

Welcome!

Comprehensive Cardiovascular Care
Tuesday, August 30



CCFMG
Central California Faculty Medical Group

University | Centers of Excellence

In affiliation with UCSF Fresno



Welcome

Ersilia R. Lacaze, MA, MSc

Director of Marketing & Communications, CCFMG

Speakers

Teresa Daniele, MD, FACC

Associate Clinical Professor, UCSF

Chief of Cardiology, UCSF Fresno

University Cardiovascular Center Physician

Richard Kiel, MD

Assistant Clinical Professor, UCSF

University Cardiovascular Center Physician

Speakers

Leigh Ann O'Banion, MD, FACS, FSVS, RPVI

Assistant Clinical Professor, UCSF
Valley Vascular Surgery Associates Physician

Sammy Siada, DO, RPVI

Assistant Clinical Professor, UCSF
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Cardiovascular Screening Project



UCSF Fresno
CHAMPIONS

Comprehensive Heart
and Multidisciplinary Limb
Preservation Outreach Networks

Teresa Daniele, M.D., FACC
Leigh Ann O'Banion, M.D.

Sponsors

University of California
San Francisco
UCSF Fresno
School of Medicine
Fresno Medical Education Program



Mission

- Outreach and screening in targeted underserved communities within the Central Valley
- CME education for primary care providers in these communities on cardiovascular health and preventative medicine
- Establish outreach networks for long term cardiovascular care in these patients

CME

Educate community medical providers about appropriate evidence based screening and Cardiovascular Care

Screening Event

Cardiovascular focused screening in identified targeted underserved area of interest.
Establish continuity with a PCP (FQ) if needed.

Medical Care

FQ follow up for risk factor modification.
Referral to Cardiac or Vascular Surgery

Cardiovascular Risk Assessment

Teresa Daniele, M.D., FACC
Chief of Cardiology, UCSF-Fresno
Associate Professor of Medicine UCSF



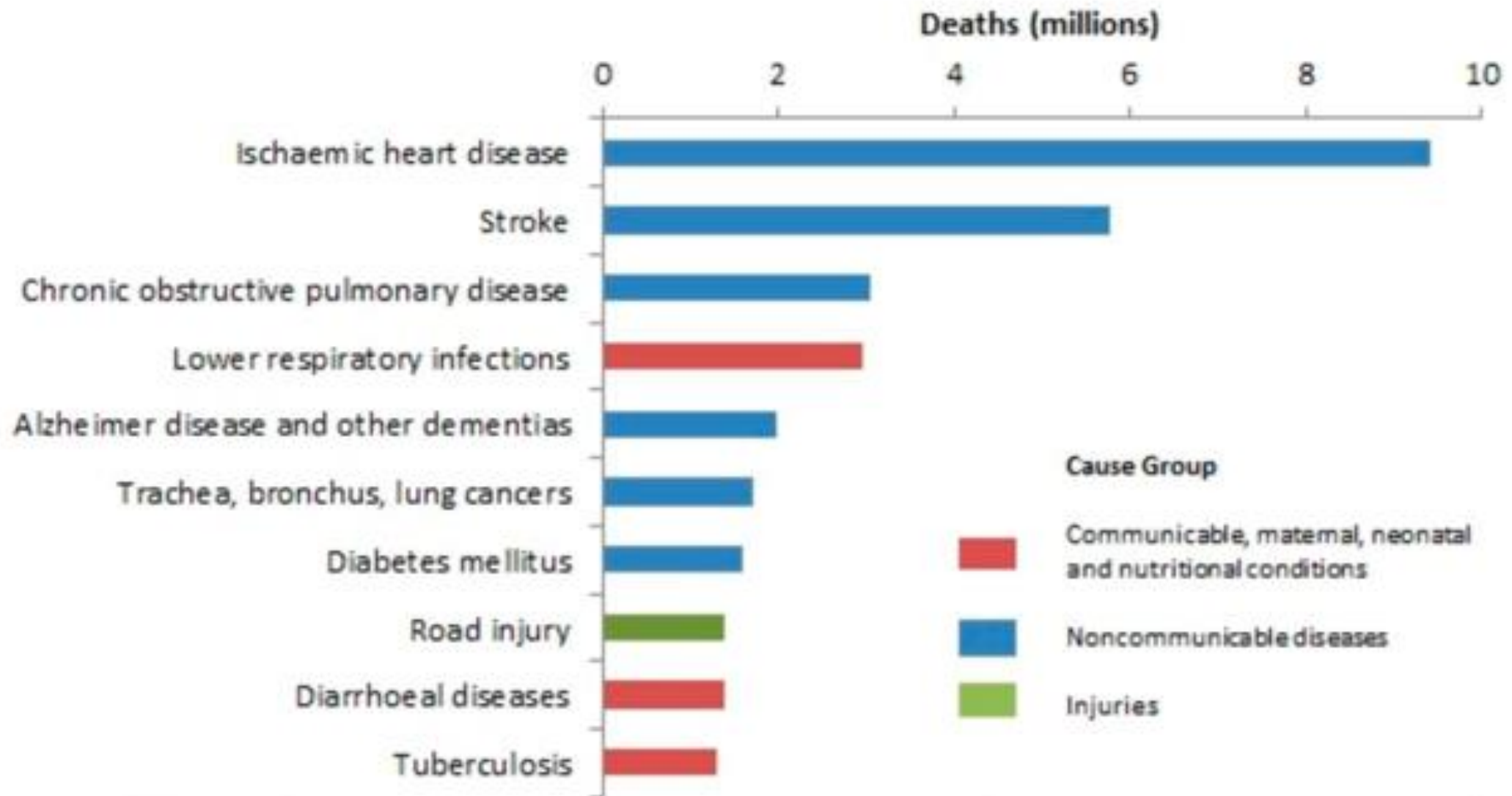
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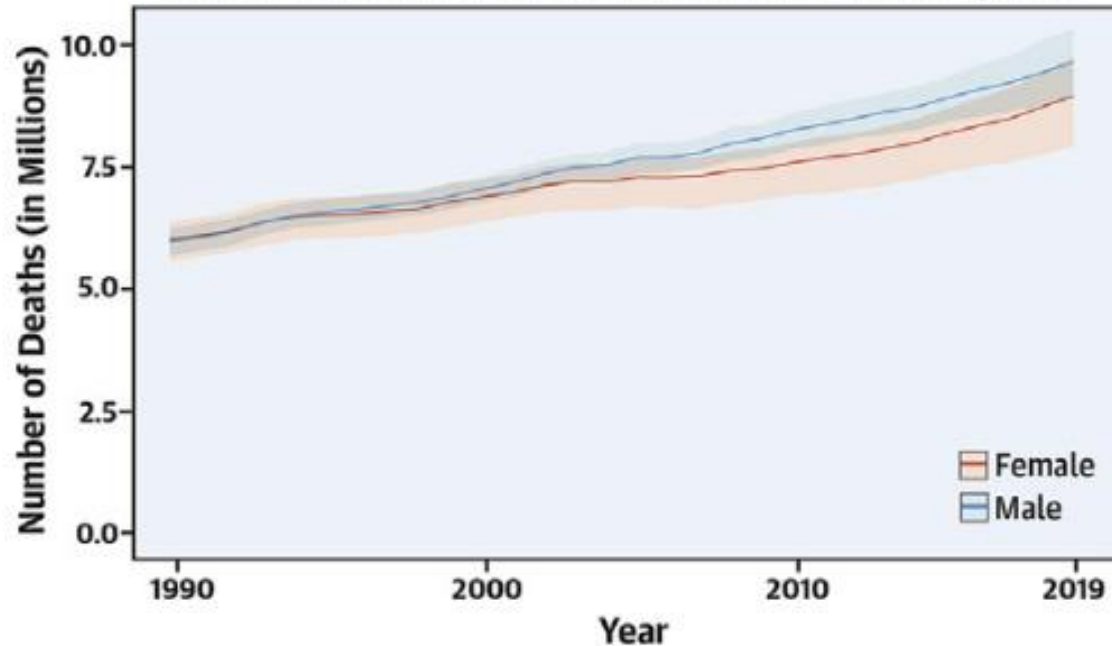
Top 10 global causes of deaths, 2016



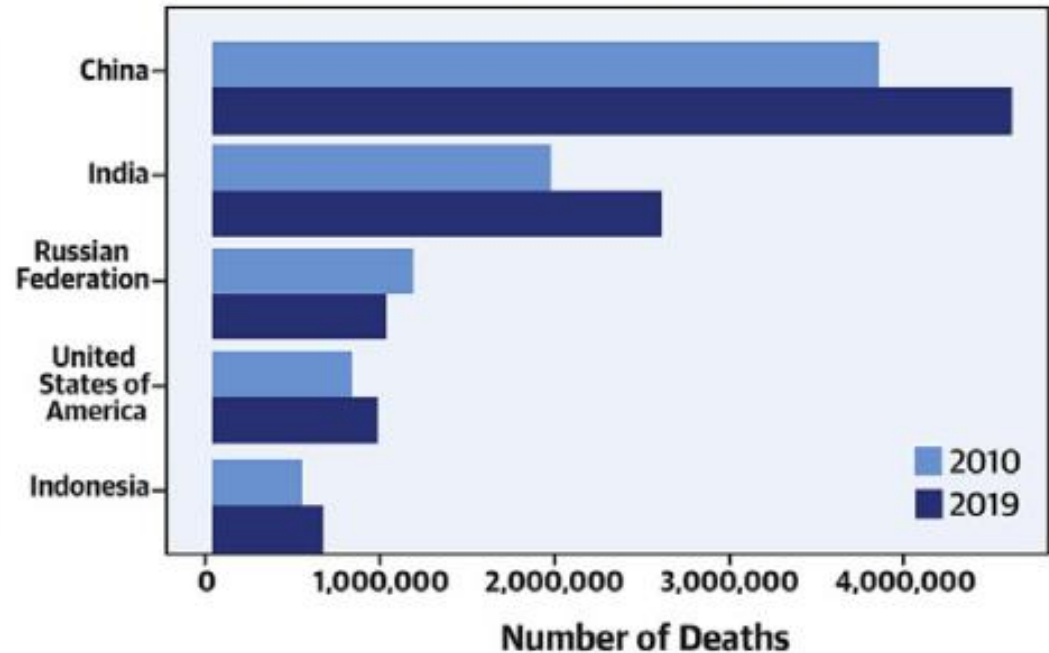
Geneva World Health Organization, 2016

Number of CVD Deaths

Number of CVD Deaths from 1990-2019 by Sex



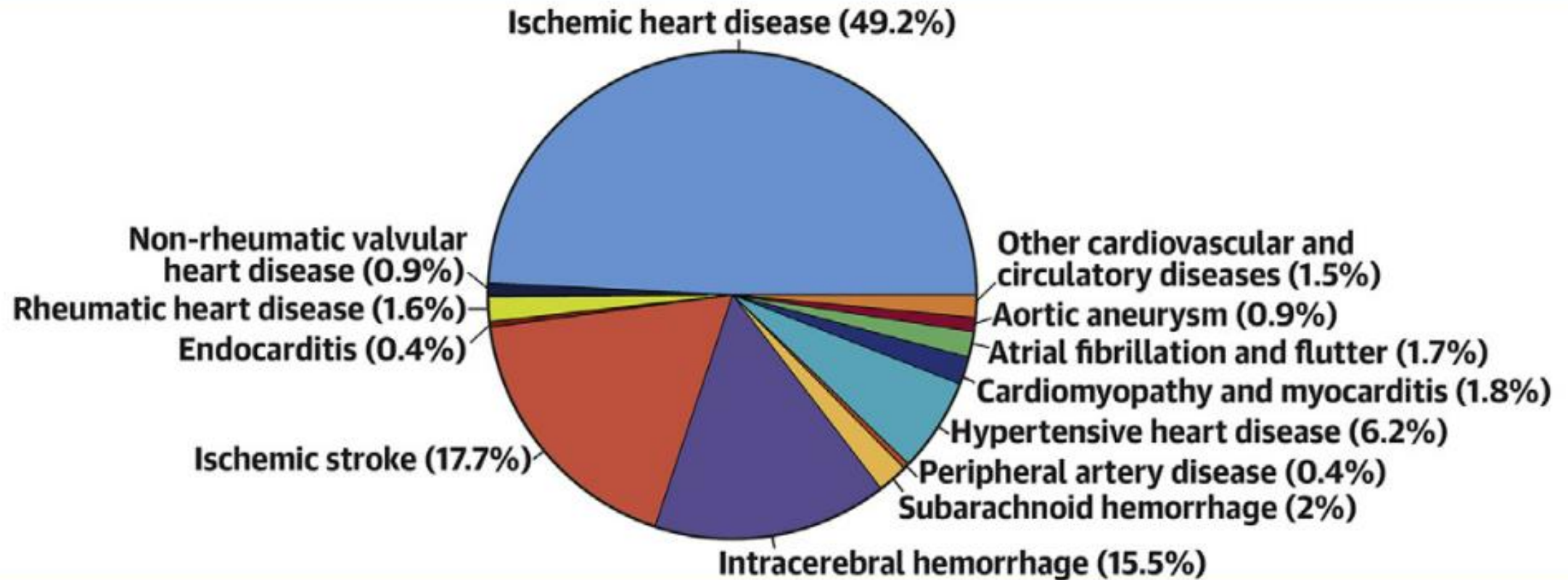
Countries with the Highest Number of CVD Deaths



Proportion of CVD Deaths by Cause (2019)

Roth, G.A. et al. J Am Coll Cardiol. 2020;76(25):2982-3021.

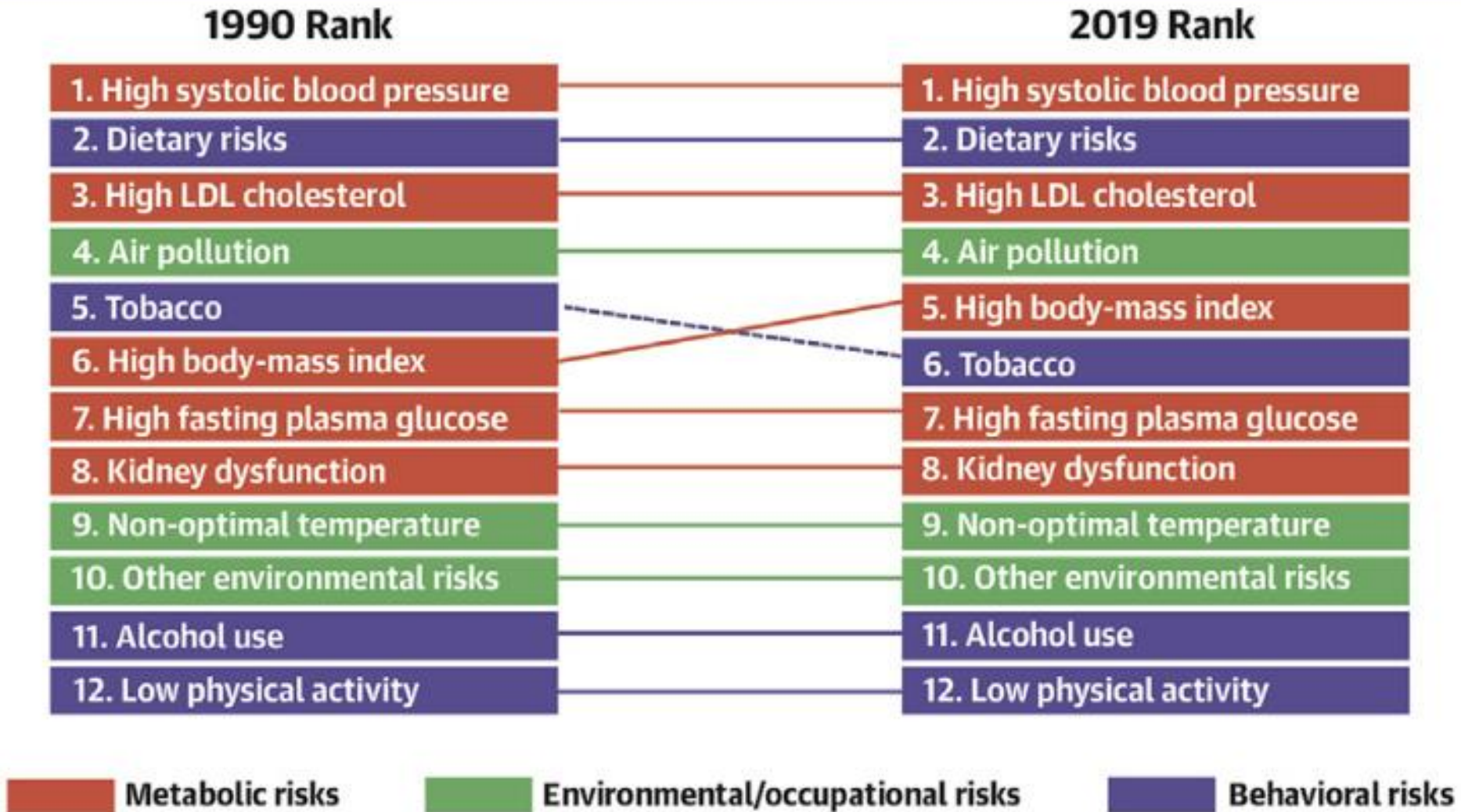
Proportion of CVD Deaths by Cause (2019)



CVD Burden Attributable to Modifiable Risk Factors

Roth, G.A. et al. J Am Coll Cardiol. 2020;76(25):2982-3021.

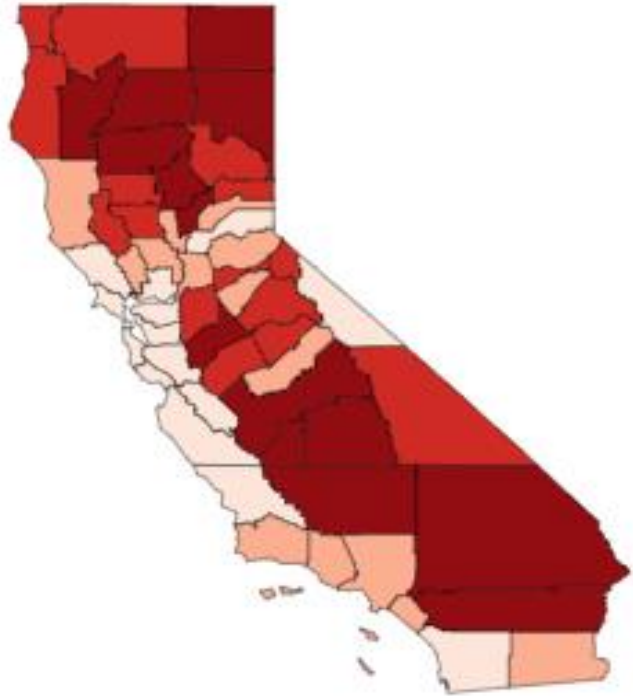
CVD Burden Attributable to Modifiable Risk Factors



Roth, G.A. et al. J Am Coll Cardiol. 2020;76(25):2982–3021.

