The Art of Cardiovascular Risk Assessment

Laurence S. Sperling, M.D., FACC, FACP, FAHA, FASPC
Professor of Medicine (Cardiology)
Professor of Global Health
Director- Center for Heart Disease Prevention
Emory University
Immediate Past President, American Society for Preventive Cardiology
Chairman of ACC Cardiometabolic Working Group
Chairman of The U.S. National Cardiometabolic Alliance
About the Presenter

Laurence S. Sperling, MD
Professor of Medicine
Director of The Center for Heart Disease Prevention
Emory University School of Medicine
Atlanta, GA

DISCLOSURES

No potential conflicts related to this presentation
Art of CV Risk Assessment

- Case
- Risk factors / Risk scores
- Risk Assessment
- Risk estimation / lifetime risk / reclassification of risk
- Precision medicine vs. population-based risk
Case:
A 52 yo African American female wants your opinion on heart attack & stroke prevention.

Moderately active, Asx. Has worked hard to make lifestyle changes for 6 mo.
BMI of 29
BP 138/78 mmHg
TC 210, HDL 32, TG 180, LDL 152
No Hx of Tob or DM
Fasting BG 110 (family Hx of DM)
QUESTION:

She is worried about her risk of diabetes. In addition, she heard statins can hurt your muscles & liver.

Thoughts about CV Risk?

How do I best assess CV Risk?
Identifying those at increased risk....

Sitting in a 3.8-metre sea kayak and watching a four-metre great white approach you is a fairly tense experience.
“In 1961 with just two words, Bill (Kannel) helped to change our understanding of the underlying causes of heart disease and stroke, and with two words, the entire field of preventive cardiology was born.”

Daniel Levy

Current Framingham Heart Study Director

Wong N., Sperling L., Baum S. The ASPC: Our 30 Year Legacy, Clinical Cardiology, 2016
Concept of cardiovascular “risk factors”

Factors of Risk in the Development of Coronary Heart Disease—Six-Year Follow-up Experience

The Framingham Study

William B. Kannel, M.D., Thomas R. Dawber, M.D., F.A.C.P.,
Abraham Kagan, M.D., F.A.C.P., Nicholas Revotskie, M.D.,
and Joseph Stokes, III, M.D.

Framingham, Massachusetts

Age, sex, hypertension, hyperlipidemia, smoking, diabetes, (family history), (obesity)

FIGURE 1. Risk of CHD according to elevated blood pressure (BP), elevated cholesterol, and left ventricular hypertrophy: Framingham cohort 6-year follow-up. Elevated BP = ≥160/95; elevated cholesterol = ≥260 mg/dl.
Why Use Risk Scores?

1) Dr. Kannel noted risk functions provide an “economic and efficient method of identifying persons at high cardiovascular risk who need preventive treatment,” (AJC 1976)

2) The ACC Bethesda Conf. noted intensity of treatment should match a person’s risk (Califf RM, JACC 1996).

3) A physician’s “guesstimate” is only accurate 24% of the time (Pignone et al, BMC health Serv Res 2003).

4) Routine use of global risk scores leads to greater use of guideline-based therapy and modest improvements in intermediate outcomes with no harm identified (Sheridan et al. BMC Health Serv Res 2008).
Preventive cardiology efforts begin with assessment of cardiovascular disease risk

Recommendation- begin with global risk assessment using Pooled Cohort Equations to estimate 10-year ASCVD Risk
Risk Stratification

Figure 1. Implementation of Risk Assessment Work Group Recommendations

Does the patient have existing clinical ASCVD?

Yes → See AHA/ACC Secondary Prevention Guideline

No

Is the patient <20 y or >79 y of age?

Yes → See Pediatric Guidelines and ACC/AHA Adult Primary Prevention Guidelines
- Blood Cholesterol
- Obesity

No

Assess traditional risk factors every 4-6 y in patients 20-79 y of age; estimate 10-y risk in those 40-79 y of age using Pooled Cohort Equations

Elevated 10-y risk (≥7.5%)

Low 10-y risk (<7.5%)

Assess 30-y or lifetime risk in those 20-59 y of age; Communicate risk data regardless of age and refer to AHA/ACC Lifestyle Guideline
Pooled Cohort Equations for ASCVD Risk

predict 10-year risk of both CHD and stroke (ASCVD) vs. CHD (focus of 2001 ATP III)

predict nonfatal MI, CHD death, or nonfatal or fatal stroke ONLY; do not include (PCI, CABG, UA requiring hospitalization, PAD) - Risk will be higher for total CVD

