Disclosures

Faculty and Steering Committee Disclosures
The faculty and steering committee reported the following relevant financial relationships that they or their spouse/partner have with commercial interests:

Deepak L. Bhatt, MD, MPH – Research: Amarin, AstraZeneca, Bristol-Myers Squibb, Eisai, Ethicon, Medtronic, Roche, Sanofi Aventis, The Medicines Company

David A. Morrow, MD, MPH – Research: Abbott Diagnostics, Amgen, AstraZeneca, Athera, Beckman Coulter, BG Medicine, Bristol-Myers Squibb, Buhlmann Laboratories, Daiichi-Sankyo, Eisai, Eli Lilly and Co., GlaxoSmithKline, Johnson & Johnson, Merck and Company, Nanosphere, Novartis Pharmaceuticals, Ortho-Clinical Diagnostics, Pfizer, Randox, Roche Diagnostics, Sanofi-Aventis, Siemens, Singulex; Consultant/Advisory Board: Abbott Laboratories, diaDexus, Eli Lilly and Co., Gilead, Instrumentation Laboratory, Konica-Minolta, Merck, Novartis, Prevencio, Radiometer, Roche Diagnostics, Servier

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Non-faculty content contributors and/or reviewers reported the following relevant financial relationships that they or their spouse/partner have with commercial interests:

Barry Watkins, PhD; Blair St. Amand; Jay Katz, CCMEP; Dana Simpler, MD: Nothing to Disclose

Educational Objectives

• Adhere to guidelines-recommended approaches in the diagnosis and risk assessment of SIHD patients

• Adopt evidence-based risk assessment strategies to identify high-risk patients who are likely to benefit from intensive therapies and revascularization options

• Understand the management of persistent or recurrent angina in patients who have been revascularized
PATHOPHYSIOLOGY AND NATURAL HISTORY
Stable Ischemic Heart Disease (SIHD)

Changing Perspectives on Stable Ischemic Heart Disease

Morphing name
stable angina → chronic coronary disease → SIHD

Disease progression

Early Presymptom
CT evidence Carotid intimal Coronary Ca + stress test

Frank CAD
Dynamic symptoms
Shifting perception of pathobiology

Risk factors
Dyslipidemia Hypertension Smoking Diabetes Obesity Sedentary Poor nutrition Older age

150 million in U.S.

17.6 million in U.S.
Pathobiological Contributors to Ischemic Heart Disease: *Not Just Epicardial Stenosis*

- Critical Coronary Stenosis
- Inflammation
- Platelets and Coagulation
- Vasospasm
- Microvascular Dysfunction
- Endothelial Dysfunction

Abnormalities Evolving During Myocardial Ischemia

- Symptoms occur at end of ischemic cascade
- Approximately 50% of patients with angina also experience episodes of asymptomatic (silent) ischemia
- Many episodes of ischemia never become painful

THE COMPLEXITIES OF STABLE ISCHEMIC HEART DISEASE AND ITS TREATMENT

**Percentage of Patients Who Had Ischemic Heart Disease, but no Coronary Artery Disease**

![Bar graph showing the percentage of patients with no CAD in different heart conditions]


**Proposed Mechanisms in Angina Pectoris with Non-obstructive Coronary Artery Disease**

- Endothelial Dysfunction
- Microvascular Dysfunction
- Spasm

Della Rocca DG, Pepine CJ. Eur Heart J. 2014;35:873-877
THE COMPLEXITIES OF STABLE ISCHEMIC HEART DISEASE AND ITS TREATMENT

Intracellular Ischemic Cascade Effects on Late \( I_{Na} \) and Intracellular \( Ca^{++} \)

- Calcium overload:
  - Impaired Inactivation
  - Electrical instability

- Mechanical dysfunction:
  - And relaxation
  - ↑ Diastolic tension
  (↑LV wall stiffness)

- Oxygen supply and demand:
  - Increase ATP consumption
  - Decrease ATP formation

- Electrical instability:
  - Early after potentials
  - Beat-to-beat ΔAPD
  - Arrhythmias (VT)


SIHD: Major Adverse Cardiovascular Event-free Survivor Function of Women with No Obstructive Coronary Artery Disease, Age-adjusted to 60 years