California: Heart Disease Death Rates

Select/Hover Over a County to See the Rates



California

Heart Disease
Death Rate per 100,000*



Death Rate, Age 35+
Per 100,000

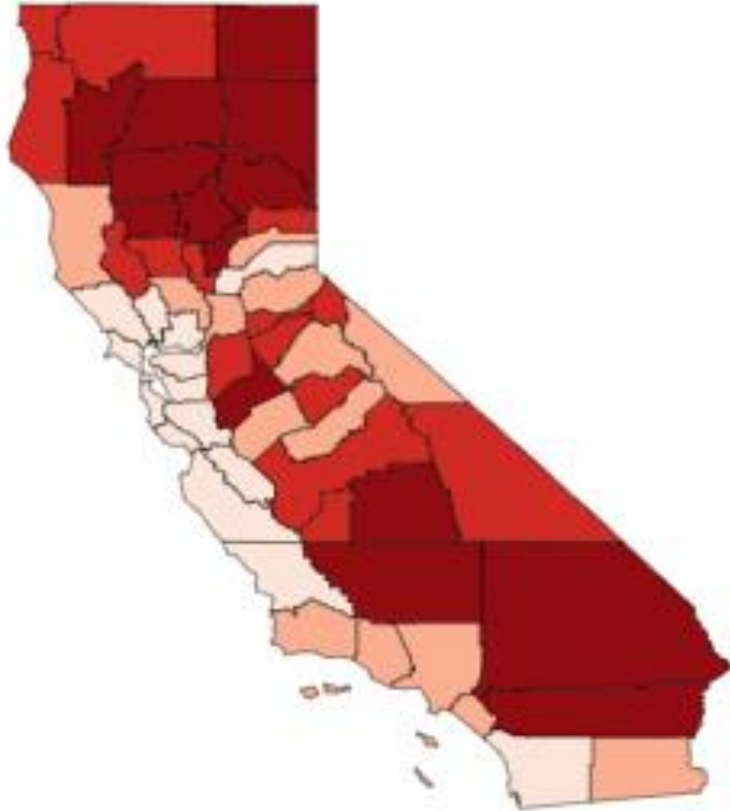
| | |
|------------|-----|
| Madera | 286 |
| Fresno | 331 |
| Tulare | 353 |
| Kern | 372 |
| Stanislaus | 353 |

2017-2019



California: Heart Disease Death Rates, Men

Select/Hover Over a County to See the Rates



California: Heart Disease Death Rates, Women

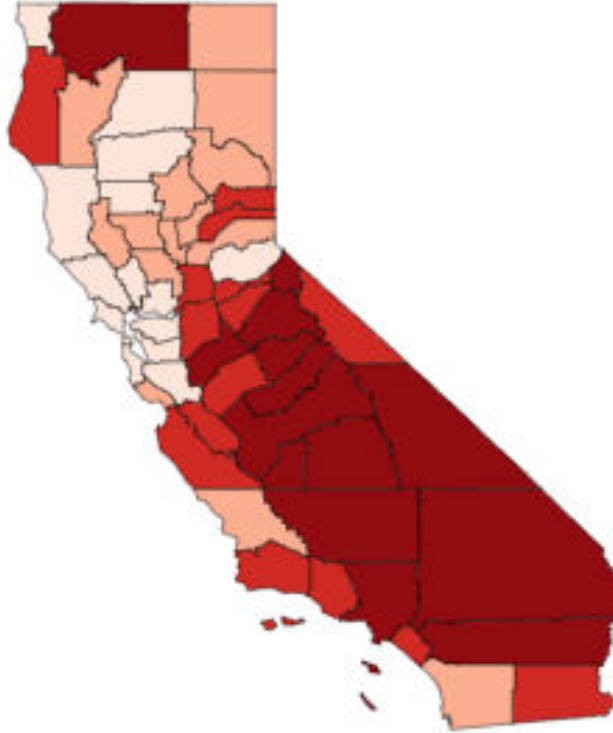
Select/Hover Over a County to See the Rates



2017-2019

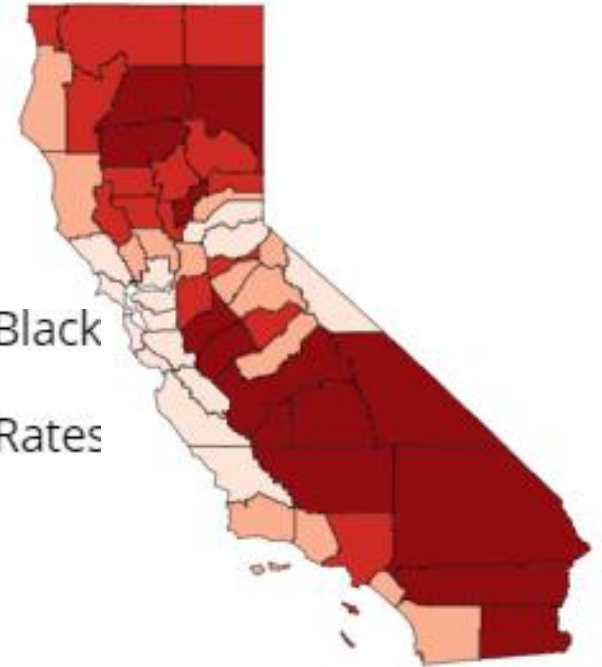
California: Heart Disease Death Rates, Hispanic

Select/Hover Over a County to See the Rates



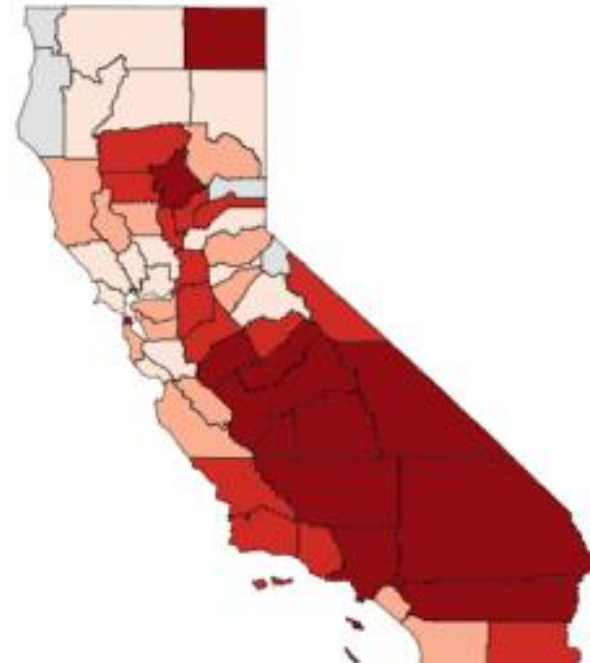
California: Heart Disease Death Rates, White

Select/Hover Over a County to See the Rates



California: Heart Disease Death Rates, Black

Select/Hover Over a County to See the Rates



2017-2019

California: Stroke Death Rates

Select/Hover Over a County to See the Rates



California

Stroke
Death Rate per 100,000*



Death Rate, Age
35+

Per 100,000

| | |
|------------|----|
| Madera | 71 |
| Fresno | 84 |
| Tulare | 85 |
| Kern | 73 |
| Stanislaus | 80 |



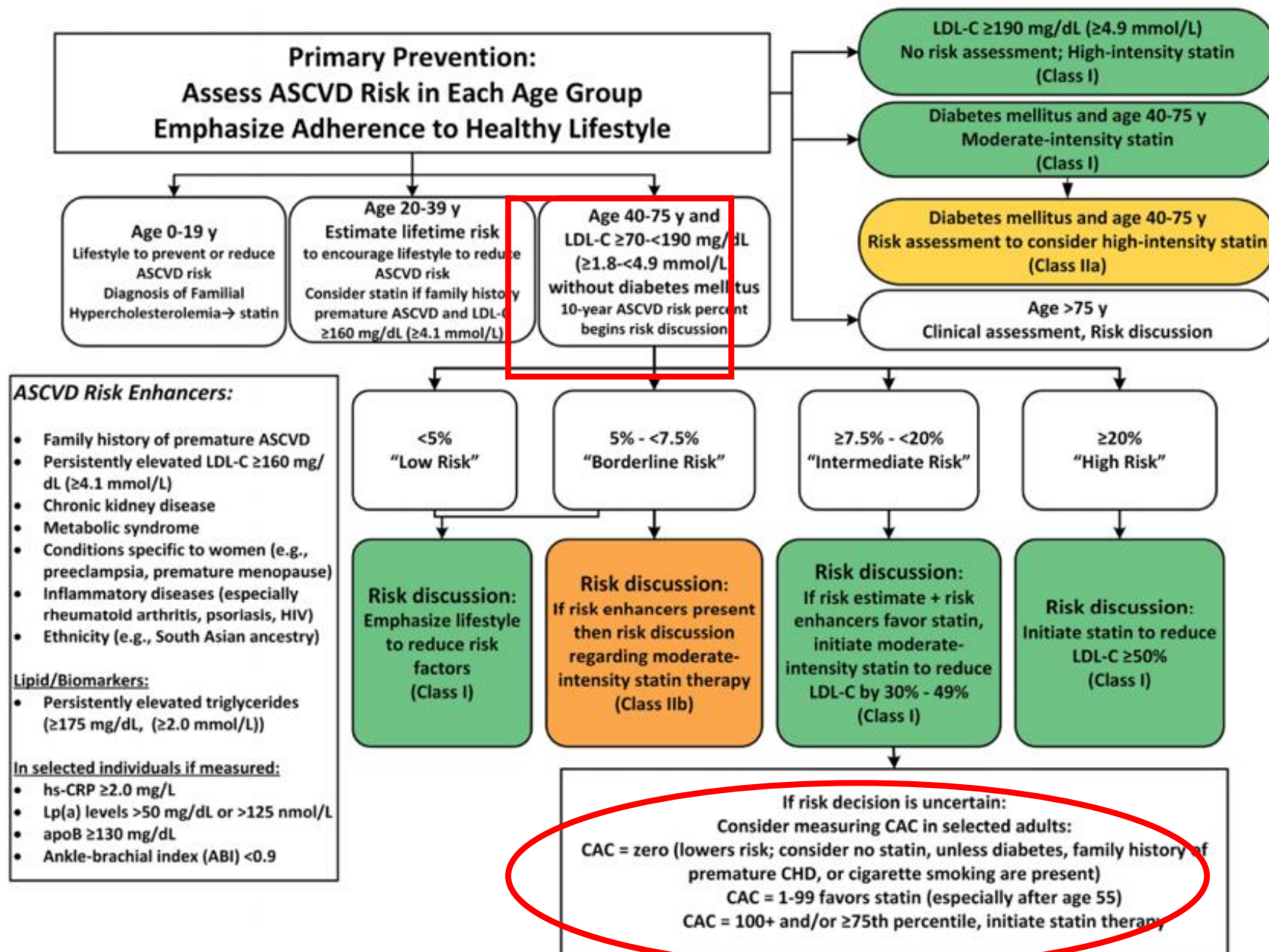
2017-2019

Case – asymptomatic patient

- 52 yo non-smoker, non-diabetic caucasian man with normal BMI, Family history of premature CAD (father)
 - BP 138/84, HDL 60, LDL 135
- Referred to you for cardiac risk stratification given FH
- Pooled Cohort Equation: 4.7% 10-year risk of ASCVD

What do you do next?

- Reassurance/lifestyle modifications
- Start statin and aspirin
- Further risk stratify

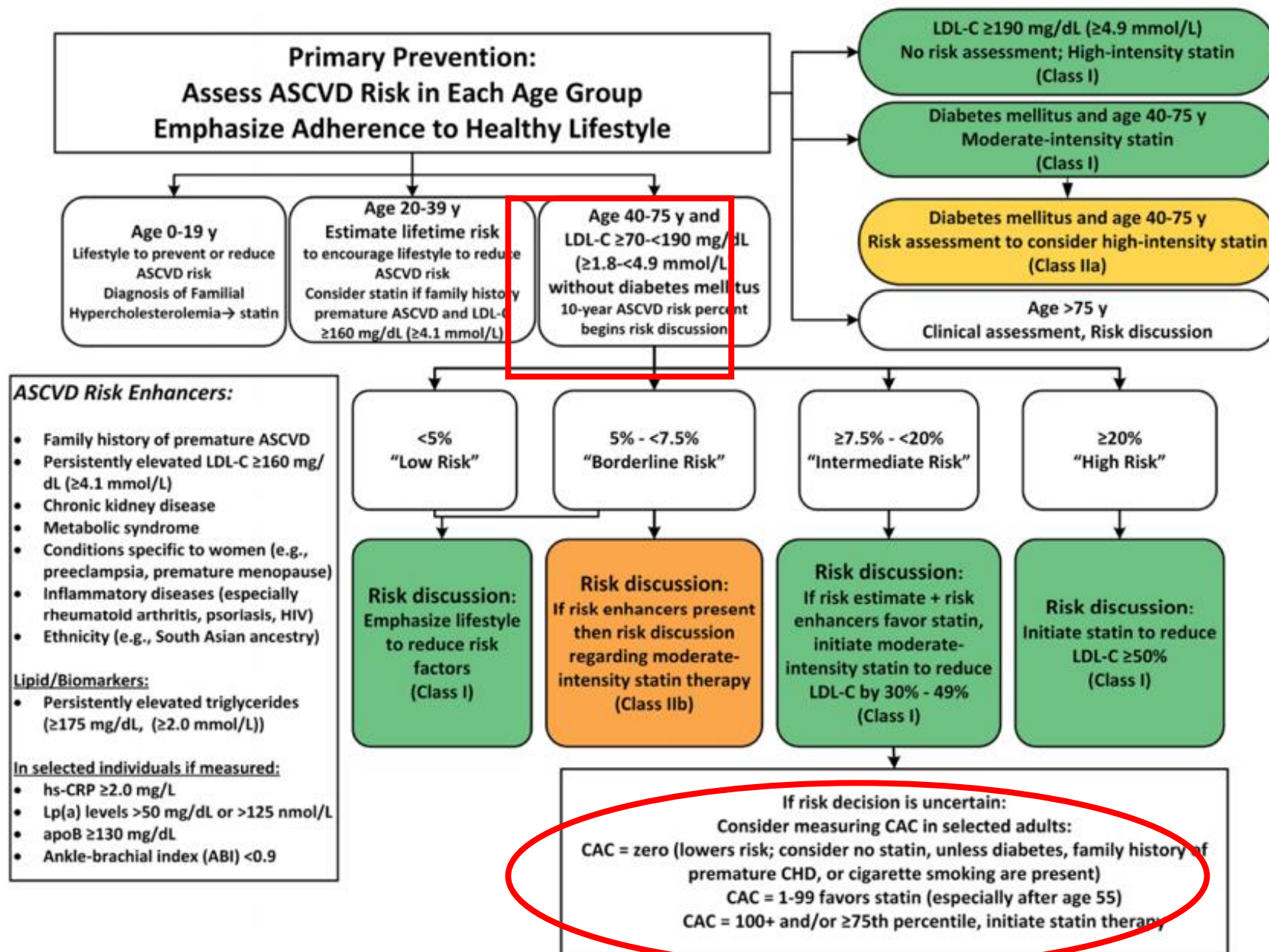


Pooled Cohort Equation

- 10-year risk of MI/Stroke, MI/Stroke death
- Age
- Sex
- Race (Black/White)
- Total Cholesterol
- HDL Cholesterol
- Systolic BP
- Hypertension
- Diabetes
- Current smoking



| Estimator | Clinicians | Patients | About |
|--|------------|---|-------|
| ASCVD Risk Estimator* | | | |
| 10-Year ASCVD Risk | | Lifetime ASCVD Risk | |
| 18.2% calculated risk | | ▲ Lifetime Risk Calculator only provides lifetime risk estimates for individuals 20 to 59 years of age. | |
| 9.6% risk with optimal risk factors** | | | |
| Recommendation Based On Calcul... > | | | |
| Total Cholesterol (mg/dL) | | <input type="text" value="180"/> | |
| HDL - Cholesterol (mg/dL) | | <input type="text" value="45"/> | |
| Systolic Blood Pressure | | <input type="text" value="140"/> | |
| Treatment for Hypertension | | <input checked="" type="radio"/> Y <input type="radio"/> N | |

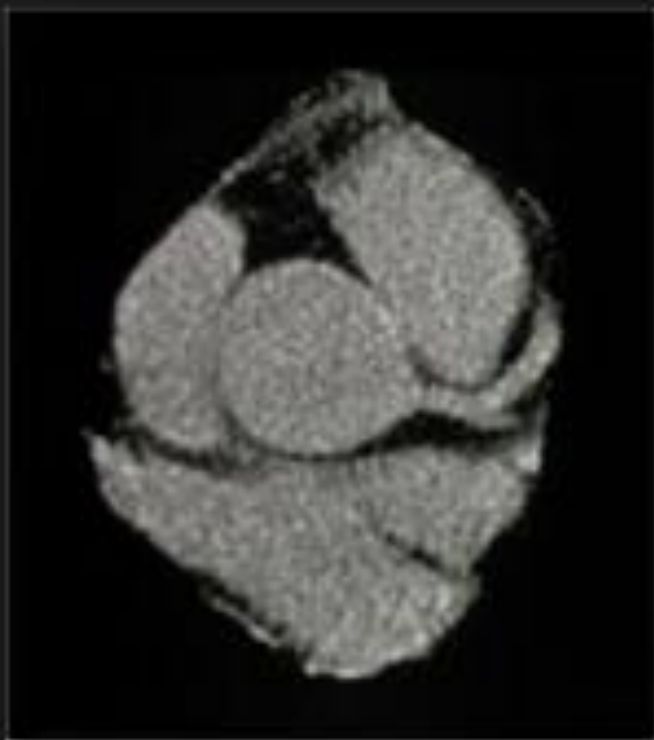


Background

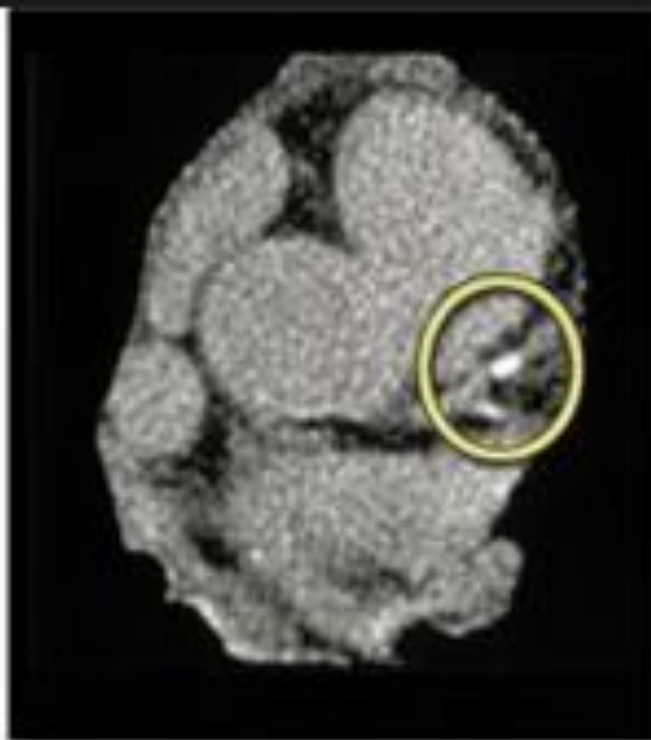
- Coronary calcification is a marker of atherosclerosis
- Proportional to the extent and severity of atherosclerotic disease
- Total coronary artery calcium score represents an anatomic measure of overall cardiac calcified plaque burden
- High sensitivity for atherosclerosis
- Does not assess for significant stenosis

Test Procedure

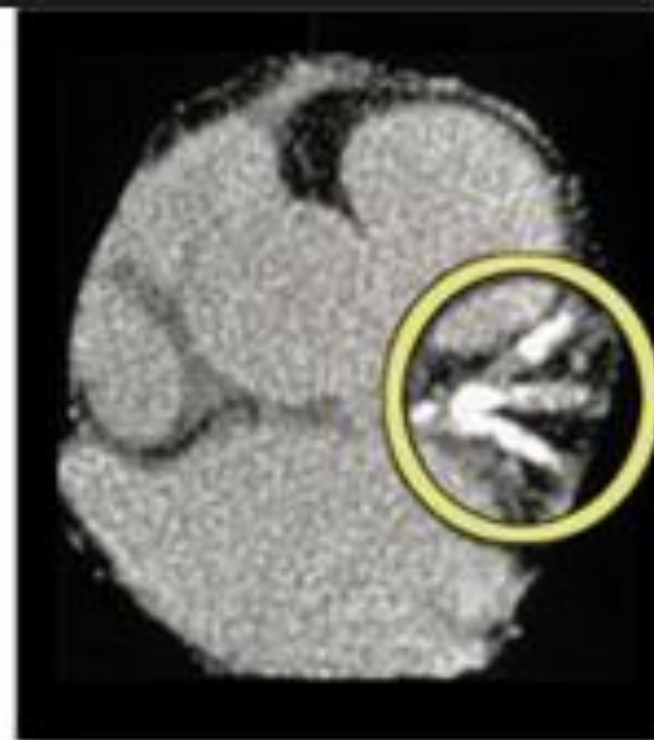
- No special preparation, nor medication restrictions. No contrast given for CAC
- Patient lies in CT scanner for approximately 10 minutes and must hold breath between 10-20 seconds during imaging
- Gated study (prospective)
- Radiation exposure: ~1.5 mSv (milli-Sieverts)
 - Avg. yearly “natural” background exposure in US: 3 mSv
 - Mammogram is about 1.5 mSv
 - Diagnostic cardiac catheterization: 6-10 mSv



Normal



**Moderate
Calcification**



**Severe
Calcification**



**How can CAC
help with risk
stratification?**

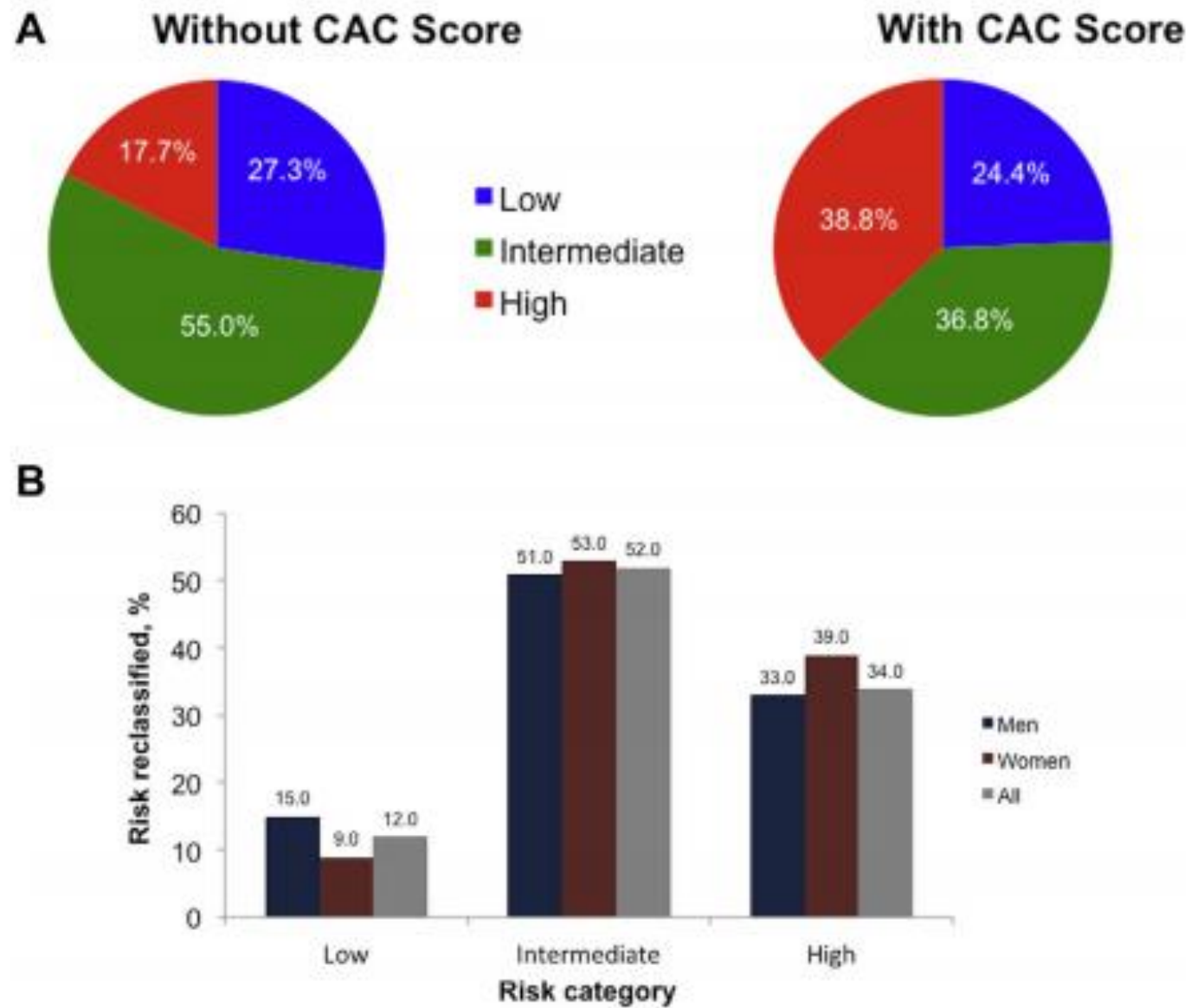


Figure 1 Select Studies Demonstrating Improved Risk Stratification of CHD Events With Use of CAC Scores

