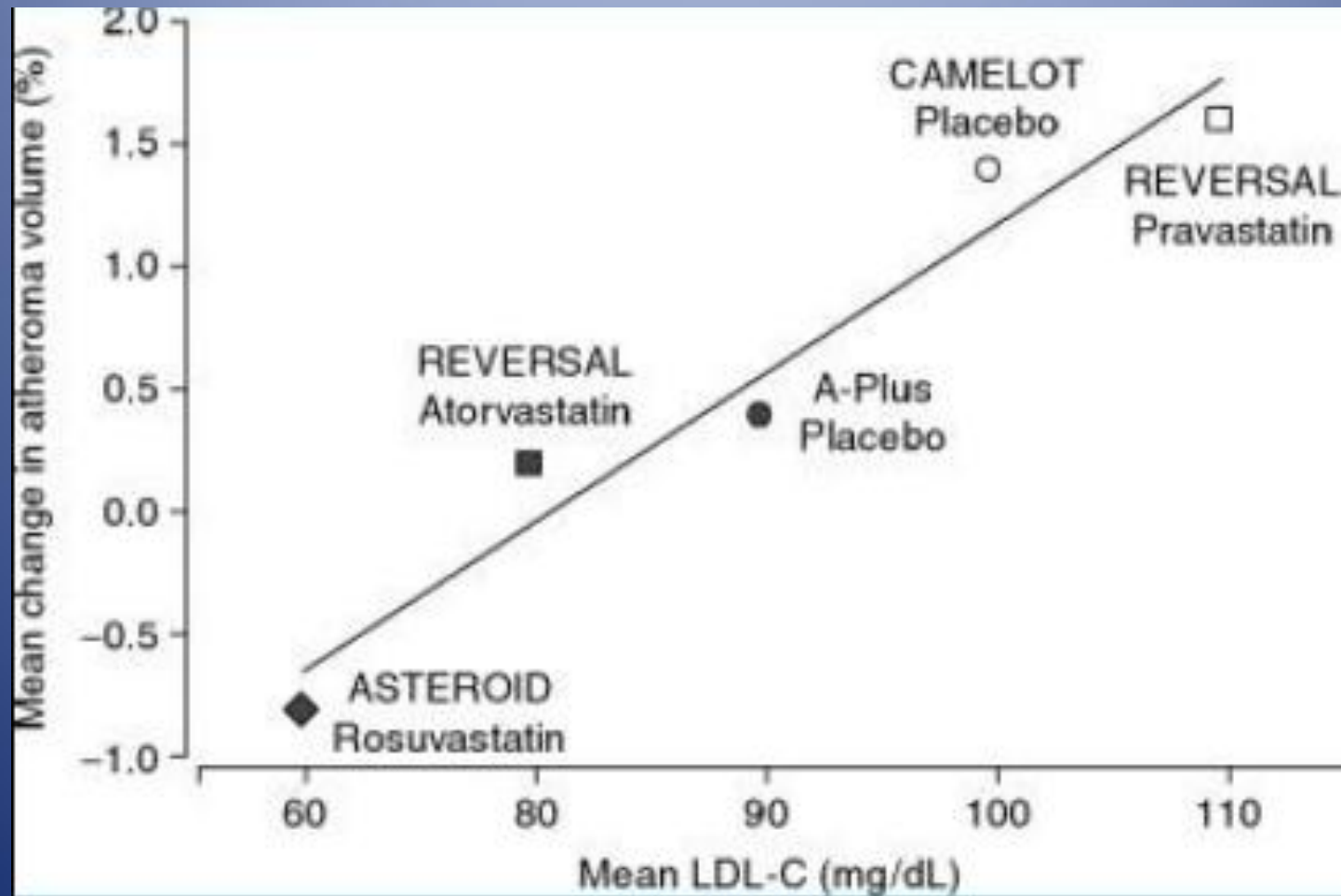
LDL achieved vs Rates of Coronary Events