The Complexities of Stable Ischemic Heart Disease and Its Treatment

Risk of CV Death or MI by History of Stable Angina: REACH Registry


Myocardial Ischemia Diminishes Quality of Life
Assessment of General Health Status During Follow-up Visits

EVALUATION OF THE PATIENT WITH SIHD

Diagnosis and Risk Stratification

Clinical Assessment

Evaluation and Diagnosis

- Patients presenting with chest pain
  - Detailed symptom history
  - Focused physical examination, including ECG
  - Directed risk-factor assessment
- Estimate the probability of significant ischemic heart disease (low, intermediate, high)
- Estimate the risk of major vascular events if ischemic heart disease is present

**Initial Diagnostic Testing**

*Patient Able to Exercise*

- **Able to Exercise**
  - No Contraindications to Stress Testing

**No Previous Revascularization**

**Interpretable Resting ECG**

**Likelihood of Ischemic Heart Disease**

- **Intermediate**
  - Standard Exercise ECG
  - MPI or Echocardiogram With Exercise

**Previous Revascularization**

**or**

**Resting ECG Not Interpretable**

**MPI or Echocardiogram**

**With Exercise**

I | IIa | IIb | III
--- | --- | --- | ---
Low |  |  |  
Intermediate |  |  |  
High |  |  |  

MPI: myocardial perfusion imaging.


---

**Duke Treadmill Score**

*4-Year Survival by Risk Group*

- **Low Risk**
  - Score: >+5
- **Moderate Risk**
  - Score: -10 to +4
- **High Risk**
  - Score: <-10

**4-Year Survival (%)**

Low Risk
Moderate Risk
High Risk

**Annual Mortality (%)**

Low Risk
Moderate Risk
High Risk

n=613 consecutive patients with suspected coronary disease who were referred for exercise testing. The Duke treadmill score was calculated as follows:

- Exercise duration in minutes – (5x maximal ST-segment deviation during or after exercise, in millimeters) – (4x treadmill angina index).
- Numerical treadmill angina index: 0 for no angina, 1 for non-limiting angina, and 2 for exercise-limiting angina.
- Treadmill scores ranged from -25 (indicating the highest risk) to +15 (indicating the lowest risk).

SIHD Diagnosis: Appropriate Appropriateness of Invasive Testing for Diagnosis

- Noninvasive stress testing is normally appropriate initial study
- Angiography is appropriate only when information derived will significantly influence patient management
  - Useful in patients with SIHD who have symptoms despite GDMT
  - Reasonable to define extent of CAD in patients with high likelihood of severe IHD
  - Reasonable in patients with suspected SIHD who cannot undergo stress testing
  - Reasonable in patients with negative stress test, but suspicion of CAD remains high

Fihn SD et al. Circulation. 2014, published online ahead of print

Initial Diagnostic Testing
Patient Not Able to Exercise

Not Able to Exercise
No Contraindications to Stress Testing

Low Likelihood of Ischemic Heart Disease (IHD)
Pharmacologic Stress Echocardiogram

Intermediate-to-High Likelihood of IHD
OR

Pharmacologic Stress MPI or Echocardiogram

Pharmacologic Stress CMRI or CCTA

Not Recommended For High Likelihood

MPI: myocardial perfusion imaging. CMRI: cardiac magnetic resonance imaging. CCT: cardiac computed tomography

Risk Stratification in Patients With Coronary Heart Disease

**Clinical Parameters**
- Patient demographics
- Risk factors
- Symptoms
- History of vascular disease

**Noninvasive Testing**
- ECG
- Chest x-ray
- LVEF
- ETT
  - Duke Treadmill Score
- Stress imaging
  - Nuclear
  - Echo
  - CMRI

**Coronary Imaging**
- Coronary calcium scoring
- CT angiography
- Coronary angiography


### Noninvasive Risk Stratification

**Low-risk (<1% annual mortality rate)**
1. Low-risk Duke treadmill score (score ≥ 5)
2. Normal or small myocardial perfusion defect at rest or with stress
3. Normal stress echocardiographic wall motion or no change of limited resting wall motion abnormalities during stress