Clincalc; omnibus risk estimator; AHA; ACC
Cardiosource
i-phone ??
Pooled ASCVD RS- How used?

incorporate 4 cohorts: Framingham (original and offspring), ARIC, CARDIA, and CHS

used as starting point to help identify those most likely to benefit from a statin; other tests may help refine the treatment decision if uncertain

should be an impetus for a “risk discussion” between the clinician and patient
2013 Prevention Guidelines
ASCVD Risk Estimator

The ACC and the American Heart Association (AHA), in collaboration with the National Heart, Lung, and Blood Institute and other specialty societies, have released four guidelines focused on the assessment of cardiovascular risk, lifestyle modifications to reduce cardiovascular risk and management of elevated blood cholesterol and body weight in adults.

In order to support the implementation of these guidelines the ACC and AHA have jointly published a new mobile application (app).

The ASCVD Risk Estimator application helps health care providers and patients estimate 10-year and lifetime risks for atherosclerotic cardiovascular disease (ASCVD) using the Pooled Cohort Equations and lifetime risk prediction tools. The ASCVD Risk Estimator provides easy access to recommendations specific to calculated risk estimates. Additionally, the app includes readily accessible guideline reference information for both providers and patients related to therapy, monitoring, and lifestyle.

The app is available on both iTunes (iPhones, iPads) and Google Play (Galaxy, Nexus, other Android devices). Use the links below from your mobile device to download the app.

Available at www.cardiosource.com or www.clinicalcalc.com
ASCVD Risk Estimator

• 10 year ASCVD Risk

• For those 20-59 risk estimator provides lifetime risk estimate

• Intended to drive discussions of greater adherence to heart-healthy lifestyle

• Part of risk discussion
Our case……
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BP 138/78 mmHg
TC 210, HDL 32, TG 180, LDL 152
No Hx of Tob or DM
Fasting BG 110 (family Hx of DM)
Risk Estimate????
Her 10 yr ACC/AHA ASCVD risk is 6.3% (optimal risk 1.3%)

Remember......she is worried about her risk of diabetes. In addition, she heard statins can hurt your muscles & liver.

Discussion & implementation of treatment recommendations?
Lifetime Risk for CVD (Age 50) – LOE C

Adjusted Cumulative Incidence

Attained Age

Men

Women

≥2 Major RFs
≥1 Major RF
≥1 Elevated RF
≥1 Not Optimal RF
Optimal RFs

50%
69%
50%
50%

36%
46%
36%
27%

39%
50%

8%
5%
Her Lifetime ACC/AHA ASCVD risk is 39% (optimal risk 8%)

Impact discussion & treatment recommendations?
**Clinician Patient Risk Discussion: Importance to Implementation of Guidelines**

**JACC 2015;65(13):1361-1368**

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**CLINICIAN-PATIENT RISK DISCUSSION (CPRD)**

**CLINICIAN**
- Present evidence-based clinical guidelines in the context of clinical judgment
- Personalize the presentation; consider visual aids (icon arrays/pictographs) to improve patient understanding

**PATIENT**
- Express personal preferences and make informed decisions

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**Present ACC/AHA Risk Estimator Application**
- Endorse the tool as a helpful resource to aid understanding of ASCVD risk, diet and physical activity recommendations, weight management, blood cholesterol, statin benefit groups, and common CV terms.
  - To be used during and in-between clinical encounters

**Discuss Patient’s 10-Year Risk Estimate**
- Review ACC/AHA Risk Estimator application tool results

**Discuss Options to Reduce ASCVD Risk**
- **Lifestyle changes (in all)**
  - Review diet and physical activity habits
  - Endorse lifestyle changes
  - Explain benefits of a healthy lifestyle to improve blood pressure and cholesterol levels and reduce the risk for ASCVD and diabetes
- **Initiation of statin (not automatic)**
  - Explain benefits to improve cholesterol levels and reduce ASCVD risk
  - Note that statin therapy is commonly lifelong: Patient will likely need to continue therapy indefinitely to maintain cholesterol levels

**Discuss Potential for Statin Adverse Effects (The S Ms)**
- **Metabolism:** Small risk of new-onset diabetes in those predisposed
- **Muscles:** Range of muscle symptoms can occur
- **Medication interactions:** Possible prescription interactions
- **Major organ effects:** Rare possibility of major organ effects
- **Memory:** The guidelines found no evidence for cognitive impairment

