Updates in Cardiology

Washington Chapter ACP

November 9, 2024

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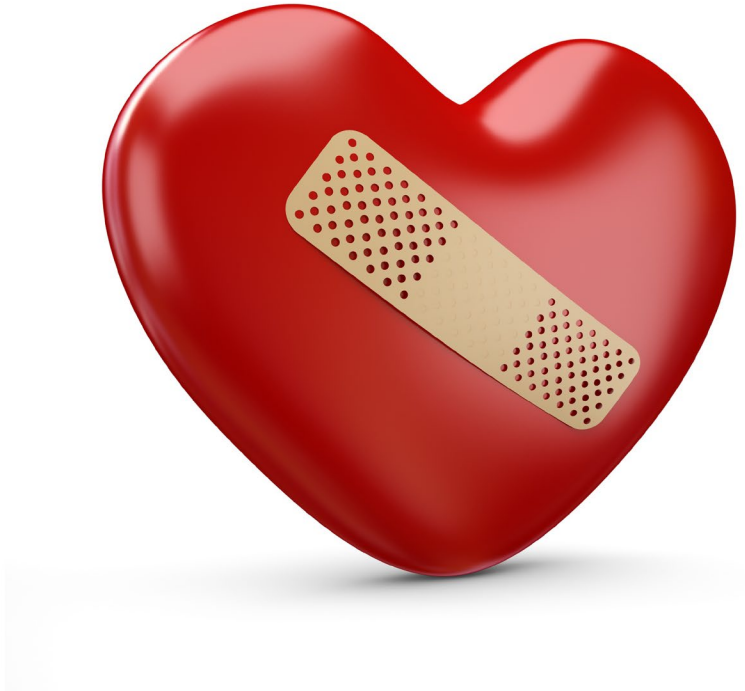
Objectives

- Review ISCHEMIA, STICHES and REVIVED-BCIS2 Trial and update in ischemic heart disease management and indications for revascularization
- Review the role of SGLT2i and GLP1 agonists with reducing CV outcomes and Heart Failure Management
- Discuss contemporary literature on Atrial Fibrillation management
- Brief updates on new percutaneous valve intervention

Ischemic Heart Disease



A 65 yo male with a PMH of HTN, HLD, DM2 presents for follow up after recent ED visit for chest pain. He underwent a treadmill stress myocardial perfusion study. He was able to achieve 11 METs but there was a large perfusion defect in the inferior wall, consistent with ischemia. He continues to endorse chest pressure with more strenuous exertion. His blood pressure is 120/80mmHg and LDL is 130. He is currently on Atorvastatin 20mg daily. What is the next best step in management?

A. Start Isosorbide mononitrate 30mg daily and uptitrate for symptoms managment
B. Refer for invasive coronary angiography and revascularization now
C. Increase Atorvastatin to 80mg daily
D. A and C
E. B and C

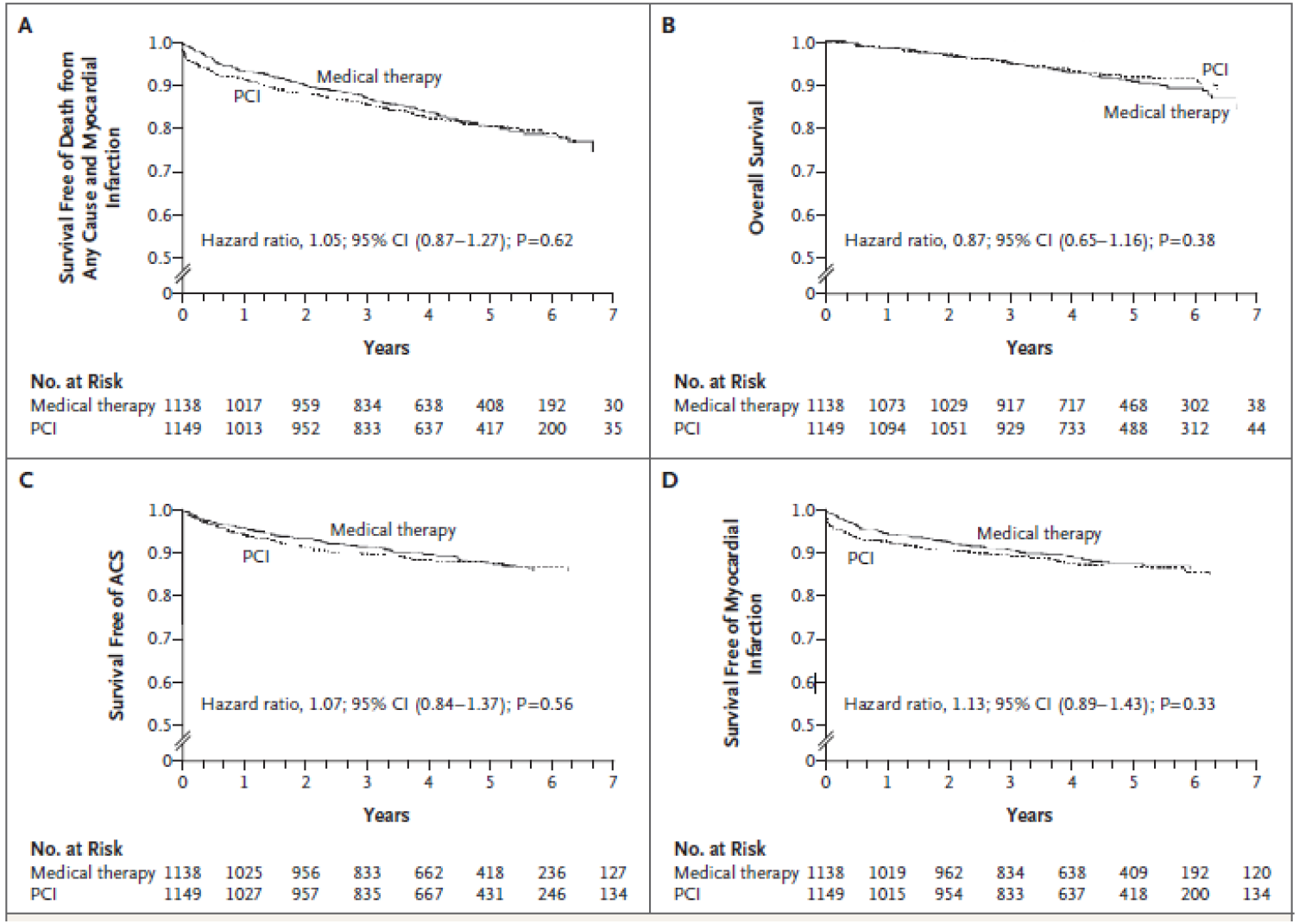
Background

- There have been NO clinical trial to show a mortality benefit with PCI vs optimal medical therapy in stable ischemic heart disease
  - Excluding Left main disease and HFrEF
- Some studies have shown a reduce in MI or need for urgent revascularization
- In HFrEF patients, CABG has been shown to have a 10 year mortality benefit

COURAGE 2007

- No difference in primary composite outcome
- No difference in all cause mortality
- No difference in rate of MI or ACS

A more contemporary trial with newer generation stents was needed….



N Engl J of Med, 356(15), 1503-1516.

ISCHEMIA Trial 2020

Inclusion Criteria:

- Age ≥21 years
- Stress Testing showing **moderate or severe** reversible ischemia

Exclusion Criteria:

- GFR <30
- Recent ACS
- **Unprotected Left Main stenosis ≥50% (most ruled out with CT coronary angio)**
- LVEF ≤35%
- NHYA class III/IV Heart Failure
- Unacceptable angina despite maximal medical therapy

N Engl J Med 2020; 382: 1395-40.7

ISCHEMIA Trial 2020

Initial Invasive Strategy: Medical Therapy, Angiography and Revascularization

Vs.

Initial Conservative Strategy: Medical Therapy Alone with Angiography if failure medical therapy

- **Primary Outcome:** composite of death from CV cause, myocardial infarction, or hospitalization for unstable angina, heart failure or resuscitated cardiac arrest

N Engl J Med 2020; 382: 1395-40.7

ISCHEMIA Trial 2020

Initial Invasive Strategy:
Medical Therapy, Angiography and Revascularization

- 96% underwent angiogram
- 79% revascularization
  - 74% PCI
  - 26% CABG

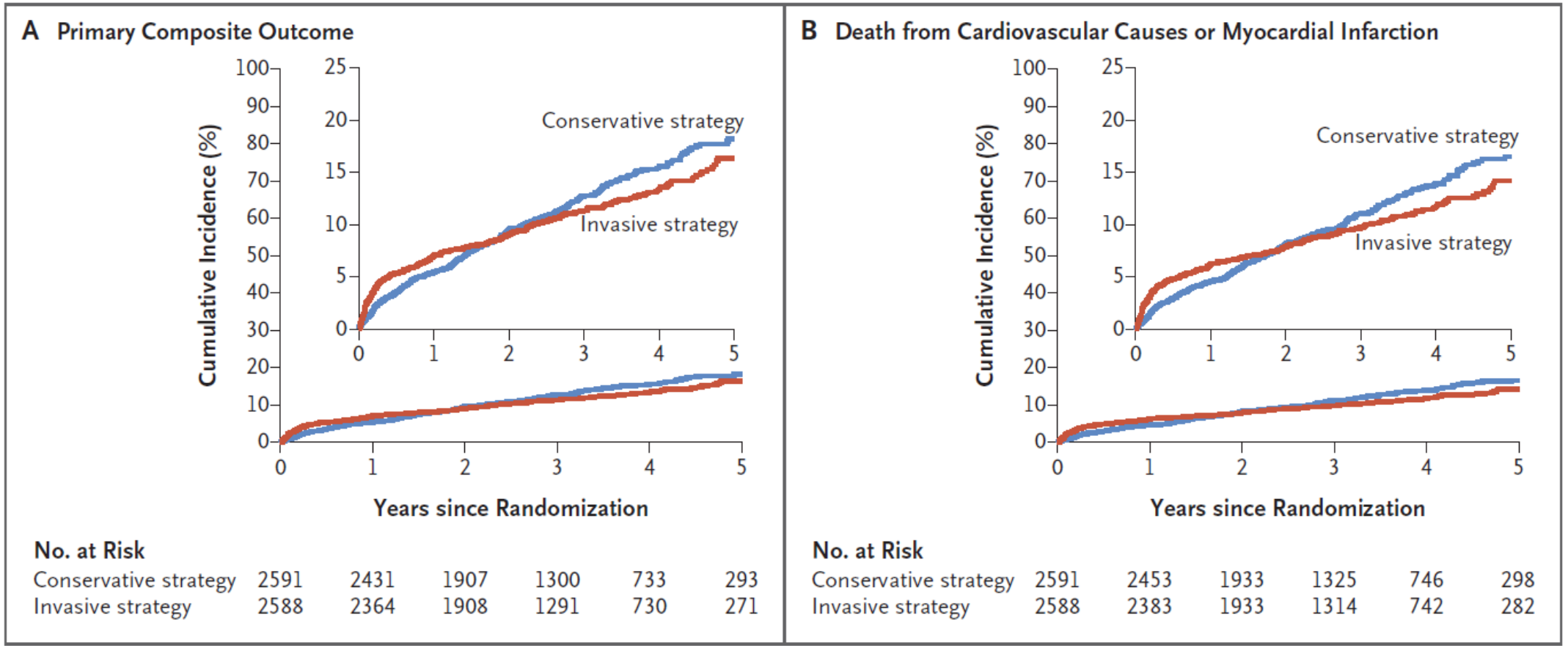
Vs.

Initial Conservative Strategy:
Medical Therapy Alone with Angiography if failure medical therapy

