TEL AVIV UNIVERSITY אוניברסיטת תל אביב

האיגוד הישראלי לרפואה פנימית
ISRAEL SOCIETY OF INTERNAL MEDICINE

וולפסון. זה בית.
המרכז הרפואי האוניברסיטאי ע"ש אדית וולפסון

Cardiology – a year in review

Doron Menachemi MD

Director, Internal Medicine F

Heart Failure & Pulmonary Hypertension Service

E. Wolfson UMC

1 April 2022

OHIO STATE Medical Center

Disclosure- Speaker on behalf of

האיגוד הישראלי לרפואה פנימית
ISRAEL SOCIETY OF INTERNAL MEDICINE

Member

האיגוד הישראלי לרפואה פנימית
ISRAEL SOCIETY OF INTERNAL MEDICINE

Member

Member

החוג לאי ספיקת לב
THE ISRAEL WORKING GROUP ON HEART FAILURE

Member VHD council

EUROPEAN SOCIETY OF CARDIOLOGY®

Member Cardio-Oncology council

EUROPEAN SOCIETY OF CARDIOLOGY®

Member HRS & EHRA

EHRA

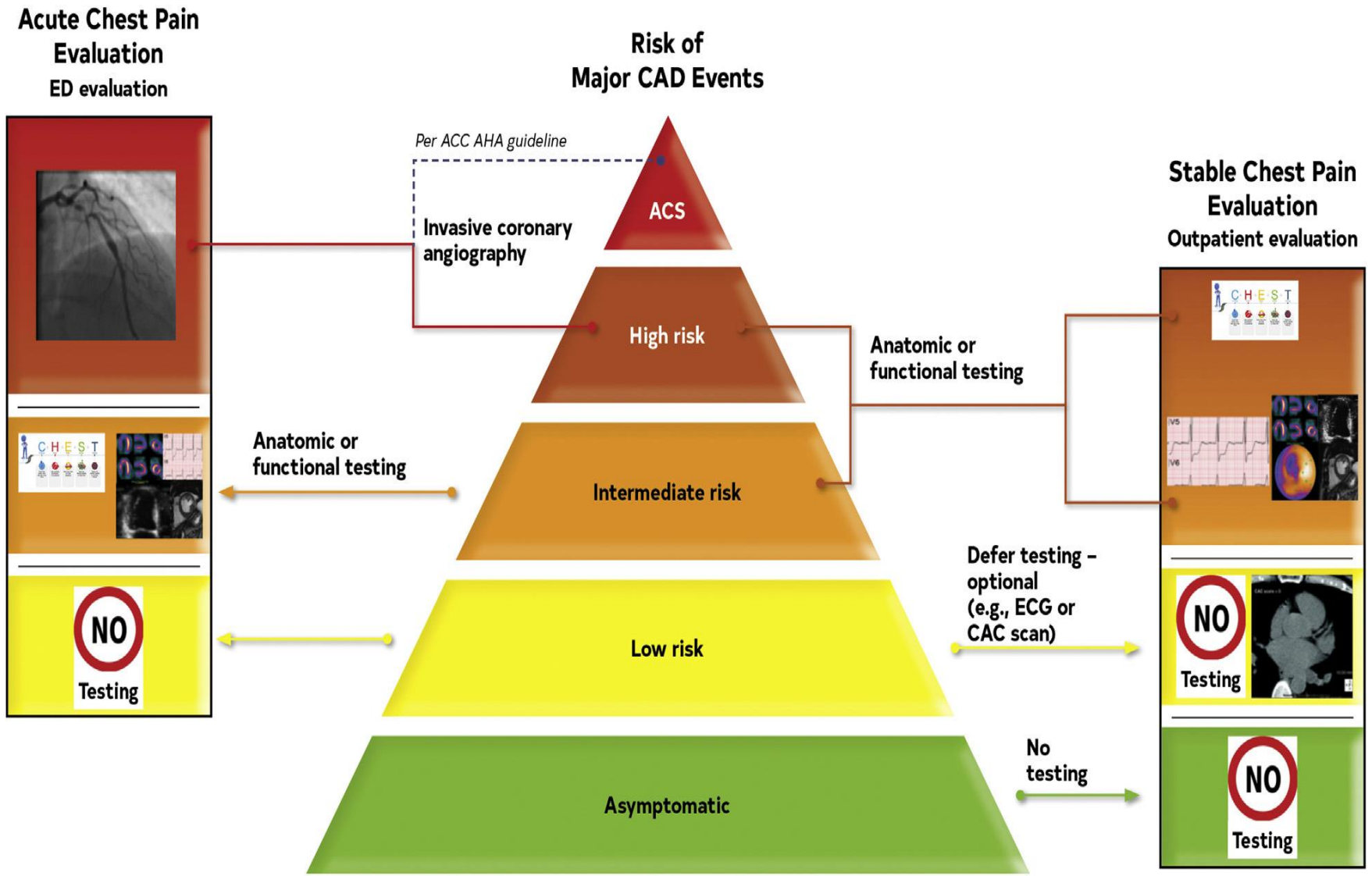
Subjects

- Guidelines- Chest pain management.
- New concept in Stable IHD & aggressive Lipid lowering treatment.
- Atrial Fibrillation- A. changing the paradigm.
  B. Silent CVA in AF.
- Interventional Cardiology.
- Valvular Heart Diseases- what's new in the guidelines?
- Cardiomyopaties- A. HCM
  B. ATTR-CMP
- Heart Failure – The 2021 new guidelines.
  The role of SGLT2Inh.
- New frontiers – Tele- Med & AI
- The GOLDEN BULT in Cardiology

Subjects

- Guidelines- Chest pain management.
