Prevention of Cardiovascular Disease: Prescient beyond COVID-19

Jamal. S. Rana MD, PhD, FACC
President-Elect, American College of Cardiology California Chapter
Assistant Physician-in-Chief, Medical Specialties & Interventional Services
Chief of Cardiology, East Bay, The Permanente Medical Group
Adjunct Investigator, Division of Research, Kaiser Permanente
Context

Primary Prevention

Risk Estimation

Coronary Calcium Scanning vs. Coronary CT Angiogram

Secondary Prevention

What it is new

Taking care of populations - Scaling Excellence
Editorial
March 27, 2020

Association of Coronavirus Disease 2019 (COVID-19) With Myocardial Injury and Mortality
Robert O. Bonow, MD, MSc2,3; Gregg C. Fonarow, MD4; Patrick T. O’Gara, MD5,6; Clyde W. Yancy, MD, MSc1,4

Viewpoint
September 22/29, 2020

Cardiology and COVID-19
Robert O. Bonow, MD, MSc2,3; Patrick T. O’Gara, MD4; Clyde W. Yancy, MD, MSc1,4

The New York Times
Opinion
Covid-19 Is Creating a Wave of Heart Disease
Emerging data show that some of the coronavirus’s most potent damage is inflicted on the heart.

By Haider Warraich
Dr. Warraich is a cardiologist.

Aug. 17, 2020
Recent Trends in Cardiovascular Mortality in the United States and Public Health Goals

Stephen Sidney, MD, MPH¹; Charles P. Quesenberry Jr, PhD¹; Marc G. Jaffe, MD²; Michael Sorel, MPH¹; Mai N. Nguyen-Huynh, MD³; Lawrence H. Kushi, ScD¹; Alan S. Go, MD¹,4,6; Jamal S. Rana, MD, PhD¹,4,7

Author Affiliations


THE WALL STREET JOURNAL.

U.S.

Annual Decline in Heart-Disease Death Rates in U.S. Flat Since 2011

Researchers say the likely culprits are obesity and the resulting increase in Type 2 diabetes
October 30, 2019

Association Between Aging of the US Population and Heart Disease Mortality From 2011 to 2017

Stephen Sidney, MD, MPH\textsuperscript{1}; Alan S. Go, MD\textsuperscript{12,3,4,5}; Marc G. Jaffe, MD\textsuperscript{6}; Matthew D. Solomon, MD, PhD\textsuperscript{7}; Andrew P. Ambrosy, MD\textsuperscript{8}; Jamal S. Rana, MD, PhD\textsuperscript{1,7,9}

» Author Affiliations  |  Article Information


THE WALL STREET JOURNAL.

Heart-Failure Deaths Rise, Contributing to Worsening Life Expectancy

Rate surges as population ages and health of younger generations worsens
# Table 1 Changes in Mortality Attributed to the Top 10 Causes of Death in the USA, 2011–2018

<table>
<thead>
<tr>
<th>Total deaths</th>
<th>Age-adjusted mortality rate (per 100,000 population)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2011</td>
</tr>
<tr>
<td>1. Heart disease (I00–I09, I11, I13, I20–I51)</td>
<td>596,577</td>
</tr>
<tr>
<td>2. Cancer (C00–C97)</td>
<td>576,691</td>
</tr>
<tr>
<td>3. Accidents (V01–X59, Y85–Y86)</td>
<td>126,438</td>
</tr>
<tr>
<td>4. Chronic lower respiratory diseases (J40–J47)</td>
<td>142,943</td>
</tr>
<tr>
<td>5. Cerebrovascular diseases (I60–I69)</td>
<td>128,932</td>
</tr>
<tr>
<td>6. Alzheimer disease (G30)</td>
<td>84,974</td>
</tr>
<tr>
<td>7. Diabetes mellitus (E10–E14)</td>
<td>73,831</td>
</tr>
<tr>
<td>8. Influenza and pneumonia (J09–J18)</td>
<td>53,826</td>
</tr>
<tr>
<td>9. Nephritis, nephrotic syndrome and nephrosis (N00–N07, N17–N19, N25–N27)</td>
<td>45,591</td>
</tr>
<tr>
<td>10. Intentional self-harm (suicide) (U03, X60–X84, Y87.0)</td>
<td>39,518</td>
</tr>
</tbody>
</table>

Heart disease remains the #1 Killer
Black men had the highest burden of mortality from leading subtypes of heart disease.
Primary Prevention

CLINICAL PRACTICE GUIDELINE: EXECUTIVE SUMMARY

2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease: Executive Summary

A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines
Top 10 Take Home Messages for Primary Prevention

1. The most important way to prevent atherosclerotic vascular disease, heart failure, and atrial fibrillation is to promote a healthy lifestyle throughout life.