- 26% underwent angiogram
- 21% revascularization

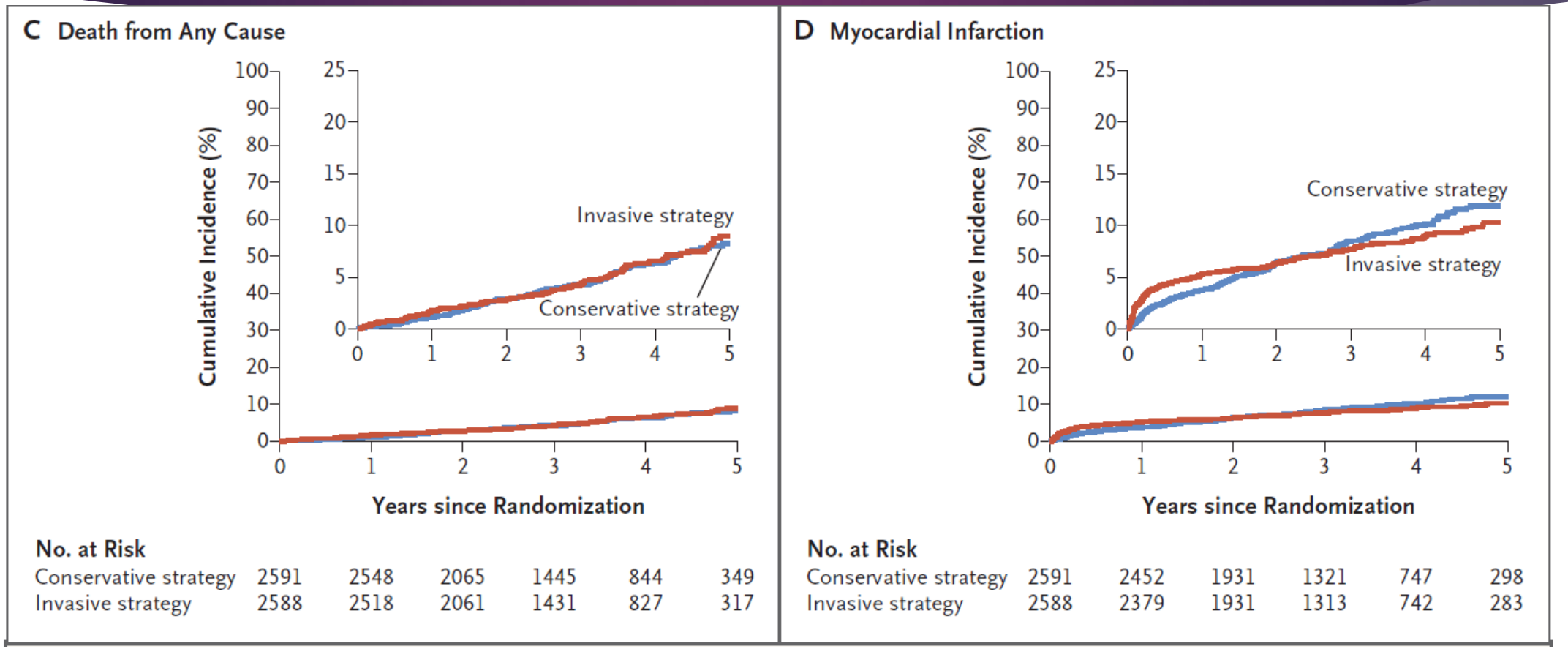
N Engl J Med 2020; 382: 1395-40.7

ISCHEMIA Trial 2020



N Engl J Med 2020; 382: 1395-40.7

ISCHEMIA Trial 2020



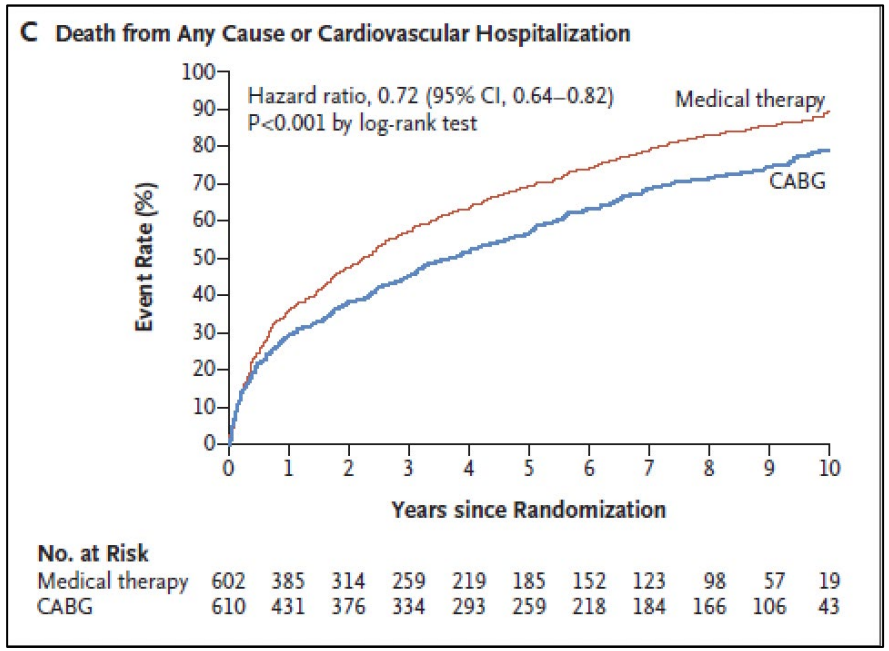
N Engl J Med 2020; 382: 1395-40.7

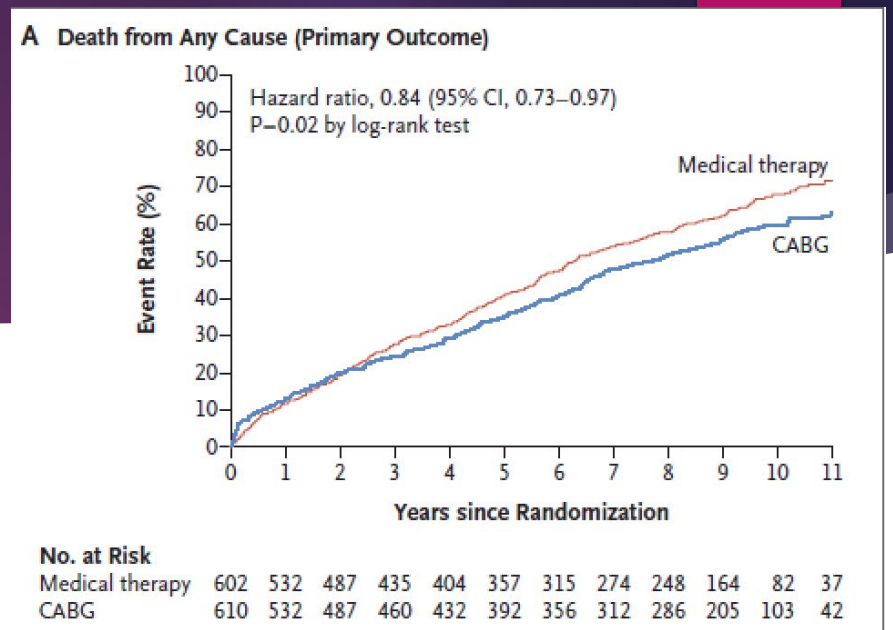
ISCHEMIA Trial 2020

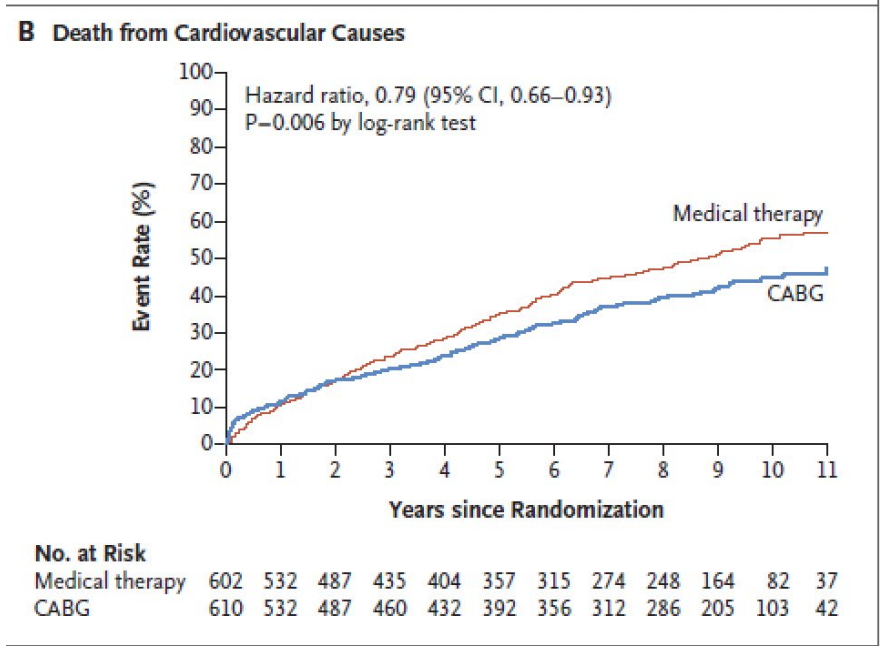
- **Clinical Practice Changes**
  - More confirmation that routine revascularization for stable ischemic heart disease, DOES NOT improve mortality
  - Not all patients with a positive stress test should undergo invasive coronary angiogram with revascularization
  - Obtaining a Coronary CT angiogram in select patients with positive stress tests to r/o left main disease and 3V disease, may be beneficial

STICHES Trial 2016

- In patients with HFrEF ≤35% with multivessel CAD, CABG vs medical therapy alone reduces mortality at 10 years







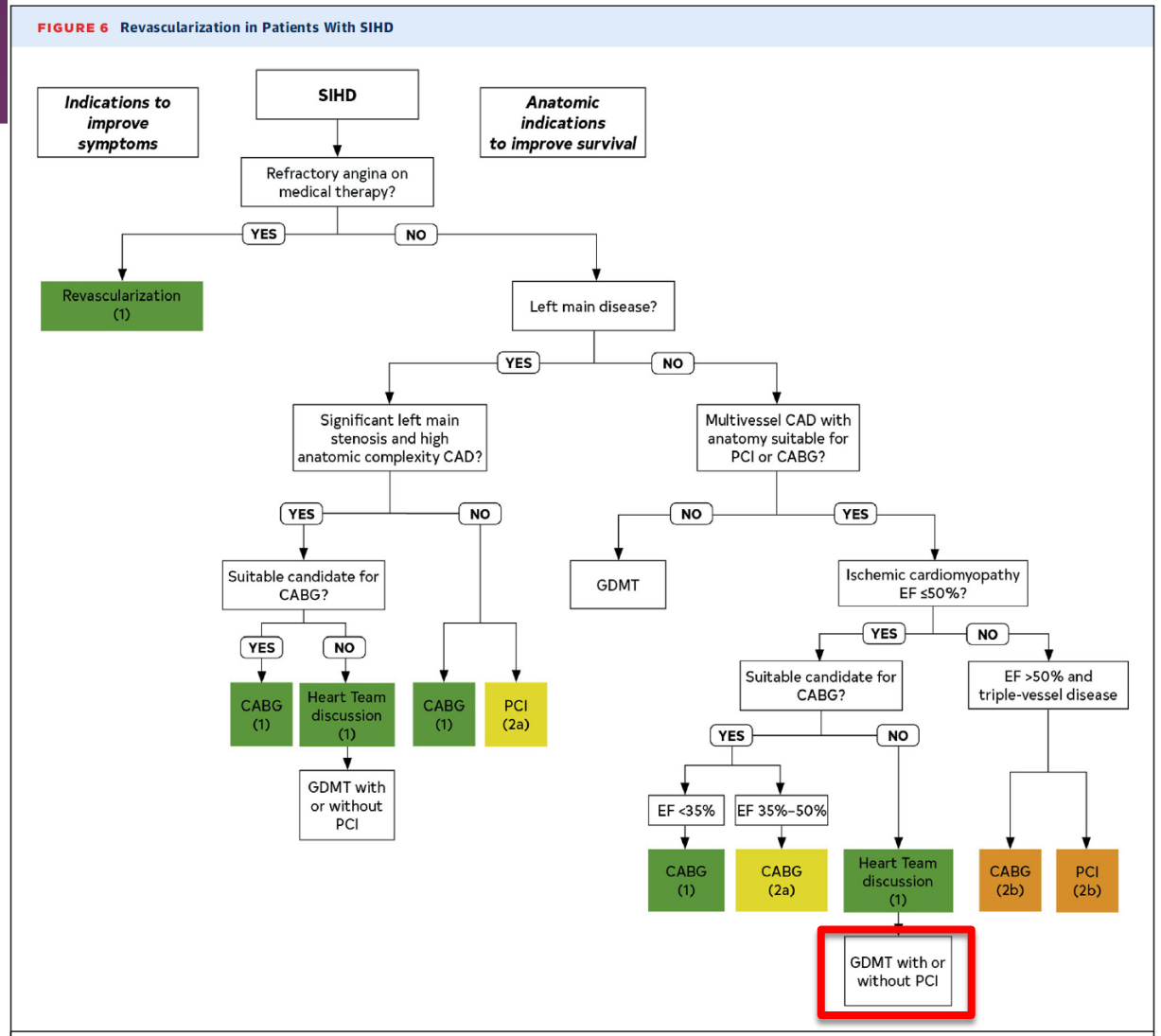
BUT does routine PCI in non-surgical candidates reduce mortality?

N Engl J Med 2016; 374: 1511-20

Revascularization Guidelines—Stable Ischemia Heart Disease

- Revascularization indications:
  - Refractory Angina
  - Left Main Disease
  - LVEF ≤35% with Multivessel disease
    - CABG has mortality benefit at 10 years

JACC 2022; 29: e21-129



REVIVED-BCIS2 2022

Inclusion Criteria:

- LVEF ≤35%
- Extensive CAD
- Demonstratable viability in at least 4 dysfunctional myocardia segments
- Amenable to PCI

Exclusion Criteria:

- Acute MI in last 4 weeks
- Acute decompensated heart failure
- Sustained VT within 72 hrs

N Engl J Med 2022; 387:1351-60

REVIVED-BCIS2 2022

PCI + Optimal Medical Therapy

- 14% Left Main disease
- 38% 3V Disease

Vs.

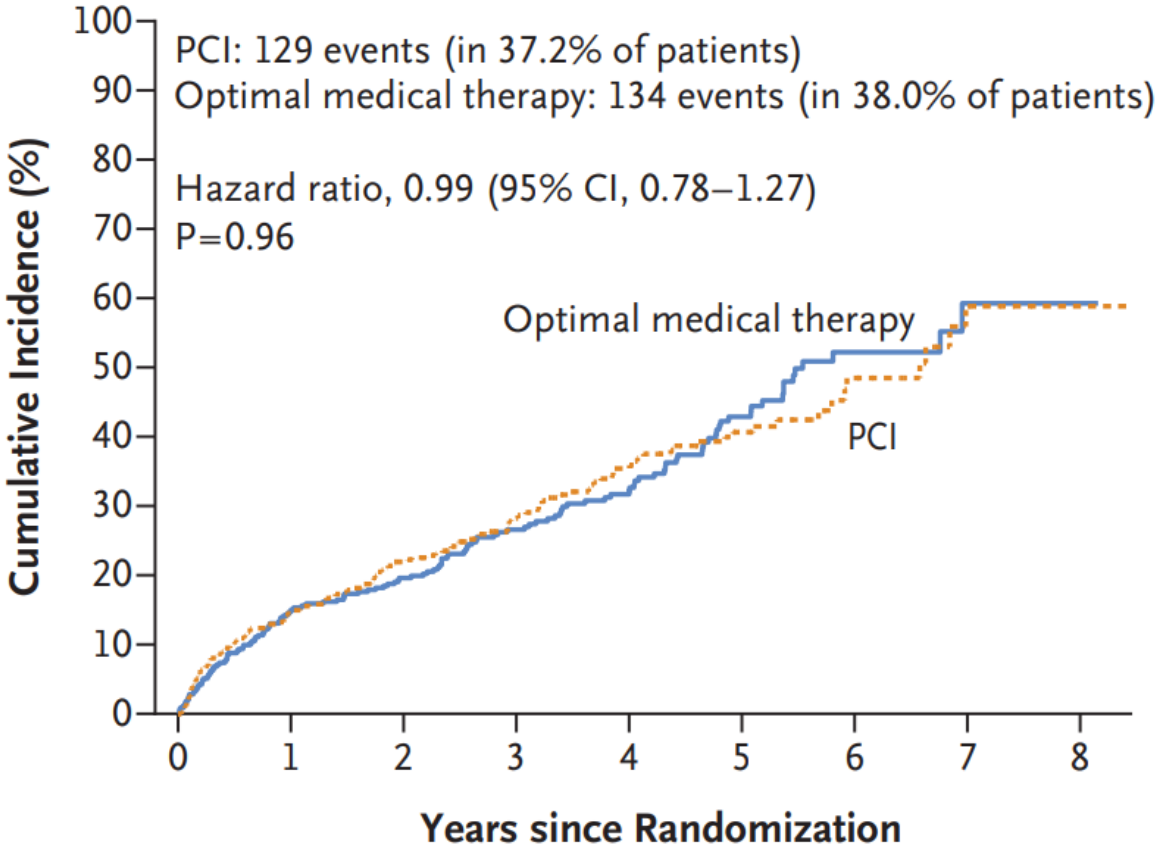
Optimal Medical Therapy Alone

- 13% Left Main disease
- 42% 3V Disease

- **Primary Outcome:** Composite of death from any cause or hospitalization for heart failure

N Engl J Med 2022; 387:1351-60

- No difference in All cause mortality or CV death
- No difference in heart failure hospitalizations
- More spontaneous MIs and unplanned revascularizations with optimal medical therapy alone



No. at Risk

PCI	347	295	262	179	130	80	32	14	3
Optimal medical therapy	353	299	276	191	142	82	33	10	1

Figure 1. Primary Outcome of Death from Any Cause or Hospitalization for Heart Failure.