- New concept in Stable IHD & aggressive Lipid lowering treatment.
- Atrial Fibrillation- A. changing the paradigm.
  B. Silent CVA in AF.
- Interventional Cardiology.
- Valvular Heart Diseases- what's new in the guidelines?
- Cardiomyopathies- A. HCM
  B. ATTR-CMP
- Heart Failure – The 2021 new guidelines.
  The role of SGLT2Inh.
- New frontiers – Tele- Med & AI
- The GOLDEN BULT in Cardiology

Chest Pain and Cardiac Testing Considerations



Pretest Probabilities of Obstructive CAD in Symptomatic Patients According to Age, Sex, and Symptoms

Pretest Probabilities of Obstructive CAD in Symptomatic Patients
(A) according to age, sex, and symptoms;
(B) according to age, sex, symptoms, and CAC

Age, y	Chest Pain		Dyspnea	
	Men	Women	Men	Women
30–39	≤4	≤5	0	3
40–49	≤22	≤10	12	3
50–59	≤32	≤13	20	9
60–69	≤44	≤16	27	14
70+	≤52	≤27	32	12

Juarez-Orozco et al. (1) and Winther et al. (2).

Subjects

✓Guidelines- Chest pain management.

- New concept in Stable IHD & aggressive Lipid lowering treatment.
- Atrial Fibrillation- A. changing the paradigm.
  B. Silent CVA in AF.
- Interventional Cardiology.
- Valvular Heart Diseases- what's new in the guidelines?
- Cardiomyopathies- A. HCM
  B. ATTR-CMP
- Heart Failure – The 2021 new guidelines.
  The role of SGLT2Inh.
- New frontiers – Tele- Med & AI
- The GOLDEN BULT in Cardiology