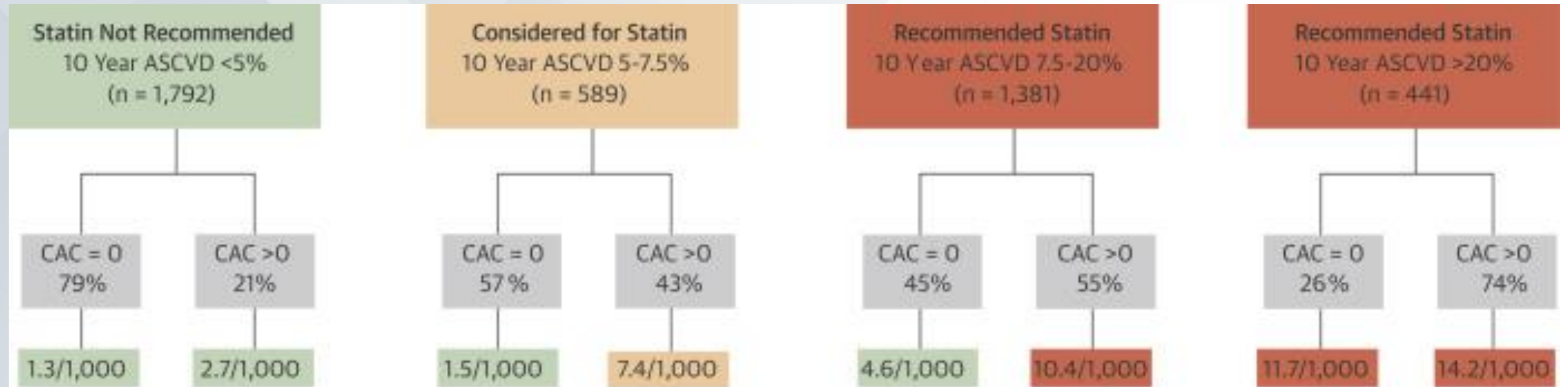
Our case

- 52 yo non-smoker, non-diabetic caucasian man with normal BMI
 - Family history of premature CAD (father)
 - BP 138/84, HDL 60, LDL 135
- Referred to you for cardiac risk stratification given FH
- Pooled Cohort Equation: 4.7% 10-year risk of ASCVD

- Underwent a CAC – Comes back at 325



**How can cac
change our
clinical
practice?**



Nasir, K. et al. J Am Coll Cardiol. 2015; 66(15):1657-68.

Nasir, K et al. J Am Coll Cardiology. 2015; 66(15):1657-68

Cac is now guideline endorsed

| | | |
|------------|-------------|---|
| Ila | B-NR | 6. In intermediate-risk or selected borderline-risk adults, if the decision about statin use remains uncertain, it is reasonable to use a CAC score in the decision to withhold, postpone or initiate statin therapy. ^{S4.4.2-15,S4.4.2-17,S4.4.2-23} |
| Ila | B-NR | 7. In intermediate-risk adults or selected borderline-risk adults in whom a CAC score is measured for the purpose of making a treatment decision, AND <ul style="list-style-type: none">▪ If the coronary calcium score is zero, it is reasonable to withhold statin therapy and reassess in 5 to 10 years, as long as higher risk conditions are absent (diabetes mellitus, family history of premature CHD, cigarette smoking);▪ If CAC score is 1 to 99, it is reasonable to initiate statin therapy for patients ≥55 years of age;▪ If CAC score is 100 or higher or in the 75th percentile or higher, it is reasonable to initiate statin therapy.^{S4.4.2-17,S4.4.2-23} |

Aspirin

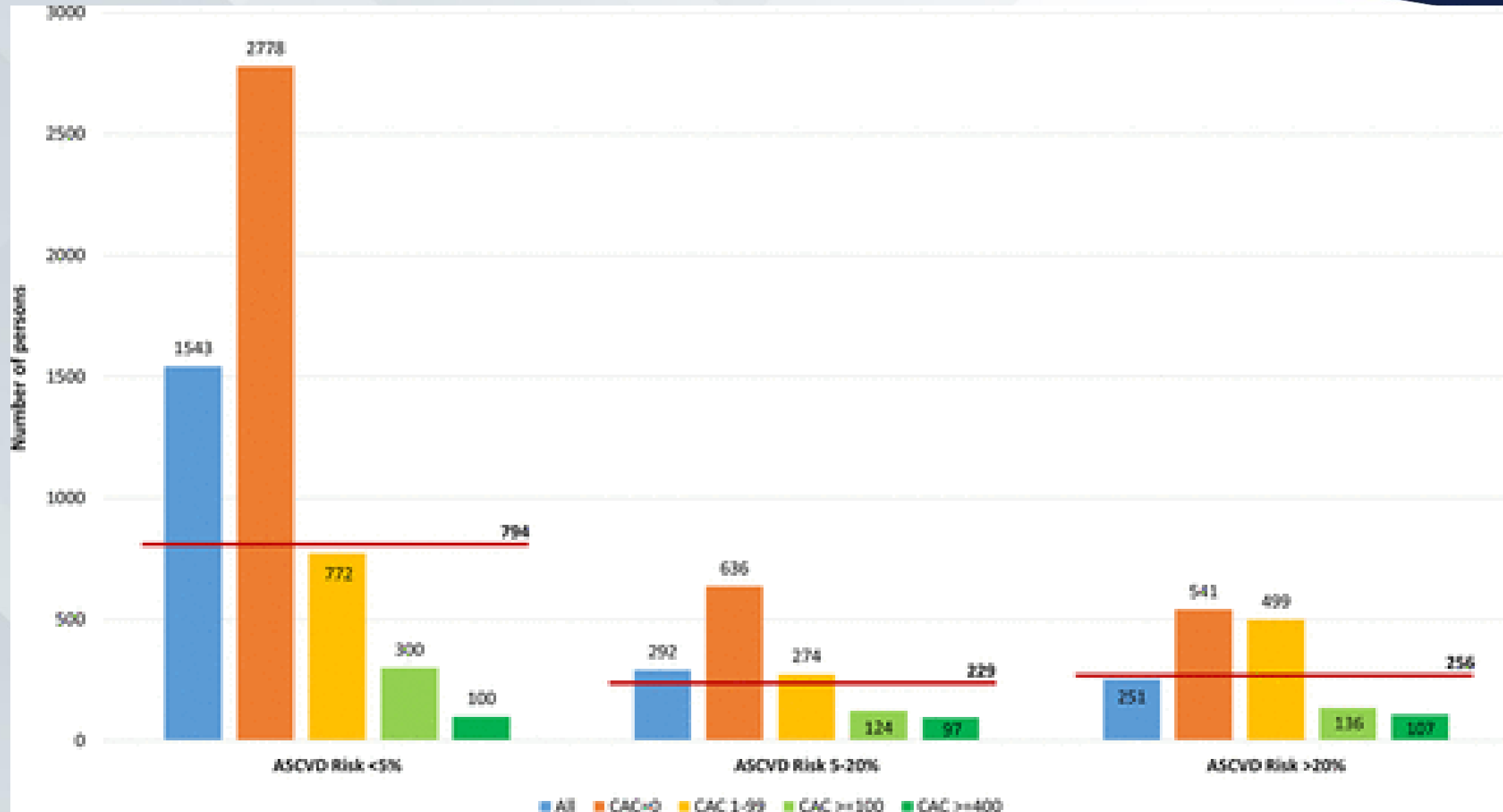
- Role of aspirin in primary prevention is controversial
- 2019 AHA/ACC guidelines downgraded use
- Level I to level IIB in “select adults at higher risk”

Recommendations for Aspirin Use

Referenced studies that support recommendations are summarized in Online Data Supplements 17 and 18.

| COR | LOE | Recommendations |
|-----------|------|--|
| IIb | A | 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. ^{S4.6-1-S4.6-8} |
| III: Harm | B-R | 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 >70 years of age. ^{S4.6-9} |
| III: Harm | C-LD | 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. ^{S4.6-10} |

ASA net benefit by CAC scores



Case – Asymptomatic patient

- 52 yo non-smoker, non-diabetic man with normal BMI Family history of premature CAD (father)
 - BP 138/84, HDL 60, LDL 135
- Referred to you for cardiac risk stratification given FH
- Pooled Cohort Equation: 4.7% 10-year risk of ASCVD
- Recommend aggressive risk stratification with Statin and Aspirin



UCSF Fresno **CHAMPIONS**

Comprehensive Heart
and Multidisciplinary Limb
Preservation Outreach Networks

Dinuba Raisin Festival September 24th



Thank you



SGLT-2 inhibitors: cardiovascular benefit in heart failure and beyond

Richard G. Kiel, M.D.

Associate Clinical Professor of Medicine, UCSF

Medical Director Advanced Heart Failure and Mechanical Circulatory Support

Program Director, Adult Cardiovascular Disease Fellowship Program

UCSF Fresno

Disclosures

No personal or financial conflict of interests

Case scenario

- 47 year old male with history of chronic non-ischemic, dilated cardiomyopathy with severely reduced left ventricular systolic function NYHA functional class II, ACC/AHA stage C. Euvolemic on exam with blood pressure of 108/64, heart rate 68 bpm. Current meds include valsartan/sacubitril 97/103 mg, carvedilol 25 mg, spironolactone 25 mg, bumetanide 1 mg bid. Hospitalized twice in last 12 months for decompensated congestive heart failure. Next step in treatment is:
 - A. add ivabradine 5 mg by mouth twice per day
 - B. Refer for cardiomechs
 - C. LVAD
 - D. Add dapagliflozin 10 mg by mouth daily

Standard of Care Heart Failure With Reduced EF

- 1st line therapy
 - Beta blockers (carvedilol, metoprolol succinate)
 - Mineral corticoid receptor antagonist
 - ACEI, ARB, or angiotensin receptor neprilysin inhibitor (ARNI)
 - SGLT2 inhibitors
 - Diuretics as needed
- 2nd line therapy
 - Ivabradine
 - Hydralazine + nitrates
 - Digoxin
 - Intravenous iron
- Soluble guanylate cyclase inhibitors

Standard of Care Heart Failure With Preserved EF

- 1st line therapies
 - Blood pressure control (less than 130/80)
 - Diuretics as needed to achieve euvolemia
 - SGLT 2 inhbitors
 - Consider MRA
 - Consider ARNI
 - Avoid nitrates
- Advanced Therapies
 - Pulmonary arterial pressure monitoring
 - Rare transplant

How we got here: cardiovascular risk testing in diabetic medications

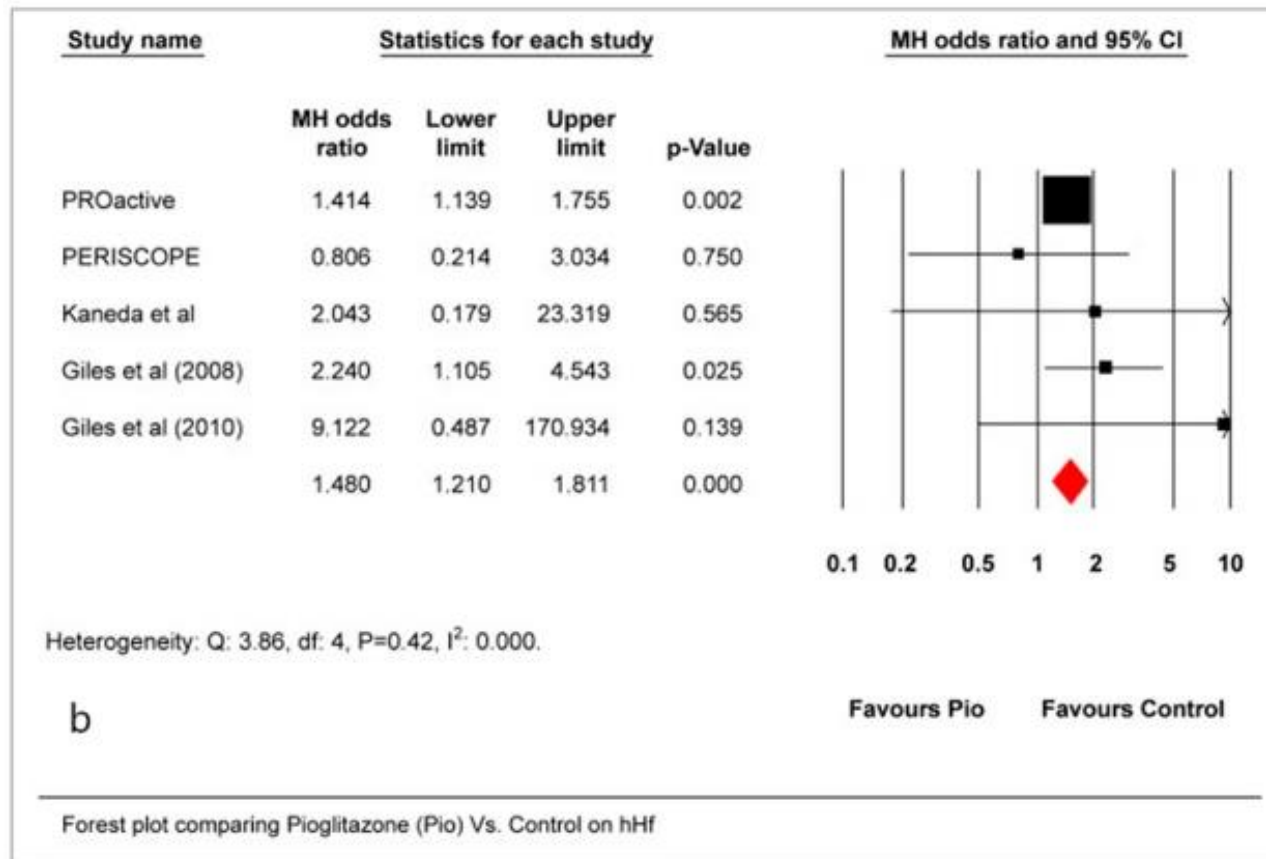
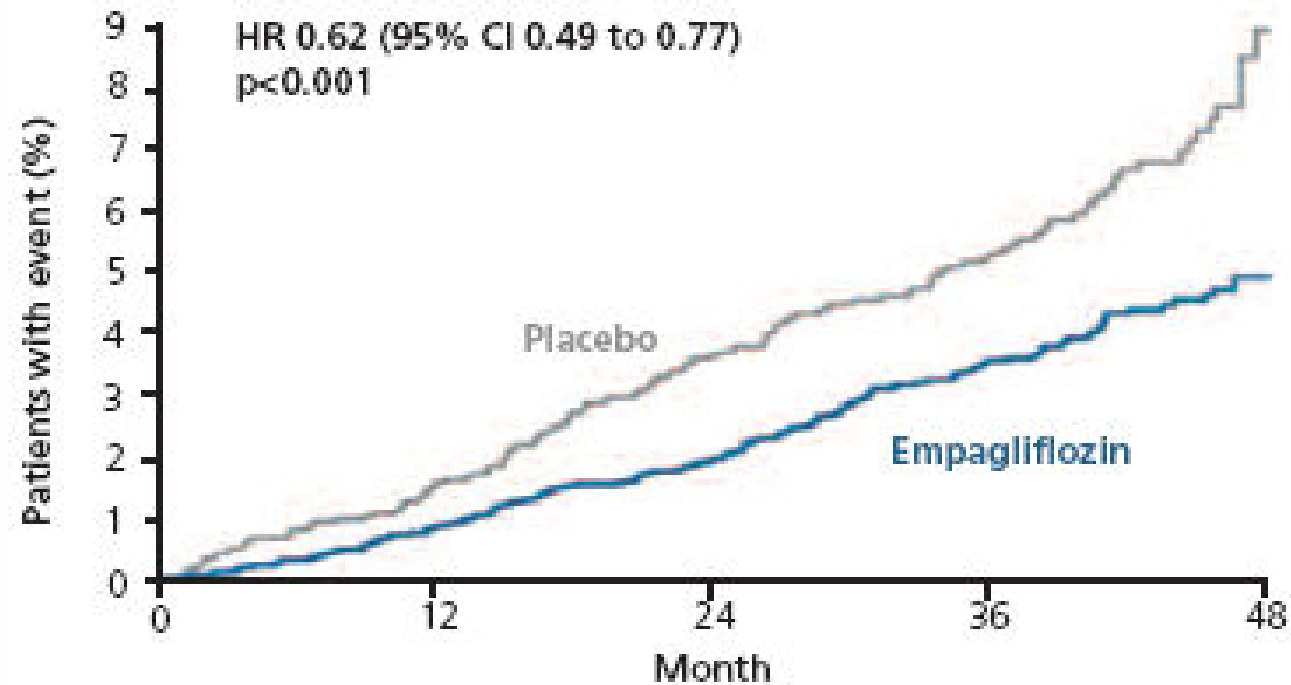
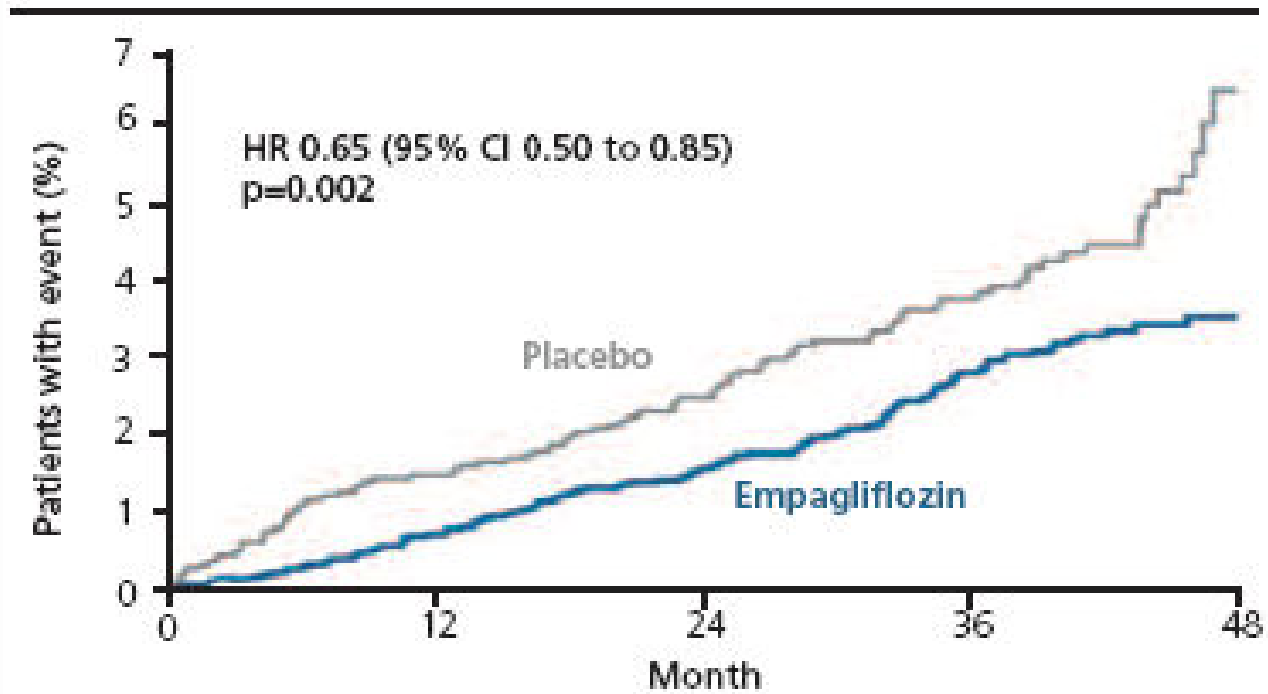