2. A team-based care approach is an effective strategy for the prevention of cardiovascular disease.Clinicians should evaluate the social determinants of health that affect individuals to inform treatment decisions.
Risk Estimation

3. Adults who are 40 to 75 years of age and are being evaluated for cardiovascular disease prevention should undergo 10-year atherosclerotic cardiovascular disease (ASCVD) risk estimation and have a clinician-patient risk discussion before starting on pharmacological therapy, such as antihypertensive therapy, a statin, or aspirin. In addition, assessing for other risk-enhancing factors can help guide decisions about preventive interventions in select individuals, as can coronary artery calcium scanning.
All adults should consume a healthy diet that emphasizes the intake of vegetables, fruits, nuts, whole grains, lean vegetable or animal protein, and fish and minimizes the intake of trans fats, red meat and processed meats, refined carbohydrates, and sugar-sweetened beverages. For adults with overweight/obesity, counseling and caloric restriction are recommended for achieving and maintaining weight loss.
U.S. News Reveals Best Diets Rankings for 2020

The NEW ENGLAND JOURNAL of MEDICINE

Primary Prevention of Cardiovascular Disease with a Mediterranean Diet
Effects of Intermittent Fasting on Health, Aging, and Disease

Rafael de Cabo, Ph.D. and Mark P. Mattison, Ph.D.

Figure 3. Cellular and Molecular Mechanisms Underlying Improved Organ Function and Resistance to Stress and Disease with Intermittent Metabolic Switching.

Periods of dietary energy restriction sufficient to cause depletion of liver glycogen stores trigger a metabolic switch toward use of fatty acids and ketones. Cells and organ systems adapt to this bioenergetic challenge by activating signaling pathways that bolster mitochondrial function, stress resistance, and antioxidant defenses while up-regulating autophagy to remove damaged molecules and recycle their components. During the period of energy restriction, cells...
Plant-centered diet quality was measured using the A Priori Diet Quality Score (APDQS); a higher score favors nutritionally rich plant foods.

Participants with the largest increase in APDQS over 20 years had a 48% (P-trend < 0.001) lower risk of diabetes over the subsequent 10 years compared with participants whose diet score remained stable.
Adults should engage in at least 150 minutes per week of accumulated moderate-intensity physical activity or 75 minutes per week of vigorous-intensity physical activity.
Physical inactivity as dangerous as smoking for heart disease, stroke
Patients with diabetes

For adults with type 2 diabetes mellitus, lifestyle changes, such as improving dietary habits and achieving exercise recommendations, are crucial. If medication is indicated, metformin is first-line therapy, followed by consideration of a sodium-glucose cotransporter 2 inhibitor or a glucagon-like peptide-1 receptor agonist.
EDITORIAL COMMENT

Are All Individuals With Diabetes Equal, or Some More Equal Than Others?*

Jamal S. Rana, MD, PhD,¹,²,³ Ron Blankstein, MD,⁴

*Figure 1: CHD Rates Stratified According to Sex and Age in 4 Cohorts Defined by History of DM or CHD

A

Women

Event Rate/1000 Person Years

30-39 40-49 50-59 60-69 70-79 ≥80

Age Categories (Years)

B

Men

Event Rate/1000 Person Years

30-39 40-49 50-59 60-69 70-79 ≥80

Age Categories (Years)

JCIM

Rana et al.: Diabetes and Coronary Heart Disease Risk
All adults should be assessed at every healthcare visit for tobacco use, and those who use tobacco should be assisted and strongly advised to quit.
Aspirin and Statins

8. Aspirin should be used infrequently in the routine primary prevention of ASCVD because of lack of net benefit.

9. Statin therapy is first-line treatment for primary prevention of ASCVD in patients with elevated low-density lipoprotein cholesterol levels (≥190 mg/dL), those with diabetes mellitus, who are 40 to 75 years of age, and those determined to be at sufficient ASCVD risk after a clinician–patient risk discussion.
Nonpharmacological interventions are recommended for all adults with elevated blood pressure or hypertension. For those requiring pharmacological therapy, the target blood pressure should generally be <130/80 mm Hg.