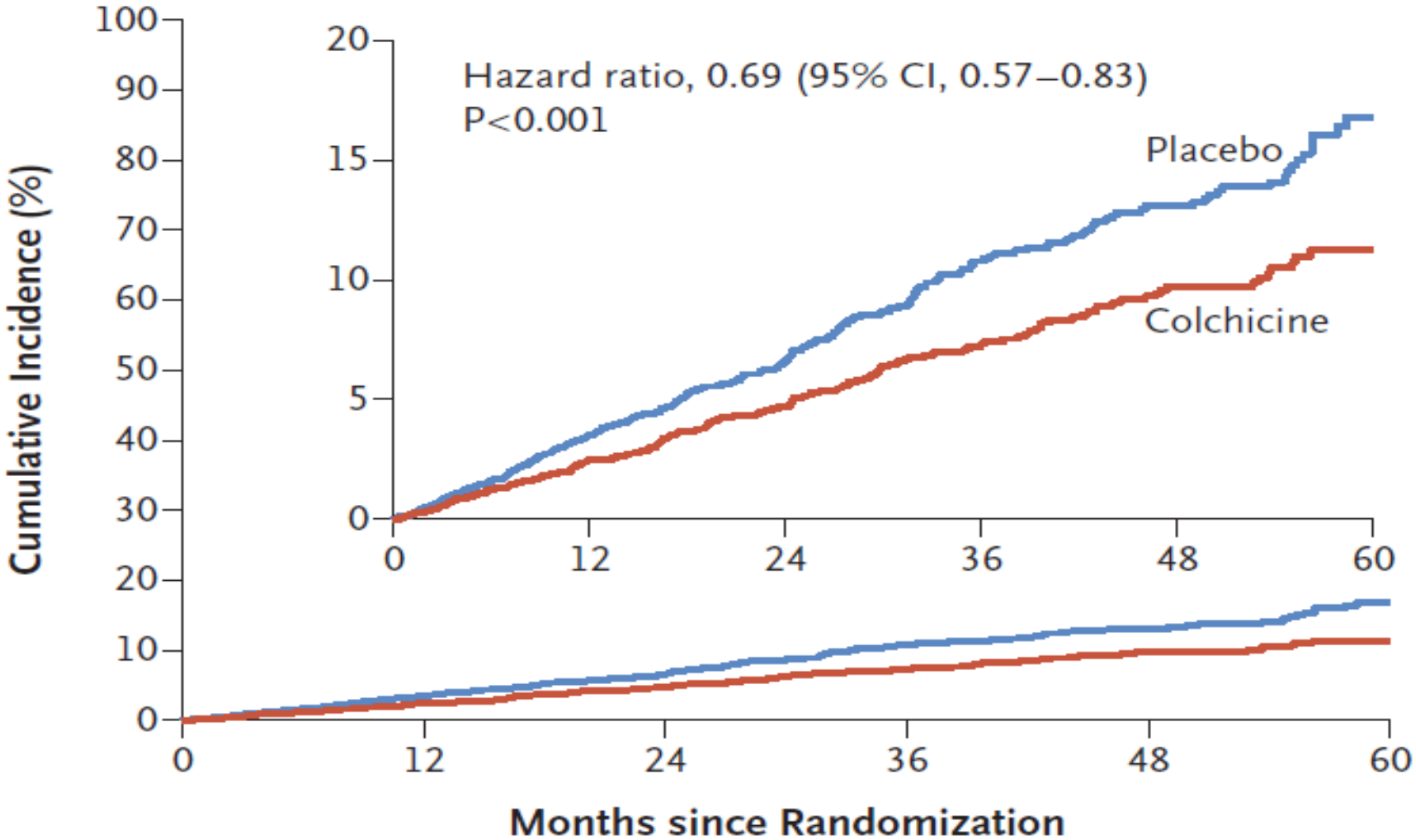
Colchicine in Patients with Chronic Coronary Disease

LoDoCo2 Australian New Zealand Clinical Trials

The NEW ENGLAND JOURNAL of MEDICINE

Characteristic	Colchicine (N = 2762)	Placebo (N = 2760)
Age — yr	65.8±8.4	65.9±8.7
Female sex — no. (%)	457 (16.5)	389 (14.1)
Country — no. (%)		
Australia	951 (34.4)	953 (34.5)
The Netherlands	1811 (65.6)	1807 (65.5)
Current smoker — no. (%)†	318 (11.5)	330 (12.0)
Hypertension — no. (%)	1421 (51.4)	1387 (50.3)
Diabetes — no. (%)		
Patients receiving any treatment for diabetes	492 (17.8)	515 (18.7)
Patients dependent on insulin	140 (5.1)	147 (5.3)
Renal function — no. (%)‡		
Stage 1 or 2	2614 (94.6)	2602 (94.3)
Stage 3a	148 (5.4)	158 (5.7)
Prior acute coronary syndrome — no. (%)	2323 (84.1)	2335 (84.6)
Time since last acute coronary syndrome — no. (%)		
≤24 mo	753 (27.3)	726 (26.3)
>24 mo	1570 (56.8)	1609 (58.3)
Prior coronary revascularization — no. (%)	2301 (83.3)	2320 (84.1)
Coronary-artery bypass grafting	319 (11.5)	391 (14.2)
Percutaneous coronary intervention	2100 (76.0)	2077 (75.3)
History of atrial fibrillation — no. (%)	332 (12.0)	317 (11.5)
History of gout — no. (%)	220 (8.0)	226 (8.2)
Medication use — no. (%)		
Single antiplatelet therapy	1849 (66.9)	1852 (67.1)
Dual antiplatelet therapy	638 (23.1)	642 (23.3)
Anticoagulant	342 (12.4)	330 (12.0)
No antiplatelet agent or anticoagulant	4 (0.1)	11 (0.4)
Statin	2594 (93.9)	2594 (94.0)
Ezetimibe	551 (19.9)	522 (18.9)
Any lipid-lowering agent	2670 (96.7)	2665 (96.6)
Renin–angiotensin inhibitor	1995 (72.2)	1965 (71.2)
Beta-blocker	1692 (61.3)	1735 (62.9)
Calcium-channel blocker	633 (22.9)	611 (22.1)