Figure 1. The cumulative incidence of death from cardiovascular causes in the empagliflozin group versus placebo group in the EMPA-REG OUTCOME



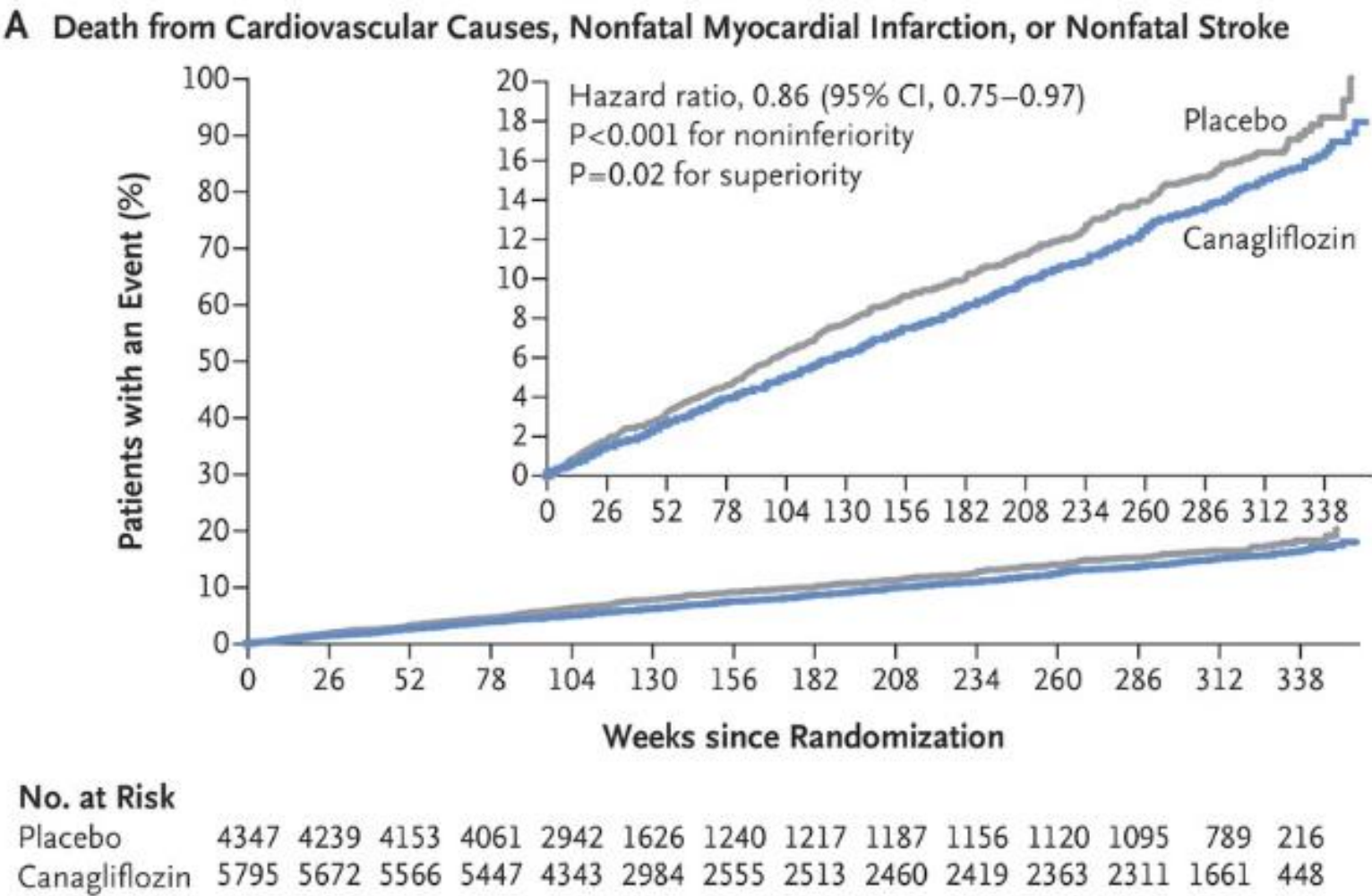
Hazard ratios (HR) are based on Cox regression analysis. Reproduced with permission from ref 2.

Figure 6. The cumulative incidence of hospitalisation for heart failure in the empagliflozin group versus placebo in the EMPA-REG OUTCOME study



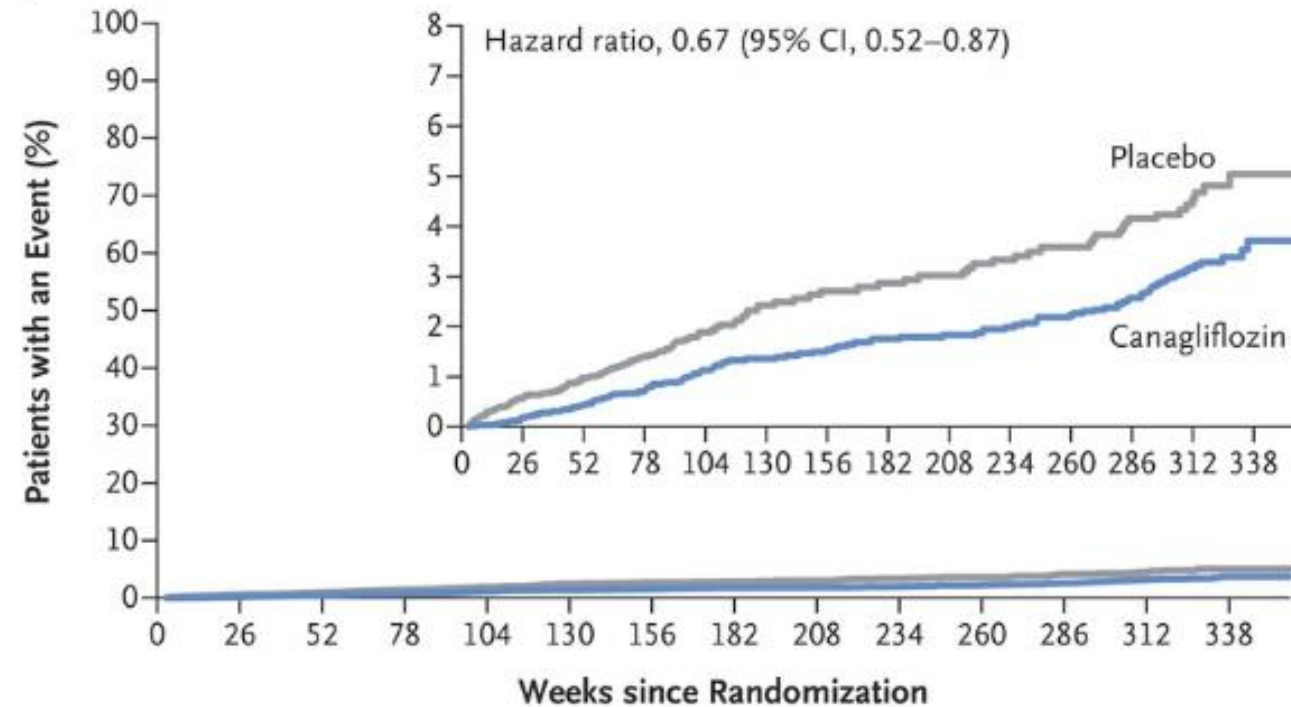
Hazard ratios (HR) are based on Cox regression analysis. Reproduced with permission from ref 2.

Canagliflozin - CANVAS Trial



Canagliflozin - CANVAS Trial

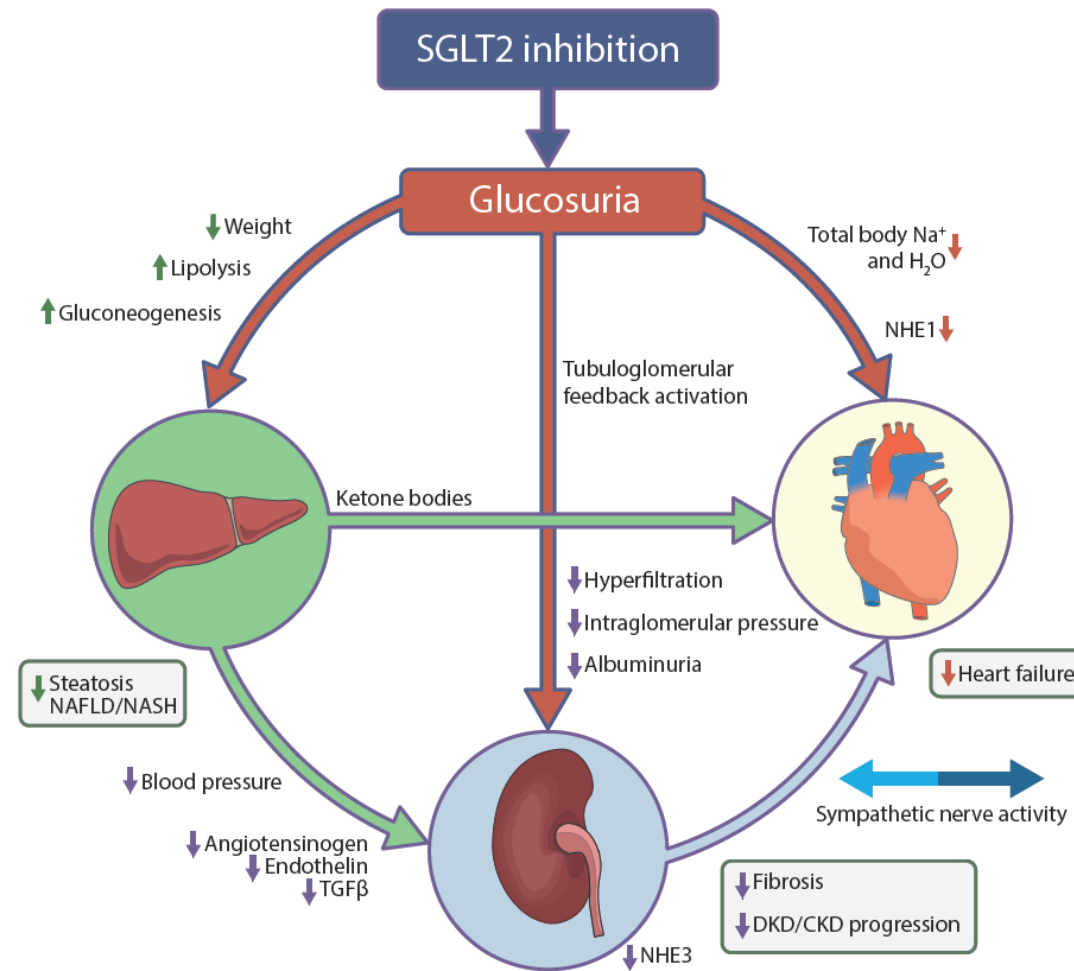
A Hospitalization for Heart Failure



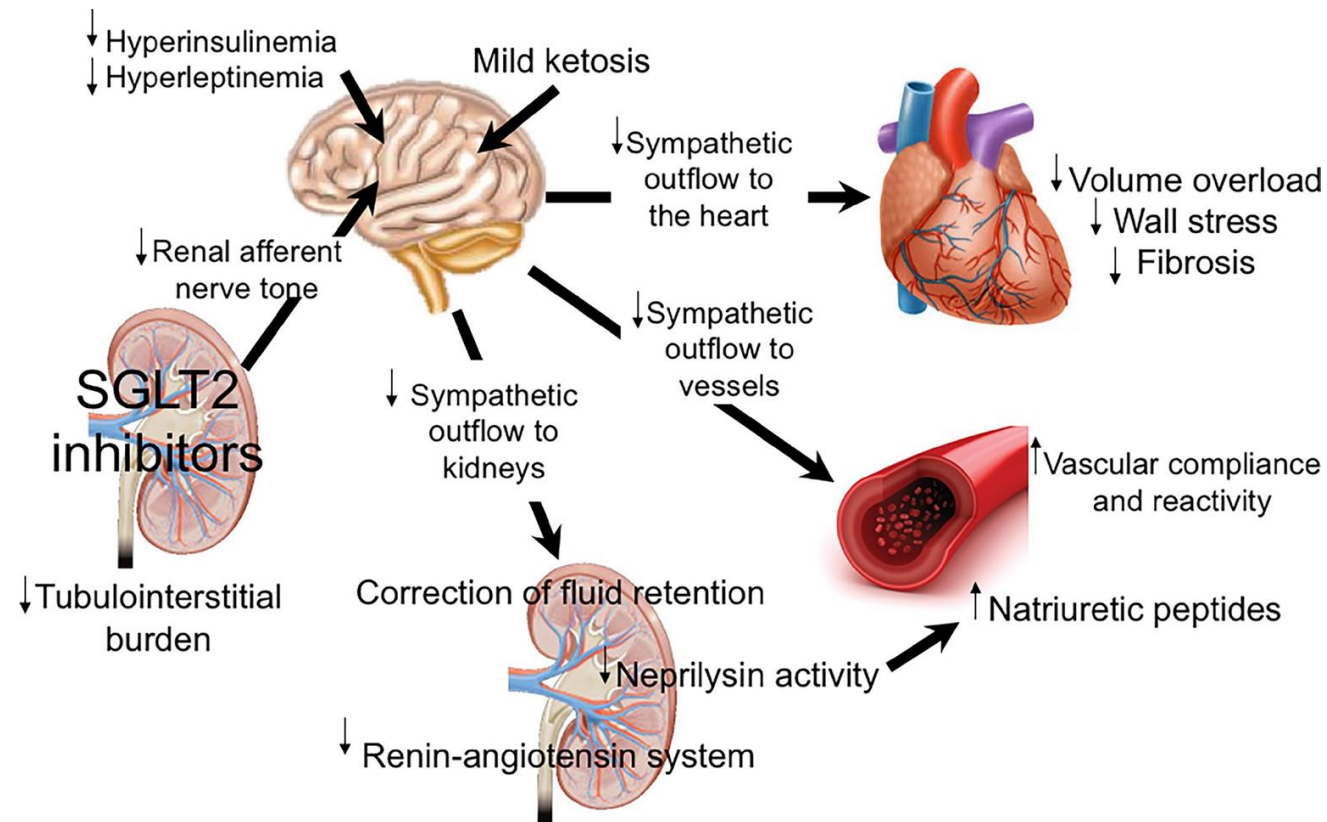
No. at Risk

| | | | | | | | | | | | | | | |
|---------------|------|------|------|------|------|------|------|------|------|------|------|------|------|-----|
| Placebo | 4347 | 4267 | 4198 | 4123 | 3011 | 1667 | 1274 | 1256 | 1236 | 1210 | 1180 | 1158 | 829 | 233 |
| Canagliflozin | 5795 | 5732 | 5653 | 5564 | 4437 | 3059 | 2643 | 2610 | 2572 | 2540 | 2498 | 2451 | 1782 | 490 |

Consequences of inhibition of SGLT2 on glucose, salt and water excretion, as well as its potential metabolic impact on kidney, liver and heart function



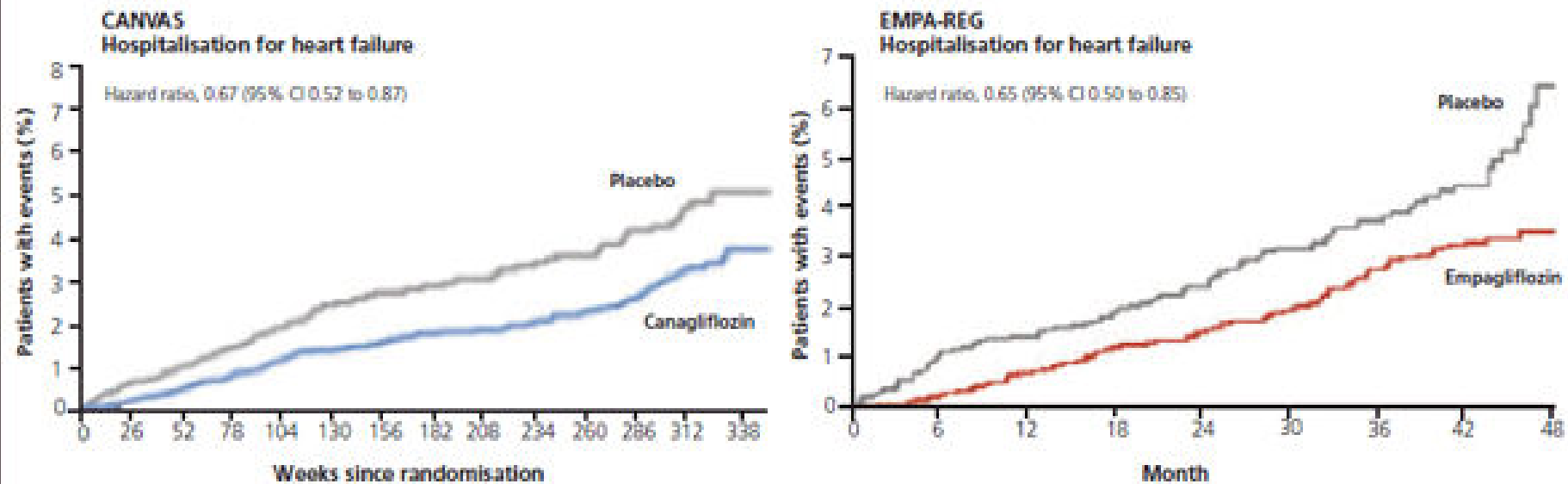
SGLT2 Effect on HF, Proposed Mechanisms



SGLT2 Inhibition in Heart Failure

- Rational
 - EMPA-REG: empagliflozin cardiovascular outcomes in type 2 diabetes mellitus patient
 - 35% RRR in CHF hospitalizations in patients with DM2 and ASCVD
 - CANVAS: canagliflozin cardiovascular assessment study:
 - 33% RRR in CHF hospitalizations in patients with DM2 and ASCVD
 - DECLARE-TIMI 58: Dapagliflozin effect on cardiovascular event:
 - 27% RRR in CHF hospitalizations in patients with DM2 and at risk or with known ASCVD

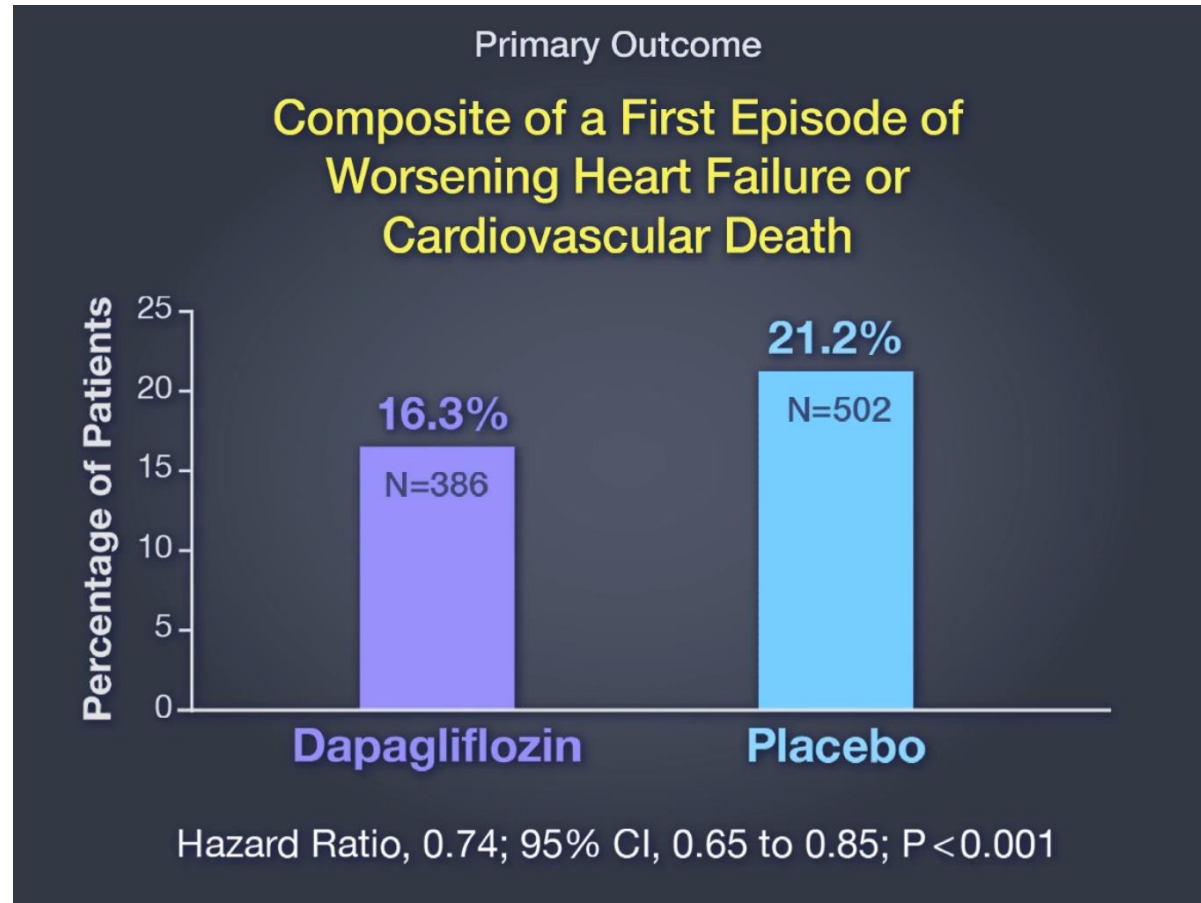
Figure 2. Side by side comparison of the effect of canagliflozin (CANVAS) and empagliflozin (EMPA-REG OUTCOME) on cumulative incidence of hospitalisation for heart failure