Proportional Reduction in MCE vs. LDL Reduction



LDL vs. IVUS Atheroma Volume



Cholesterol Treatment Trialists

26 trials with 169,138 participants

- MVEs were reduced 22% (0.76-0.80, $p < 0.0001$) for every 1.0 mmol/L (39 mg/dL) reduction in LDL-C cholesterol with 5 years of treatment
- A similar reduction in MVE was achieved regardless of baseline LDL-C levels

| Baseline LDL-C | RR per 39 mg/dL reduction |
|----------------|---------------------------|
| < 78 mg/dL | 0.78 (0.61-0.99) |
| ≥78-<97 mg/dL | 0.77 (0.67-0.89) |
| ≥98-<116 mg/dL | 0.77 (0.70-0.85) |
| ≥116-135 mg/dL | 0.76 (0.70-0.82) |
| ≥136 | 0.80 (0.76-0.83) |
| TOTAL | 0.78 (0.76-0.80) |

MVE = major vascular events (nonfatal MI, CHD death, stroke, revascularization)

Number of Additional Patients Rx with New ACC/AHA Guidelines

- 12.8 million additional Americans vs. ATP III
- 10.4 million additional for primary prevention
- 48% of adults
- 30% of adults 40-60
- 77% of adults age 60-75

Application of New Cholesterol Guidelines to a Population-Based Sample

Michael J. Pencina, Ph.D. et.al. March 19, 2014 DOI: 10.1056/NEJM

Increased sensitivity vs. specificity

- The increased number of adults who would be newly eligible for statin therapy suggests higher treatment rates among those expected to have future cardiovascular events (increased sensitivity) but also an increased number of adults receiving therapy who are not expected to have events (decreased specificity).

Application of New Cholesterol Guidelines to a Population-Based Sample

Michael J. Pencina, Ph.D., et.al. March 19, 2014 DOI: 10.1056/NEJM

Individuals Not in a Statin Benefit Group

- In those not clearly in a statin benefit group, additional factors may inform treatment decision-making:
 - *Family history of premature ASCVD*
 - *Elevated lifetime risk of ASCVD*
 - *LDL-C ≥ 160 mg/dL*
 - *hs-CRP ≥ 2.0 mg/L*
 - *Subclinical atherosclerosis*
 - *CAC score $\geq 300/75^{\text{th}}$ ile or ABI < 0.9*
- Discussion of potential for ASCVD risk reduction benefit, potential for adverse effects, drug-drug interactions, and patient preferences



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Risk Factors Not Included in Guidelines

- Non-HDL Cholesterol
- Apo B
- LDL-P
- Lp-Pla2
- Lp(a)

Unintended Consequences

- HEDIS guidelines 2015 propose to remove repeat assessment of lipids as a quality measure
- Adverse public commentary lowers patient compliance to treatment
- Provider confusion about recommendations
- Worsening outcomes from withdrawn therapy

Communication Issues

- Excessively long delay in release
- Complaints about collaboration
- Unanticipated paradigm change to therapy
- Health professionals uninformed
- Public relations / media missteps

Gaps Requiring Further RCT Studies According to Expert Committee

- Primary prevention in adults >75 years of age.
- Alternative treatment strategies for ASCVD risk reduction eg. titration to specific cholesterol or apolipoprotein goals
- In statin-intolerant patients, determine whether submaximal statin doses, combined with non-statin therapies, reduce ASCVD risk
- Evaluate outcomes of new-onset diabetes with statin therapy.
- New lipid-modifying agents when added to statin therapy.

Other Gaps

- Therapeutic lifestyle recommendations not supported by RCTs
- Treatment of patients with recurrent MCE with LDL already on high dose statin
- Treatment of patients with very elevated cholesterol already on high dose statin
- Prospective testing of the new risk calculator



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2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol

Reduce Atherosclerotic Cardiovascular

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

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RN⁺; Sidney C.

Peter W. F. Wil

Other Guidelines

- National Lipid Association
- American Association of Clinical Endocrinologist
- American Diabetic Association
- National Kidney Foundation
- International Society of Atherosclerosis
- European Society Cardiology

New Directions

- PCSK9 outcome trials will test the LDL hypothesis
- Prospective RCTs using the Risk Calculator
- New RCTs filling many of the gaps in these guidelines
- 2015 HEDIS Guidelines on cholesterol testing

2013 ACC/AHA disclaimers

- “...our process did not provide for a comprehensive approach to the detection, evaluation, and treatment of lipid disorders...”
- “For the many questions about complex lipid disorders that are beyond the scope of our systematic evidence review, or for which little or no RCT data are available, it is anticipated that clinicians with lipid expertise can contribute to their management. “