**Discuss Patient Questions/Values/Preferences**
- Review patient values and preferences
- If patient lacks confidence to make decisions, review factors that modify risk if a risk decision is uncertain; family history of premature ASCVD; LDL-C ≥ 160 mg/dl; an elevated coronary artery calcium score or ≥75th percentile based on age, sex, and ethnicity; hs-C-reactive protein (CRP) level ≥ 2.0 mg/L; ankle brachial index (ABI) < 0.9
- Patient may desire time to review information before making decisions

**Benefits of CPRD**
- Strengthen clinician-patient relationships
- Boost patient engagement and medication adherence
- Heighten patient satisfaction: Patient preference is for shared decision making (SDM) and patients appreciate evidence-based guidelines
- Acknowledges that each case is unique and patient preferences matter

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NET CLINICAL BENEFIT by diabetes status (for a near 40 mg/dL reduction in LDL cholesterol) from a meta-analysis of 14 clinical trials of statin therapy.

A

Non-diabetics
- All-cause mortality
- Cardiac death
- Stroke
- Coronary revascularization
- Major coronary event

Diabetics
- All-cause mortality
- Cardiac death
- Stroke
- Coronary revascularization
- Major coronary event

Relative Risk of Event

Statin therapy better

Control therapy better

B

**BENEFIT**
- Reduction in cardiovascular risk (primary and secondary prevention in diabetics and non-diabetics)

**RISK**
- New-onset diabetes
- Liver and muscle toxicity
- Rare serious side effects (rhabdomyolysis, death)

Should I start a statin in my patient?

What is the underlying patient-specific risk of a cardiac event?
(by conventional risk algorithms, e.g., Framingham score; primary vs. secondary prevention)

Ravi V. Shah, and Allison B. Goldfine Circulation.
2012;126:e282-e284
Efficacy & Safety of Statins

- Atorva 40 mg in 10K with ASCVD / High Risk
  - Prevent **1000** events with ASCVD (10% absolute RR)
  - Prevent **500** events in high risk population (5% RR)
  - **5** cases myopathy / **50-100** myalgias
  - **50-100** new cases of diabetes

“Evidence-Based” Not “Evidence-Bound”

Three Key Dimensions

Scientific evidence

Patient preference

Clinical Judgment
Receiver Operating Characteristic Curves and Disease Prediction

![Graph showing ROC curves]

- **Sensitivity (True Positives)**
  -更好测试(Better test)
  -良好测试(Good test)
  -机会线(Chance Line)

- **1-Specificity (False Positives)**
  -范围从0到1
Comparison of Novel Risk Markers for Improvement in Cardiovascular Risk Assessment in Intermediate-Risk Individuals (n=1330)

C-statistics:

- FRS alone 0.623
- FRS+CAC 0.784 (p<0.001)
- FRS+CIMT 0.652 (p=0.01)
- FRS+FMD 0.639 (p=0.06)
- FRS+CRP 0.640 (p=0.03)
- FRS+FamHx 0.675 (p=0.001)
- FRS+ABI 0.650 (p=0.01)

Yeboah J et al, JAMA 2012
“…risk estimation is based on group averages...applied to individual patients in practice. This process is admittedly imperfect..”

2013 ACC / AHA Guidelines on the Assessment of CV Risk
The Detection Gap in CHD

“Despite available RA approaches substantial gap in detection of asymptomatic individuals who develop CHD”

Current risk scores… “emphasize classic risk factors…. only moderately accurate for prediction of short- and long-term risk of major events…”

Pasternak and Abrams et al. 34th Bethesda conf. JACC 2003; 41: 1855-1917
Predicting ASCVD Risk?

- Arterial imaging/function
- Biomarkers
- Metabolic syndrome
- Family history
- Pooled 10 yr ASCVD Risk Equation

Identification of the Metabolic Syndrome

• Abdominal obesity (waist circumference)
  – Men >40 in
  – Women >35 in

• Triglycerides >150 mg/dL

• HDL-cholesterol
  – Men <40 mg/dL
  – Women <50 mg/dL

• Blood pressure >130/85 mm Hg

• Fasting glucose >100 mg/dL
Affirmed Concepts

• MetS associated with risk for DM & ASCVD
• MetS cluster of under-recognized causally inter-related RFs
• Risk increases with # of components
• Ectopic and visceral adiposity central
• Treatment-prioritize TLC / focus on specific components

Sperling LS, et al. JACC 2015;66(9):1050-1067
Staging system for MetS- A Framework
Sperling LS et al., JACC 2015;66(9):1050-67