**Intermediate-risk (1-3% annual mortality rate)**
1. Mild-moderate resting LV dysfunction (LVEF – 35% to 49%)
2. Intermediate-risk treadmill score (-10 to +4)
3. Stress-induced moderate perfusion defect, indicating 1 vascular territory, without LV dilatation or increased lung intake of thallium-201
4. Limited stress echocardiographic ischemia with a wall motion abnormality only at higher doses of dobutamine involving two or more segments

**High-risk (>3% annual mortality rate)**
1. Severe resting LV dysfunction (LVEF <35%) not readily explained by non-coronary causes
2. High-risk treadmill score (score ≤-11)
3. Severe exercise left ventricular dysfunction (LV EF <35%)
4. Stress-induced large perfusion defect (particularly if anterior)
5. Stress-induced multiple perfusion deficits of moderate size
6. Large fixed perfusion defect with LV dilation or increased lung intake of thallium-201
7. Echocardiographic wall motion abnormality, involving more than 2 segments, developing at low dose of dobutamine (< 10 mg/kg/min) or low heart rate (< 120 bpm)
8. Stress echocardiographic evidence of extensive ischemia

Adapted from Topol EJ, Griffin BP. Manual of Cardiovascular Medicine. 3rd Edition. Lippincott Wilkins and Williams. 2007
THE COMPLEXITIES OF STABLE ISCHEMIC HEART DISEASE AND ITS TREATMENT

**COURAGE Trial Nuclear Substudy**
5-year Survival of CAD Patients with 0% to >10% Residual Ischemia

![Graph showing 5-year survival rates for CAD patients with different residual ischemia levels.](image)


**Intermediate Stenosis without Evidence of Ischemia**
Cardiac Death and Acute MI after 5 Years

![Bar graph showing the percentage of patients with cardiac death and acute MI after 5 years based on PCI reference and FFR levels.](image)

THE COMPLEXITIES OF STABLE ISCHEMIC HEART DISEASE AND ITS TREATMENT

SYNTAX
Angiographic Risk Stratification Coronary Tree Segments

Example Weighting

<table>
<thead>
<tr>
<th>SEGMENT NUMBER</th>
<th>R DOMINANCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 RCA proximal</td>
<td>1</td>
</tr>
<tr>
<td>2 RCA mid</td>
<td>1</td>
</tr>
<tr>
<td>3 RCA distal</td>
<td>1</td>
</tr>
<tr>
<td>4 PDA</td>
<td>1</td>
</tr>
<tr>
<td>16 PLB from RCA</td>
<td>0.5</td>
</tr>
<tr>
<td>5 Left Main</td>
<td>5</td>
</tr>
<tr>
<td>6 LAD proximal</td>
<td>3.5</td>
</tr>
<tr>
<td>7 LAD mid</td>
<td>2.5</td>
</tr>
<tr>
<td>8 LAD apical</td>
<td>1</td>
</tr>
<tr>
<td>9 First diagonal</td>
<td>1</td>
</tr>
</tbody>
</table>

Syntax-Score: Low (≤8)
Syntax-Score: Middle (>8 and ≤16)
Syntax-Score: High (>16)

Patients in the highest tertile of SYNTAX score have an increased major adverse cardiac event rate (P=0.0002).

Kaplan-Meier Curves for MACE at 360 Days
According to the SYNTAX Angiographic Risk Stratification

Example SYNTAX Weighting

<table>
<thead>
<tr>
<th>SEGMENT</th>
<th>R DOMINANCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 RCA proximal</td>
<td>1</td>
</tr>
<tr>
<td>2 RCA mid</td>
<td>1</td>
</tr>
<tr>
<td>3 RCA distal</td>
<td>1</td>
</tr>
<tr>
<td>4 PDA</td>
<td>1</td>
</tr>
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<td>16 PLB from RCA</td>
<td>0.5</td>
</tr>
<tr>
<td>5 Left Main</td>
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</tr>
<tr>
<td>6 LAD proximal</td>
<td>3.5</td>
</tr>
<tr>
<td>7 LAD mid</td>
<td>2.5</td>
</tr>
<tr>
<td>8 LAD apical</td>
<td>1</td>
</tr>
<tr>
<td>9 First diagonal</td>
<td>1</td>
</tr>
</tbody>
</table>

