Perspectives on the 2013 AHA/ACC Guidelines for Risk Assessment: What’s the Worry?

Donald M. Lloyd-Jones, MD ScM FACC FAHA
Senior Associate Dean
Chair, Dept. of Preventive Medicine
Director, NUCATS Institute
Eileen M. Foell Professor of Heart Research

Disclosures

• No relevant RWI/COI
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Outline

• Why do we estimate absolute risk?
• Review of 2013 AHA/ACC Guideline on Risk Assessment for ASCVD
  ▪ Integration with Cholesterol Treatment Guidelines
  ▪ Development of new risk equations
  ▪ Ancillary testing when risk assessment/decision-making is uncertain
• Evidence since publication
• Summary/Take-home

CTT 2005: Statin vs placebo

Everyone has similar RRR benefit!
CTT 2010: Statin/More vs Control/Less Baseline LDL Subgroups

CTT 2012: RRR Similar; Absolute Risk Rules
2013 ACC/AHA Guideline on the Assessment of Cardiovascular Risk

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

NHLBI Charge to the Work Group

- Examine the scientific evidence on risk assessment for initial ASCVD events, and develop an approach for risk assessment that could be used in practice and used or adapted by the risk factor panels in their guidelines.

- Specifically, the Work Group was charged with 2 tasks:
  1. To develop or recommend an approach to quantitative risk assessment that could be used to guide care; and
  2. To pose and address a small number of questions judged to be critical to refining and adopting risk assessment in clinical practice, using systematic review methodology.
Secondary and Primary Prevention

Initiating Statin Therapy

Heart-healthy lifestyle habits are the foundation of ASCVD prevention (see 2013 AHA/ACC Lifestyle Management Guideline)

- Age ≥25 y and a candidate for statin therapy
- Definitions of High- and Moderate-Intensity Statin Therapy (see Table 5)
- Regularly monitor adherence to lifestyle and drug therapy with test and safety assessments (see Fig 5)

Clinical ASCVD

- LDL-C ≥190 mg/dL
- Regularly monitor adherence to lifestyle and drug therapy with test and safety assessments (see Fig 5)

Secondary Prevention

Initiating Statin Therapy (cont’d)

Primary prevention (no diabetes, LDL-C 70 to 189 mg/dL, and not receiving statin therapy)

- Estimate 10 y ASCVD risk every 4–6 y using Pooled Cohort Equation

- In selected individuals, additional factors may be considered to inform treatment decision-making

Primary prevention

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- Regularly monitor adherence to lifestyle and drug therapy with test and safety assessments (see Fig 5)
- Emphasize adherence to lifestyle, manage other risk factors, monitor adherence

- Yes to statin

- Yes to statin

- Repeat every 4–6 y

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ASCVD Risk Estimator
Considerations

- RAWG endorsed the paradigm of 10-year risk estimation
- Existing risk scores vary with regard to:
  - Derivation populations
    - Age, sex, race, birth cohort, country/region of origin
  - Inputs
    - Traditional RFs ± family hx, BMI, SES, region, CRP
  - Outcomes
    - CVD death, Total CHD (incl revasc), Total CHD, Hard CHD, Total CVD (revasc), Hard CVD (incl HF)

ASCVD Risk Estimator
Development

- RAWG judged new risk tool was needed
  - Inclusive of African Americans and with expanded endpoint including stroke
- Sought cohorts representative of the US population as a whole
  - Community- or population-based
  - Whites and African Americans (at a minimum)
  - Recent follow up data of at least 10 years
- Reflect more contemporary risk factor trends and event rates, ideally without significant downstream uptake of statins/revascularization
ASCVD Risk Estimator
Development

- Pooled Cohort Equations
  - Atherosclerosis Risk in Communities (ARIC)
  - Cardiovascular Heath Study (CHS)
  - Coronary Artery Risk Development in Young Adults (CARDIA)
  - Framingham Original and Offspring
- Hard ASCVD
  - CHD death, non-fatal MI, fatal/non-fatal stroke
- Models tested using traditional RFs + newer markers when possible (family hx, CRP, etc)
- Internal and external validation

ASCVD Risk Estimator
Model Characteristics

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<th>White Women</th>
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</table>
ASCVD Risk Estimator

Search “ASCVD risk estimator”

55 yo AA and White Women

- African American Women: 7.7% 10-Year ASCVD Risk, 1.8% Optimal (%)
- White Women: 3.6% 10-Year ASCVD Risk, 1.4% Optimal (%)

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Recommendations for 10-Year ASCVD Risk Estimation

The race- and sex-specific Pooled Cohort Equations to predict 10-year risk for a first hard ASCVD event should be used in non-Hispanic African Americans and non-Hispanic Whites, 40 to 79 years of age.