N Engl J Med 2022; 387:1351-60

Take Home Points

- In patients with HFrEF and multivessel coronary artery disease, CABG provides a 10 year mortality benefit over optimal medical therapy (STITCH Trial); HOWEVER….

- In those who are not candidates for CABG, PCI does not offer a mortality benefit, but may reduced spontaneous Mis
  - Still referring patients with HFrEF ≤35% for invasive angiography, however, routine revascularization without symptoms, is not being performed----more shared decision making

SGLT2i and CV risk reduction

EMPA-REG OUTCOME 2015

Inclusion Criteria:

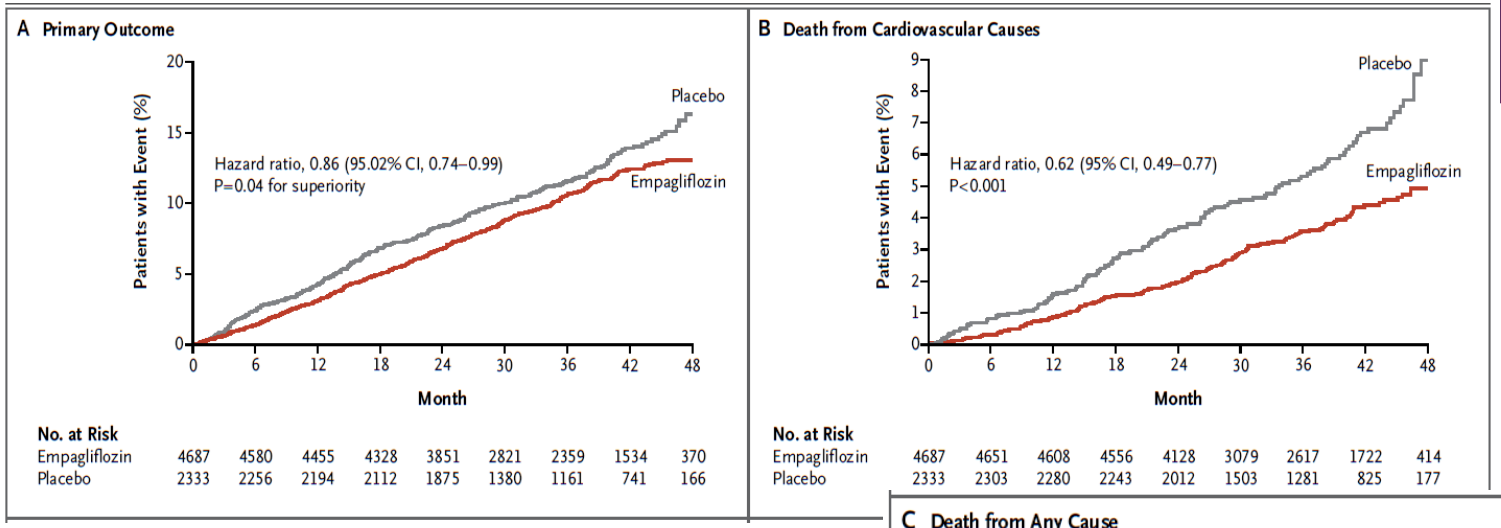
- DM2
- HbA1C 7-9%
- ≥18 year
- BMI ≤45
- eGFR ≥30
- Established CV disease

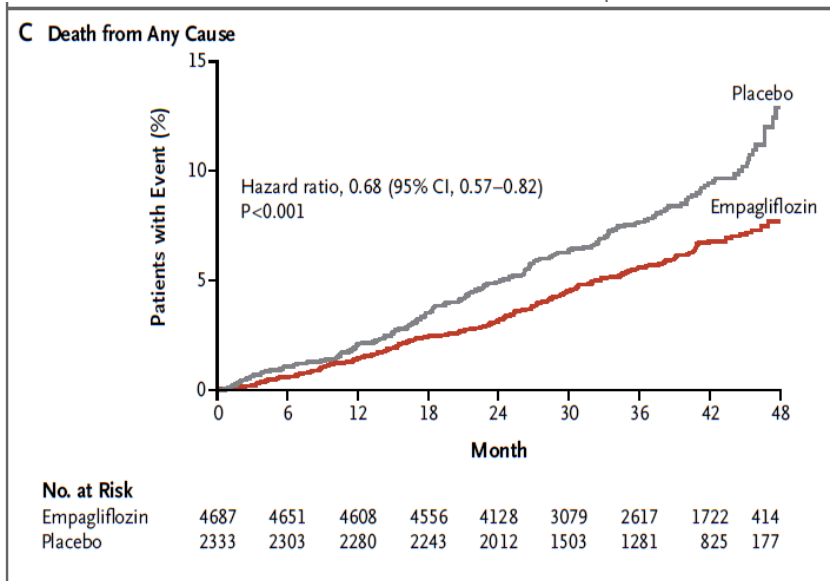
Empagliflozin 10mg daily **Vs.** **Empagliflozin 25mg daily** **Vs.** **Placebo**

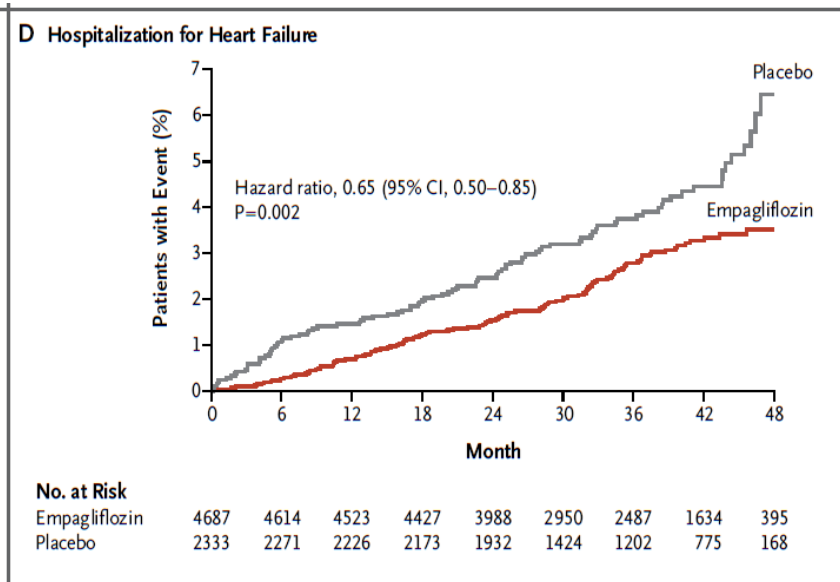
- **Primary outcome-** composite of death from CV causes, non-fatal MI or non-fatal stroke

N Engl J Med 2015; 373: 2117-28xc

EMPA-REG OUTCOME 2015







*Also noted significant reduction in HF hospitalization…

N Engl J Med 2015; 373: 2117-28xc

A 54 yo male with a PMH of HFrEF with an LVEF of 30% presents for follow up. He is currently taking Carvedilol 12.5mg BID and Entresto 97/103mg BID. His blood pressure is 110/75 mmHg and heart rate is 60 bpm. He appears to be very minimally volume overloaded on exam. Most recent labs show normal Cr and Potassium. What is the next best change to medical therapy?

A. Start Spironolactone 12.5mg daily
B. Start Empagliflozin 10mg daily
C. Start Furosemide 20mg daily
D. A and B
E. A and C

SGLT2i for Heart Failure with Reduced LVEF

DAPA-HF 2019

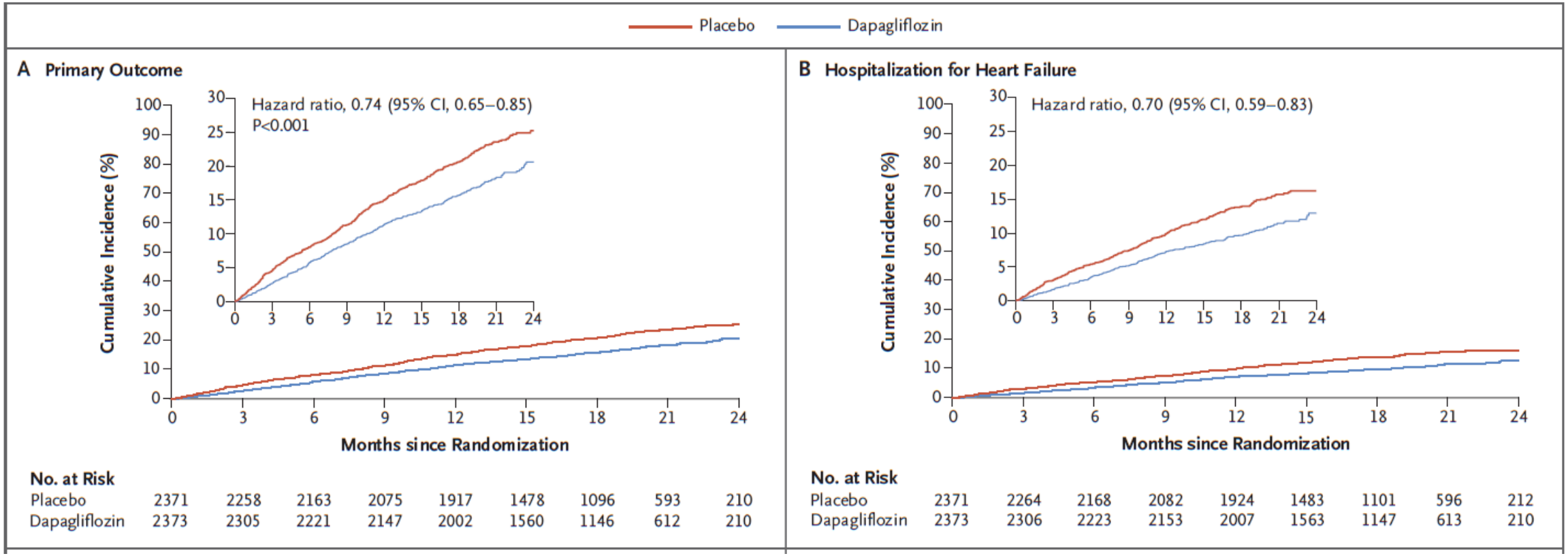
Inclusion Criteria:
- ≥ 18 years old
- HFrEF ≤40%
- NYHA class II-IV
- Elevated BNP

Dapagliflozin 10mg daily **Vs.** **Placebo**

- **Primary outcome-** composite of worsening heart failure or death from CV cause

N Engl J Med 2019; 381: 1995-2008

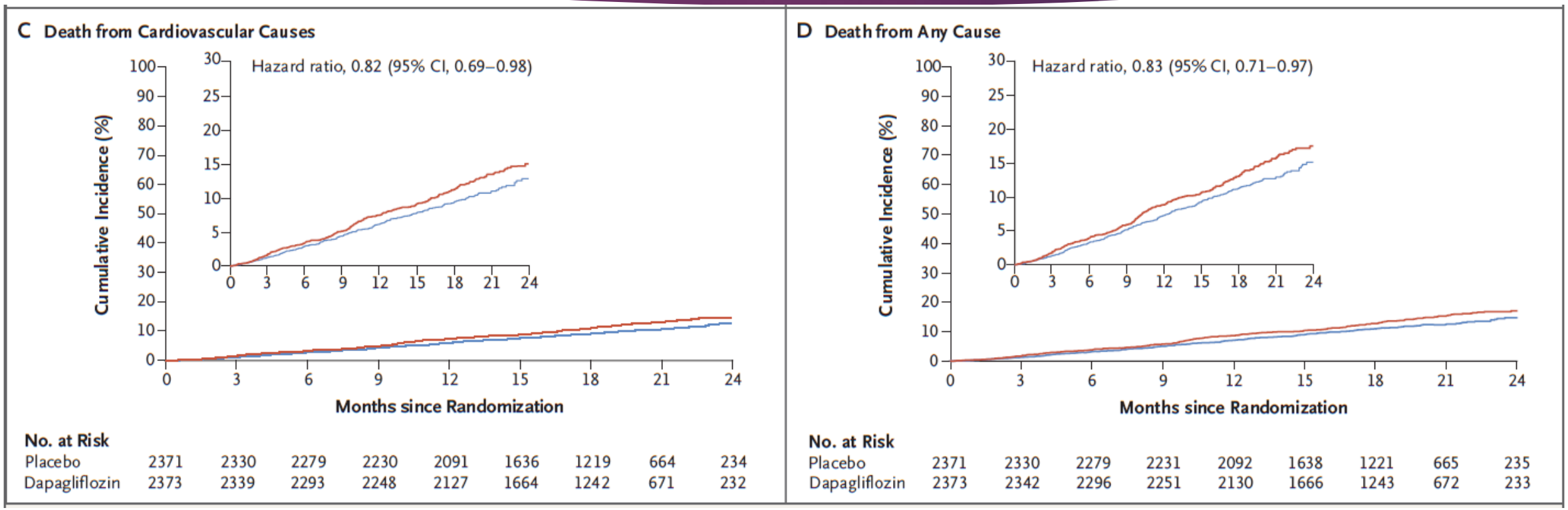
DAPA-HF 2019



NNT=21

N Engl J Med 2019; 381: 1995-2008

DAPA-HF 2019



N Engl J Med 2019; 381: 1995-2008

EMPEROR-Reduced 2020

Inclusion Criteria:

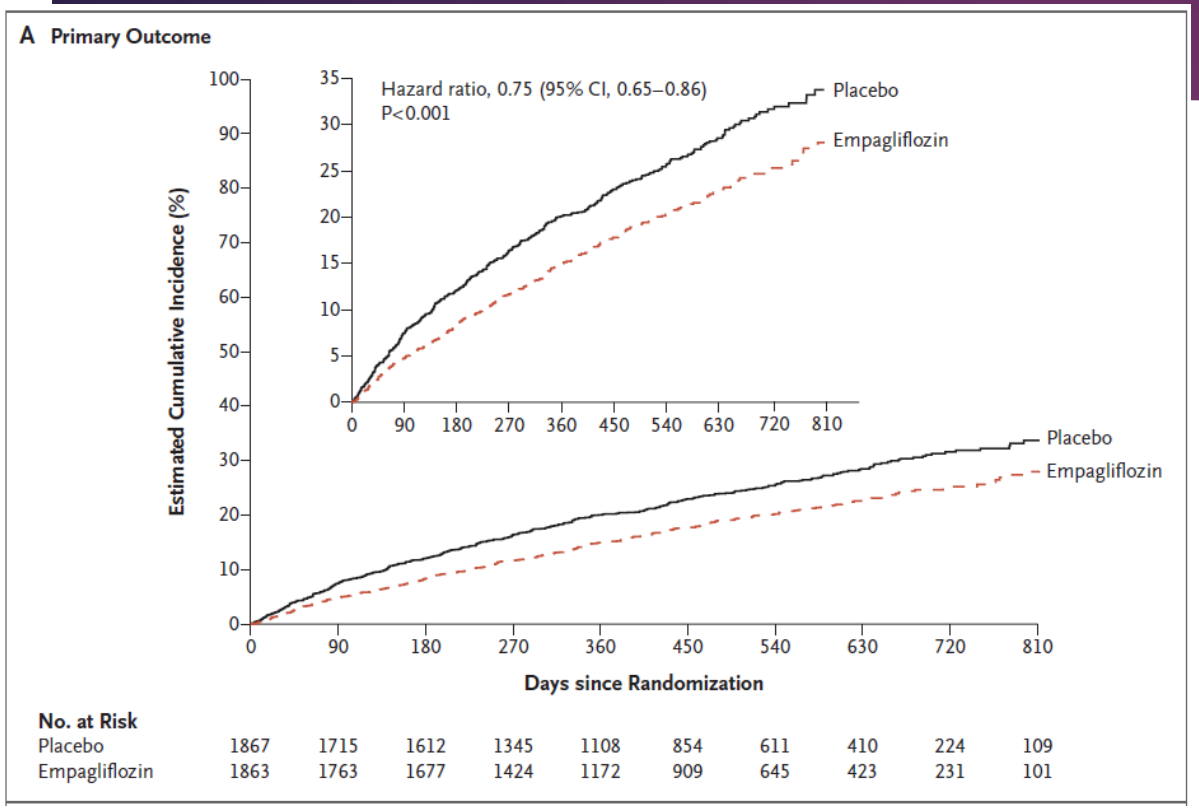
- ≥18 years old
- LVEF ≤40%
- NYHA class II-IV
- Elevated BNP
- Recent HF hospitalization