High Blood Pressure

**BP Thresholds and Recommendations for Treatment**

- **Normal BP** (BP <120/80 mm Hg):
  - Promote optimal lifestyle habits
  - Reassess in 1 y (Class IIa)

- **Elevated BP** (BP 120-129/<80 mm Hg):
  - Nonpharmacologic therapy (Class I)
  - Reassess in 3-6 mo (Class I)

- **Stage 1 Hypertension** (BP 130-139/80-89 mm Hg):
  - Nonpharmacologic therapy (Class I)
  - Nonpharmacologic therapy and BP-lowering medication (Class I)

- **Stage 2 Hypertension** (BP ≥ 140/90 mm Hg):
  - Nonpharmacologic therapy and BP-lowering medication (Class I)

*Clinical ASCVD or estimated 10-y CVD risk ≥10%*
## Aspirin Use

### Recommendations for Aspirin Use

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>IIb</td>
<td>A</td>
<td>1. Low-dose aspirin (75-100 mg orally daily) might be considered for the primary prevention of ASCVD among select adults 40 to 70 years of age who are at higher ASCVD risk but not at increased bleeding risk.</td>
</tr>
<tr>
<td>III: Harm</td>
<td>B-R</td>
<td>2. Low-dose aspirin (75-100 mg orally daily) should not be administered on a routine basis for the primary prevention of ASCVD among adults &gt;70 years of age.</td>
</tr>
<tr>
<td>III: Harm</td>
<td>C-LD</td>
<td>3. Low-dose aspirin (75-100 mg orally daily) should not be administered for the primary prevention of ASCVD among adults of any age who are at increased risk of bleeding.</td>
</tr>
</tbody>
</table>
Primary Prevention: Lifestyle Changes and Team-Based Care

- **Cholesterol**: Assess ASCVD Risk, personalize with risk enhancers, reclassify with CAC as needed.
- **High Blood Pressure**: Maintain blood pressure below 130/80 mm Hg.
- **Physical Activity**: Perform ≥150 mins/week of moderate or ≥75 mins/week of vigorous physical activity.
- **Aspirin Use**: Low-dose aspirin for primary prevention now reserved for select high-risk patients.
- **Type II Diabetes**: Control through diet and exercise. Metformin (primary therapy), SGLT-2 Inhibitor or GLP-1 receptor agonist (secondary).
- **Diet**: Emphasis on intake of vegetables, fruits, nuts, legumes, fish and whole grains.
- **Tobacco**: Pharmacotherapy + behavior interventions recommended to maximize quit rates.
## Risk Estimation

### 60 year old white man

- **Height**: 69 inches (175 cm)
- **Blood Pressure (BP)**: 144/86 mm Hg

### Medical History
- No medications
- Non-smoker
- No CVD
- No family history of CVD

### Fasting Lipid Panel
- Total cholesterol: 195 mg/dL
- LDL-C: 125 mg/dL
- HDL-C: 50 mg/dL
- Triglycerides: 100 mg/dL

### Recommendations According to Different Guidelines

<table>
<thead>
<tr>
<th>Guideline</th>
<th>10-year Global Risk Assessment (outcome)</th>
<th>Statin Recommended</th>
</tr>
</thead>
<tbody>
<tr>
<td>2013 ACC/AHA</td>
<td>10.3% (ASCVD)</td>
<td>Yes</td>
</tr>
<tr>
<td>ATP III</td>
<td>10% (CHD)</td>
<td>No</td>
</tr>
<tr>
<td>2011 ESC/EAS</td>
<td>3-5% (CVD mortality)</td>
<td>Yes</td>
</tr>
<tr>
<td>2014 NICE</td>
<td>10.4% (CVD)</td>
<td>Yes</td>
</tr>
<tr>
<td>2012 CCS</td>
<td>16.6% (CVD)</td>
<td>No</td>
</tr>
</tbody>
</table>

*Circulation. 2016;133:1795-1806.*
The 2013 ACC/AHA guideline for cholesterol treatment made several notable changes to the older ATP III guidelines.

- Introduced the Pooled Cohort equations as the preferred risk assessment tool
- Added Stroke to definition of ASCVD
- Added White and African Americans
- Lowered the risk threshold for considering statin in primary prevention settings to a 10-year absolute ASCVD risk of 7.5%
- Removed cholesterol treatment targets.
Levels of Risk (2019 ACC/AHA Guidelines)

- Aged 40-75 years without diabetes and with low-density lipoprotein cholesterol (LDL-C) levels of 70-189 mg/dL, clinicians should estimate 10-year atherosclerotic CVD (ASCVD) risk.