- Identify
- Risk-stratify
- Apply evidence-based therapeutic interventions
  - **imperative that Rx decisions incorporated within context of absolute risk**
Stages in Evolution of MetS
(Therapy by Stage)
Sperling LS et al., JACC 2015;66(9):1050-67
Spectrum / Lifecourse of Health

- Acute CV Events
- Stable CVD
- Subclinical CVD
- Promotion of CV Health
- Optimal Window at 3-5 years

Adapted from Fuster V., JACC 2015; 66(4):482.
Selective consideration

Biomarkers and Noninvasive Testing
Can Inform Treatment Decision (when Uncertain Based on Risk Assessment)

1) Primary LDL-C $>160$ mg/dl or other genetic evidence of hyperlipidemia
2) Family history of premature ASCVD with onset $<65$ in a female first degree or $<55$ years of age in a male first degree relative
3) C-reactive protein $\geq 2$ mg/L
4) CAC score $\geq 300$ or $\geq 75^{\text{th}}\%$tile for age and sex
5) ABI $<0.9$ indicative of PAD
6) Elevated lifetime risk of CVD
Contribution to RA is uncertain at present

1) ApoB
2) CKD
3) Albuminuria
4) Cardiorespiratory fitness
Non-traditional CV Risk Factors

- Lp(a)
- Autoinflammatory / HIV
- XRT
- X-plant recipients
- Stress / Anxiety / depression
- Pregnancy-related disorders
  - Gest DM, preeclampsia
- Drugs / Toxins
  - Cocaine, HRT, NSAIDS

Major Risk Factors for Coronary Artery Disease

-Age (men ≥ 45 years; women ≥ 55 years)
-Family history of premature coronary artery disease (CAD in male first-degree relative < 65 years)
-Hypertension (BP > 140/90 mmHg or on antihypertensive medications)
-Cigarette Smoking
-Diabetes
-Hypercholesterolemia
-Low HDL cholesterol (< 40 mg/dl)
-Hypertriglyceridemia (> 200 mg/dl)
-Obesity
Criteria for Marker of CV Risk

• Proof of concept
• Prospective validation
• Incremental value
• Clinical utility
• Clinical outcomes
• Cost-effectiveness

– AHA Scientific Statement, Hlatky MA et al., Circulation, 2009;119
Use All Available Information

- Contemporary Risk Score Calculators
- Clinical Markers of ASCVD
- Advanced Measures of Subclinical Atherosclerosis (CAC) For Difficult Cases

<table>
<thead>
<tr>
<th>Table: Clinical Markers of Coronary Heart Disease Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Historical markers</td>
</tr>
<tr>
<td>Family history</td>
</tr>
<tr>
<td>Transient ischemic attack</td>
</tr>
<tr>
<td>Claudication</td>
</tr>
<tr>
<td>Erectile dysfunction</td>
</tr>
<tr>
<td>Physical inactivity</td>
</tr>
<tr>
<td>Physical examination markers</td>
</tr>
<tr>
<td>Widened pulse pressure</td>
</tr>
<tr>
<td>Ankle–brachial index</td>
</tr>
<tr>
<td>Increased waist circumference</td>
</tr>
<tr>
<td>Retinal arteriolar narrowing</td>
</tr>
<tr>
<td>Aortic sclerotic murmur</td>
</tr>
<tr>
<td>Carotid bruit</td>
</tr>
<tr>
<td>Femoral bruit</td>
</tr>
<tr>
<td>Absent lower extremity pulses</td>
</tr>
<tr>
<td>Radiologic markers</td>
</tr>
<tr>
<td>Aortic knob calcification</td>
</tr>
<tr>
<td>Abdominal aortic calcification</td>
</tr>
<tr>
<td>Breast arterial calcification (mammogram)</td>
</tr>
<tr>
<td>Laboratory/electrocardiographic markers</td>
</tr>
<tr>
<td>Fasting blood glucose</td>
</tr>
<tr>
<td>Serum creatinine/microalbuminuria</td>
</tr>
<tr>
<td>Left ventricular hypertrophy</td>
</tr>
</tbody>
</table>

DeFilippis A, Sperling LS. Prev Card 2007
PRECISION MEDICINE?
POPULATION HEALTH?
President Obama’s Precision Medicine Initiative
January 30, 2015

- effort to revolutionize approach to health & disease.
- Patient-powered research to accelerate biomedical discoveries.
- innovative approach (individual differences - genes, environments & lifestyles)

Key Investments to Launch the Precision Medicine Initiative:
- $130 million NIH
- $70 million National Cancer Institute (NCI).
- $10 million FDA.
Precision Medicine: Biomarkers of Cardiovascular risk