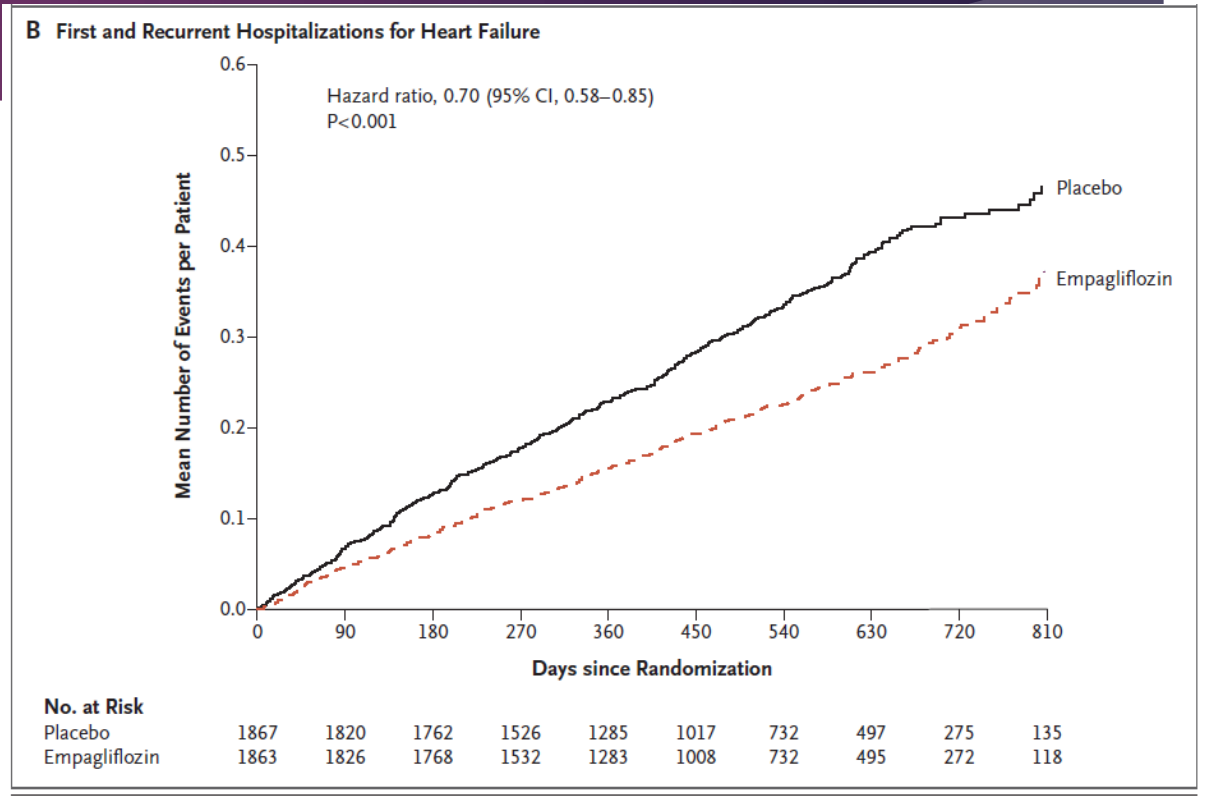
Empagliflozin 10mg daily **Vs.** **Placebo**

- **Primary outcome-** composite of CV deaths or hospitalizations for heart failure

N Engl J Med 2020;383:1413-1424

EMPEROR-Reduced 2020





- NNT= 19
- No difference in CV Death

N Engl J Med 2020;383:1413-1424

A 75 yo male with HFpEF with LVEF 70% presents after discharge for recent heart failure hospitalization. His blood pressure is 120/75 mmHg and heart rate is 80 bpm. He is currently taking Losartan 100mg daily, Spironolactone 25mg daily and Lasix 80mg BID. What is the next best step in management?

A. Switch Losartan to Entresto
B. Start Metoprolol Succinate 25mg daily
C. Start Empagliflozin 10mg daily

SGLT2i for Heart Failure with Preserved LVEF

EMPEROR-PRESERVED 2021

Inclusion Criteria:

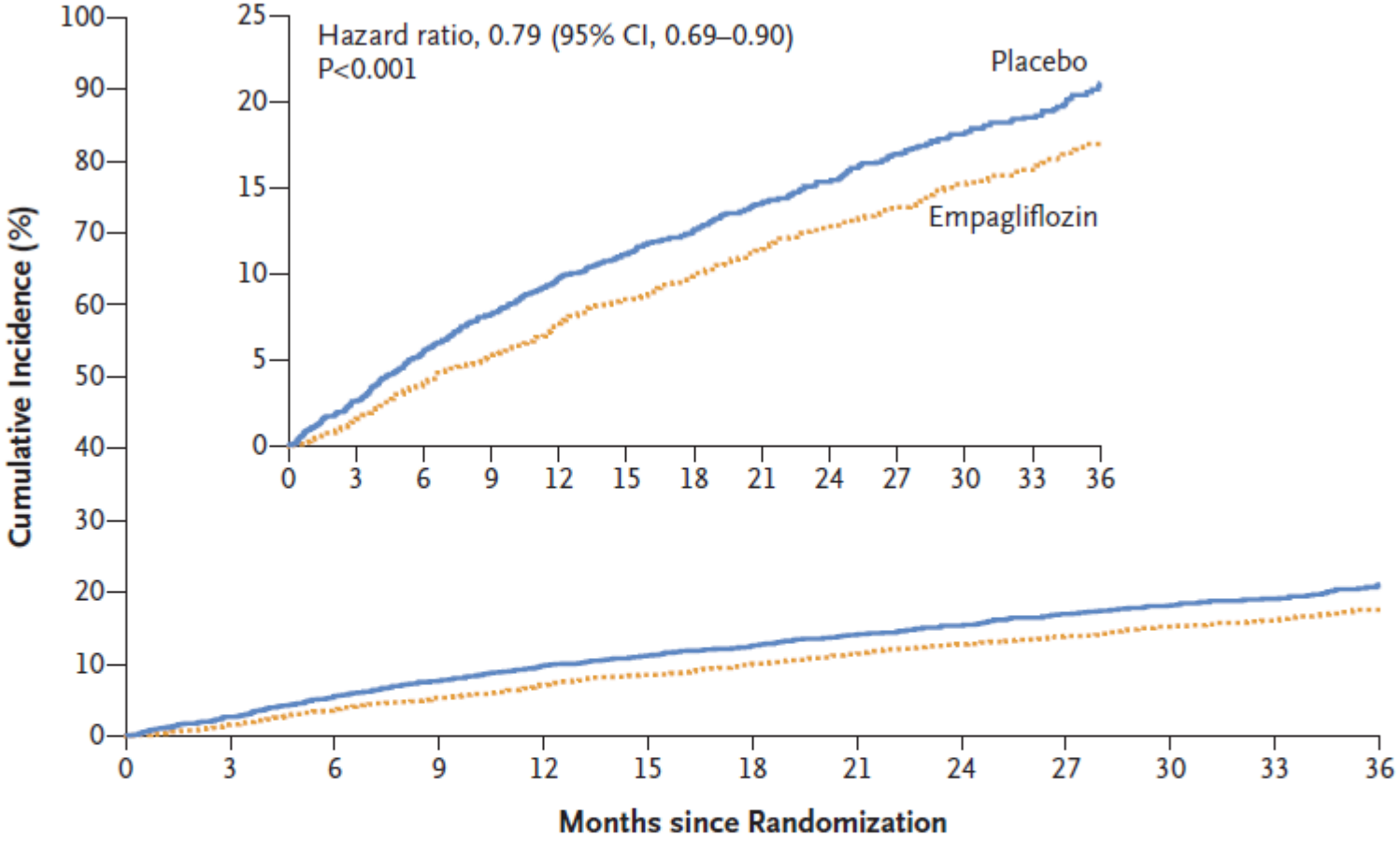
- ≥18 years old
- NYHA class II-IV
- LVEF >40%
- Elevated BNP

Empagliflozin 10mg daily **Vs.** **Placebo**

- **Primary outcome-** composite of CV death or HF hospitalizations

N Engl J Med 2021;385:1451-1461

Largely driven by reduced hospitalization and not CV death



No. at Risk													
Placebo	2991	2888	2786	2706	2627	2424	2066	1821	1534	1278	961	681	400
Empagliflozin	2997	2928	2843	2780	2708	2491	2134	1858	1578	1332	1005	709	402

Figure 1. Primary Outcome, a Composite of Cardiovascular Death or Hospitalization for Heart Failure.

The estimated cumulative incidence of the primary outcome in the two groups is shown. The inset shows the same data on an expanded y axis.

N Engl J Med 2021;385:1451-1461

DELIVER 2022

Inclusion Criteria:

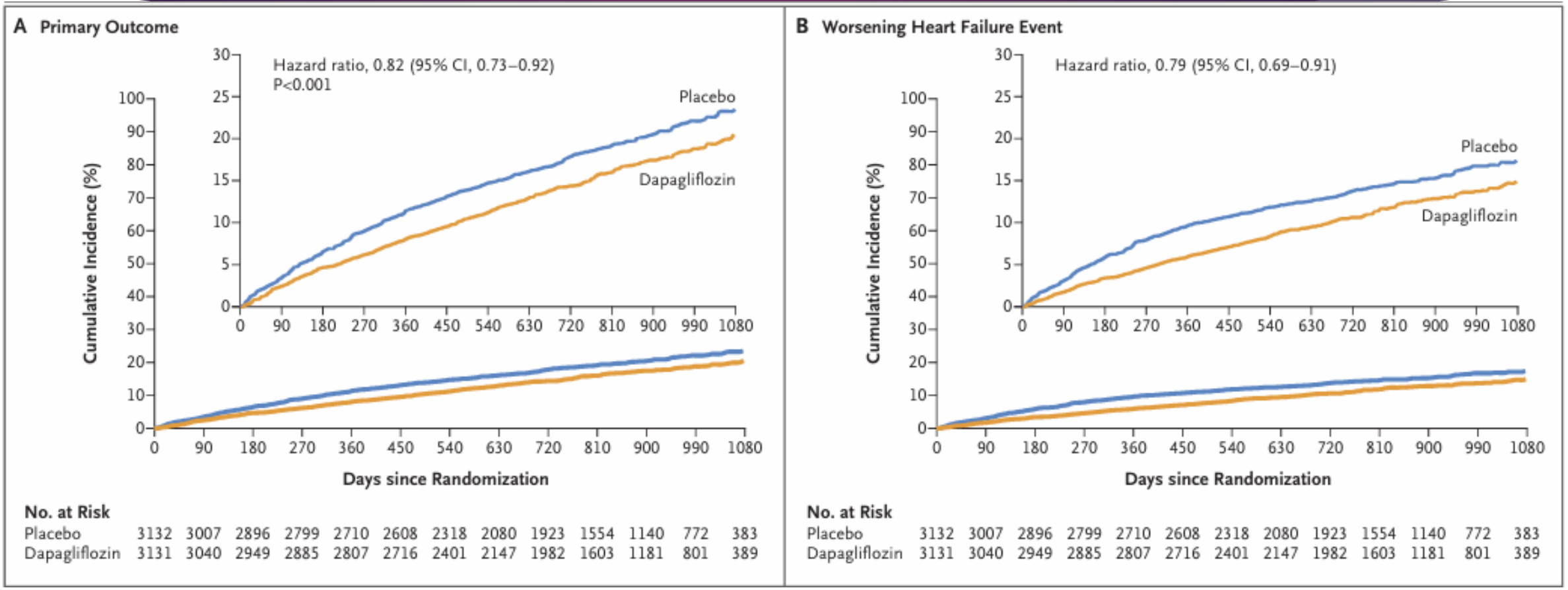
- ≥40 years old
- LVEF ≥40%
- Evidence of structural heart disease
- Elevated BNP