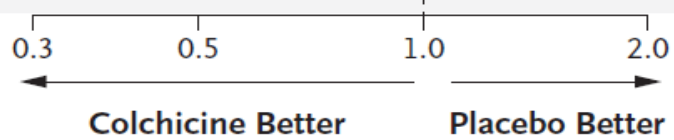
A Primary End Point



No. at Risk

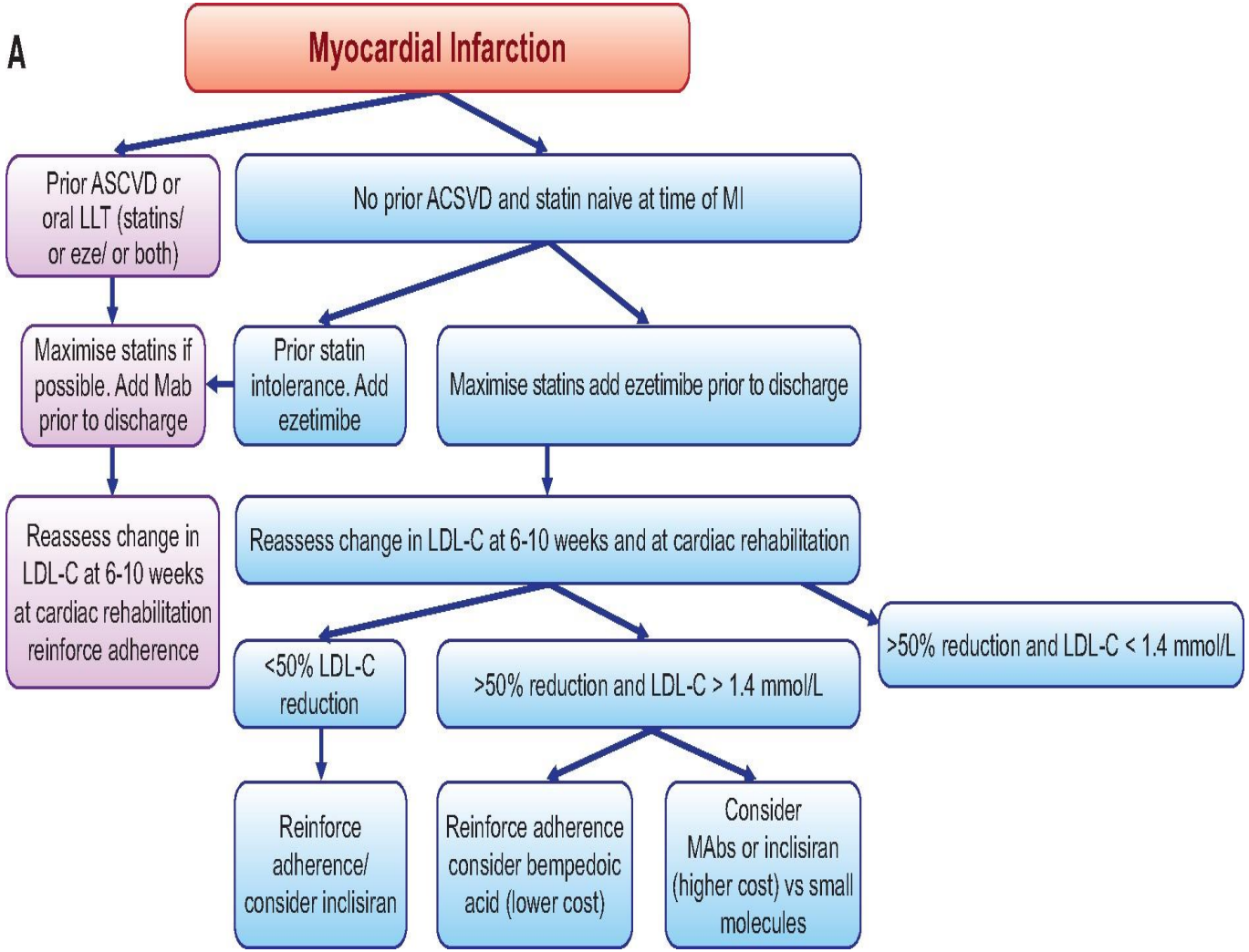
Placebo	2760	2655	1703	821	590	161
Colchicine	2762	2685	1761	890	629	166