- High-intensity statin therapy, which lowers LDL-C by ≥ 50% for patients at high risk for CVD (> 20% 10-year risk).

- Low risk for CVD (< 5% 10-year risk), lifestyle modifications alone may be sufficient for prevention.
Intermediate risk for CVD (≥ 7.5%-19.9%) a moderate-intensity statin, which lowers LDL-C by ≥ 30%, is recommended.

Borderline (≥ 5%-7.5%) risk for CVD should have a risk discussion with their clinician before initiating pharmacologic therapy, with special attention to risk-enhancing factors that could increase the benefit of statin therapy.

Diabetes or severe primary hypercholesterolemia (LDL-C level ≥ 190 mg/dL), clinicians should forgo the 10-year risk assessment and initiate statin therapy immediately.
Accuracy of the Atherosclerotic Cardiovascular Risk Equation in a Large Contemporary, Multiethnic Population

Jamal S. Rana, MD, PhD,a,b,c Grace H. Tabada, MPH,b Matthew D. Solomon, MD, PhD,a,b,c,d, Joan C. Lo, MD,a,b,c,e
Marc G. Jaffe, MD,a,b,d Sue Hee Sung, MPH,a Christie M. Ballantyne, MD,a Alan S. Go, MD,a,c,d
Patient Case

44 yr old male, history of HTN (on Losartan), Family hx of premature CHD

Total Cholesterol 219
LDL-C 167
HDL-C 42
TG 219
Chest pain - STEMI
Coronary Angiography

**LMCA:** No obstructive coronary artery disease

**LAD:** Large vessel with mid vessel very short "napkin ring" lesion with narrowing of 80%, at the origin of a large first septal branch, distal vessel 70% narrowing.

**LCx:** Medium sized nondominant vessel.

**RCA:** Large dominant vessel. 95% proximal vessel stenosis. Distal vessel 90% narrowing. 99% narrowing of the proximal posterior AV groove branch, beyond the large PDA

Interventions

Primary PCI to Proximal RCA: 3.5 x 15 mm Resolute Onyx DES
PCI to distal RCA: 3.5 x 26 mm Resolute Onyx DES
PCI to RCA PAV branch: 2.75 x 15 mm Resolute Onyx DES
Residual LAD lesions: Later Staged PCI
New in 2019!

Risk-Enhancing Factors for Clinician-Patient Risk Discussion

- **Family history of premature ASCVD** (males, age <55 y; females, age <65 y)
- **Primary hypercholesterolemia** (LDL-C, 160-189 mg/dL [4.1-4.8 mmol/L]; non-HDL-C 190-219 mg/dL [4.9-5.6 mmol/L])*  
- **Metabolic syndrome** (increased waist circumference [by ethnically appropriate cutpoints], elevated triglycerides (>150 mg/dL, nonfasting), elevated blood pressure, elevated glucose, and low HDL-C [<40 mg/dL in men; <50 mg/dL in women] are factors; a tally of 3 makes the diagnosis)
- **Chronic kidney disease** (eGFR 15–59 mL/min/1.73 m2 with or without albuminuria; not treated with dialysis or kidney transplantation)
- **Chronic inflammatory conditions**, such as psoriasis, RA, lupus, or HIV/AIDS
- **History of premature menopause** (before age 40 y) and history of pregnancy-associated conditions that increase later ASCVD risk, such as preeclampsia
- **High-risk race/ethnicity** (e.g., South Asian ancestry)
- **Lipids/biomarkers**: associated with increased ASCVD risk
  - Persistently elevated,* primary hypertriglyceridemia (>175 mg/dL, nonfasting)
  - If measured:
    - **Elevated high-sensitivity C-reactive protein** (>2.0 mg/L)
    - **Elevated Lp(a)**: A relative indication for its measurement is family history of premature ASCVD. An Lp(a) >50 mg/dL or >125 nmol/L constitutes a risk-enhancing factor, especially at higher levels of Lp(a).
    - **Elevated apoB (≥130 mg/dL)**: A relative indication for its measurement would be triglyceride ≥200 mg/dL. A level ≥130 mg/dL corresponds to an LDL-C >160 mg/dL and constitutes a risk-enhancing factor
    - **ABI (<0.9)**
South Asian: Risk Enhancer for Heart Disease