Dapagliflozin 10mg daily **Vs.** **Placebo**

- **Primary outcome-** composite of worsening heart failure or CV death

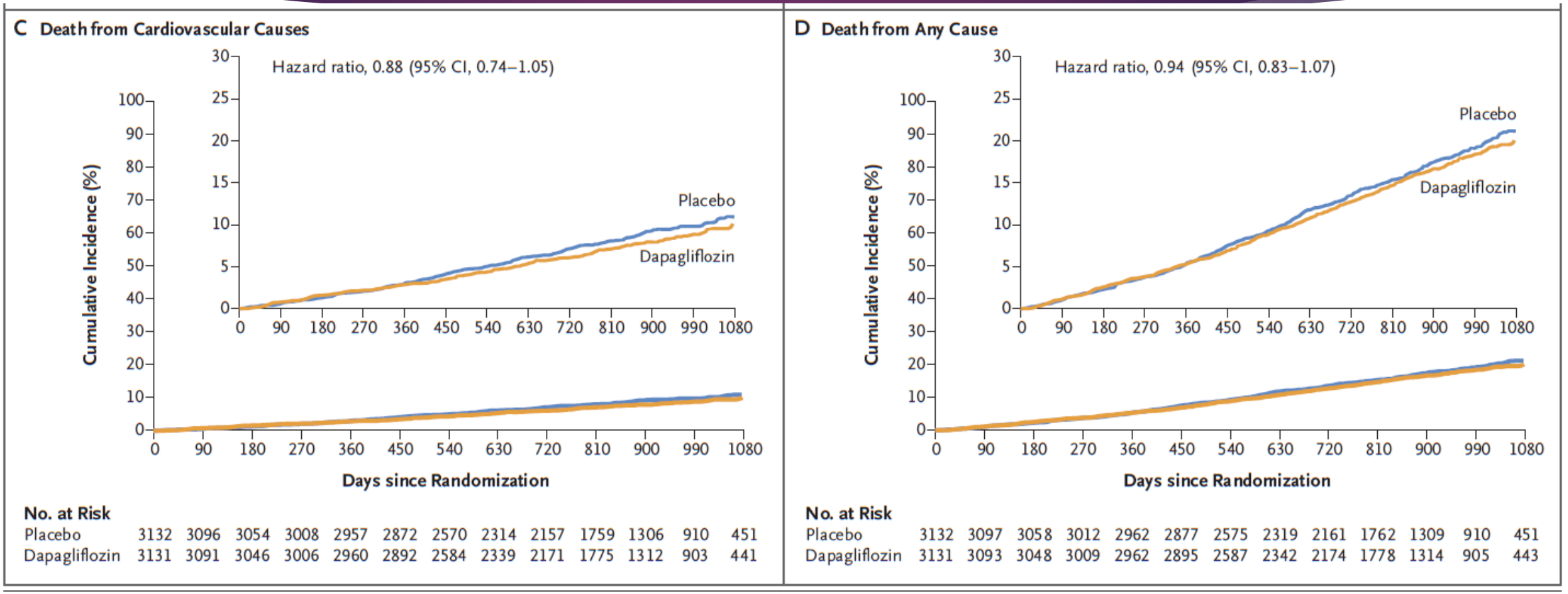
N Engl J Med 2022;387:1089-1098

DELIVER 2022



N Engl J Med 2022;387:1089-1098

DELIVER 2022



N Engl J Med 2022;387:1089-1098

SGLT2i for Heart failure: Bottom Line

- **In patients with HFrEF, SGLT2i reduced**
  - Compositive outcome worsening heart failure or CV death
  - All cause mortality (DAPA-HF)

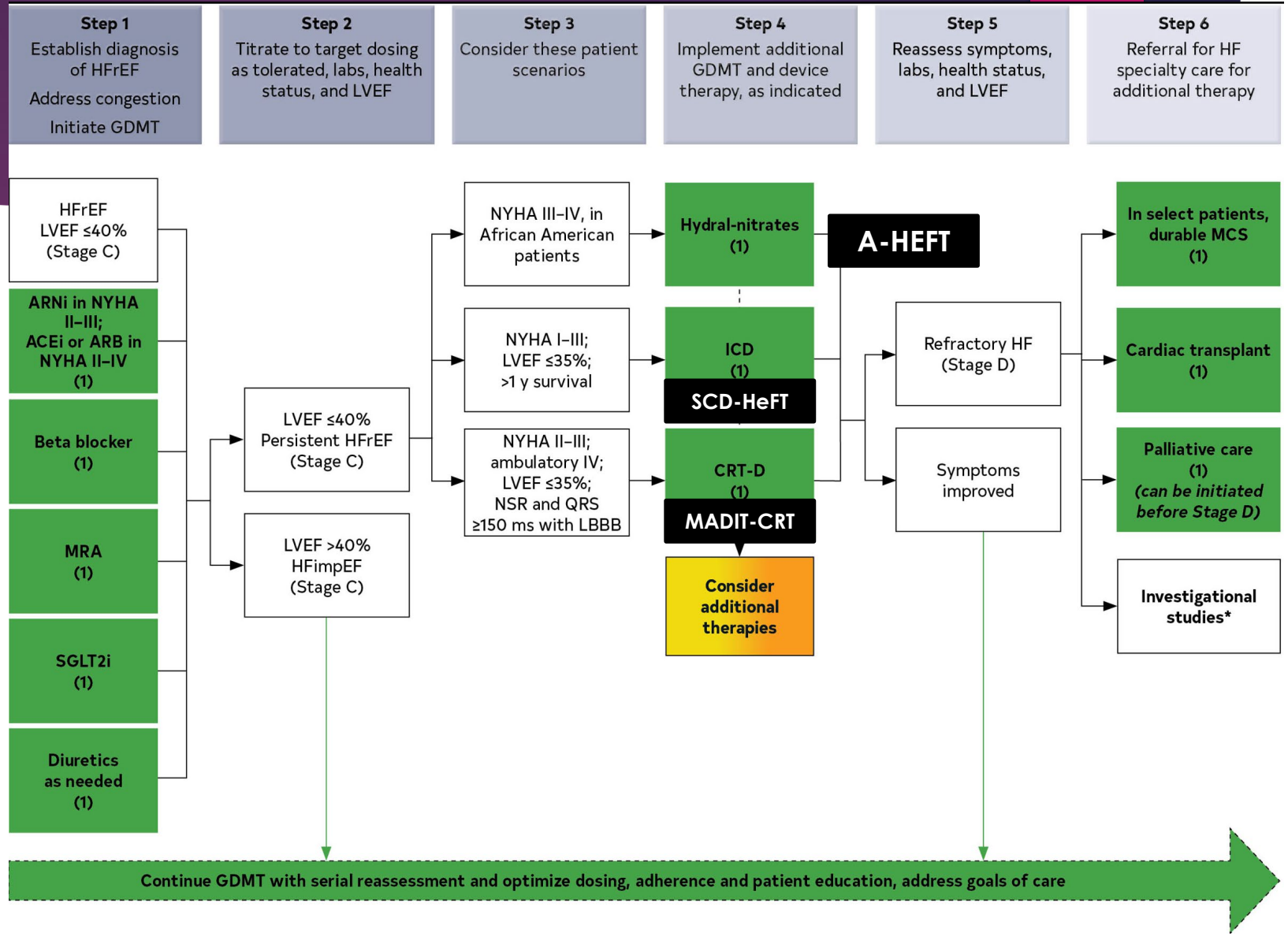
- **In patients with HFpEF, SGLT2i reduced**
  - Composite outcome of worsening heart failure or CV death, largely driven by heart failure hospitalization
  - No major difference in all cause or CV mortality

HFrEF Guidelines

Early initiation and up titration of **quadruple** therapy has been shown effective and beneficial

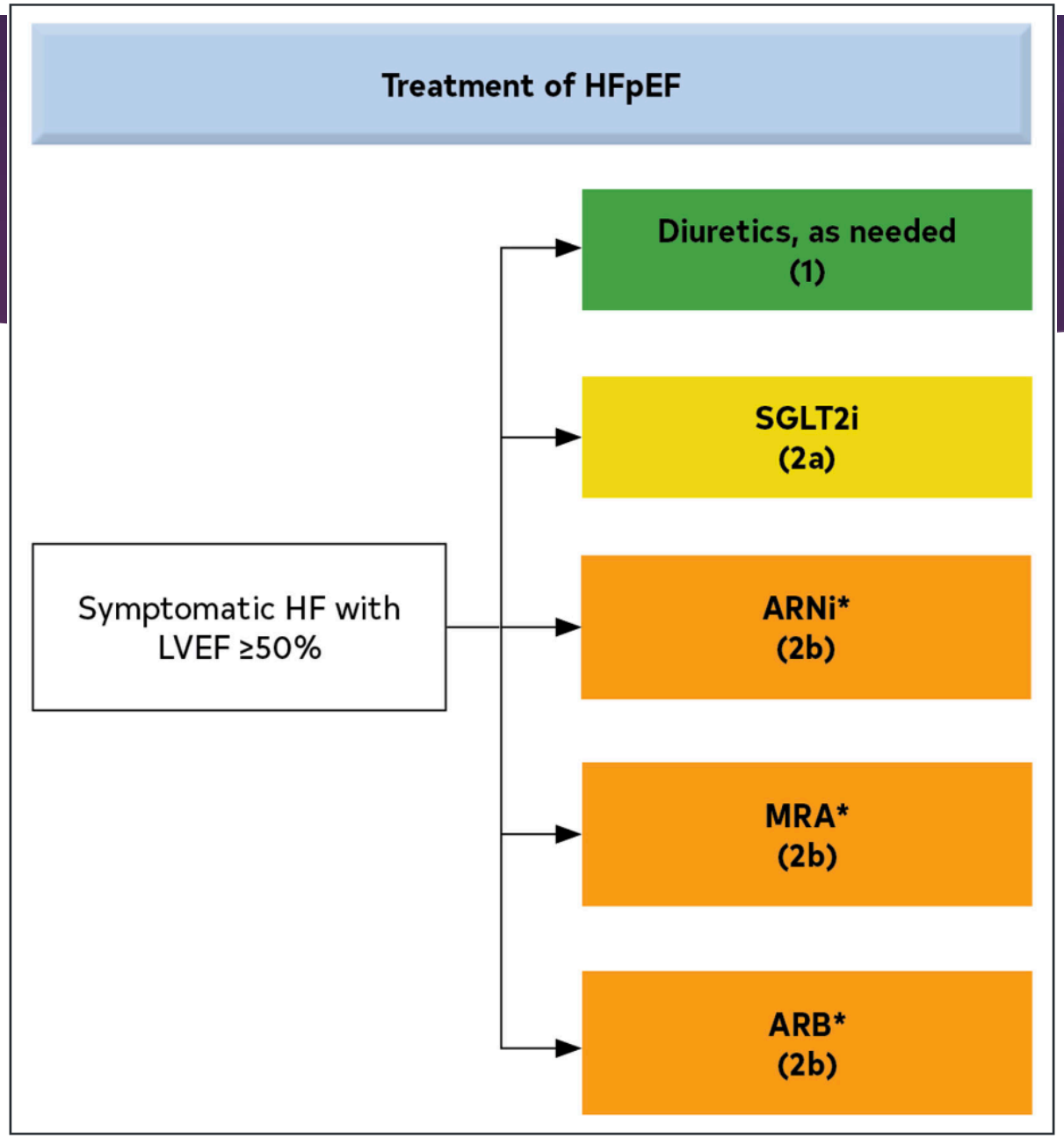
Often can reduce need for loop diuretic

Supporting Clinical Trials
PARADIGM-HF
MERIT-HF, COPERNICUS, CIBIS II
RALES and EMPHASIS
DAPA-HF and EMPEROR-REDUCED



Circulation 2022;145:e895–e1032.

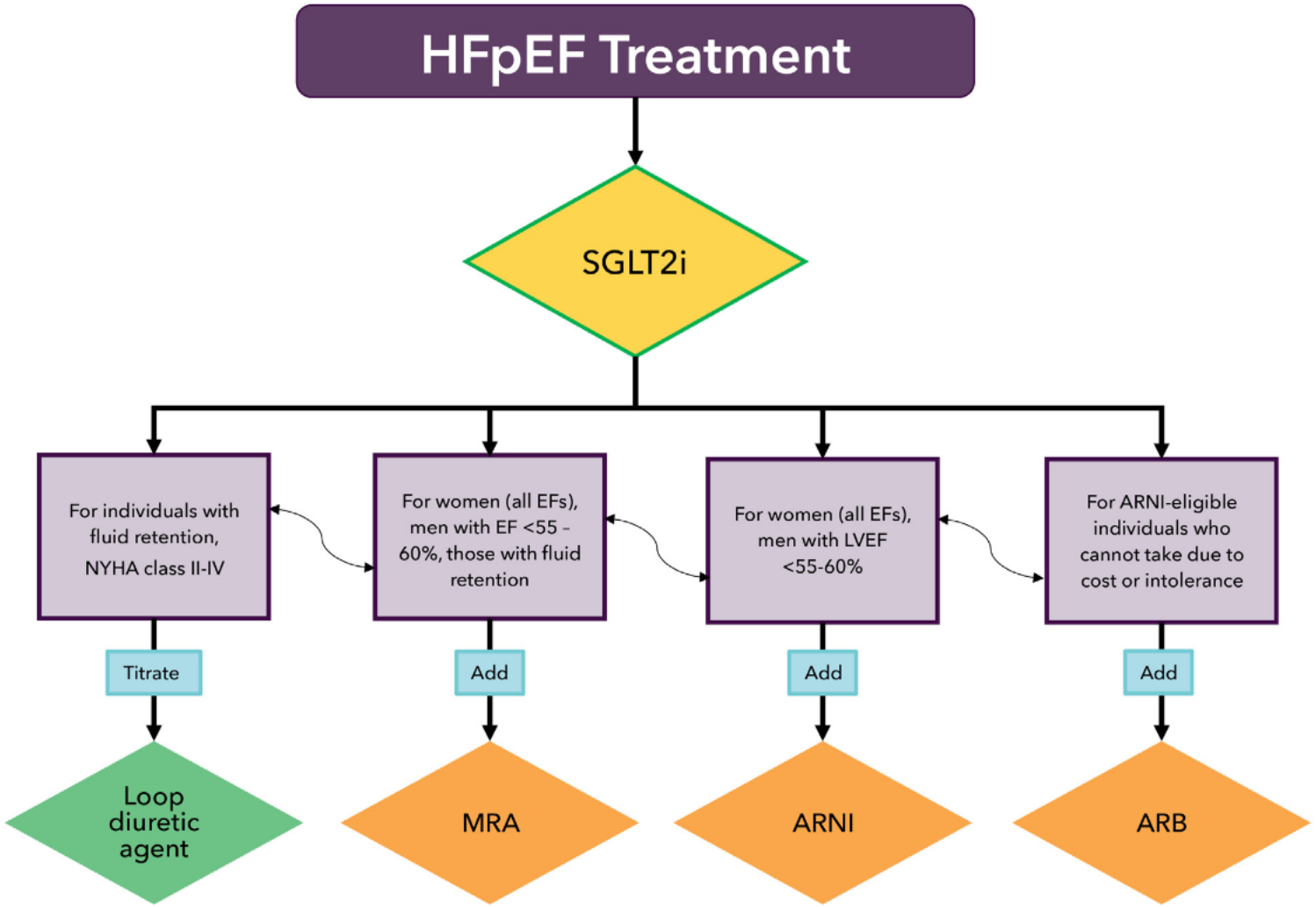
HFpEF



Circulation 2022;145;18:e895-1032

HFpEF

FIGURE 9 Treatment Algorithm for Guideline-Directed Medical Therapy in HFpEF*



*Green color identifies a Class 1 therapy from clinical practice guidelines,[14] yellow color indicates a Class 2a therapy, and orange color denotes a Class 2b therapy. SGLT2is receive a Class 2a indication in the 2022 AHA/ACC/HFSA HF Guidelines,[14] but the benefit, now confirmed in 2 randomized trials,[60,61] suggests that SGLT2is may receive a stronger class of recommendation in future guidelines, and thus the box is shaded yellow with a green border. AF = atrial fibrillation; ARB = angiotensin receptor blocker; ARNI = angiotensin receptor-neprilysin inhibitor; EF = ejection fraction; HFpEF = heart failure with preserved ejection fraction; LVEF = left ventricular ejection fraction; MRA = mineralocorticoid antagonist; NYHA = New York Heart Association; SGLT2i = sodium-glucose cotransporter 2 inhibitor.