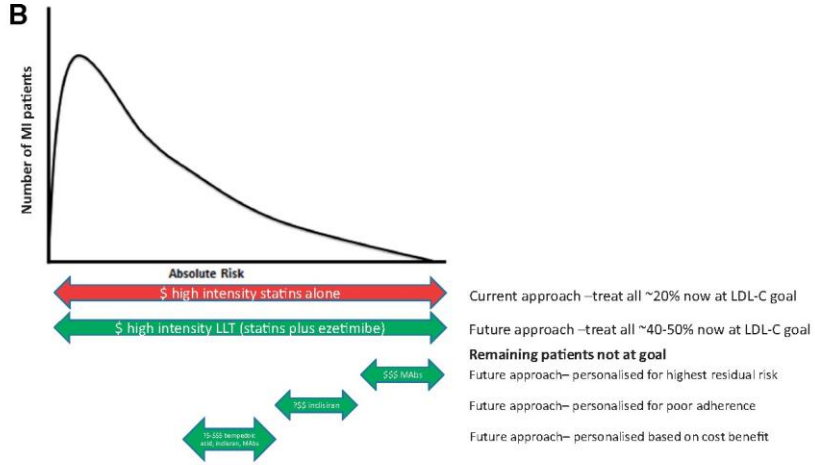
End Point	Colchicine (N=2762)		Placebo (N=2760)		Hazard Ratio (95% CI)	P Value
	no. of patients (%)	*no. of events/100 person-yr*	*no. of patients (%)*	*no. of events/100 person-yr*		
Primary end point						
Cardiovascular death, myocardial infarction, ischemic stroke, or ischemia-driven coronary revascularization	187 (6.8)	2.5	264 (9.6)	3.6	0.69 (0.57–0.83)	<0.001
Secondary end points in ranked order						
Cardiovascular death, myocardial infarction, or ischemic stroke	115 (4.2)	1.5	157 (5.7)	2.1	0.72 (0.57–0.92)	0.007
Myocardial infarction or ischemia-driven coronary revascularization	155 (5.6)	2.1	224 (8.1)	3.0	0.67 (0.55–0.83)	<0.001
Cardiovascular death or myocardial infarction	100 (3.6)	1.3	138 (5.0)	1.8	0.71 (0.55–0.92)	0.01
Ischemia-driven coronary revascularization	135 (4.9)	1.8	177 (6.4)	2.4	0.75 (0.60–0.94)	0.01
Myocardial infarction	83 (3.0)	1.1	116 (4.2)	1.5	0.70 (0.53–0.93)	0.01
Ischemic stroke	16 (0.6)	0.2	24 (0.9)	0.3	0.66 (0.35–1.25)	0.20
Death from any cause	73 (2.6)	0.9	60 (2.2)	0.8	1.21 (0.86–1.71)	
Cardiovascular death	20 (0.7)	0.3	25 (0.9)	0.3	0.80 (0.44–1.44)	
Additional end points						
The primary end point in the first LoDoCo trial	201 (7.3)	2.7	290 (10.5)	4.0	0.67 (0.56–0.81)	
New onset or first recurrence in atrial fibrillation or atrial flutter	126 (4.6)	1.7	148 (5.4)	2.0	0.84 (0.66–1.07)	
Deep-vein thrombosis or pulmonary embolism or both	17 (0.6)	0.2	16 (0.6)	0.2	1.06 (0.53–2.10)	
Any myocardial infarctions	85 (3.1)	1.1	117 (4.2)	1.5	0.72 (0.54–0.95)	
New-onset diabetes	34 (1.2)	—	49 (1.8)	—	0.69 (0.44–1.06)	