INTEGRATED TREATMENT APPROACH

Patient Education and Behavior Modification

Patient Education

• Patients with SIHD should have an individualized education plan to optimize care and promote wellness
  – Education on the importance of medication adherence
  – Explanation of medication management and cardiovascular risk reduction strategies
  – Comprehensive review of all therapeutic options
  – A description of appropriate levels of exercise
  – Self-monitoring skills and information on how to recognize worsening cardiovascular symptoms
  – Lifestyle elements that could influence prognosis
### Lifestyle/Risk Factor Goals

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Goal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking</td>
<td>Cessation</td>
</tr>
<tr>
<td>Total Dietary Fat / Saturated Fat</td>
<td>&lt;30% calories / &lt;7% calories</td>
</tr>
<tr>
<td>Fish/Omega 3</td>
<td>≥3 servings/week / 1 g/day</td>
</tr>
<tr>
<td>Dietary Cholesterol</td>
<td>&lt;200 mg/day</td>
</tr>
<tr>
<td>Dietary Sodium</td>
<td>&lt;2,000 mg/day (DASH diet goal)</td>
</tr>
<tr>
<td>Physical Activity</td>
<td>≥30 min/day; 5 times/week (daily Ila)</td>
</tr>
<tr>
<td>Weight Loss / Maintenance</td>
<td></td>
</tr>
<tr>
<td>BMI (Plus Waist Circumference)</td>
<td></td>
</tr>
<tr>
<td>Blood Pressure</td>
<td></td>
</tr>
<tr>
<td>LDL Cholesterol (primary goal)</td>
<td>25-27.5</td>
</tr>
<tr>
<td>HDL Cholesterol</td>
<td>BMI &lt;25 (WC &lt;40in/35)</td>
</tr>
<tr>
<td>Non-HDL Cholesterol (secondary goal)</td>
<td>&gt;27.5</td>
</tr>
<tr>
<td>Diabetes</td>
<td>10% relative weight loss</td>
</tr>
<tr>
<td>Blood Pressure</td>
<td>&lt;140/90 mmHg</td>
</tr>
<tr>
<td>LDL Cholesterol (primary goal)</td>
<td>Intensive statin therapy</td>
</tr>
<tr>
<td>HDL Cholesterol</td>
<td>&gt;40 mg/dL for men; &gt;50 mg/dL women</td>
</tr>
<tr>
<td>Non-HDL Cholesterol (secondary goal)</td>
<td>&lt;130 mg/dL(&lt;100 Ila) if TG ≥200 mg/dL</td>
</tr>
<tr>
<td>Diabetes</td>
<td>HbA1c &lt;7.0%</td>
</tr>
</tbody>
</table>

Stone JN et al. J Am Coll Cardiol 2014;63:2889-2934

---

### INTEGRATED TREATMENT APPROACH

**Pharmacological Treatment**
THE COMPLEXITIES OF STABLE ISCHEMIC HEART DISEASE AND ITS TREATMENT

Pathobiology of Angina Pectoris

Targets for Pharmacologic Therapy


Treatment Strategies for the Management of SIHD

Progressive patient management concerns
Primary prevention
Reverse early pre symptomatic
Secondary prevention

Relieve symptoms
HR, BP, preload
BB, CAI, nitrates
Myocardial oxygen
(ranolazine)
Revascularization
(PCI, CABG)

Treatment strategies

Pharmacotherapy
(antiplatelet, BB, RAA5, statin, flu vaccine)
Secondary prevention
(smoking, lipids, BP, HbA1c, BMI, exercise)

Treat pathology
Guideline-directed Medical Therapy

Disease Modification: Prevent MI and Death – “Live Longer”

PHARMACOTHERAPY
- Antiplatelet therapy
  - ASA 75-162 mg; ADP antagonist post-ACS or stent
- Beta-blocker (post-MI, low EF)
- ACEI / ARB (especially if DM, HF [EF <40%], HTN)
- Moderate or high-dose statin
- Influenza vaccine

SECONDARY PREVENTION GOALS
- Smoking cessation
- LDL: intensive statin therapy
- BP <140/90 mm Hg
- HbA1c <7%
- BMI = 18.5-24.9
- Exercise: 30-60 min, at least 5 days/week


Cholesterol Guidelines for Management of SIHD; Atherosclerotic Cardiovascular Disease (ASCVD)

Colors correspond to the ACC/AHA Classification of Recommendations and Levels of Evidence