J Am Coll Cardiol. 2023 81 (18): 1835-1878

A 67 year old with a PMH of morbid obesity (BMI 39), coronary artery disease with prior revascularization, HTN, HLD and sleep apnea who presents for follow up. He is current taking Aspirin 81mg daily, Atorvastatin 80mg daily, Metoprolol 25mg daily and Lisinopril 20mg daily. Blood pressure is 120/80 mmHg and heart rate is 65 bpm. Last LDL was 50 and Triglycerides were 100. He is not a diabetic and does not have evidence of heart failure. What medication change would be beneficial for cardiovascular risk reduction?

A. Start Empagliflozin 10mg daily
B. Start Semaglutide subq
C. Start Ezetimibe 10mg daily
D. Start Icosopent ethyl 2g BID

GLP1 agonists and CV risk reduction

Several trials have established CV risk reduction with GLP1 agonists in Diabetics……

- LEADER
- SUSTAIN-6
- REWIND
- And Others…

But what about in obese, NON-diabetics?

SELECT 2023

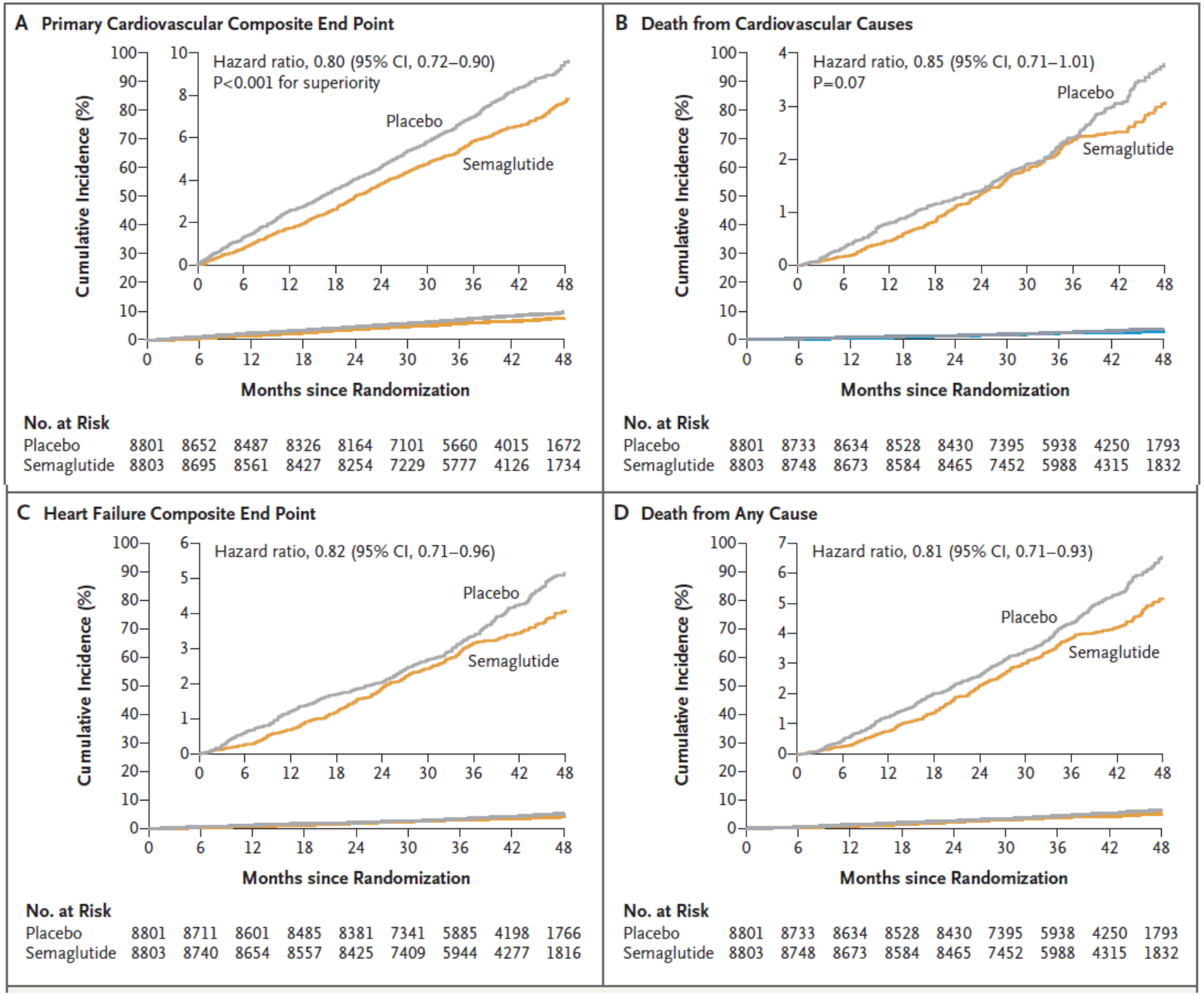
Inclusion Criteria:
- ≥45 years
- BMI ≥27
- Establish CV disease

Exclusion Criteria:
- Diabetes diagnosis

Semaglutide 2.4mg subQ **Vs.** **Placebo**

- **Primary outcome-** composite of death from CV cause, non-fatal MI, non fatal stroke

N Engl J of Med 2023; 384(11), 989-1002.



N Engl J of Med, 384(11), 989-1002.

GLP1 agonists for Heart Failure and Obesity

STEP-HFpEF 2023

Inclusion Criteria:

- ≥ 18 years
- LVEF ≥45%
- BMI ≥30
- NYHA class II-IV
- KCCQ-CSS score <90
- 6 minutes walk test <100m

AND

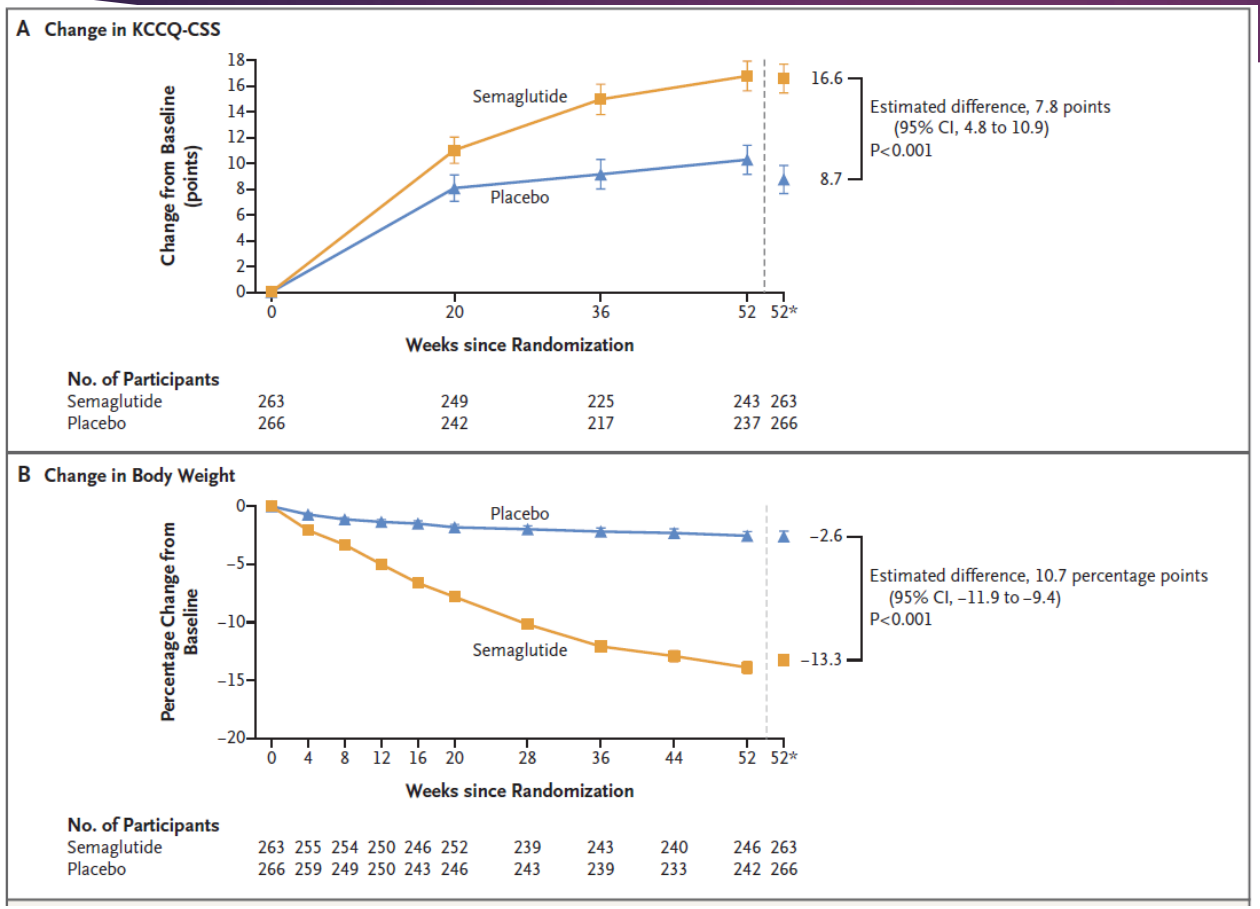
- Evidence of heart failure

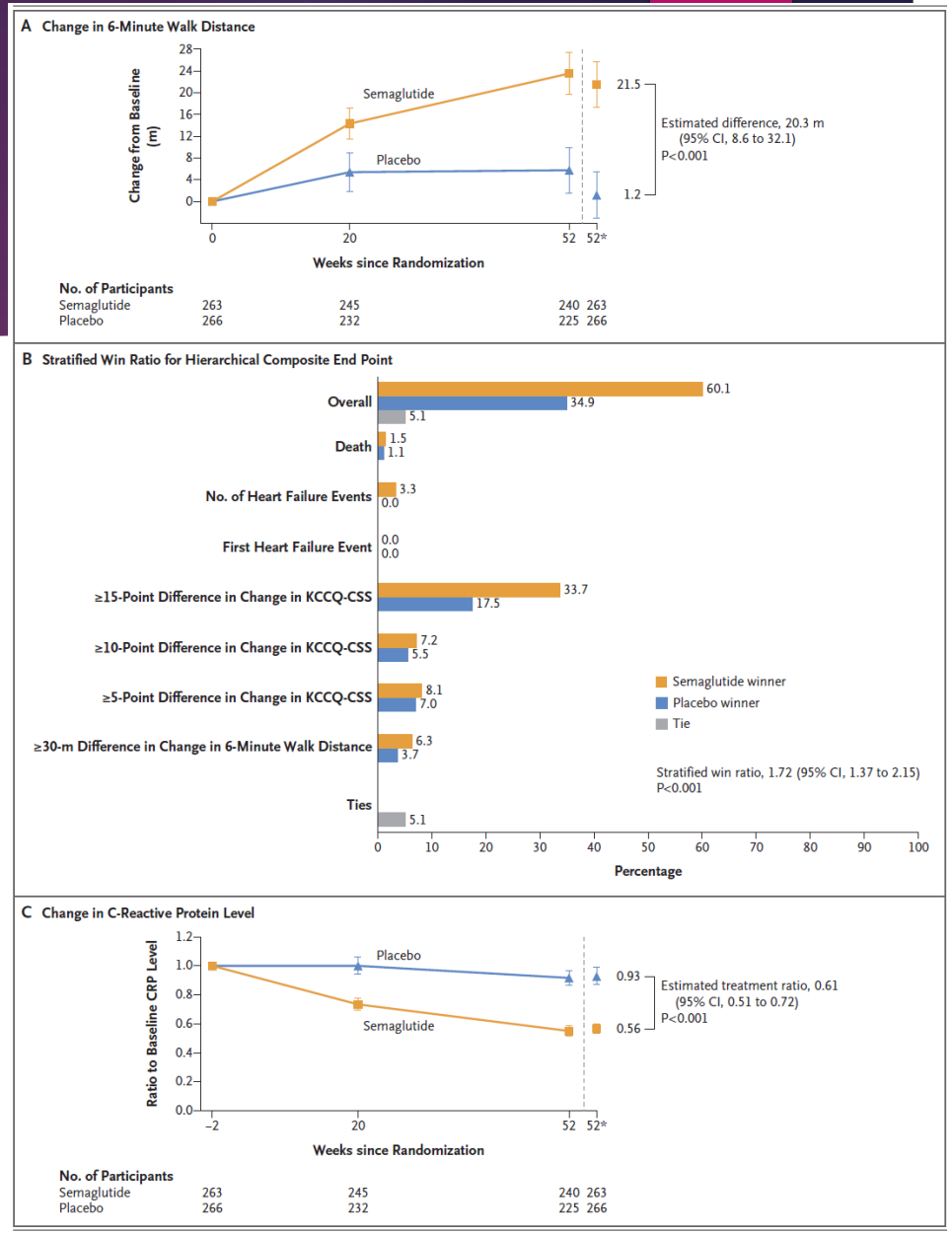
Semaglutide 2.4mg subQ **Vs.** **Placebo**

- **Primary outcome-** change in KCCQ-CSS and the percentage of change in body weight

New Engl J of Med 2023; 389(12), 1043-1056.

STEP-HFpEF 2023





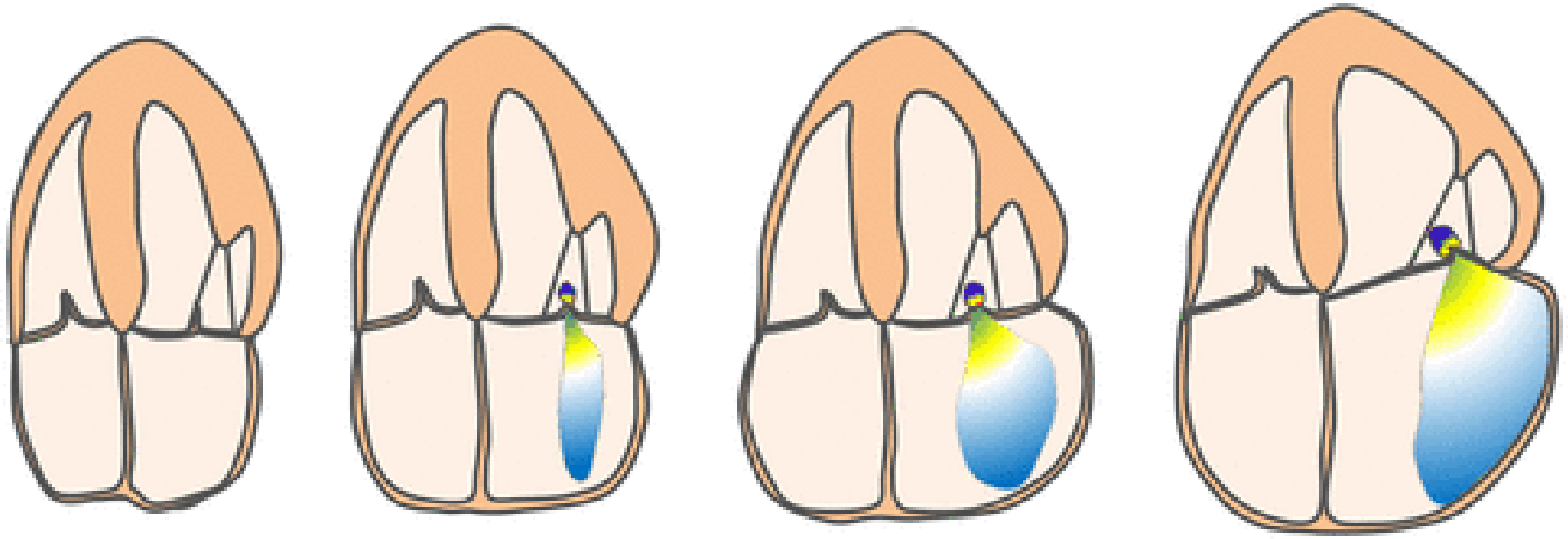
New Engl J of Med 2023; 389(12), 1043-1056.