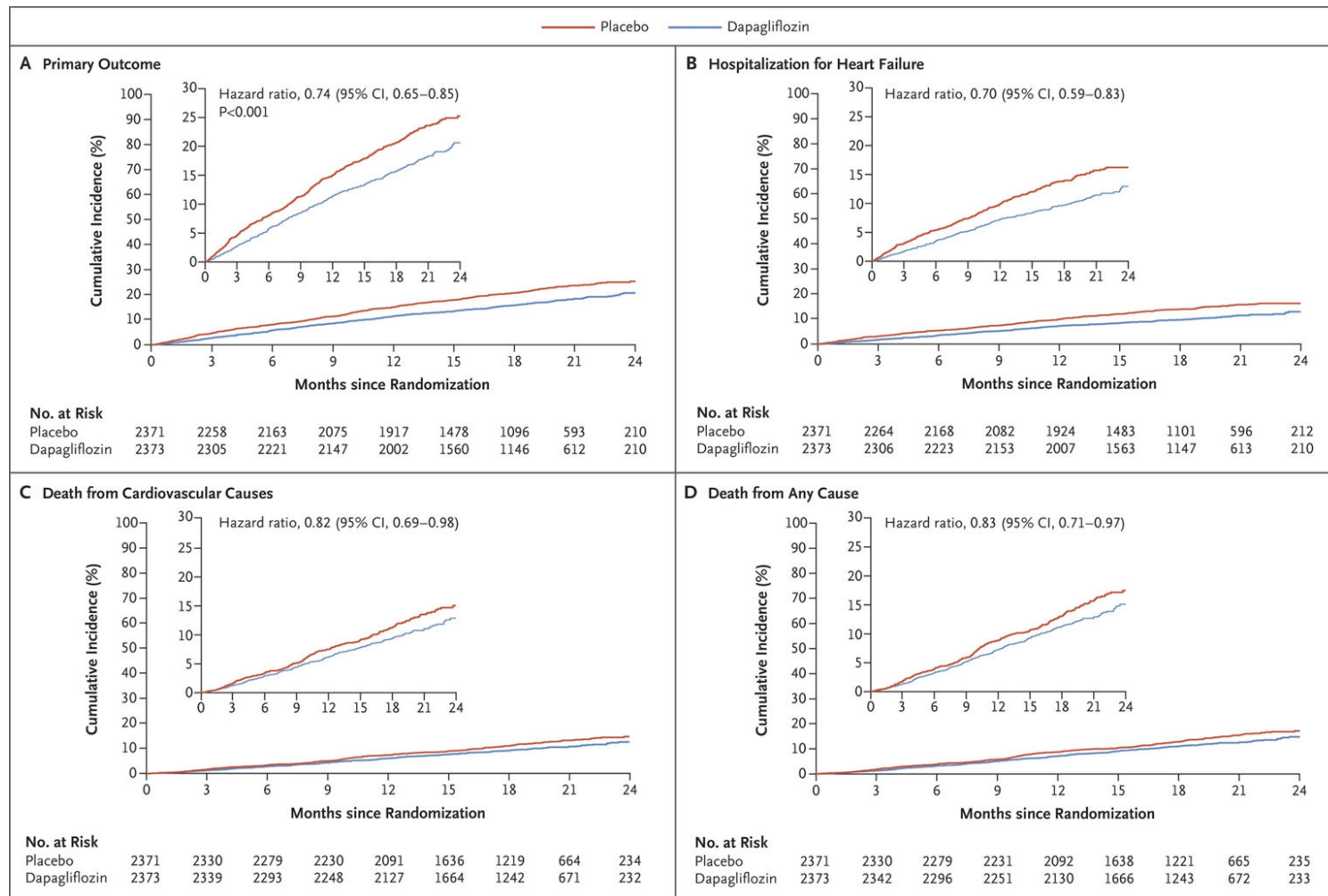
Hazard ratios [HR (95%CI)] based on Cox regression analysis. Graphs adapted from reference 11.

- Multicenter, double blind, randomized placebo controlled trial evaluating efficacy of dapagliflozin on reducing CV outcomes in patients with or without diabetes with symptomatic heart failure with reduced ejection fraction (LVEF \leq 40%)
- N = 4744
- 410 centers in 20 countries
- Median follow up 18.2 months
- Analysis: intention to treat
- Primary outcome: composite of worsening of heart failure (hospitalization or urgent IV diuretics for HF) or CV death

DAPA-HF: Primary Outcome



DAPA-HF Primary Outcomes



DAPA-HF: Secondary Outcomes

- Cardiovascular death or heart-failure hospitalization
 - 16.1% vs 20.9% (HR 0.75; 95% CI 0.65-0.85; $P < 0.001$)
- Changes in KCCQ (Kansas City Cardiomyopathy Questionnaire) total symptom score at 8 months
 - 6.1 ± 18.6 vs 3.3 ± 19.2 (HR 1.18; 95% CI 1.11-1.26; $P < 0.001$)
- Worsening renal function
 - 1.2% vs 1.6% (HR 0.71; 95% CI 0.44-1.16; P not given)
- All cause mortality
 - 11.6% vs 13.9% (HR 0.83; 95% CI 0.71-0.97; P not given)

DAPA-HF: Subgroup Analysis

- Diabetes Status
 - T2DM at baseline: HR 0.75 (95% CI 0.63-0.90)
 - No T2DM at baseline: HR 0.73 (95% CI 0.60-0.88)

DAPA-HF: Takeaway

- Dapagliflozin is effective at reducing a composite of cardiovascular mortality, heart failure hospitalizations and need for urgent diuretics regardless of if patient has diabetes
- Uncertain of efficacy in patients on ARNI (10% enrolled in study)
- Not clear if effect is driven by diuretic effect or other mechanism
- Patients enrolled had primarily moderate heart failure, uncertain of utility in more severe patients

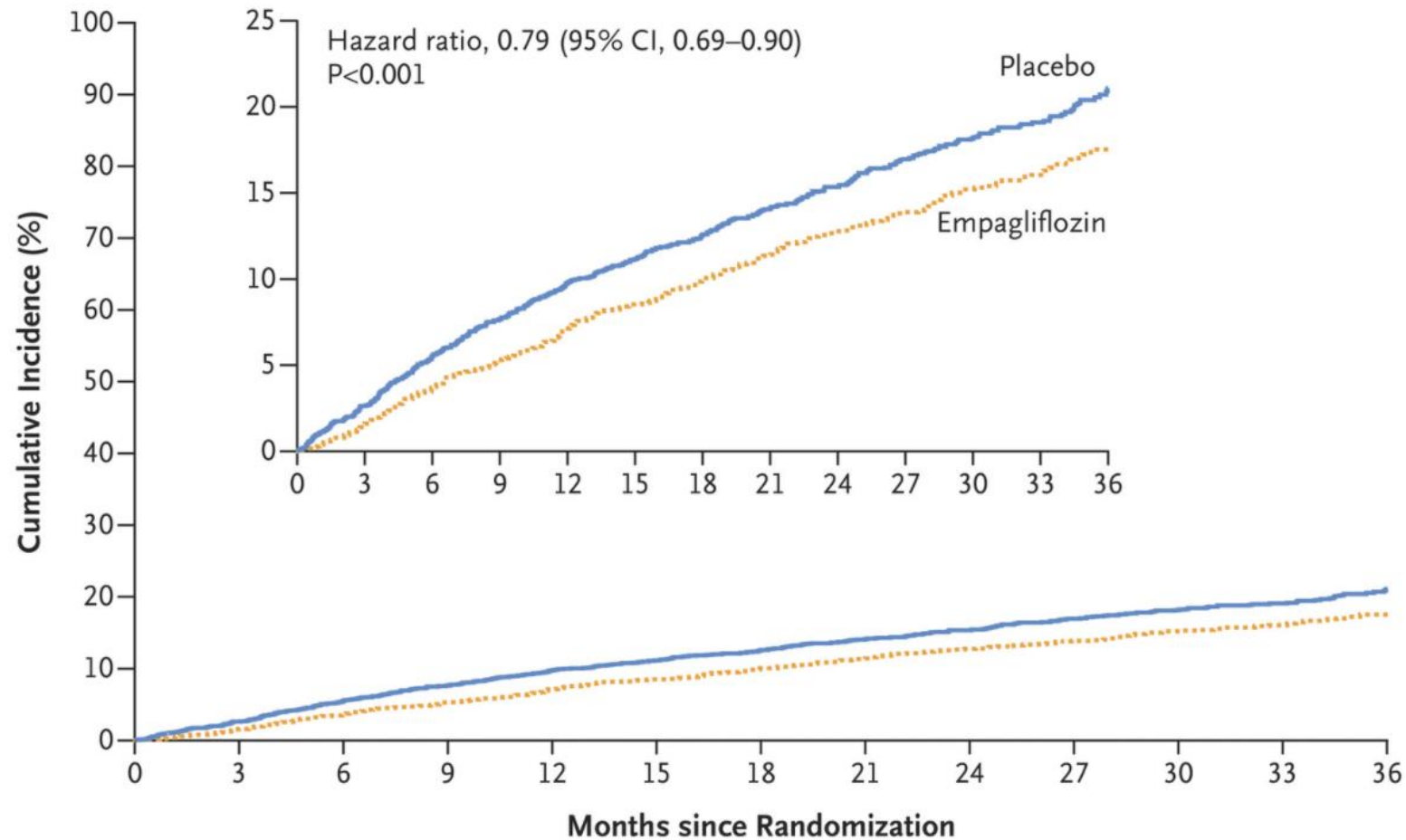
EMPEROR-Preserved

- Multicenter, double-blind, parallel-group, randomized, controlled trial
- N=5988
 - Empagliflozin (n=2997)
 - Standard (n=2991)
- Setting: 622 centers in 23 countries
- Enrollment: 2017-2020
- Median follow-up: 26.2 months
- Analysis: Intention-to-treat
- Primary outcome: Death from cardiovascular causes or hospitalization for heart failure

EMPEROR-Preserved: Inclusion criteria

- NYHA class II-IV with LVEF >40% while clinically stable (and no prior LVEF ≤40 while clinically stable)
- NT-proBNP >300 pg/mL if no AF or >900 pg/mL if AF
- Aged ≥18 years
- Evidence of hypertensive heart failure or structural heart disease characterized by LAE or LVH
- Stable diuretic use
- BMI <45 kg/m²

EMPEROR-Preserved



Primary outcome:
composite of death and HF
Hospitalization

EMPEROR-Preserved

Primary Outcomes

Death from cardiovascular causes or hospitalization for heart failure

13.8% vs.17.1% (HR 0.79; 95% CI 0.69-0.90; P<0.001; NNT=30)

Secondary Outcomes

Hospitalization for heart failure

8.6% vs.11.8% (HR 0.71; 95% CI 0.60-0.83; NNT=31)

Death from cardiovascular causes

7.3% vs.8.2% (HR 0.91; 95% CI 0.76-1.09)

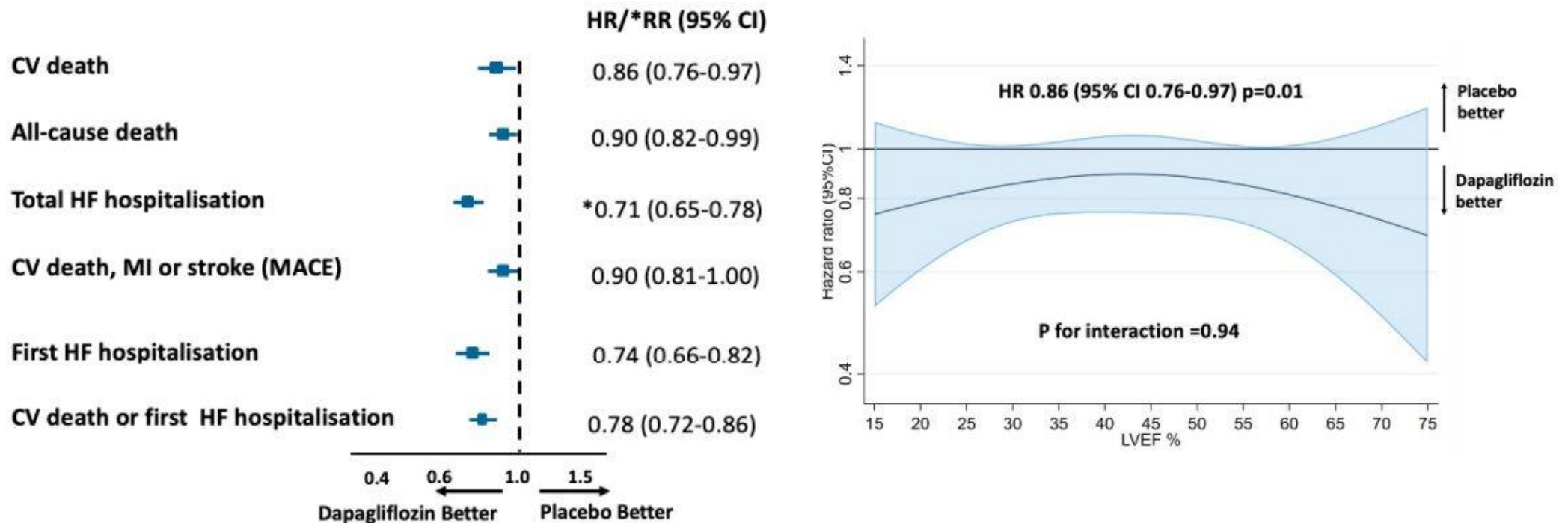
EMPEROR-Preserved: takeaway

SGLT 2 inhibition useful for preventing heart failure hospitalization in patients with heart failure with preserved ejection fraction

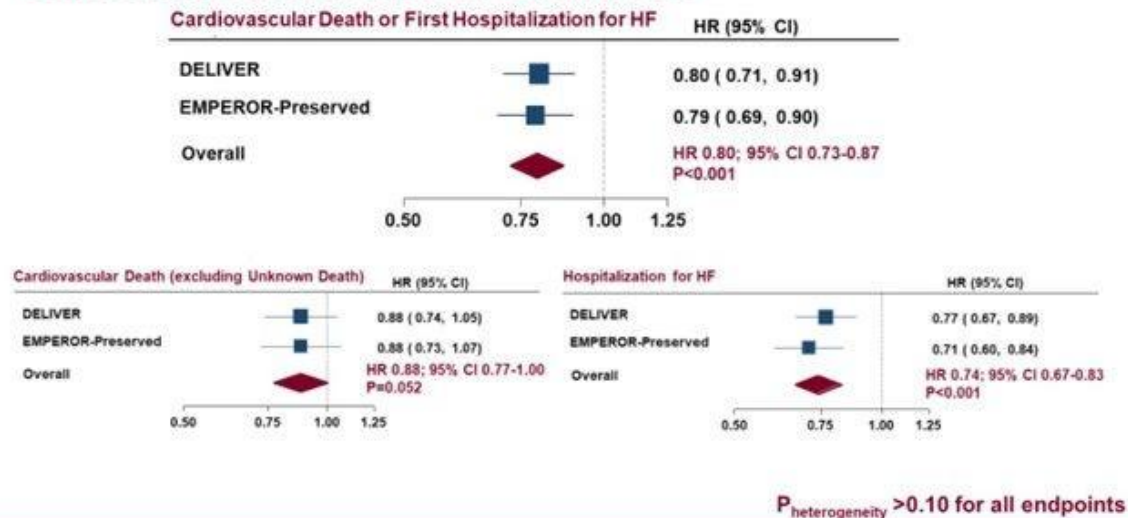
Effect strongest in patients with LVEF < 55%

Pooled Analysis of DAPA-HF and Deliver

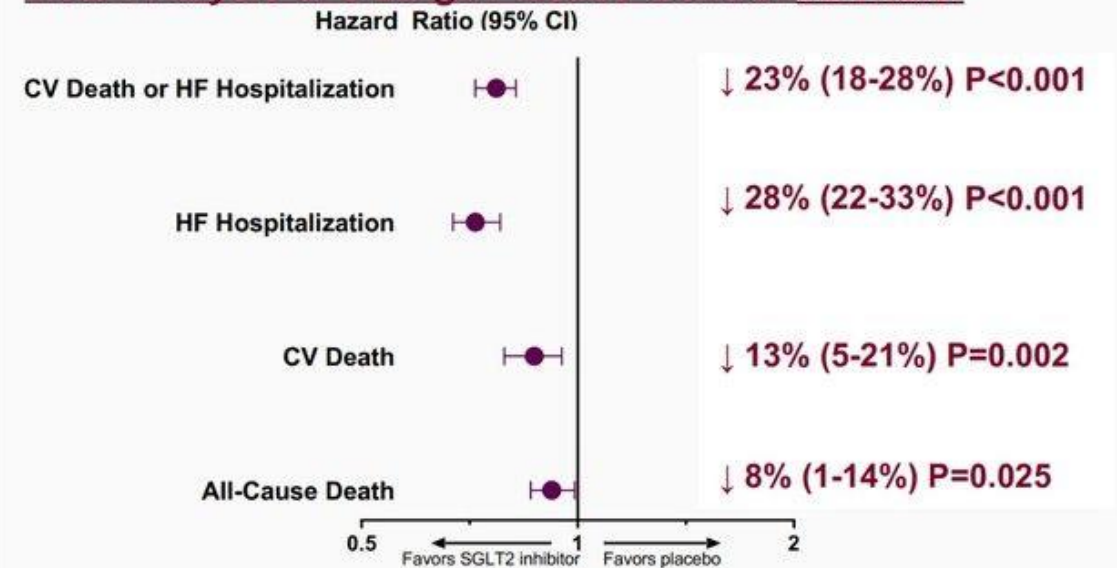
Results - For every outcome the benefit of dapagliflozin was seen in all patients regardless of ejection fraction



DELIVER and EMPEROR-Preserved Meta-Analysis: ↓ 20% (13-27%) Relative Risk Reduction of Primary Endpoint with Consistent Reductions in Both Components



Meta-Analysis of 5 Large Placebo-Controlled Trials:



2022 ACC/AHA/HFSA Clinical Practice Guidelines

Circulation

AHA/ACC/HFSA CLINICAL PRACTICE GUIDELINE

2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines

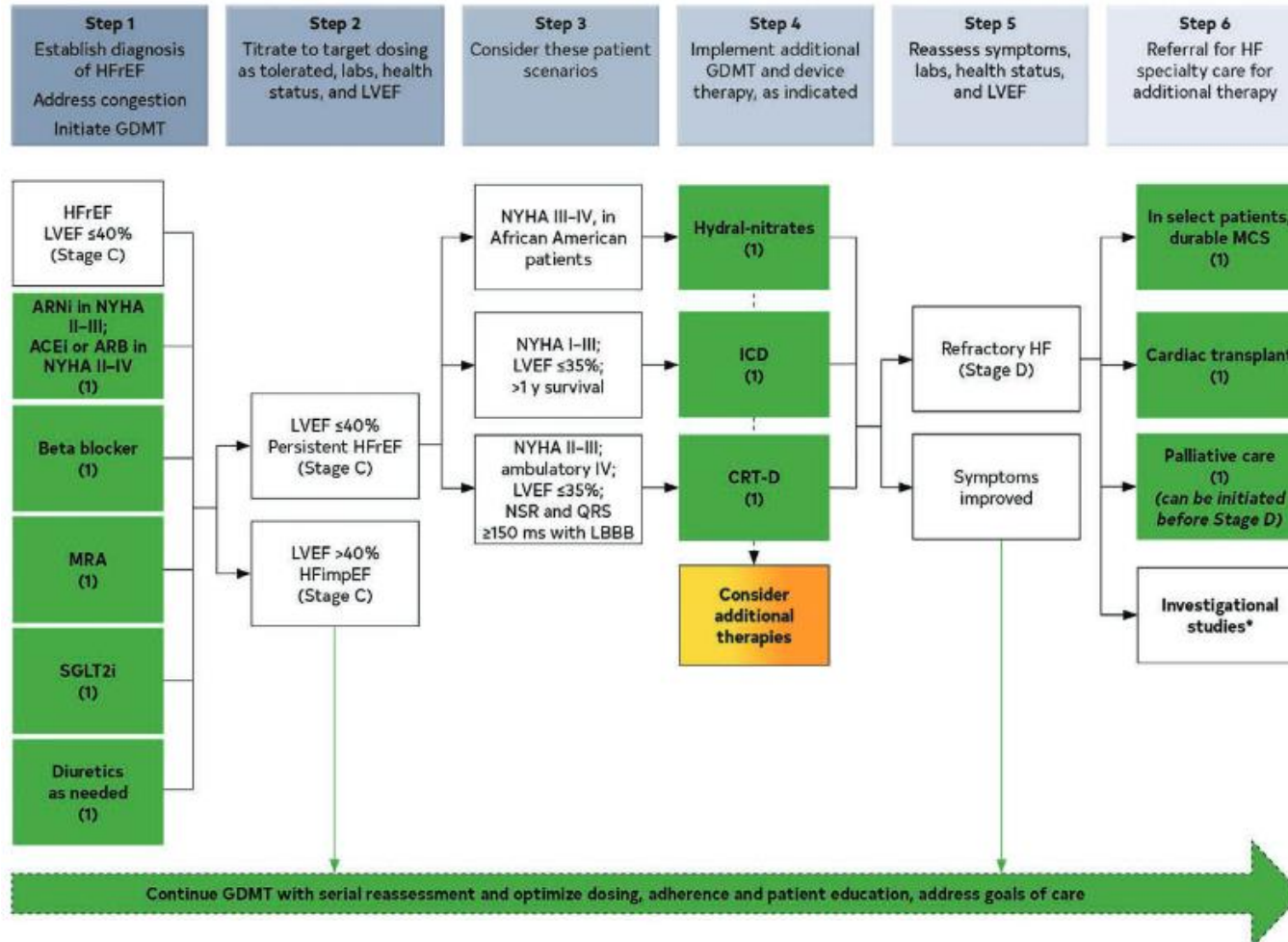
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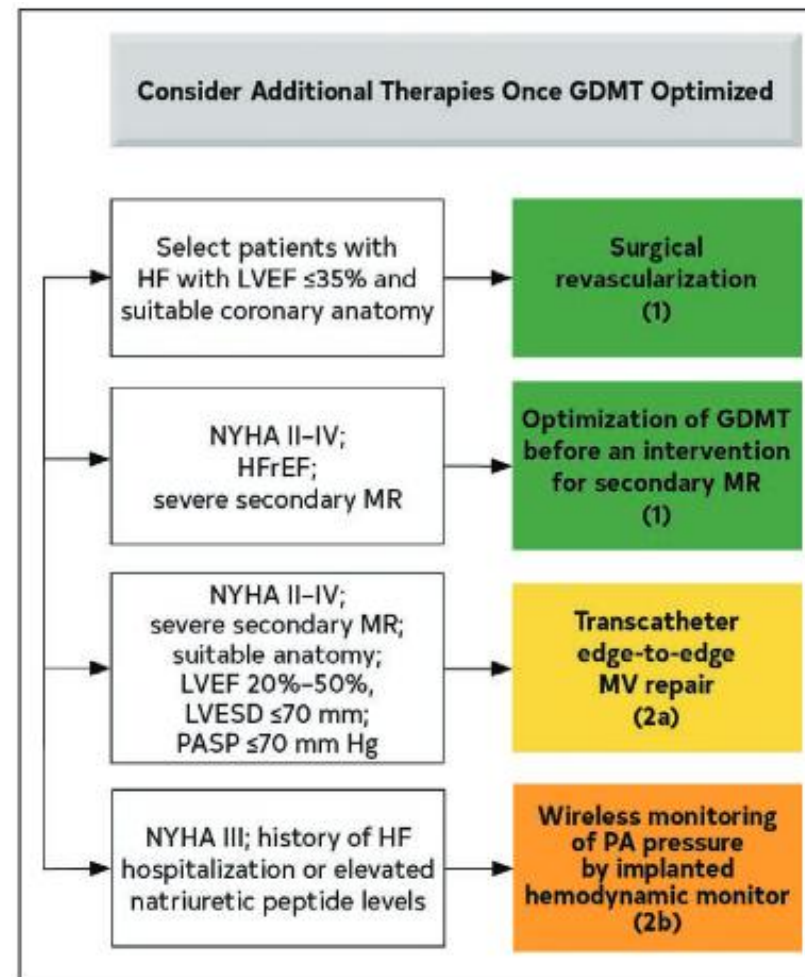
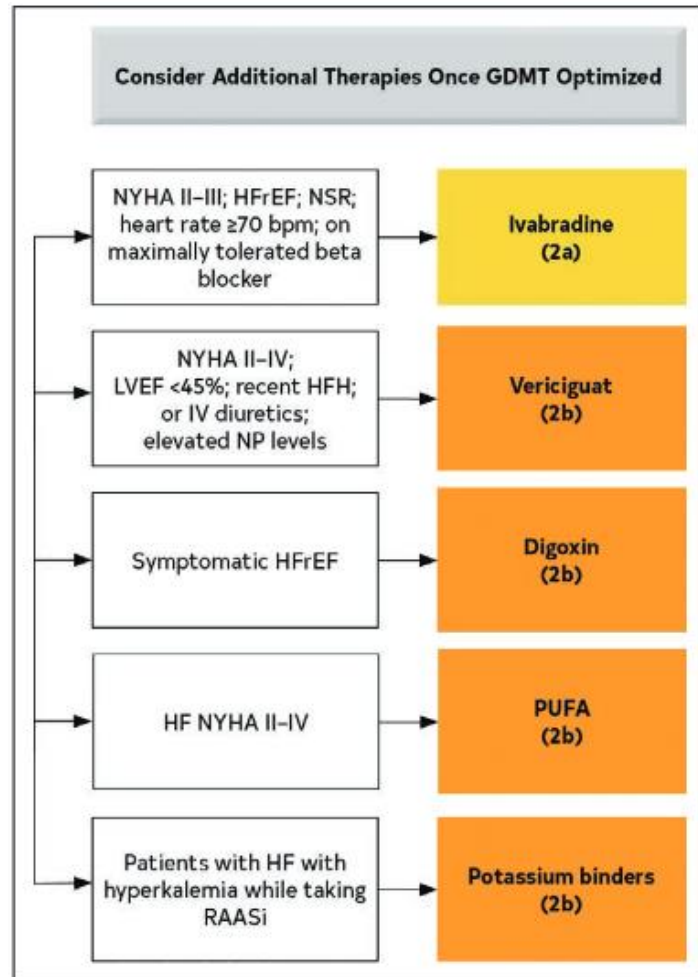
AIM: The "2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure" replaces the "2013 ACCF/AHA Guideline for the Management of Heart Failure" and the "2017 ACC/AHA/HFSA Focused Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure." The 2022 guideline is intended to provide patient-centric recommendations for clinicians to prevent, diagnose, and manage patients with heart failure.

METHODS: A comprehensive literature search was conducted from May 2020 to December 2020, encompassing studies, reviews, and other evidence conducted on human subjects that were published in English from MEDLINE (PubMed), EMBASE, the Cochrane Collaboration, the Agency for Healthcare Research and Quality, and other relevant databases. Additional relevant clinical trials and research studies published through September 2021 were also considered. This

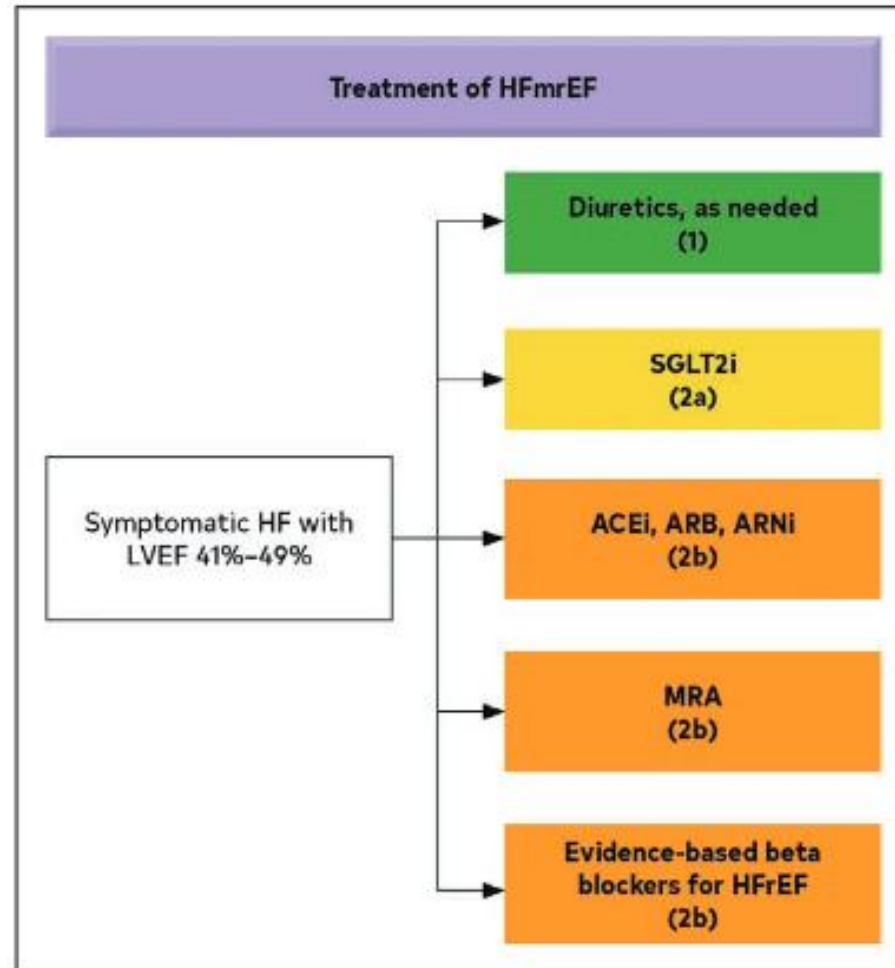
Management of Patients with HFrEF (LVEF $\leq 40\%$)



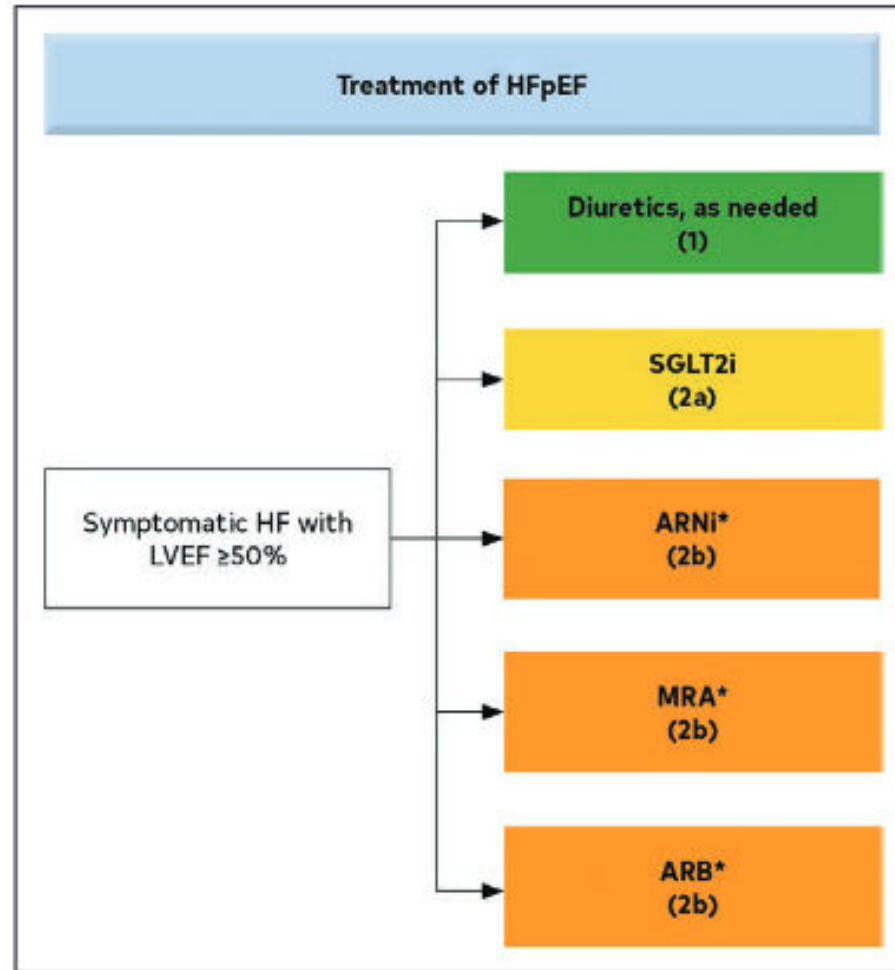
Additional Therapies for HFrEF



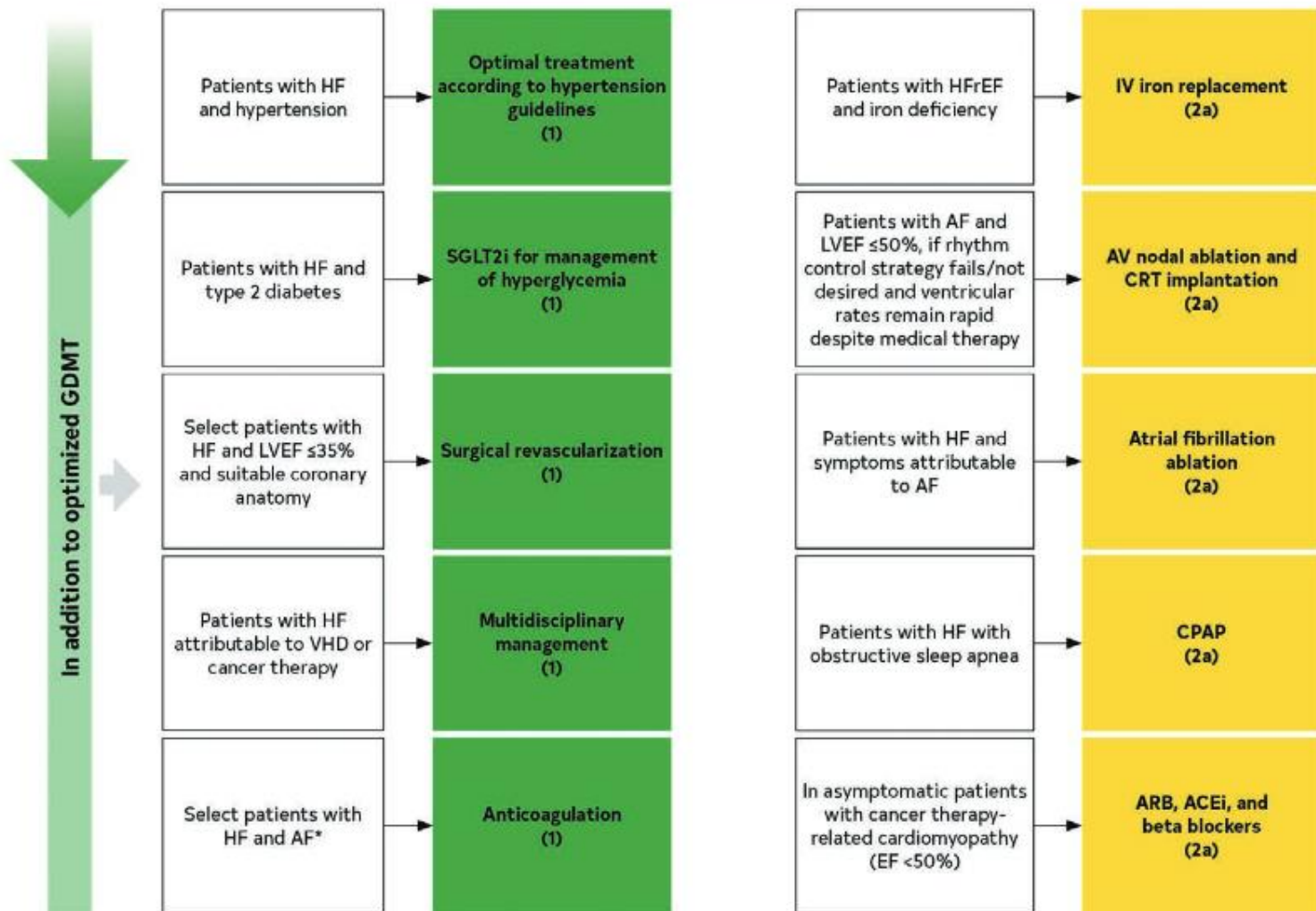
Treatment of HFmEF (LVEF 41-49%)



Management of HFpEF (LVEF $\geq 50\%$)



Additional Therapies in Patients With HF and Comorbidities



Case scenario

- 47 year old male with history of chronic non-ischemic, dilated cardiomyopathy with severely reduced left ventricular systolic function NYHA functional class II, ACC/AHA stage C. Euvolemic on exam with blood pressure of 108/64, heart rate 68 bpm. Current meds include valsartan/sacubitril 97/103 mg, carvedilol 25 mg, spironolactone 25 mg, bumetanide 1 mg bid. Hospitalized twice in last 12 months for decompensated congestive heart failure. Next step in treatment is:
 - A. add ivabradine 5 mg by mouth twice per day
 - B. Refer for cardiomechs
 - C. LVAD
 - D. Add dapagliflozin 10 mg by mouth daily

UCSF Fresno

Peripheral Arterial Disease

Leigh Ann O'Banion, MD



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University | Centers of Excellence

In affiliation with UCSF Fresno



Disclosures

- Relationships with commercial interests:
 - Grants/Research Support: Medtronic, Abbott, Shockwave
 - Speakers Bureau/Honoraria: none
 - Consulting Fees: none

Learning Objectives

- How to diagnose PAD
- Current medical management of PAD and why it is important
- Role of the specialist

Outline

- What is it?
- Why does it matter?
- Diagnostic work-up
- Medical Management
- Role of Vascular Surgery

PAD: What is it?

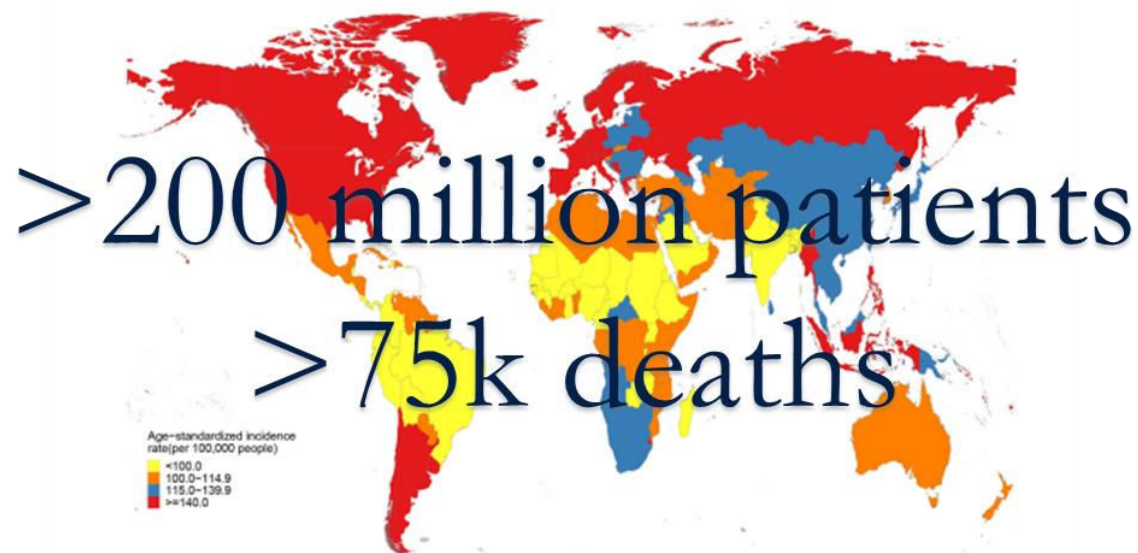
- Peripheral artery disease is a chronic narrowing of arteries in the lower extremities related to atherosclerotic plaque build-up
- It can be asymptomatic in up to 70% of people

PAD: What is It?