### Major Adverse Cardiovascular Events Comparing Influenza Vaccine vs Control

In Patients at High Risk for CVD*

<table>
<thead>
<tr>
<th>Study</th>
<th>Influenza Vaccine</th>
<th>Placebo or Control</th>
<th>Risk Ratio (95% CI)</th>
<th>Favors Influenza Vaccine</th>
<th>Favors Placebo or Control</th>
<th>Weight %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Govaert et al., 41 1994</td>
<td>7</td>
<td>927</td>
<td>5</td>
<td>911</td>
<td>1.38 (0.44-4.32)</td>
<td>6.2</td>
</tr>
<tr>
<td>FLUVACS, 20, 21 2004</td>
<td>32</td>
<td>145</td>
<td>54</td>
<td>147</td>
<td>0.60 (0.41-0.87)</td>
<td>33.6</td>
</tr>
<tr>
<td>FLUCAD, 22, 23 2008</td>
<td>16</td>
<td>325</td>
<td>30</td>
<td>333</td>
<td>0.55 (0.30-0.98)</td>
<td>18.9</td>
</tr>
<tr>
<td>De Villers et al., 42 2009</td>
<td>20</td>
<td>1620</td>
<td>20</td>
<td>1622</td>
<td>1.00 (0.54-1.85)</td>
<td>17.6</td>
</tr>
<tr>
<td>Phrommintikul et al., 24 2011</td>
<td>20</td>
<td>221</td>
<td>42</td>
<td>218</td>
<td>0.47 (0.29-0.77)</td>
<td>23.7</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>95</td>
<td>3238</td>
<td>151</td>
<td>3231</td>
<td>0.64 (0.48-0.86)</td>
<td>100.00</td>
</tr>
</tbody>
</table>

Heterogeneity: \( I^2 = 0.03; \chi^2 = 5.59, (P = 0.23); I^2 = 28\%

Test for overall effect: \( Z = 2.93 (P = 0.003) \)

*Through 1-year follow-up.

**FLUCAD** indicates FLU Vaccination Coronary Artery Disease; **FLUVACS**, FLU Vaccination Acute Coronary Syndromes. Square data markers represent risk ratios (RRs); horizontal lines, the 95% CIs with marker size reflecting the statistical weight of the study using random-effects meta-analysis. A diamond data marker represents the overall RR and 95% CI for the outcome of interest evaluated using the random-effects Mantel-Haenszel test.

Udell JA et al. JAMA 2013;310:1711-1720

### Vorapaxar: Secondary Prevention (PAD, post MI)

**Death from Cardiovascular Causes, Myocardial Infarction, or Stroke**

- **N = 26449 pts with prior MI, PAD, or stroke**
- **Median follow-up 2.5 years**
- **Hazard Ratio 0.87; 95% CI 0.80 to 0.94**
- **\( p < 0.001 \)**

**Placebo**

**Vorapaxar**

- **10.5%**
- **9.3%**

**Bleeding**

- **GUSTO Mod/Sev at 3 yrs**
- **4.2 v. 2.5%, HR 1.66, \( p < 0.001 \)**

Vorapaxar: 2º Prevention (post-MI cohort)

Occurrence of Cardiovascular Death, Myocardial Infarction, or Stroke

HR 0.80, 95% CI 0.72-0.89; P<0.0001

Goals of Therapy in SIHD, 2014

Reduce Symptoms – “Live Better”

- Medications to reduce HR, BP, contractility, preload
  - β-blockers
  - Ca++ blockers
  - Nitrates
- Medication to enhance myocardial O₂ supply
  - Ranolazine
- Revascularization
  - PCI or CABG

Chaitman BR. Circulation. 2006;113:2462-2477.
**Anti-Ischemic Medications**

- **Beta blockers** should be prescribed as initial therapy for relief of symptoms in patients with SIHD.

- **Calcium channel blockers** or **long-acting nitrates** should be prescribed for relief of symptoms when beta blockers are contraindicated or cause unacceptable side effects in patients with SIHD; or when initial treatment with beta blockers is unsuccessful.

- **Sublingual nitroglycerin or nitroglycerin spray** is recommended for immediate relief of angina in patients with SIHD.