India, Pakistan, Bangladesh, Sri Lanka, Nepal, Bhutan

1.9 billion or about quarter of the world's population
Primary Prevention:
Assess ASCVD Risk in Each Age Group
Emphasize Adherence to Healthy Lifestyle

Age 0-19 y
Lifestyle to prevent or reduce ASCVD risk
Diagnosis of Familial Hypercholesterolemia → Statin

Age 20-39 y
Estimate lifetime risk to encourage lifestyle to reduce ASCVD risk
Consider statin if family history premature ASCVD and LDL-C ≥160 mg/dL (≥4.1 mmol/L)

Age 40-75 y and LDL-C ≥70-<190 mg/dL (≥1.8-<4.9 mmol/L)

Age >75 y
Clinical assessment, Risk discussion

ASCVD Risk Enhancers:
- Family history of premature ASCVD
- Persistently elevated LDL-C ≥160 mg/dL (≥4.1 mmol/L)
- Chronic kidney disease
- Metabolic syndrome
- Conditions specific to women (e.g., preeclampsia, premature menopause)
- Inflammatory diseases (especially rheumatoid arthritis, psoriasis, HIV)
- Ethnicity (e.g., South Asian ancestry)

Lipid/Biomarkers:
- Persistently elevated triglycerides (≥175 mg/dL, ≥2.0 mmol/L)

In selected individuals if measured:
- hs-CRP ≥2.0 mg/L
- Lp(a) levels >50 mg/dL or >125 nmol/L
- apoB ≥130 mg/dL
- Ankle-brachial index (ABI) <0.9

Risk discussion: Emphasize lifestyle to reduce risk factors (Class I)

Risk discussion: If risk enhancers present then risk discussion regarding moderate-intensity statin therapy (Class IIb)

Risk discussion: If risk estimate + risk enhancers favor statin, initiate moderate-intensity statin to reduce LDL-C by 30% - 49% (Class I)

Risk discussion: Initiate statin to reduce LDL-C ≥50% (Class I)

If risk decision is uncertain:
Consider measuring CAC in selected adults:
CAC = zero (lowers risk; consider no statin, unless diabetes, family history of premature CHD, or cigarette smoking are present)
CAC = 1-99 favors statin (especially after age 55)
CAC = 100+ and/or ≥75th percentile, initiate statin therapy
Coronary Artery Calcium (CAC) assessment

If risk decision is uncertain:
Consider measuring CAC in selected adults:
CAC = zero (lowers risk; consider no statin, unless diabetes,
family history of premature CHD, or cigarette smoking are present)
CAC = 1-99 favors statin (especially after age 55)
CAC = 100+ and/or ≥75th percentile, initiate statin therapy

Selected Examples of Candidates for Coronary Artery Calcium Measurement Who Might Benefit From Knowing Their Coronary Artery Calcium Score Is Zero

- Patients reluctant to initiate statin who wish to understand their risk and potential for benefit more precisely
- Patients concerned about need to reinstitute statin therapy after discontinuation for statin-associated symptoms
- Older patients (men 55-80 y of age; women 60-80 y of age) with low burden of risk factors who question whether they would benefit from statin therapy
- Middle-aged adults (40-55 y of age) with PCE-calculated 10-year risk of ASCVD 5% to <7.5% with factors that increase their ASCVD risk, although they are in a borderline risk group.

Caveats: If patient is at intermediate risk and if a risk decision is uncertain and a coronary artery calcium score is obtained, it is reasonable to withhold statin therapy unless higher-risk conditions, such as cigarette smoking, family history of premature ASCVD, or diabetes mellitus, are present and to reassess coronary artery calcium score in 5 to 10 years. Moreover, if coronary artery calcium scoring is recommended, it should be performed in facilities that have current technology and expertise to deliver the lowest radiation possible.
Patient example

ASCVD risk 7%, decision regarding statin initiation

CAC score 312
CAC Scan

Asymptomatic
No contrast

Coronary CT Angiogram

Symptomatic
Contrast
What about radiation!

Background Radiation – 3 mSv
Mammography – 0.7 mSv

Calcium Scan – 0.5-0.6 mSv
CT Angiogram – 3-6 mSv (256 slice 1-3 mSv!)
Coronary Angiography – Avg 8 mSv (2-10)
Nuclear Imaging – 9 – 15 mSv
Is resistance to screening for heart disease rational?