- PAD can be broken into three categories:
 - Asymptomatic
 - Intermittent Claudication
 - Most common manifestation
 - Pain in the calf, thigh, or buttock induced by exertion and relieved with rest
 - Very low risk of progression of disease with appropriate risk factor modification and medical management
 - “Disabling” = everyday life, reported by patient and agreed upon by clinician
 - Chronic limb threatening Ischemia (formerly CLI-critical limb ischemia)
 - Defined by rest pain **OR** tissue loss
 - WIfI classification
 - High rate of limb loss without urgent revascularization

PAD Prevalence

- PAD affects >200 million people worldwide
- It is an independent risk factor for MI, stroke, total and cardiovascular mortality, and poorer CV outcomes such as CHF
- The diagnosis, treatment, and management of PAD cost >\$21 billion in 2008 in the US alone



Global PAD burden from 1990-2019

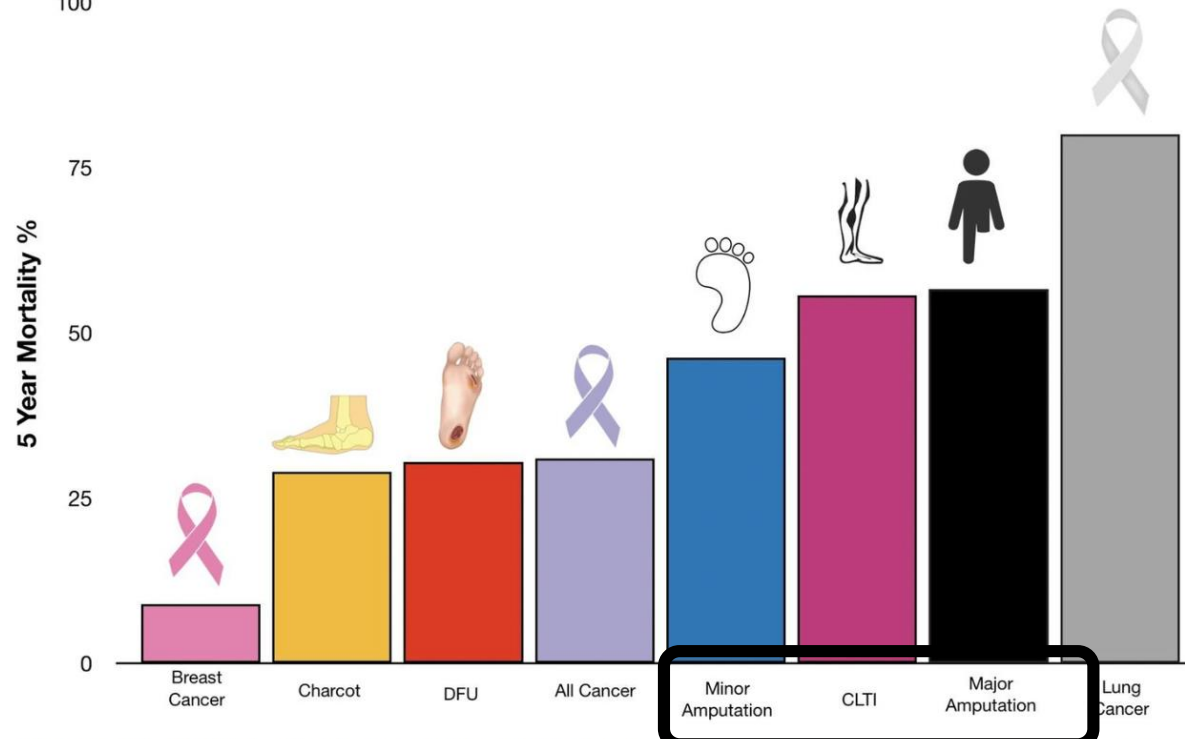
Epidemiology

- Prevalence is 4.3% in the US, as defined by ABI <0.9 in people greater than 40 yoa
 - <50 yoa: 0.9%
 - 60-69yoa: 7%
 - 70-79yoa: 12.5%
 - >79 yoa: 23.2%
- Men $>$ Women
 - Black men & women and Mexican American women have higher risks than non-Hispanic white men and women
- Mortality of claudicants over 5 yrs – 42% and 10 yrs – 65%
 - 66% of deaths were due to MI
- Risk of major amputation in claudicants: 5%/5yrs
- Increased risk of progression of claudication to CLI:
 - IDDM
 - Smoking
 - Initial low ABI
- Association with CAD and Cerebrovascular disease

5-Year Mortality Rates

Fig. 1

From: [Five year mortality and direct costs of care for people with diabetic foot complications are comparable to cancer](#)
100

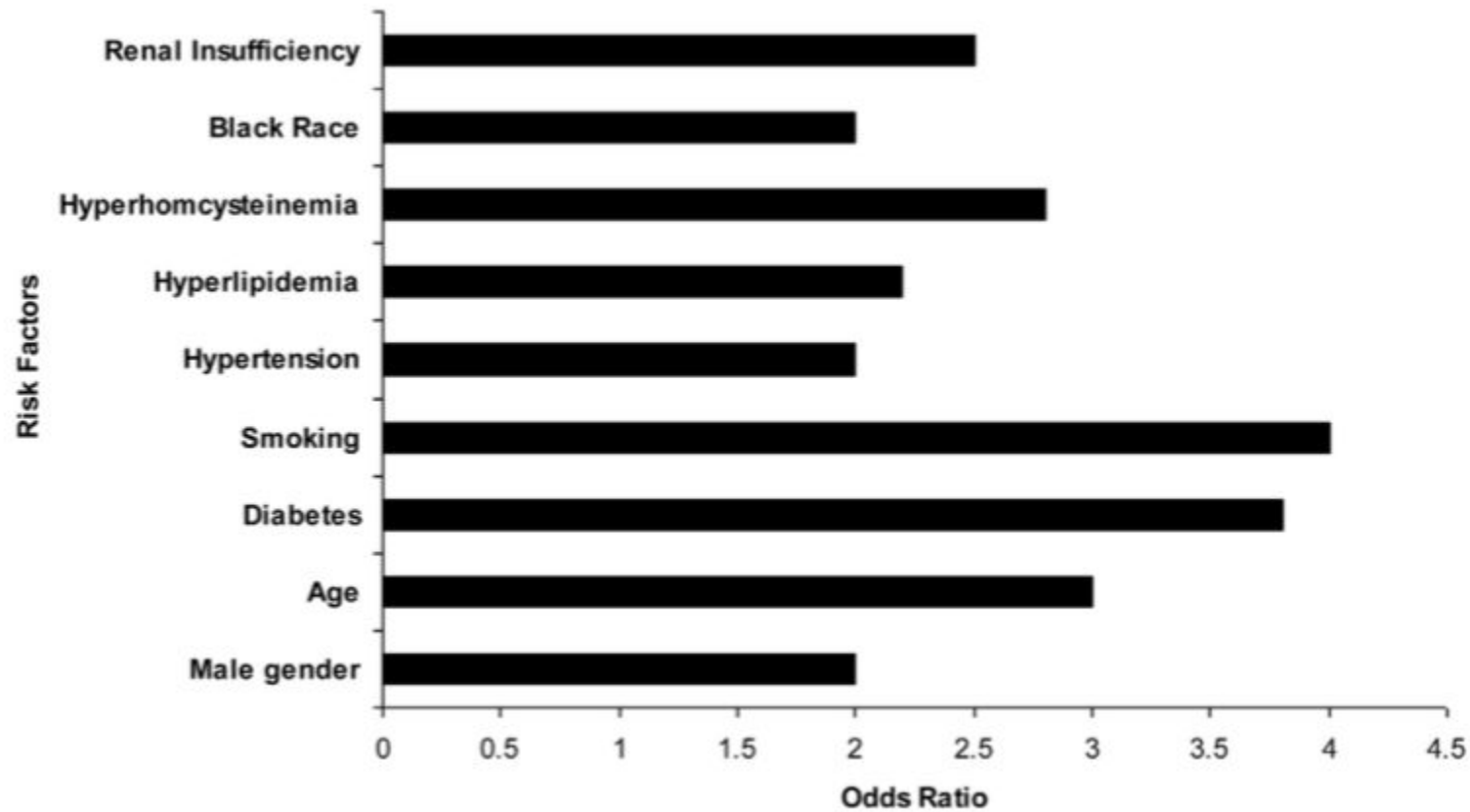


Five Year Mortality of Diabetic Foot Complications and Cancer. Diabetic foot complications compared to cancer. DFU = diabetic foot ulcers [11] = 30.5%. Charcot = Charcot neuroarthropathy of the foot [14]. All Cancer = pooled 5 year survival of all cancers [11]. CLTI = chronic limb threatening ischemia [28, 29]. Major Amputation = above foot amputation [20, 21, 22, 26, 27]. Minor Amputation = foot level amputation [17, 27]

Diagnosis

- Clinical suspicion:
 - Presence of risk factors: age > 65, male sex, history of or current smoking, HTN, DM, ESRD, known cardiovascular disease in other vascular bed
- Physical exam findings:
 - decreased hair growth on lower legs, poor nail quality, decreased skin health, decreased pulse exam, dependent rubor, ulcers (forefoot and toes)

Weight of Risk Factors



- Society for Vascular Surgery practice guidelines for atherosclerotic occlusive disease of the lower extremities: Management of asymptomatic disease and claudication

Clinical Presentation: Claudication

- **Asymptomatic** w/ reduced ABI
- **Claudication:**
 - Calf fatigue or cramping when walking
 - Pain is only with exertion
 - Relieved by rest
 - Pathophysiology of pain:
 - Anaerobic metabolism → Local intramuscular acidosis → stimulation of pain fibers by substance
 - Ischemic neuropathy of small unmyelinated A delta & C sensory nerves
 - Single level of disease
- Hip / Thigh / Buttock claudication due to Iliac disease
 - Symptoms often begin more proximally and progress toward the calf
- Erectile Dysfunction

Clinical presentation:

Chronic limb threatening ischemia

- ABI <0.4
- Ankle Pressure <50 mmHg
- Toe pressure <30 mmHg
- **Rest pain:**
 - Burning, cold temperature, paresthesia, awakening from sleep, worsening with elevation
 - Forefoot, toes
 - Physical exam:
 - Atrophy, dependent rubor, lack of hair growth



Clinical presentation:

Chronic limb threatening ischemia

- **Ischemic ulceration**

- Soft tissue trauma → shallow, nonhealing skin erosion
- Aching / burning / severe pain (exposed nerve & ischemic neuropathy)
- Inadequate skin perfusion
 - poor healing
- Can be associated with osteomyelitis and ascending infection

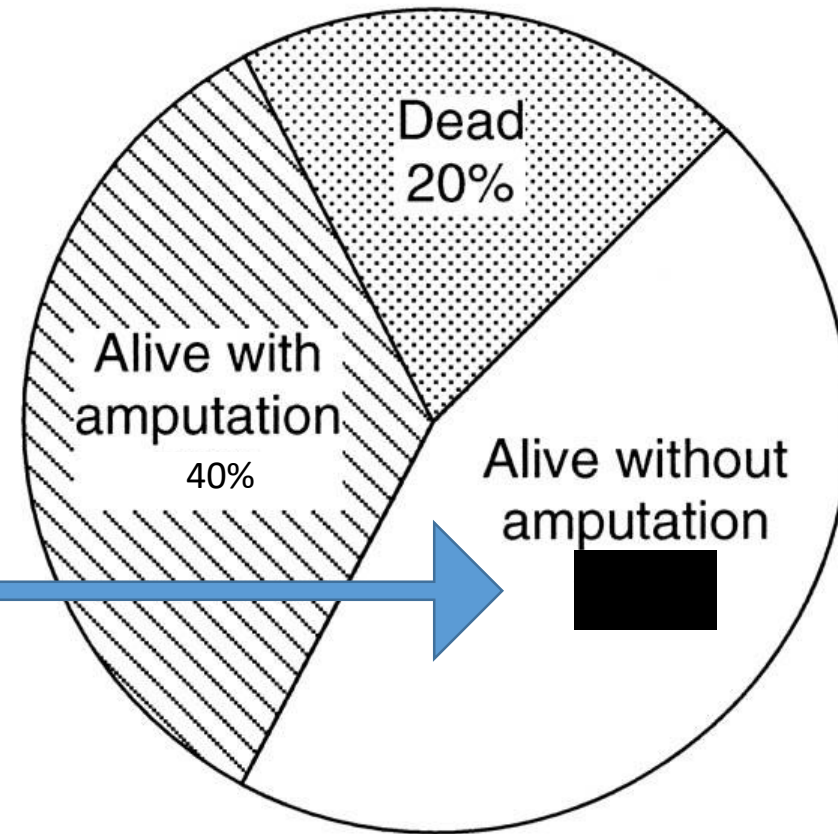


- **Gangrene**



Natural History of Chronic Limb Threatening Ischemia

6 months after diagnosis:



What is the most common cause of death in a patient with CLTI?

CARDIAC DISEASE

Workup

- Identification of **risk factors & associated conditions**:
 - CBC, fasting glucose and lipid panel, creatinine, UA, HbA1c
 - Screening for carotid artery stenosis & AAA

Diagnostic Screening

- Ankle Brachial Index
 - Often with PVR and PPG
 - Toe PPG most helpful in diabetics and patients with ESRD
- TcPO₂
- Other tests such as arterial duplex, CTA or MRA should not be used as screening

Toe-Brachial Index Measurement



Useful for noncompressible vessels (ABI > 1.3)

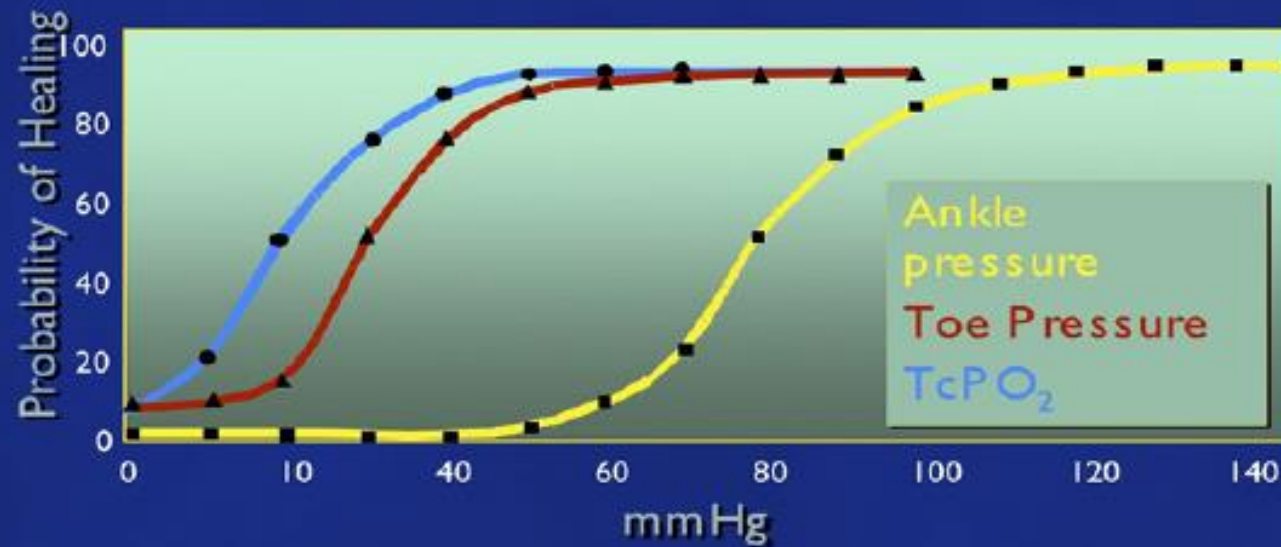
Digital cuff, PPG probe

Normal > 0.75

Severe ischemia < 0.25

Absolute pressure < 30 mm Hg associated with poor healing rates

Hemodynamics and Probability of Healing of a Diabetic Foot Ulcer



Healing unlikely if toe pressure < 55 mmHg

Ankle Brachial Index

Normal: 0.90-1.29

- No discrepancy between ABI and waveform data*
- Mild, moderate, moderate-severe: 0.41-0.89
- Severe or critical: 0.40 or less
- *Additional diagnostic testing such as exercise ABIs may be recommended



**Therapy of all patients with PAD begins
with modification of risk factors for
atherosclerosis**

Guideline Directed Medical Therapy

- SMOKING CESSATION
- Diabetes Control
- Lipid lowering Agent
- Antiplatelet Medication
- Low Dose Rivaroxaban
- Cilostazol (physician discretion)
 - *CHF contraindication
- Supervised vs Unsupervised Exercise Therapy
 - 6 months
 - Three 30 min sessions/week
 - Walking



Guideline Directed Medical Therapy

SMOKING

- Mechanism of accelerated atherosclerosis:
 - Carbon monoxide → arterial wall injury → influx of LDL...
 - Decreased HDL
 - Peripheral vasoconstriction
 - Increased platelet reactivity
- Directly related to amputation risks, ischemic heart disease, graft failure (femoropopliteal & aortic)
- Claudication & smoking:
 - 8% of quitters will progress to CLI
 - 79% of smokers will progress to CLI
- Structured smoking cessation programs have a 22% success rate/5 yrs (vs. 5% without program)
- Bupropion increases this success rate
 - Partial agonist of alpha-4-beta-2 nicotine acetylcholine receptor
 - Stimulates release of dopamine

Guideline Directed Medical Therapy

DIABETES

- Each 1% increase in HbA1c → 28% increased PAD risk
- Abnormal lipid metabolism
- Procoagulant state
 - Increased platelet aggregation
 - Increased blood viscosity
 - Increased fibrinogen
- Glycosylation of arterial wall components → accelerated atherosclerosis
- LDL entry into macrophages increased due to glycosylation → foam cells → atherosclerosis
- Insulin and glucose stimulate smooth muscle cell growth
- Altered vasoactivity
- **GOALS OF THERAPY:**
 - **HbA1c < 7%**
 - **Fasting glucose < 110**
 - **BP < 130/80**
 - **LDL < 100**
 - **TG < 150**

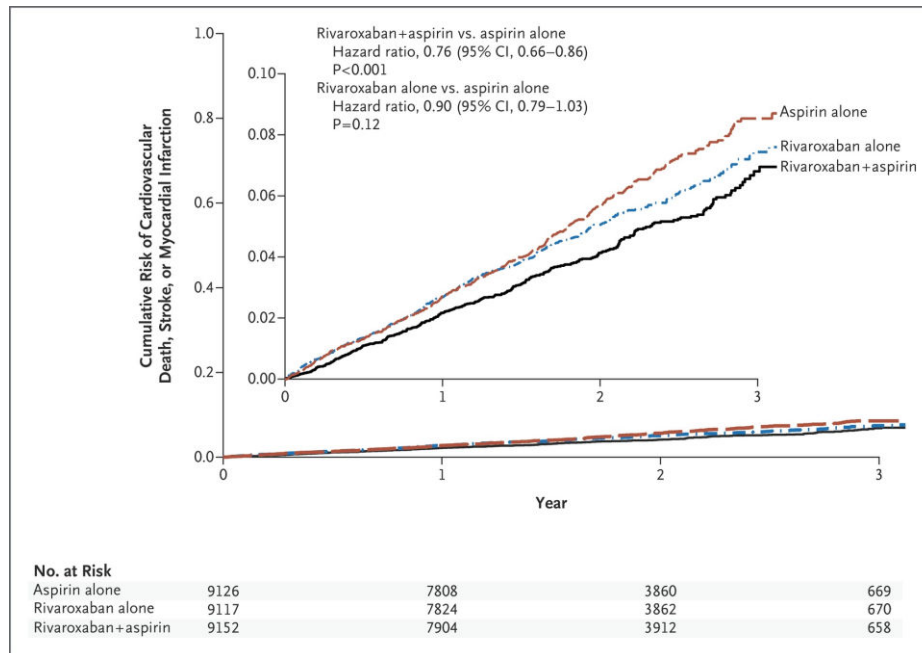
Guideline Directed Medical Therapy

HYPERLIPIDEMIA

- Statins:
 - 3-hydroxyflutaryl Coenzyme A reduction: inhibition of hepatic cholesterol synthesis
 - Antiinflammatory
 - Better clinical result in conjunction w/ smoking cessation
 - Reduction in stroke, MI and cardiac related death
 - Improved walking distance in claudicants
- Other agents:
 - Gemfibrozil
 - Cholestyramine / colestipol: bile acid sequestrants
 - Niacin (niacin + statin in nondiabetics → reduced incidence of CAD)
 - Ezetimibe (selectively inhibits intestinal absorption of cholesterol / phytosterol) (works well in conjunction w/ statins)
- **GOAL OF THERAPY:**
 - **LDL <70 in pt with high risk / generalized atherosclerosis**
 - **LDL <100 in pt with PAD**
 - **Total cholesterol <130 if LDL cannot be calculated (due to high TG)**
 - **Dietary modification for all patients**

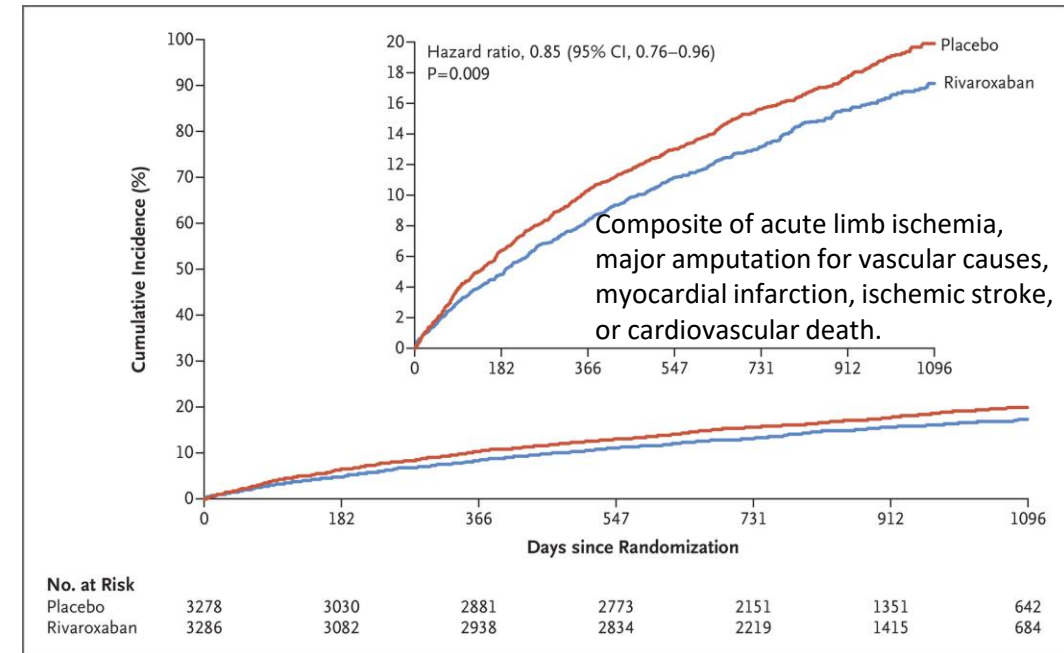
Guideline Directed Medical Therapy

COMPASS TRIAL



Stable Cardiovascular Disease

VOYAGER TRIAL



After Revascularization

- Low-dose Rivaroxaban (2.5mg BID) and ASA 81mg reduce major cardiovascular events and adverse limb events
- 2016 AHA/ACC Guideline on the Management of Patients With Lower Extremity Peripheral Artery Disease

Guideline Directed Medical Therapy

CILOSTAZOL (Pletal)

- Phosphodiesterase III inhibitor
 - Increase cAMP
 - Inhibits smooth muscle cell contraction and platelet aggregation
 - Beneficial effect on plasma lipid concentrations (decreased TG and increased HDL)
 - VEGF modulation may lead to angiogenesis
- 50% increase in walking distance
- Side effects: headache, diarrhea, GI discomfort
 - 15% of patients cannot use medication due to adverse events
- Contraindicated in CHF because it can exacerbate ventricular dysfunction

Effects of Supervised Exercise Therapy on Blood Pressure and Heart Rate During Exercise and Associated with Improved Walking Performance



Post hoc analysis of a randomized clinical trial



210 patients with peripheral artery disease randomized to:



Supervised Exercise Therapy (SET) vs. No Exercise Control

6 months of SET resulted in:



- Decreased systolic blood pressure (-12mmhg, $p < .001$)
- Decreased pulse pressure (-9mmhg, $p < .001$)
- Decreased heart rate (-7 beats/min, $p < .01$) during a graded treadmill exercise test.