- **Ranolazine** can be useful when prescribed as a substitute for beta blockers for relief of symptoms in patients with SIHD if initial treatment with beta blockers leads to unacceptable side effects or is ineffective, or is contraindicated.

- **Ranolazine in combination with beta blockers** can be useful when prescribed for relief of symptoms when initial treatment with beta blockers is not successful in patients with SIHD.

**REACH Registry**

*CV Death, Nonfatal MI, Nonfatal Stroke in Patients with Known CAD without MI*

Consistent Anti-anginal Effects of Ranolazine in Combination with Other Anti-anginals

3 Randomized Trials

CARISA
n=823

36% ↓
P < 0.001

23% ↓
P = 0.028

ERICA
n=565

MERLIN-TIMI 36
n=6560

23% ↓
P = 0.023

Other anti-anginals: CARISA: atenolol, diltiazem, or amlodipine, ERICA: amlodipine + long acting nitrates, MERLIN TIMI 36: standard antianginal therapy


INTEGRATED TREATMENT APPROACH

Pharmacological Treatment and Revascularization
### Risk Stratification and Therapeutic Implications

#### Low-risk
- (<1% annual mortality)
  - Low Duke treadmill score (DTS) \( \leq 5 \)
  - Minimal/No perfusion defects
  - No WMA during stress

#### Intermediate-risk
- (1%-3% annual mortality)
  - LVEF 35% to 49%
  - Intermediate DTS -11 to 5
  - Mod. defects w/out LV dilatation / ↑ lung uptake

#### High-risk
- (>3% annual mortality)
  - LVEF < 35%
  - High DTS \( \leq -11 \)
  - Large and/or mult. defects
  - LV dilatation/↑ lung uptake

Adapted from Fihn SD et al. J Am Coll Cardiol. 2012;60:e44-e164.

### COURAGE Primary Outcome

**Overall Survival**

<table>
<thead>
<tr>
<th>Years</th>
<th>Medical Therapy</th>
<th>PCI</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1138</td>
<td>1149</td>
</tr>
<tr>
<td>1</td>
<td>1073</td>
<td>1094</td>
</tr>
<tr>
<td>2</td>
<td>1029</td>
<td>1051</td>
</tr>
<tr>
<td>3</td>
<td>917</td>
<td>929</td>
</tr>
<tr>
<td>4</td>
<td>717</td>
<td>733</td>
</tr>
<tr>
<td>5</td>
<td>468</td>
<td>488</td>
</tr>
<tr>
<td>6</td>
<td>302</td>
<td>312</td>
</tr>
<tr>
<td>7</td>
<td>46</td>
<td>44</td>
</tr>
</tbody>
</table>

Hazard ratio: 0.87
95% CI (0.65-1.16)
\( P = 0.38 \)

Mean Follow-up: 4.6 yrs

Recent Changes in Practice of Elective PCI for Stable Angina

**COURAGE 2007**

- PCI for chronic stable angina at high (20.9%) before COURAGE and decreased after publication in Q2 2007 to 16.1%
- PCI for chronic stable angina had significant 26% peak decrease in post-COURAGE PCI volumes compared with pre-COURAGE


**BARI 2D Trial**

**Primary Endpoint**

The 5-year death rate for the group receiving revascularization plus optimal medical therapy was 13.2% versus 13.5% in the group receiving optimal medical therapy alone.

THE COMPLEXITIES OF STABLE ISCHEMIC HEART DISEASE AND ITS TREATMENT

BARI 2
Angiographic Risk Stratification and Impact on Clinical Outcomes

![Graph showing PCI stratification and CABG stratification for low and high risk groups.](image)


FAME 2
FFR-Guided PCI versus Medical Therapy in Stable CAD

<table>
<thead>
<tr>
<th>Stented vessels</th>
<th>PCI + MT</th>
<th>MT</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>73%</td>
<td>27%</td>
</tr>
<tr>
<td>2</td>
<td>73%</td>
<td>27%</td>
</tr>
<tr>
<td>3</td>
<td>73%</td>
<td>27%</td>
</tr>
</tbody>
</table>

Follow-up after 1, 6 months, 1, 2, 3, 4, and 5 years

FFR = fractional flow reserve

SIHD in setting of Fractional Flow Reserve (FFR) ≤0.80: FFR-guided PCI vs GDMT on EQ-5D Quality-of-Life Measure