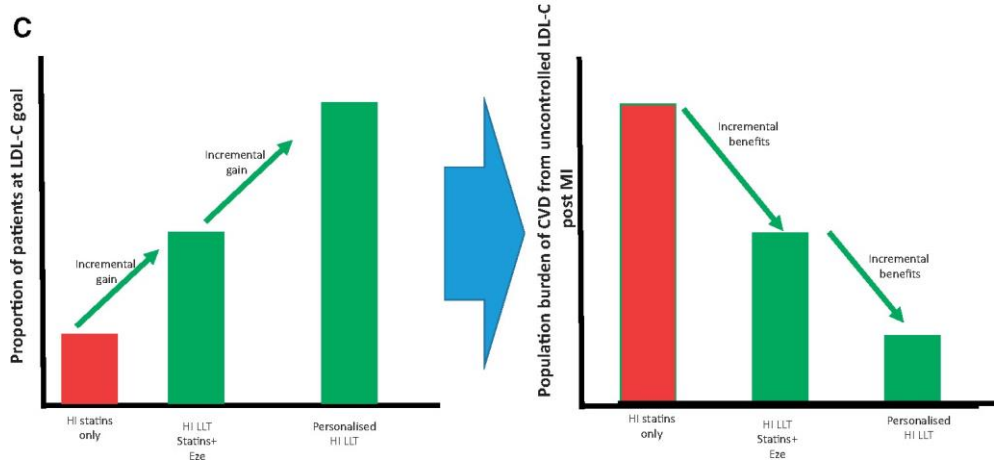


In a randomized trial involving patients with chronic coronary disease, the risk of cardiovascular events was significantly lower among those who received **0.5 mg of colchicine once daily** than among those who received placebo.

Improving population level LDL-C goal attainment through a personalized approach to intensive LDL-C lowering.







Eur Heart J, Volume 42, Issue 3, 14 January 2021, Pages 253–256,
Eur Heart J, Volume 42, Issue 3, 14 January 2021, Pages 253–256

Subjects

✓Guidelines- Chest pain management.

✓New concept in Stable IHD & aggressive Lipid lowering treatment.

- Atrial Fibrillation- A. changing the paradigm.
  B. Silent CVA in AF.
- Interventional Cardiology.
- Valvular Heart Diseases- what's new in the guidelines?
- Cardiomyopathies- A. HCM
  B. ATTR-CMP
- Heart Failure – The 2021 new guidelines.
  The role of SGLT2Inh.
- New frontiers – Tele- Med & AI
- The GOLDEN BULT in Cardiology