Specialty Care

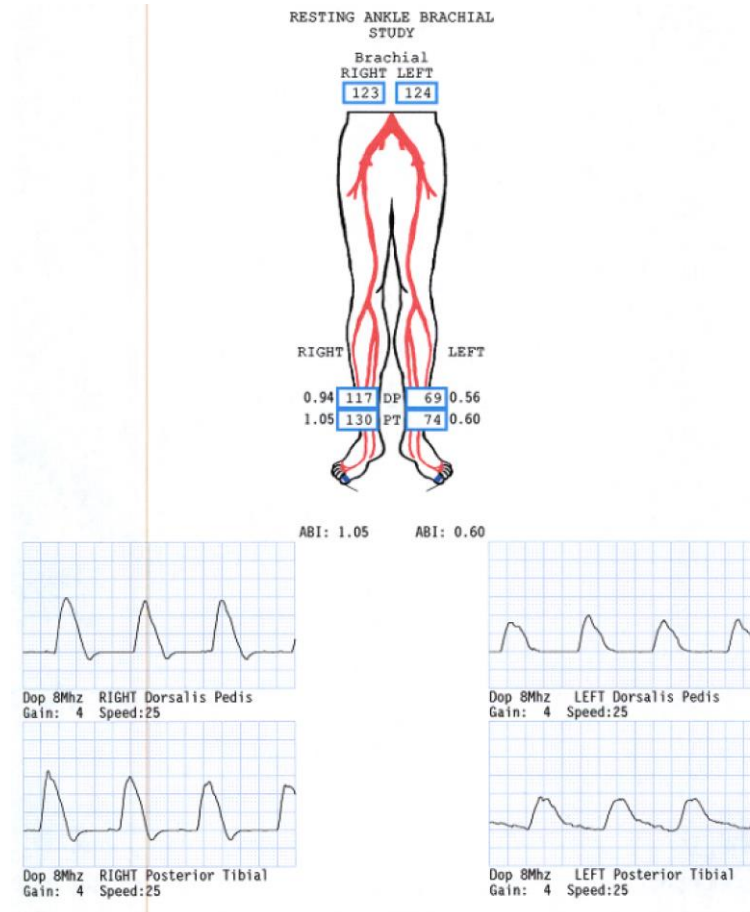
- Counselling of patients
 - Risk of progression and risks and benefits of intervention
 - Importance of medical compliance
 - Smoking cessation
- Further work-up to localize level of disease
- Open or endovascular interventions
- Long term follow-up and multidisciplinary collaboration

When in doubt...Give us a call!

Case Example

- 58 M former smoker presents with 4 years of short distance claudication
- HPI:
 - Current daily smoker, has previously quit for 6 months
 - Works as a mail person and is having issues completing his route on time due to having to rest so much
 - Meds: ACEi

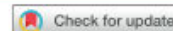
ABIs



Next Steps

- Maximal medical therapy
 - ASA + 2.5mg Xarelto
 - high intensity statin
 - Walking program
 - Smoking Cessation
- Diagnostic imaging
 - Duplex US
 - CT angiogram
 - Diagnostic angiogram
- Surgical decision making
 - Endovascular versus open

SOCIETY FOR VASCULAR SURGERY DOCUMENTS



Society for Vascular Surgery appropriate use criteria for management of intermittent claudication

Karen Woo, MD, PhD,^a Jeffrey J. Siracuse, MD, MBA,^c Kyle Klingbeil, MD, MS,^b Larry W. Kraiss, MD,^d Nicholas H. Osborne, MD,^e Niten Singh, MD,^f Tze-Woei Tan, MD,^g Shipra Arya, MD, SM,^h Subhash Banerjee, MD,ⁱ Marc P. Bonaca, MD, MPH,^j Thomas Brothers, MD,^k Michael S. Conte, MD,^l David L. Dawson, MD,^m Young Erben, MD,ⁿ Benjamin M. Lerner, MD,^o Judith C. Lin, MD, MBA,^p Joseph L. Mills Sr, MD,^q Derek Mittleider, MD,^r Deepak G. Nair, MD, MS, MHA,^s Leigh Ann O'Banion, MD,^t Robert B. Patterson, MD,^u Matthew J. Scheidt, MD,^v and Jessica P. Simons, MD, MPH,^w for the Society for Vascular Surgery Appropriateness Committee, Los Angeles, Stanford, San Francisco, and Fresno, CA; Boston and Worcester, MA; Salt Lake City, UT; Ann Arbor and East Lansing, MI; Seattle, WA; Tucson, AZ; Dallas, Temple, and Houston, TX; Aurora, CO; Charleston, SC; Jacksonville, Melbourne, and Sarasota, FL; Louisville, KY; Providence, RI; and Milwaukee, WI

ABSTRACT

The Society for Vascular Surgery appropriate use criteria (AUC) for the management of intermittent claudication were created using the RAND appropriateness method, a validated and standardized method that combines the best available evidence from medical literature with expert opinion, using a modified Delphi process. These criteria serve as a framework on which individualized patient and clinician shared decision-making can grow. These criteria are not absolute. AUC should not be interpreted as a requirement to administer treatments rated as appropriate (benefit outweighs risk). Nor should AUC be interpreted as a prohibition of treatments rated as inappropriate (risk outweighs benefit). Clinical situations will occur in which moderating factors, not included in these AUC, will shift the appropriateness level of a treatment for an individual patient. Proper implementation of AUC requires a description of those moderating patient factors. For scenarios with an indeterminate rating, clinician judgement combined with the best available evidence should determine the treatment strategy. These scenarios require mechanisms to track the treatment decisions and outcomes. AUC should be revisited periodically to ensure that they remain relevant. The panelists rated 2280 unique scenarios for the treatment of intermittent claudication (IC) in the aortoiliac, common femoral, and femoropopliteal segments in the round 2 rating. Of these, only nine (0.4%) showed a disagreement using the interpercentile range adjusted for symmetry formula, indicating an exceptionally high degree of consensus among the panelists. Post hoc, the term "inappropriate" was replaced with the phrase "risk outweighs benefit." The term "appropriate" was also replaced with



THANK YOU

Carotid and Aortic Screening

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Stroke

- Symptoms of stroke due to carotid disease:
 - Sudden contralateral sensorimotor loss
 - Speech deficit
 - Ipsilateral monocular blindness
- Transient Ischemic Attack (TIA): ischemic parenchyma recovers and returns to baseline
- Full impact of a stroke can often not be apparent for up to two weeks

Epidemiology of Stroke

- In 2013, total cost in the US of stroke was \$33.9 billion
- Prevalence in 2013 was 25.7 million
- Stroke causes 5.5 million deaths and > 44 million disabilities every year
- ~800,000 Americans have a stroke every year
- One stroke occurs every 40 seconds

Risk Factors for Stroke

- Sex
- Age
- Race
- HTN
- Family History
- Atrial Fibrillation
- Tobacco use
- Hyperlipidemia
- Physical activity
- Diabetes
- Diet
- Obesity
- Alcohol
- Renal failure

Duplex Ultrasound

| Degree of Stenosis (%) | PRIMARY PARAMETERS | | ADDITIONAL PARAMETERS | |
|----------------------------------|---------------------------|----------------------------------|-----------------------|----------------|
| | ICA PSV (cm/s) | Plaque Estimate (%) ^a | ICA/CCA PSV (ratio) | ICA EDV (cm/s) |
| Normal | <125 | None | <2.0 | <40 |
| <50 | <125 | <50 | <2.0 | <40 |
| 50-69 | 125-230 | ≥50 | 2.0-4.0 | 40-100 |
| >70 but less than near occlusion | >230 | ≥50 | >4.0 | >100 |
| Near occlusion | High, low or undetectable | Visible | Variable | Variable |
| Total occlusion | Undetectable | Visible, no detectable lumen | Not applicable | Not applicable |

Screening Guidelines

- The USPSTF does not recommend screening adults without a history of transient ischemic attack, stroke, or other neurologic signs or symptoms referable to the carotid arteries.
- The 2014 guidelines for the primary prevention of stroke from the American Heart Association/American Stroke Association indicate that screening low-risk populations for asymptomatic carotid artery stenosis is not recommended

Screening Guidelines

- SVS/ACC/AHA: It is reasonable to screen asymptomatic individuals who have a carotid bruit, and that duplex ultrasonography screening of the carotid arteries "may be considered" for patients who have symptomatic atherosclerotic disease in another vascular bed (ie, peripheral arterial disease, coronary disease, or aortic aneurysm), or have two or more risk factors for atherosclerotic disease.

Abdominal Aortic Aneurysms

- Dilation to 1.5 x normal diameter (>3 cm)
- Risk Factors:
 - **Smoking**
 - Age > 65
 - Male gender
 - Family history
 - Other aneurysms
- Symptoms: 95% of AAA are asymptomatic

Risk of Rupture

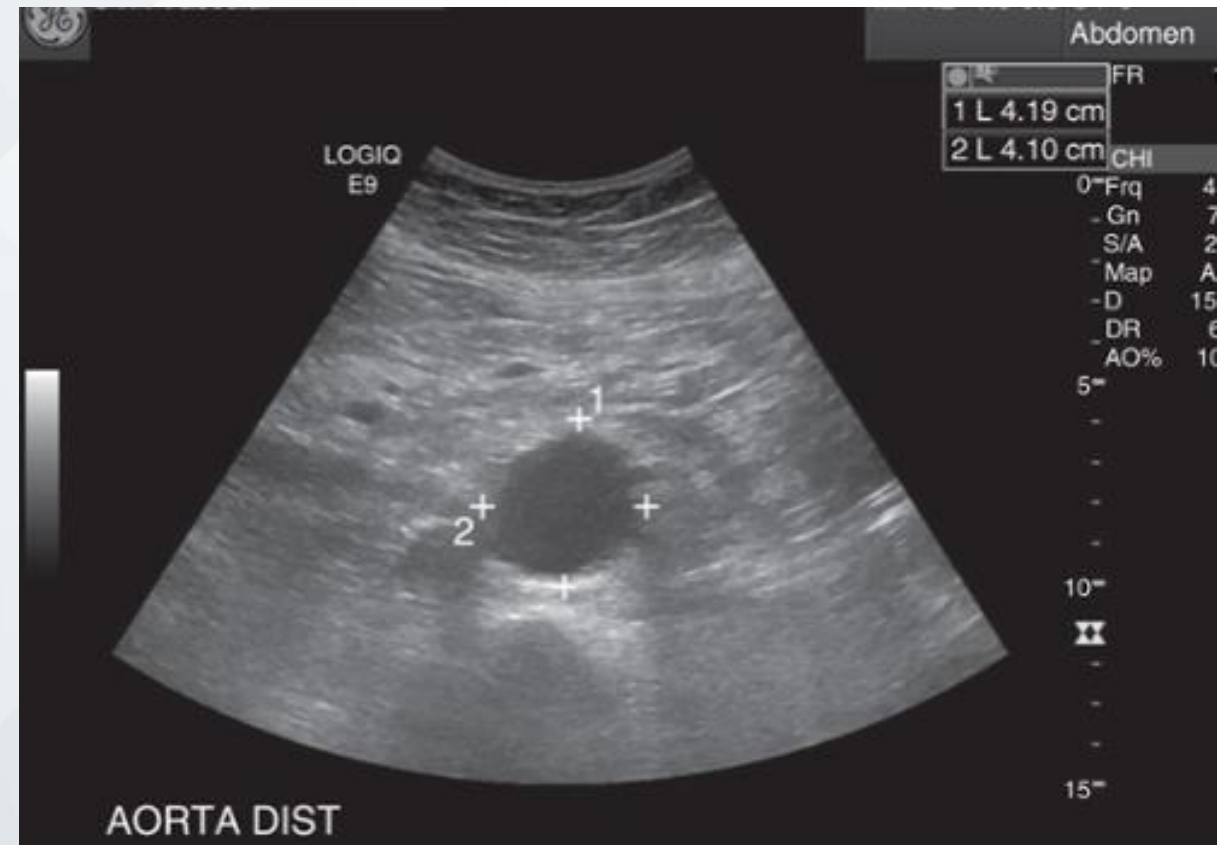
- Dilation to 1.5 x normal diameter (>3 cm)

| AAA Diameter (cm) | Rupture Risk (%) |
|-------------------|------------------|
| 3.0–3.9 | 0.3 |
| 4.0–4.9 | 0.5–1.5 |
| 5.0–5.9 | 1–11 |
| 6.0–6.9 | 11–22 |
| >7 | >30 |

AAA, Abdominal aortic aneurysms.

Ultrasound

- Cheap
- Fast
- Reliable
- Ideal for screening
- Not great in obese patients
- Cannot reliably detect rupture



Screening Recommendations

USPSTF

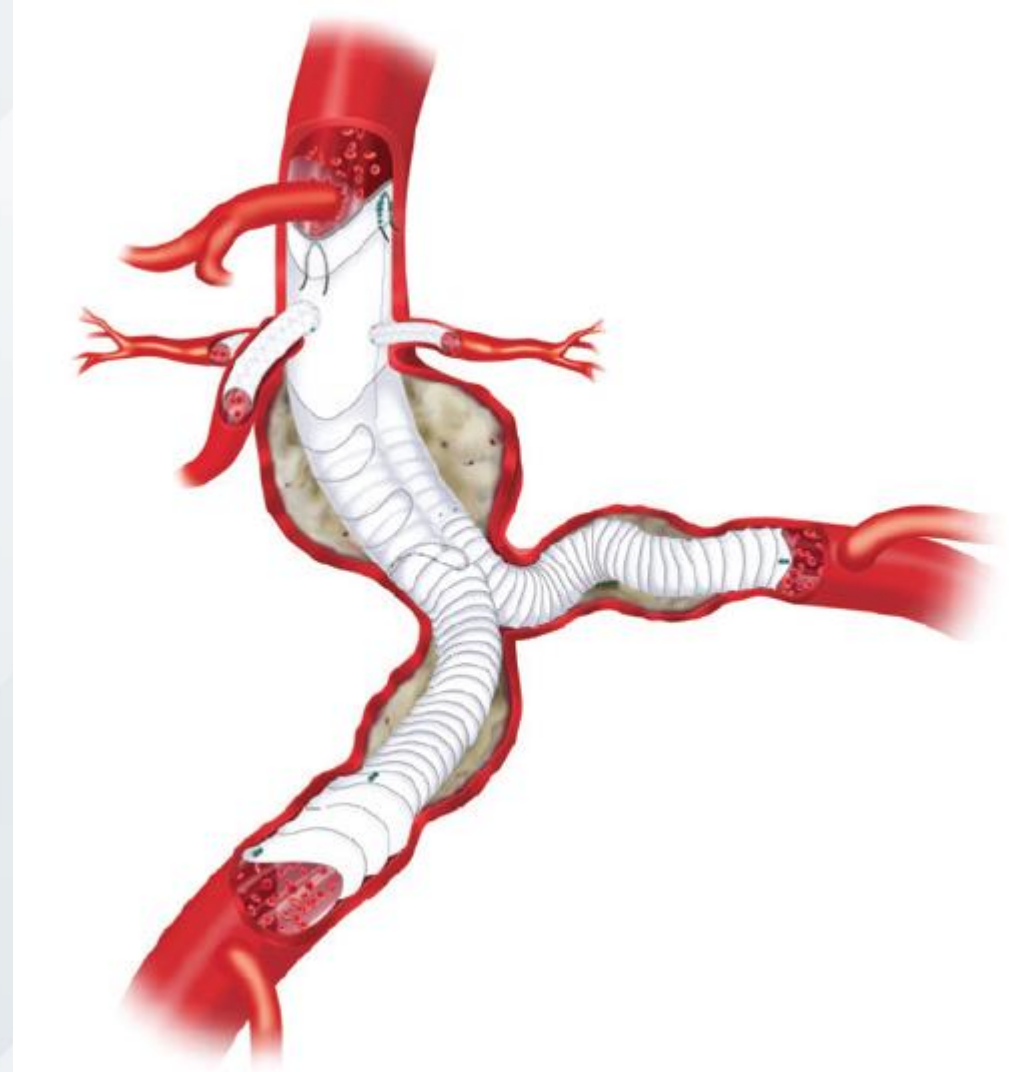
| Population | Recommendation | Grade |
|--|--|----------|
| Men aged 65 to 75 years who have ever smoked | The USPSTF recommends 1-time screening for abdominal aortic aneurysm (AAA) with ultrasonography in men aged 65 to 75 years who have ever smoked. | B |
| Men aged 65 to 75 years who have never smoked | The USPSTF recommends that clinicians selectively offer screening for AAA with ultrasonography in men aged 65 to 75 years who have never smoked rather than routinely screening all men in this group. Evidence indicates that the net benefit of screening all men in this group is small. In determining whether this service is appropriate in individual cases, patients and clinicians should consider the balance of benefits and harms on the basis of evidence relevant to the patient's medical history, family history, other risk factors, and personal values. | C |
| Women who have never smoked | The USPSTF recommends against routine screening for AAA with ultrasonography in women who have never smoked and have no family history of AAA. | D |
| Women aged 65 to 75 years who have ever smoked | The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening for AAA with ultrasonography in women aged 65 to 75 years who have ever smoked or have a family history of AAA. | I |

Screening Recommendations

- **SVS: one time screening in men > 65 or those with first degree relative with AAA**
- **National Screening Committee (UK): All men > 65**
- **ACC/AHA: all men >65; women 60-85 with family hx**

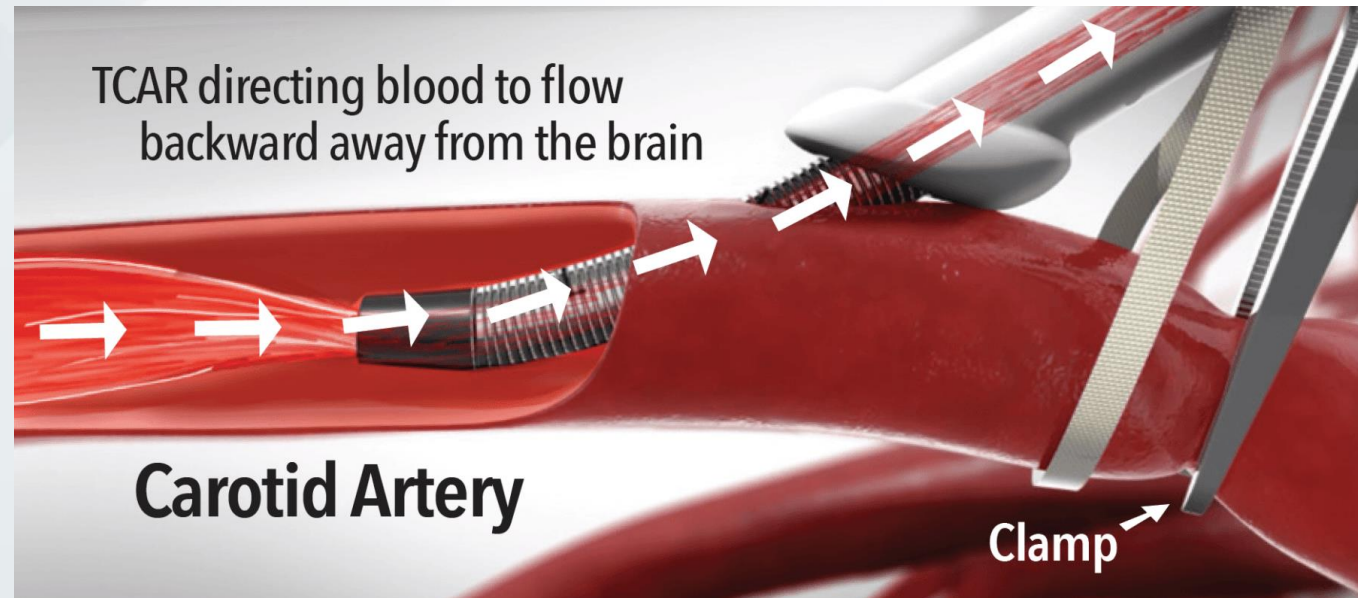
Valley Vascular Surgery Associates

- Aortic disease:
 - Thoracic aortic aneurysms
 - AAA
 - Thoracoabdominal aneurysms
 - Aortic dissection
- Peripheral Arterial Disease:
 - Intermittent claudication
 - Ischemic rest pain
 - Diabetic foot ulcer
 - Wounds



Valley Vascular Surgery Associates

- Carotid disease:
 - Medical management
 - Carotid endarterectomy
 - Carotid stenting (TCAR/TF-CAS)
- Venous disease:
 - Venous insufficiency
 - Varicose veins
 - Leg edema
 - Pelvic congestion syndrome
- Trauma





THANK YOU

Q & A

Thank you!

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Comprehensive Cardiovascular Care

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