<table>
<thead>
<tr>
<th>Treatment Arm</th>
<th>Baseline EQ-5D</th>
<th>1 month EQ-5D</th>
<th>Difference</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FFR-guided PCI</td>
<td>0.817 ± 0.160</td>
<td>0.871 ± 0.154</td>
<td>0.054</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Medical therapy (GDMT)</td>
<td>0.845 ± 0.114</td>
<td>0.846 ± 0.148</td>
<td>0.001</td>
<td>0.867</td>
</tr>
</tbody>
</table>


FAME 2
FFR-Guided PCI versus Medical Therapy in Stable CAD

**Urgent Revascularization**

- PCI+MT vs. MT: HR 0.13 (0.06-0.30); p<0.001
- PCI+MT vs. Registry: HR 0.63 (0.19-2.03); p=0.43
- MT vs. Registry: HR 4.65 (1.72-12.62); p=0.009

THE COMPLEXITIES OF STABLE ISCHEMIC HEART DISEASE AND ITS TREATMENT

FAME 2
FFR-Guided PCI versus Medical Therapy in Stable CAD

Myocardial Infarction

- PCI+MT vs. MT: HR 1.05 (0.51-2.19); p=0.89
- PCI+MT vs. Registry: HR 1.61 (0.48-5.37); p=0.41
- MT vs. Registry: HR 1.65 (0.30-9.47); p=0.41

INTEGRATED TREATMENT APPROACH
Revascularization Options
SIHD Treatment
Revascularization to Improve Survival

- A Heart Team approach to revascularization is recommended for patients with diabetes mellitus and complex multivessel disease
- CABG is generally recommended in preference to PCI in patients with diabetes mellitus and multivessel CAD

2011 – AHA/ACC PCI and CABG Guidelines
Indication for Revascularization for Symptom Relief

<table>
<thead>
<tr>
<th>Level of Rec.</th>
<th>CABG or PCI to improve symptoms is beneficial in patients with one or more significant (≥70% diameter) stenoses amenable to revascularization with unacceptable angina:</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Despite GDMT</td>
</tr>
<tr>
<td>Ila</td>
<td>For whom GDMT cannot be implemented because of medication contraindications, adverse effects, or patient preferences</td>
</tr>
<tr>
<td>III</td>
<td>CABG or PCI to improve symptoms should not be performed in patients who do not meet anatomic (≥50% left main or ≥70% non-left main stenosis) or physiologic (e.g., abnormal fractional flow reserve) criteria for revascularization</td>
</tr>
</tbody>
</table>

GDMT = guideline-directed medical therapy
Hillis LD et al. Circulation 2011;124:e652-e735
Algorithm for Revascularization to Improve Survival of Patients With SIHD

Colors correspond to the ACCF/AHA Classification of Recommendations and Levels of Evidence Table.


Referral for PCI or CABG?

- **PCI**: less invasive, fewer complications, shorter LOS, faster recovery
- **CABG**: more durable, more complete revascularization

SYNTAX

TRIAL DESIGN: Patients with severe 3-vessel disease or left main (LM) disease were randomized to either CABG or DES-PCI with paclitaxel-eluting stents; clinical outcomes were compared at 12 months.

CABG was associated with fewer repeat revascularizations compared with DES-PCI, but a higher rate of stroke. No difference in death, MI, or thrombosis. Diabetics are especially more likely to benefit with CABG compared with DES-PCI.

THE COMPLEXITIES OF STABLE ISCHEMIC HEART DISEASE AND ITS TREATMENT

FREEDOM
Trial Design

Eligibility: DM patients with MV-CAD eligible for stent or surgery
Exclude: Patients with acute STEMI

Randomized 1:1

MV-Stenting
With Drug-eluting

CABG
With or Without CPB

All concomitant Meds shown to be beneficial were encouraged, including: clopidogrel, ACE inhib., ARBs, b-blockers, statins