Atrial Fibrillation Contemporary Management

Paradigm Shift

- AFFIRM Trial from 2002 is often cited to support no benefit in rate vs rhythm control
  - Flawed trial designs
  - Lot of cross over
  - Advances in ablation techniques
- NOW there is data to support rhythm control

Sinus Rhythm → Atrial Fibrillation



LA and annular dilation
Leaflet expansion
Mild-moderate MR

reversible stage

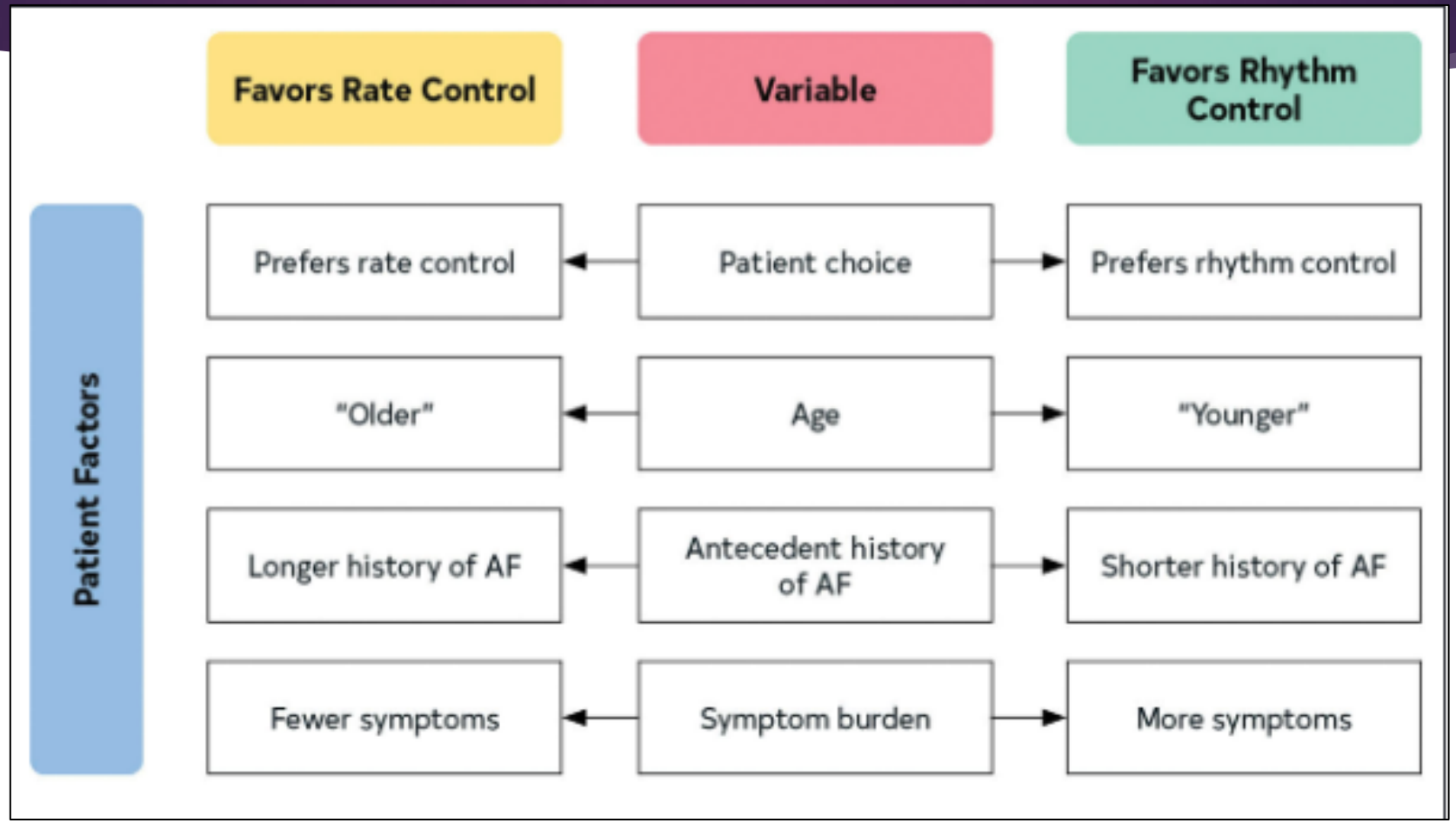
Giant LA
Excessive annular dilation
Leaflet elongation
LV dilation
Severe MR

irreversible stage

Catheter Ablation

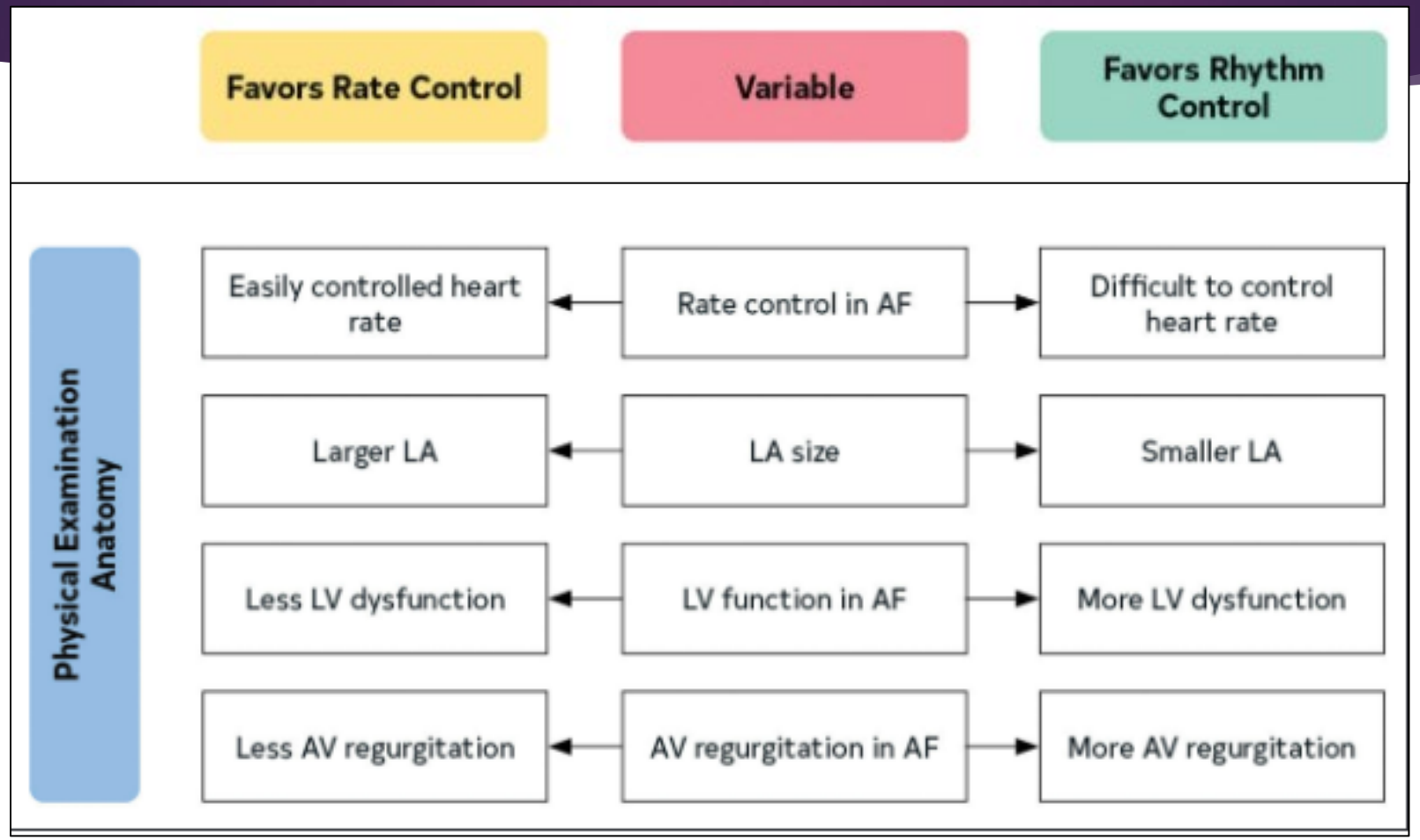
Circ Cardiovas Imaging.019;12:e009317

Who should you consider rhythm control?



Circulation 2023, 147(4), e000-e000.

Who should you consider rhythm control?



Circulation 2023, 147(4), e000-e000.

CASTLE-AF 2018

- **Inclusion Criteria**
- Paroxysmal or Persistent symptomatic Atrial Fibrillation
- No response, side effects or unwilling to take antiarrhythmic
- NYHA II-IV
- LVEF <=35%
- ICD/CRT-D

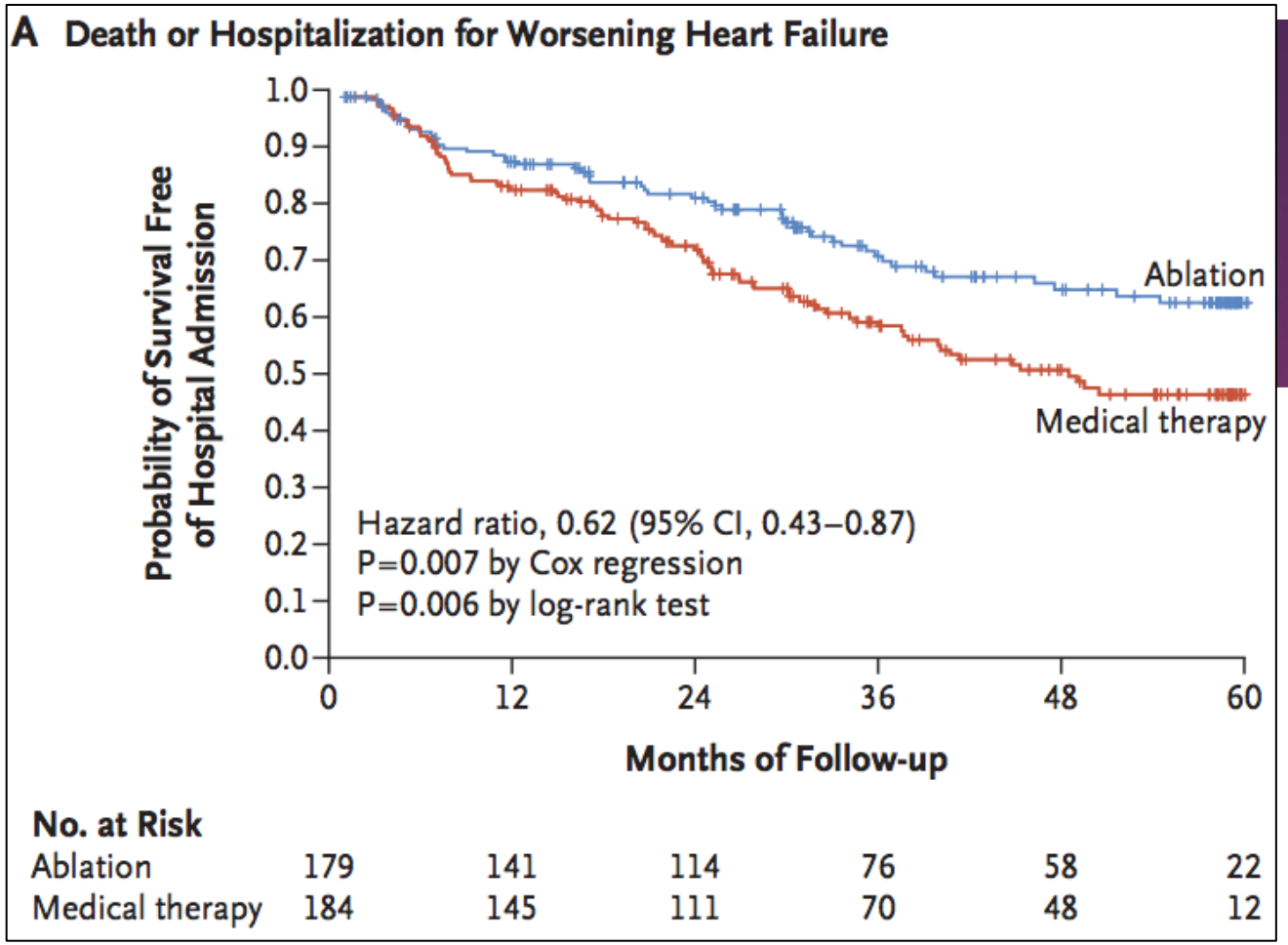
Medical therapy group: Strict rate control or rhythm control

VS.