42,690 deaths attributed to breast cancer

53,200 deaths attributed to colorectal cancer

360,000 deaths attributed to ischemic heart disease

(of the 655,00 deaths attributed to heart disease)
Heart disease is the leading cause of death (LCOD) in women

**Circulation**

**AHA SPECIAL REPORT**

Ten-Year Differences in Women’s Awareness Related to Coronary Heart Disease: Results of the 2019 American Heart Association National Survey

A Special Report From the American Heart Association

- Online surveys of US women were conducted in 2009 and 2019.
- In 2009, awareness of heart disease as the LCOD was 65%, decreasing to 44% in 2019.
- In 2019, women were more likely than in 2009 to incorrectly identify breast cancer as the LCOD (odds ratio, 2.59).
- An urgent redoubling of efforts by organizations interested in women’s health is required to reverse these trends.
Coronary CTA important takeaways

- Excellent for low to intermediate risk symptomatic patients
- Negative predictive value 99%
- Even non obstructive plaque finding can trigger statin, aspirin and lifestyle changes.
- Endorsed by ESC and ACC/AHA
Secondary Prevention
Secondary Prevention

Clinical ASCVD

Healthy Lifestyle

ASCVD not at very high-risk*

Age ≤ 75 y

High-intensity statin (Goal: ↓ LDL-C ≥ 50%) (Class I)

If high-intensity statin not tolerated, use moderate-intensity statin (Class I)

If on maximal statin therapy and LDL-C ≥ 70 mg/dL (≥ 1.8 mmol/L), adding ezetimibe may be reasonable (Class IIb)

Initiation of moderate- or high-intensity statin is reasonable (Class IIa)

Continuation of high-intensity statin is reasonable (Class IIa)

Age > 75 y

Very high-risk* ASCVD

High-intensity or maximal statin (Class I)

If on maximal statin and LDL-C ≥ 70 mg/dL (≥ 1.8 mmol/L), adding ezetimibe is reasonable (Class IIa)

If PCSK9-I is considered, add ezetimibe to maximal statin before adding PCSK9-I (Class I)

Dashed arrow indicates RCT-supported efficacy, but is less cost effective

If on clinically judged maximal LDL-C lowering therapy and LDL-C ≥ 70 mg/dL (≥ 1.8 mmol/L), or non-HDL-C ≥ 100 mg/dL (≥ 2.6 mmol/L), adding PCSK9-I is reasonable (Class IIa)
Lipid Testing

- 4 to 12 weeks after the initiation of a statin or dose adjustment to assess patient adherence to the prescription and the extent of reduction in the LDL cholesterol level.

- Subsequently, periodic measurement of lipids (12 months) is reasonable.

- For most patients, fasting is not required, fasting lipid profile may be for evaluation of genetic hyperlipidemia, or persistent hypertriglyceridemia.
<table>
<thead>
<tr>
<th>Myth (Fake News)</th>
<th>Fact</th>
</tr>
</thead>
<tbody>
<tr>
<td>Statins cause frequent muscle problems</td>
<td>• Myopathy occurs about 1 case per 10,000 (0.01%) people treated per year&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>• Rhabdomyolysis occurs about 2–3 cases per 100,000 (0.002-0.003%) treated per year</td>
</tr>
<tr>
<td></td>
<td>• Over 90% re-challenged taking a statin 12 months after the original statin-related event&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
<tr>
<td>Statins cause diabetes</td>
<td>• &lt;0.4% develop DM from taking statins.</td>
</tr>
<tr>
<td></td>
<td>• In patients with high had propensity to develop diabetes regardless due to the presence of one or more major DM risk factor. Studies show that diabetes may show up sooner by 1 month in these patients by being on a statin</td>
</tr>
<tr>
<td>Statins cause memory loss</td>
<td>• Statin therapy was not associated with cognitive impairment in randomized control trials.</td>
</tr>
<tr>
<td></td>
<td>• Studies have found a significant protective effect against all-cause dementia and Alzheimer’s disease with statin users.</td>
</tr>
<tr>
<td>Statins cause liver damage</td>
<td>• Asymptomatic increases in LFTs are a statin class effect and it is common and do not indicate liver dysfunction.</td>
</tr>
<tr>
<td></td>
<td>• Significant hepatotoxicity is extremely rare and occurs in &lt;1%</td>
</tr>
<tr>
<td></td>
<td>• Patients with pre-existing chronic liver disease and compensated liver cirrhosis are not at higher risk for statin hepatotoxicity.</td>
</tr>
</tbody>
</table>
In Summary