FREEDOM
Primary Outcome – Death, Stroke, or MI

5-Year Event Rates: 26.6% vs. 18.7%

Log rank P=0.005

PCI/DES N 953 848 788 625 416 219
CABG N 943 814 758 613 422 221

The Complexities of Stable Ischemic Heart Disease and Its Treatment

FREEDOM

Stroke

Severely Disabling Scale

<table>
<thead>
<tr>
<th></th>
<th>CABG</th>
<th>PCI/DES</th>
</tr>
</thead>
<tbody>
<tr>
<td>NIH &gt; 4</td>
<td>55%</td>
<td>27%</td>
</tr>
<tr>
<td>Rankin &gt;1</td>
<td>70%</td>
<td>60%</td>
</tr>
</tbody>
</table>

Logrank P = 0.034


INTEGRATED TREATMENT APPROACH

Appropriateness Criteria
Performance Measures
### Revascularization of SIHD 2012

**Revascularization Indications in Stable Angina**

#### FOR PROGNOSIS

<table>
<thead>
<tr>
<th>Subset of CAD by Anatomy</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left main &gt;50%</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>Any proximal LAD &gt;50%</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>2VD or 3VD with impaired LV function</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Proven large area of ischemia (&gt;10% LV)</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Single remaining vessel &gt;50% stenosis</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>IVD without proximal LAD and without &gt;10% ischemia</td>
<td>III</td>
<td>A</td>
</tr>
</tbody>
</table>

#### FOR SYMPTOMS

<table>
<thead>
<tr>
<th>Subset of CAD by Anatomy</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any stenosis &gt;50% with limiting angina or angina equivalent, unresponsive to GDMT</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>Dyspnea/CHF and &gt;10% LV ischemia/viability supplied by &gt;50% stenotic artery</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>No limiting symptoms with GDMT</td>
<td>III</td>
<td>C</td>
</tr>
</tbody>
</table>


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### ACCF/AHA/AMA-PCPI Performance Measures for Adults with CAD and Hypertension

- ACCF/AHA Performance Measures: Define what should or should not be done in the care of patients with cardiovascular disease
- ACCF/AHA performance measurement sets may serve as vehicles to accelerate appropriate translation of scientific evidence into practice
- Standard Metrics
  - Blood Pressure and Lipid Control
  - Tobacco Use: Screening, cessation, and intervention
  - B-blocker Therapy: Prior MI or LV systolic dysfunction
  - ACEI/ARB Therapy: DM or LV systolic dysfunction

ACCF = American College of Cardiology Foundation; AHA = American Heart Association; AMA = American Medical Association; PCP-I = Physician Consortium for Performance Improvement

ACCF/AHA/AMA-PCPI CAD Measurement
New Metrics and Gaps of Care

• Symptom Management
  – An evaluation of level of activity, AND with an evaluation of presence or absence of anginal symptoms, with appropriate management of anginal symptoms
    ▪ There is a significant gap in measures addressing critical patient-centric outcomes for chronic stable CAD care and effective management of ischemic symptoms

• Cardiac Rehabilitation Patient Referral from an Outpatient Setting
  – All patients who, in previous 12 months, had an AMI, CABG, PCI, valve surgery, or cardiac Tx or who have chronic stable angina are referred to such a program
    ▪ Cardiac rehabilitation programs remain underused; the writing committee recognized a significant gap in this area


Key Take-home Messages

• A standard exercise test is the first choice to diagnose IHD for patients with an interpretable ECG and able to exercise
  – Un-interpretable ECG ➔ exercise stress with MPI or echo
  – Unable to exercise ➔ MPI or echo with pharmacologic stress

• Coronary revascularization may be performed either to improve survival (high-risk patients) or improve symptoms

• Patients should have a trial of GDMT before considering revascularization to improve symptoms
  – Deferring revascularization does not ➔ worse outcomes

• Patients with SIHD should be carefully followed to monitor progression of disease, complications, and adherence
  – Stress testing should generally be repeated only when there is a change in clinical status
THE COMPLEXITIES OF STABLE ISCHEMIC HEART DISEASE AND ITS TREATMENT

Changing Perspectives on Stable Ischemic Heart Disease

- Morphing name (stable angina → chronic coronary disease → SIHD)
- Disease progression
- Risk factors: Dyslipidemia, Hypertension, Smoking, Obesly, Sedentary, Poor nutrition, Older age
- Early Presentation: CT evidence, Carotid intimal, Coronary Ca + stress test
- Frank CAD: Dynamic symptoms
- Shifting perception of pathobiology

150 million in U.S.
17.6 million in U.S.

150 million in U.S.