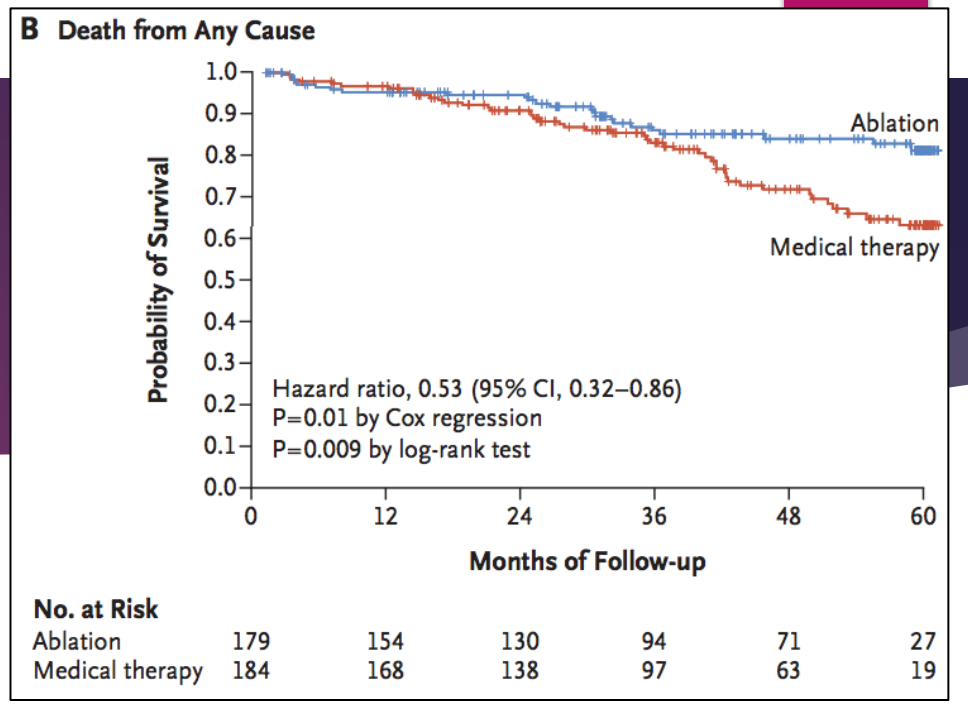
Ablation group: Pulmonary vein isolation

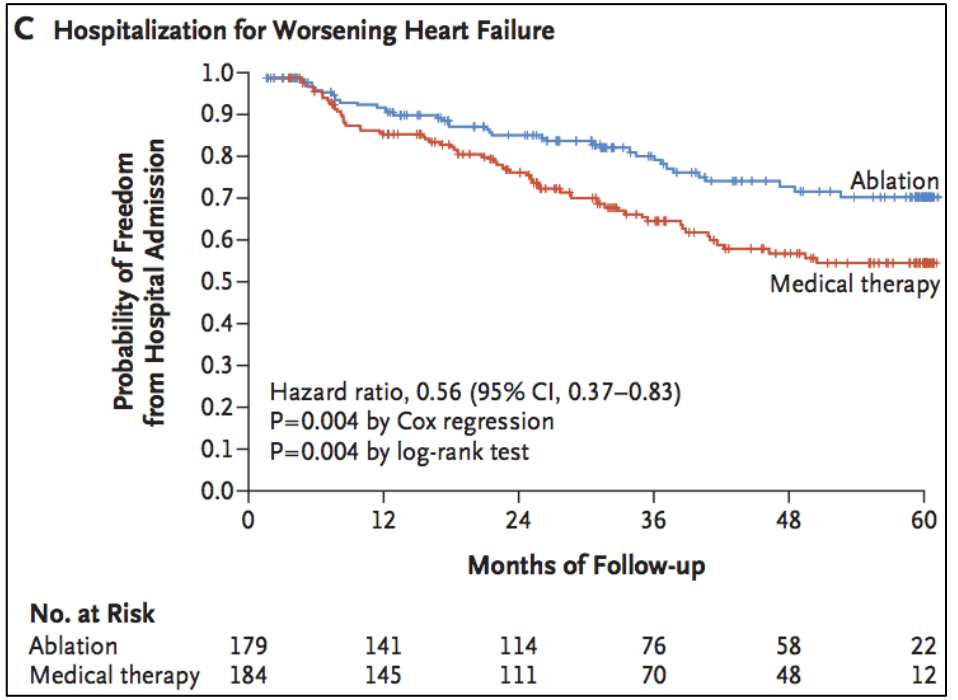
Primary outcome- composite of death from any cause or worsening of heart failure to led to an admission

N Engl J Med. 2018;378:417-27



NNT of 8.3 at 36 months





N Engl J Med. 2018;378:417-27

Atrial Fibrillation- EAST AF NET4 2020

Inclusion Criteria:

- Early Atrial Fibrillation (diagnosed ≤ 12 months)
- ≥75 years old

  AND
- Prior TIA or stroke

  OR
- 2 of the following: >65 years old, female, HF, HTN, DM2, CKD, LVH

N Engl J Med. 2020;383:1305-16

Atrial Fibrillation- EAST AF NET4 2020

Early Rhythm Control:
- Antiarrhythmics or ablation and DCCV

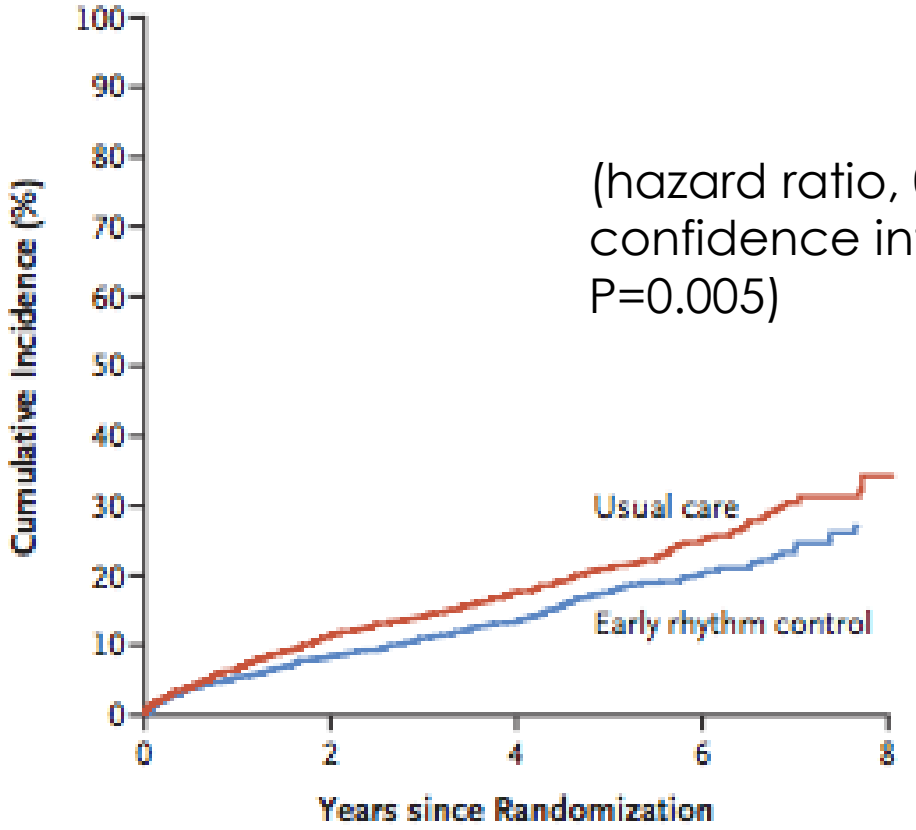
Vs.

Usual Care:
- Initial rate control
- Rhythm control only to mitigate uncontrolled symptoms despite rate control

Primary endpoint: composite of death from cardiovascular causes, stroke or hospitalization with worsening of heart failure or acute coronary syndrome AND number of nights in the hospital per year

N Engl J Med. 2020;383:1305-16

Atrial Fibrillation- EAST AF NET4 2020

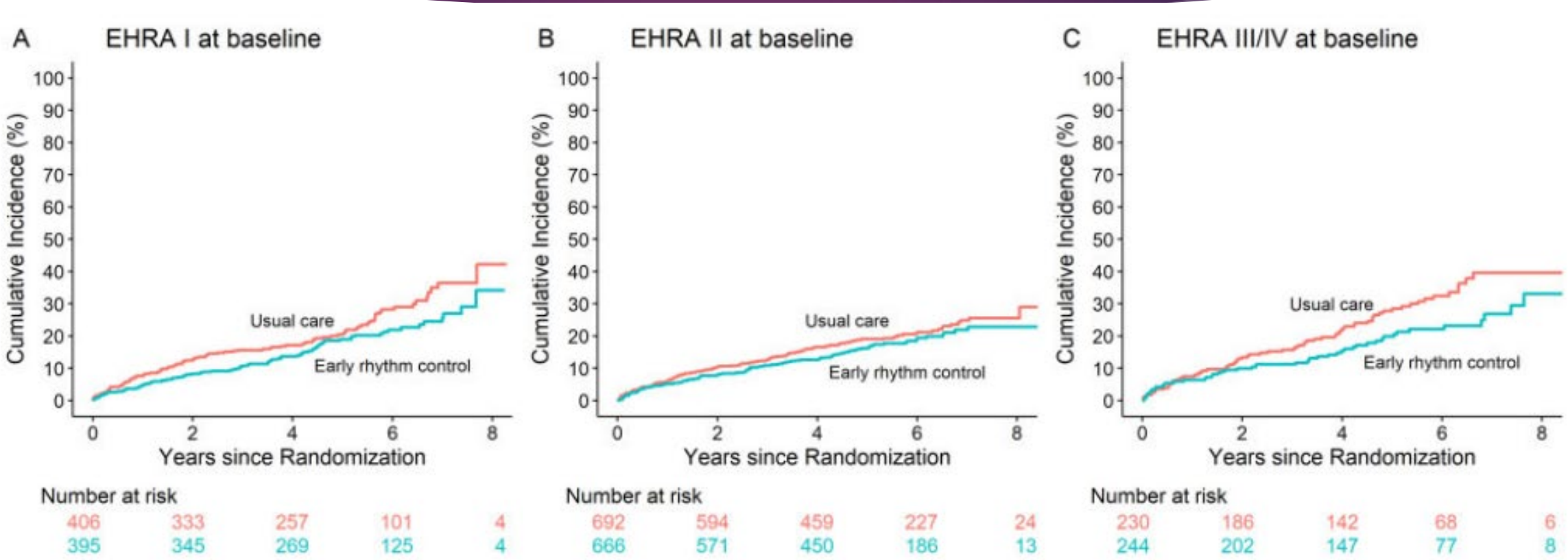


No. at Risk					
Usual care	1394	1169	888	405	34
Early rhythm control	1395	1193	913	404	26

(hazard ratio, 0.79; 96% confidence interval, 0.66 to 0.94; P=0.005)

N Engl J Med. 2020;383:1305-16

EAST-AFNET4 Follow up Study: Symptom Driven



Rhythm Control Guidelines

CLASS I

- **Reduced LVEF** and persistent (or high burden) AF, trial of rhythm control should be recommended to evaluate if AF is contributing to reduced LVEF
- Symptomatic AF in whom **antiarrhythmics have been ineffective**, contraindicated, not tolerated, and rhythm control is desired, **catheter ablatio**n is useful to improve symptoms
- Younger patient/few comorbidities with symptomatic paroxysmal Afib, catheter ablation is useful as **first line** therapy to improve symptoms and reduced AF progression
- **AF and HFrEF** who are on GDMT, catheter ablation is beneficial to improve symptoms, QOL, ventricular function and CV outcomes

Bottom line:

- Reduced LVEF deserves attempt at rhythm control
- Ablation when medications not effective, younger patients and HFrEF

Circulation 2023, 147(4), e000-e000.

Left Atrial Appendage Occlusion

Class 2a

In patients with Afib, moderate to high risk of stroke (CHADS-VasC ≥2), and a **contraindication** to long-term anticoagulation, due to non-reversible cause, percutaneous LAAO is reasonable

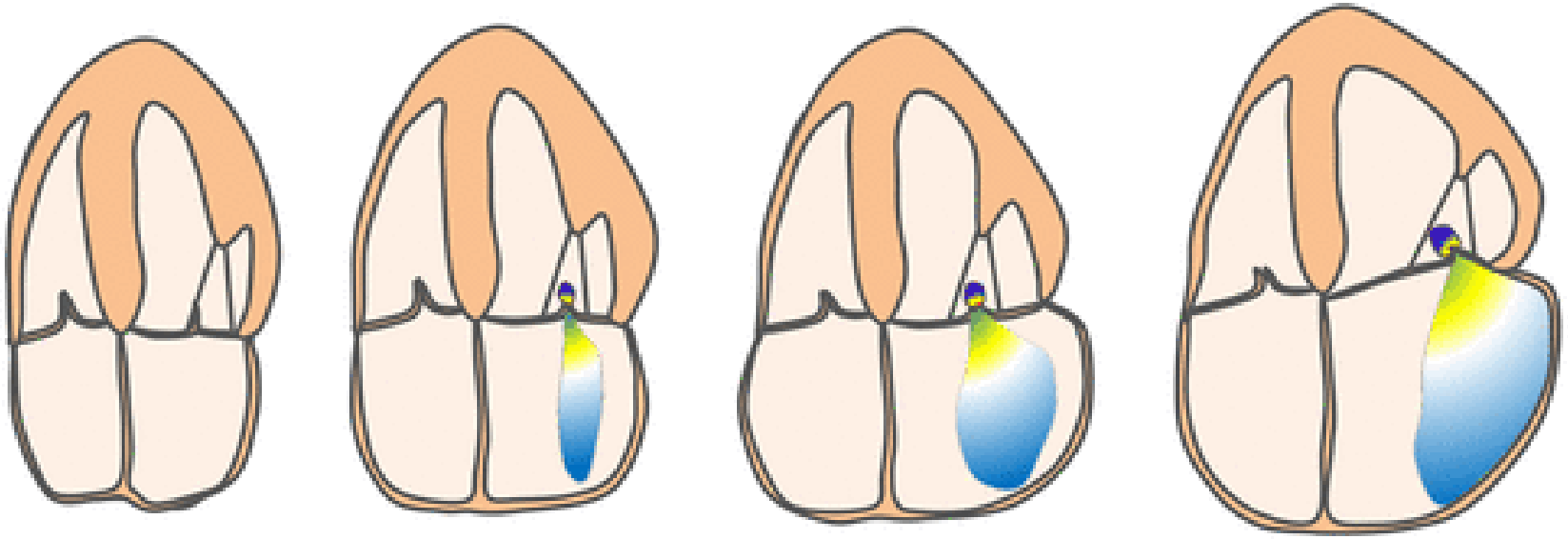
Class 2b

In patients with Afib, moderate to high risk of stroke and high risk for major bleeding, pLAAO may be a **reasonable alternative** to oral anticoagulation based on **patient preference**, with careful consideration of procedural risk and with the understanding the evidence for oral anticoagulation is more extensive

Circulation 2023, 147(4), e000-e000.

Brief Updates on Upcoming Percutaneous Valve Interventions

Sinus Rhythm → Atrial Fibrillation



LA and annular dilation
Leaflet expansion
Mild-moderate MR

reversible stage

Giant LA
Excessive annular dilation
Leaflet elongation
LV dilation
Severe MR

irreversible stage

Catheter Ablation

Circ Cardiovas Imaging.019;12:e009317

Treating Atrial Functional MR and TR and other etiologies…

- **Percutaneous Mitral Valve Repair/Replacement**
  - MitraClip offers mitral repair
    - COAPT Trial (HFrEF with function MR)
  - Several Percutaneous Mitral Valve REPLACEMENTS in clinical trial

- **Percutaneous Tricuspid Valve Repair/Replacement**
  - Tricuspid Clip offers tricuspid repair
    - TRILUMINATE Trial
  - EVOQUE Valve- Percutaneous Tricuspid Valve REPLACEMENT
    - TRISCEND II Trial

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