- Emphasize statins for primary/secondary prevention.
- Joint decision-making with a clinician-patient discussion.
- Awareness about Risk Enhancers and decline in LDL-C
What is new ...
PCSK9 Inhibitors

Proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors

THE PRESENT AND FUTURE

JACC STATE-OF-THE-ART REVIEW

The Evolving Future of PCSK9 Inhibitors

Robert S. Rosenson, MD, a Robert A. Hegele, MD, b Sergio Fazio, MD, PhD, c Christopher P. Cannon, MD d
PCSK9 Background

- Genetic studies identified *gain of function (GOF)* PCSK9 mutations causative gene for familial hypercholesterolemia (FH), which prompted extensive investigations into its relationship with LDL-R.

- Individuals with PCSK9 *loss of function (LOF)* mutations were found to have lifelong low LDL cholesterol (LDL-C) levels, reduced ASCVD risk, and were otherwise healthy.

- These discoveries led to the development of PCSK9 inhibitors as a therapy to lower LDL-C.
PCSK9 inhibits LDL-R recycling. The binding of PCSK9 to the LDL-R targets LDL-R to the lysosome for degradation, preventing LDL-R from returning to the surface of the hepatocyte to bind to additional LDL particles. Antibodies against PCSK9 upon binding to PCSK9, PCSK9 is unable to bind to LDL-R and cause its degradation. Result is more LDL-Rs on hepatocytes, leading to accelerated clearance of LDL particles, and large decreases in LDL-C levels.
Alirocumab (ODYSSEY)

Evolocumab (FOURIER)
PCSK9 Inhibitors Guidelines Recommendations

- Guidelines recommended adding PCSK9 inhibitors in patients with very high ASCVD risk only.
- Should be considered after patient is already on maximal statin therapy and ezetimibe. (Class I)
- If LDL-C > 70 mg/dl or non-HDL-C > 100 mg/dl despite being on maximal lipid lowering therapy, PCSK9 inhibitors addition is reasonable. (Class IIa)
- In terms of primary prevention, Familial hypercholesterolemia is an FDA-approved indication for both PCSK9 inhibitors.
Economic Impact

Institute for Clinical and Economic Review (ICER) performed cost-effectiveness analyses to establish value-based price benchmarks for alirocumab.

- $2,300-$3,400 per year would be cost-effective if used to treat all patients who meet trial eligibility criteria.

- $14K decreased to $5-6 K per year
Among those with ASCVD, statin use was 50% and 58% in 2002-03 and 2012-13, respectively, and < 1/3 were prescribed a high-intensity dose.
Ethyl eicosapentaenoic acid (EPA)

EPA and DHA Have Distinct Roles in Human Physiology Mediated by Membrane Interactions

Hypothetically, DHA undergoes rapid conformational changes and promotes formation of cholesterol-rich lipid domains and fluidity (necessary for neuronal function.)

EPA incorporates itself into the membrane and inhibits free radical propagation while maintaining a more even cholesterol distribution.

CONCLUSIONS

Among patients with elevated triglyceride levels despite the use of statins, the risk of ischemic events, including cardiovascular death, was significantly lower among those who received 2 g of icosapent ethyl twice daily than among those who received placebo. (Funded by the National Heart, Lung, and Blood Institute.)

The U.S. Food and Drug Administration today approved the use of Vasepa (icosapent ethyl) as an adjunctive (secondary) therapy to reduce the risk of cardiovascular events among adults with elevated triglyceride levels (a type of fat in the blood) of 150 milligrams per deciliter or higher. Patients must also have either established cardiovascular disease or diabetes and two or more additional risk factors for cardiovascular disease. Patients are advised to continue physical activity and maintain a healthy diet.

Vasepa is the first FDA approved drug to reduce cardiovascular risk among patients with elevated triglyceride levels as an add-on to maximally tolerated statin therapy. Statins are drugs used to treat elevated cholesterol levels and reduce the risk of cardiovascular events.
CONCLUSIONS