Use of the sex-specific Pooled Cohort Equations for non-Hispanic Whites may be considered when estimating risk in patients from populations other than African Americans and non-Hispanic Whites.

Recommendations for Additional Testing if Uncertainty Remains After 10-Year Risk Assessment

If, after quantitative risk assessment, a risk-based treatment decision is uncertain, assessment of 1 or more of the following — family history, hs-CRP, CAC score, or ABI — may be considered to inform treatment decision making.

CIMT is not recommended for routine measurement in clinical practice for risk assessment for a first ASCVD event.
Developments and Evidence since Publication of the Risk Assessment Guidelines

“Evidence”

Risk Calculator for Cholesterol Appears Flawed

The New York Times

Last week, the nation’s leading heart organizations released a sweeping new set of guidelines for lowering cholesterol, along with an online calculator meant to help doctors assess risk and treatment options. But, in a major embarrassment to the health groups, the calculator appears to greatly overestimate risk, so much so that it could mistakenly suggest that millions more people are candidates for statin drugs.

The apparent problem prompted one leading cardiologist, a past president of the American College of Cardiology, to call on Sunday for a halt to the implementation of the new guidelines.

“It’s stunning,” said the cardiologist, Dr. Steven Nissen, chief of cardiovascular medicine at the Cleveland Clinic. “We need a pause to further evaluate this approach before it is implemented on a widespread basis.”

The controversy set off turmoil at the annual meeting of the American Heart Association, which started this weekend in Chicago.
Women’s Health Study

• Applied Pooled Cohort Equations to the Women’s Health Study Population
  ▪ 27,000 female health professionals 45 to 79 yo
  ▪ Followed for 10 years

• Unadjusted calibration
  ▪ 45%-90% “over-estimation”

*Does not account for in-trial and downstream ASA, downstream anti-HTN Rx, or healthy volunteer effect

Cook, Ridker. JAMA IM, 2014
Rotterdam: Poor Calibration (Unadjusted)

ACC/AHA 2013

EPIC-Norfolk: Excellent Calibration (Unadjusted)

Ray, EHJ 2014
**Methodological problems**

1. Repeated CAC scoring
   - Those more likely to have events more likely to be treated at all risk levels (+ behavior change?)

2. Prevalence/initiation of preventive Rx: Natural history?
   - ASA ↑ 25% - 55%
   - AntiHTN ↑ 35% - 60%
   - Lipid meds ↑ 15% - 44%
   - Any Rx ↑ 53% - 80%

3. Inadequate accounting for effects of therapy
   - a la Cook/Ridker approach

4. Inclusion of Latino- and Chinese-American pts

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**REGARDS**

*5-year follow up
Muntner et al, JAMA 2014
REGARDS

Participants without diabetes, LDL-C of 70 to 189 mg/dL, not taking statins
Medicare-linked sample

- *5-year follow up
- Muntner et al, JAMA 2014

Performance of Pooled Cohort Equations in Diverse Population Samples: Predictable

Estimated 10-y ASCVD Risk

- Low risk, high SES, medicated populations
- Broad US Population (REGARDS, DHS)
- Well Calibrated
- HIV, Inflammatory/Rheum dz
- Underestimate Risk

Patient-Clinician Discussion
Summary

• Absolute risk estimation remains an important framing principle for identifying those at risk/most likely to benefit
  ▪ Short- and long-term

• The Pooled Cohort Equations provide a major step forward in assessing risk for ASCVD (not just CHD)
  ▪ Better representation of risk for women and AA
  ▪ Well calibrated to the broad US population seen in 1st care
  ▪ Well suited for starting a clinician-patient discussion

Perspective: What’s the Worry?

• We are in an era of significant use of medical therapy for primary prevention
  ▪ Contemporary cohorts with true natural history are hard to find
  ▪ Risk estimates attempt to predict natural history to assist with decision-making

• “Over-prediction” vs mismatch
  ▪ Newer methods/approaches needed to understand mismatch

• Demanding perfect precision is unrealistic and unnecessary
  ▪ Decision thresholds using the risk estimates are well above demonstrated “net benefit” and far above cost-effectiveness thresholds
  ▪ Clinician judgment is back in play

• Further evidence needed regarding the optimal role for disease screening