Conventional Risk factors
Age, smoking, hypertension, hypercholesterolemia, diabetes, obesity, LV function, renal dysfunction

Social, psychological, environmental determinants

Glutathione/Cystine
HsCRP, FDPs
HSP-70
Supar

HsTroponin

Cardiovascular Events
Death, MI, Heart Failure

Gene risk score
Gene Expression score
Metabolome
Proteome
microRNA

CD34+/CD133+ cells

Social, psychological, environmental determinants

Glutathione/Cystine
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Cardiac Events
Death, MI, Heart Failure

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microRNA

CD34+/CD133+ cells
A Framework for Public Health Action: The Health Impact Pyramid

- Physical environment
- Food environment
- Social environment
- Economy and poverty

FIGURE 1—The health impact pyramid.

Frieden, Am J Public Health, 2009
Focus on CV Population Health: The Health/Disease Continuum
JACC 2015;66:960-7

Normal
Low risk

Normal
High risk

Pre
disease

Early
disease

Late
disease

Health Promotion & Disease Prevention

Contemporary Medicine
Making Healthcare Better: CV Health
White House Briefing, Sept. 9, 2016

• Progress on CV Health
  – Research, access, and coverage
• Deepening the conversation on CV Health
  – Compelling stories from patient / advocates
• Improving CV Health in our Communities
  – Where we live, work, learn, play (and pray)
Population Health measures

- Impact of moving bell curve toward better health vs. individual & episodic HC
Geomapping- Social Determinants of Health

- Health varies at a very LOCAL level

- National Health Index
  - Profile of Diabetes
Mandatory Reporting of A1C

• Introduced 2006 by Board of Health
• A1C lab tests on NYC residents reportable to Health Department
• Majority not well controlled
  – ~132,000 with diabetes between 2006-2012
  – Nearly 2/3 not consistently A1C <8
• Hot spotting to target intervention

Courtesy Sonia Angell, MD, MPH, Deputy Commissioner NYC Dept. Health
Using Clinical Data to Inform a Population Response

Source: NYC A1C Registry, 2006 - 2012
Community Health Worker Initiative – Harlem Health Advocacy Partners

**Targets** Residents of 5 NYCHA Developments

**Goals:**
- Improve health of residents
- Decrease existing disparities in chronic diseases
- Policy agenda to advocate for CHW certification & reimbursement

**Design Components**
- Community Engagement
- Wellness Activities
- Health Insurance Navigation
- Health Coaching

[Map showing hotspot distribution with uncontrolled diabetes per A1C registry (>9)]
Social Determinants of Health: Zip Code vs. Genetic Code?

- Health varies at a very LOCAL level
- Life expectancy in Atlanta
Socio-economic determinants of vascular disease (Food Deserts)- Presence of “L & MIC” in HIC
Mohamed Kelli, H. et al. ACC 2016

- Food desert: Locations with low food access and low income (USDA).
- 23.5 million U.S. residents live in food deserts.
- 1421 subjects residing in the Atlanta (MetaHealth, Pred Health studies)

Food deserts in the Atlanta metropolitan area (USDA map)
Cardiovascular Prevention Dashboard Command Center?

- Home-based
- Greater focus on those out of range or at increased risk, i.e. in the “red zone”
Art of CV Risk Assessment - Summary

• RA begins with population-based risk score

• Importance of
  – Clinician-patient risk discussion
  – Net clinical benefit

• Consider select use
  – Biomarkers
  – Measures of subclinical atherosclerosis

• GLs are a starting point

• Better understanding of precision medicine & population-based risk
Cardiovascular Prevention Center – Founded 1997

- Primary and secondary prevention clinics
- HeartWise Risk Reduction Program
- Optimal Living
- Women’s Heart Program
- Cardio-oncology
- Cardio-inflammatory
- Sports Cardiology
- Subclinical markers of atherosclerosis
- Screenings and Risk Factor management
- LDL apheresis
- Housestaff / fellow training programs
- Clinical and Translational Science Research
From: Clinician-Patient Risk Discussion for Atherosclerotic Cardiovascular Disease Prevention: Importance to Implementation of the 2013 ACC/AHA Guidelines

Biomarkers & Noninvasive Testing that Can Inform Treatment Decision (when Uncertain Based on RA)

1) Primary LDL-C >=160 mg/dl or other genetic evidence of hyperlipidemia
2) Family history of premature ASCVD with onset <65 in a female first degree or <55 years of age in a male first degree relative
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