After an ischemic stroke or TIA with evidence of atherosclerosis, patients who had a target LDL cholesterol level of less than 70 mg per deciliter had a lower risk of subsequent cardiovascular events than those who had a target range of 90 mg to 110 mg per deciliter. (Funded by the French Ministry of Health and others; Treat
Taking care of populations
In stratified analyses of Kaiser and other health plans in the West, significant disparities between black enrollees and white enrollees in the frequency of blood-pressure control were not evident in Kaiser health plans in 2006 (67% vs. 73%, P = 0.18) or 2011 (89% vs. 85%, P = 0.41), but there were significant disparities between the two groups in other health plans in 2006 (52% vs. 57%, P = 0.04) and in 2011 (58% vs. 66%, P<0.001)
Kaiser Permanente Study Shows Minorities Had Lower Risk of Coronary Heart Disease Than Whites

“Racial and ethnic differences in diabetes, cardiovascular disease risk factors and their outcomes, especially in blacks, are well documented, but population health estimates are often confounded by differences in access to high-quality health care,” said lead author Jamal S. Rana, MD, PhD, of the Division of Cardiology and Clinical Adjunct with Division of Research at Kaiser Permanente Northern California.

The findings echo those of a 2014 study published in the New England Journal of Medicine, which showed that racial disparities between black and white Medicare beneficiaries covered by Kaiser Permanente in the western United States have been nearly eliminated for cardiac risks and diabetes markers, even as these disparities persisted among patients in managed health care systems in other regions of the United States.

In the study just published, “we were able to evaluate ethnic differences in risk of future coronary heart disease within a diverse population, which included not only black, but also large Asian and Latino populations, with uniform access to care in an integrated health care delivery system,” Rana noted. “The results in our report may reflect, not only access to high quality heart disease care, but also systematic efforts by the health plan to improve risk factors such as high blood pressure and promote smoking cessation across its member population.”
Improved Cardiovascular Risk Factors Control Associated with a Large-Scale Population Management Program Among Diabetes Patients

Jamal S. Rana, MD, PhD,1,5 Andrew J. Karter, PhD,2,6 Jennifer Y. Liu, MPH,7 Howard H. Moffet, MPH,7 Marc G. Jeffe, MD*  
1Division of Cardiology, Kaiser Permanente Northern California, Oakland; 2Department of Medicine, University of California, San Francisco; 3Division of Research, Kaiser Permanente Northern California, Oakland; 4Department of General Internal Medicine, University of California, San Francisco; 5Division of Endocrinology, Kaiser Permanente Northern California, South San Francisco.

Kaiser Permanente’s PHASE program outperforms nation on controlling 3 cardiovascular risk factors for diabetes patients*

![Graph showing improved blood pressure, lipid, and blood sugar control among diabetes patients.](image-url)
Comparative Trends in Heart Disease, Stroke, and All-Cause Mortality in the United States and a Large Integrated Healthcare Delivery System

Stephen Sidney, MD, MPH,* Michael E. Sorel, MPH,* Charles P. Quesenberry, PhD,* Marc G. Jaffe, MD,* Matthew D. Solomon, MD, PhD,** Mai N. Nguyen-Huynh, MD,† Alan S. Go, MD,†† Jamal S. Rana, MD, PhD†††

From 2000 to 2015

In Reducing Deaths from Heart Disease and Stroke, KAISER PERMANENTE Outpaces Nation

Kaiser Permanente

U.S. 23.6%

Kaiser Permanente

U.S. 26.0%

DECLINE IN ADULT DEATHS from HEART DISEASE

DECLINE IN ADULT DEATHS from STROKE

*NCal region, 45-64 year olds; Sidney et al., Am J Med 2018.
Improving the Quality of U.S. Health Care — What Will It Take?

Elizabeth A. McGlynn, Ph.D.


Changes in the percentages of people with hypertension at Kaiser Permanente Northern California whose blood pressure was controlled are shown in comparison with percentages in U.S. commercial health maintenance organizations (HMOs) and U.S. averages. Data for the United States are from the National Health and Nutrition Examination Surveys, 2000–2016. Data for U.S. HMOs and Kaiser Permanente are from the National Committee on Quality Assurance (www.ncqa.org/health/measures/controlling-high-blood-pressure) and were current as of July 17, 2020. The listed interventions that were implemented at Kaiser Permanente are from Jaffs and Young. †JNC denotes Joint National Commit-
“As the Covid-19 epidemic has demonstrated, we need to explicitly link health care systems with appropriately resourced public health and community-based services. These approaches must undergo systematic evaluations that will assess whether and under what conditions they work. As we recover from the pandemic and address structural racism and inequities, we have an opportunity to invest in quality in ways that lay a foundation for a healthier America.”
Prevention of Cardiovascular Disease is Prescient beyond COVID-19
Thank You and Stay Well!