2020 ESC Guidelines

ESC European Society of Cardiology

European Heart Journal (2020) **00**, 1–125
doi:10.1093/eurheartj/ehaa612

ESC GUIDELINES

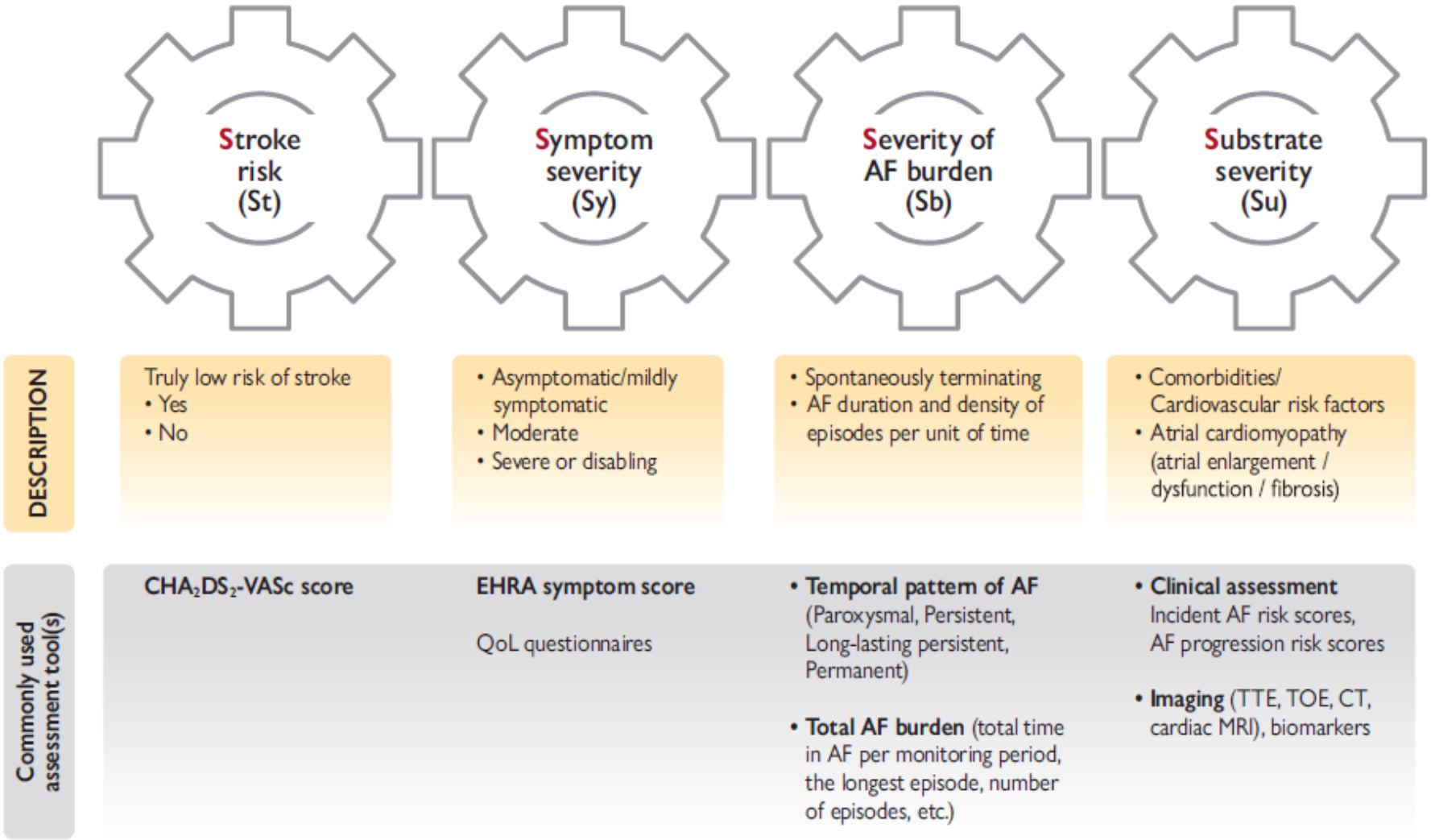
2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association of Cardio-Thoracic Surgery (EACTS)

The Task Force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC)

Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC

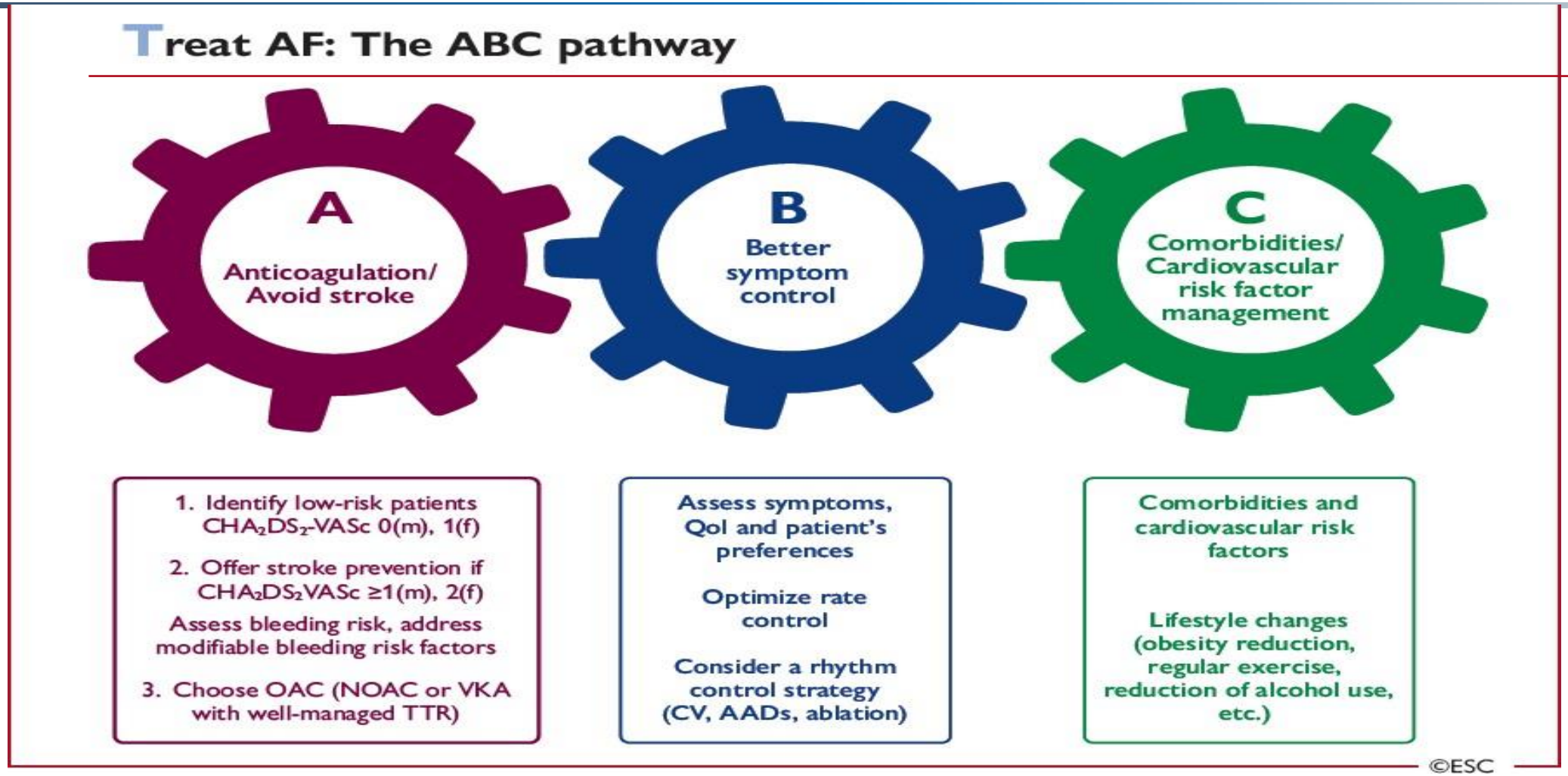
Authors/Task Force Members: Gerhard Hindricks* (Chairperson) (Germany), Tatjana Potpara* (Chairperson) (Serbia), Nikolaos Dagres (Germany), Elena Arbelo (Spain), Jeroen J. Bax (Netherlands), Carina Blomström-Lundqvist (Sweden), Giuseppe Boriani (Italy), Manuel Castella[1] (Spain), Gheorghe-Andrei Dan (Romania), Polychronis E. Dilaveris (Greece), Laurent Fauchier (France), Gerasimos Filippatos (Greece), Jonathan M. Kalman (Australia), Mark La Meir[1]

4S-AF scheme as an example of structured characterization of AF



Gerhard Hindricks, Tatjana Potpara, Gregory Y H Lip et al, 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association of Cardio-Thoracic Surgery (EACTS): The Task Force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC) Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC, European Heart Journal, , ehaa612, https://doi.org/10.1093/eurheartj/ehaa612

Management of AF (2)



Gerhard Hindricks, Tatjana Potpara, Gregory Y H Lip et al, 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association of Cardio-Thoracic Surgery (EACTS): The Task Force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC) Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC, European Heart Journal, , ehaa612, https://doi.org/10.1093/eurheartj/ehaa612

Recommendations for the prevention of thromboembolic events in AF

Recommendations	Class	Level
For stroke prevention in AF patients who are eligible for OAC, NOACs are recommended in preference to VKAs (excluding patients with mechanical heart valves or moderate-to-severe mitral stenosis).	I	A
For stroke risk assessment, a risk-factor–based approach is recommended, using the CHA_2DS_2-VASc clinical stroke risk score to initially identify patients at 'low stroke risk' (CHA_2DS_2-VASc score = 0 in men, or 1 in women) who should not be offered antithrombotic therapy.	I	A
OAC is recommended for stroke prevention in AF patients with CHA_2DS_2-VASc score ≥2 in men or ≥3 in women.	I	A

Gerhard Hindricks, Tatjana Potpara, Gregory Y H Lip et al, 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association of Cardio-Thoracic Surgery (EACTS): The Task Force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC) Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC, European Heart Journal, , ehaa612, https://doi.org/10.1093/eurheartj/ehaa612

Better Symptom Control

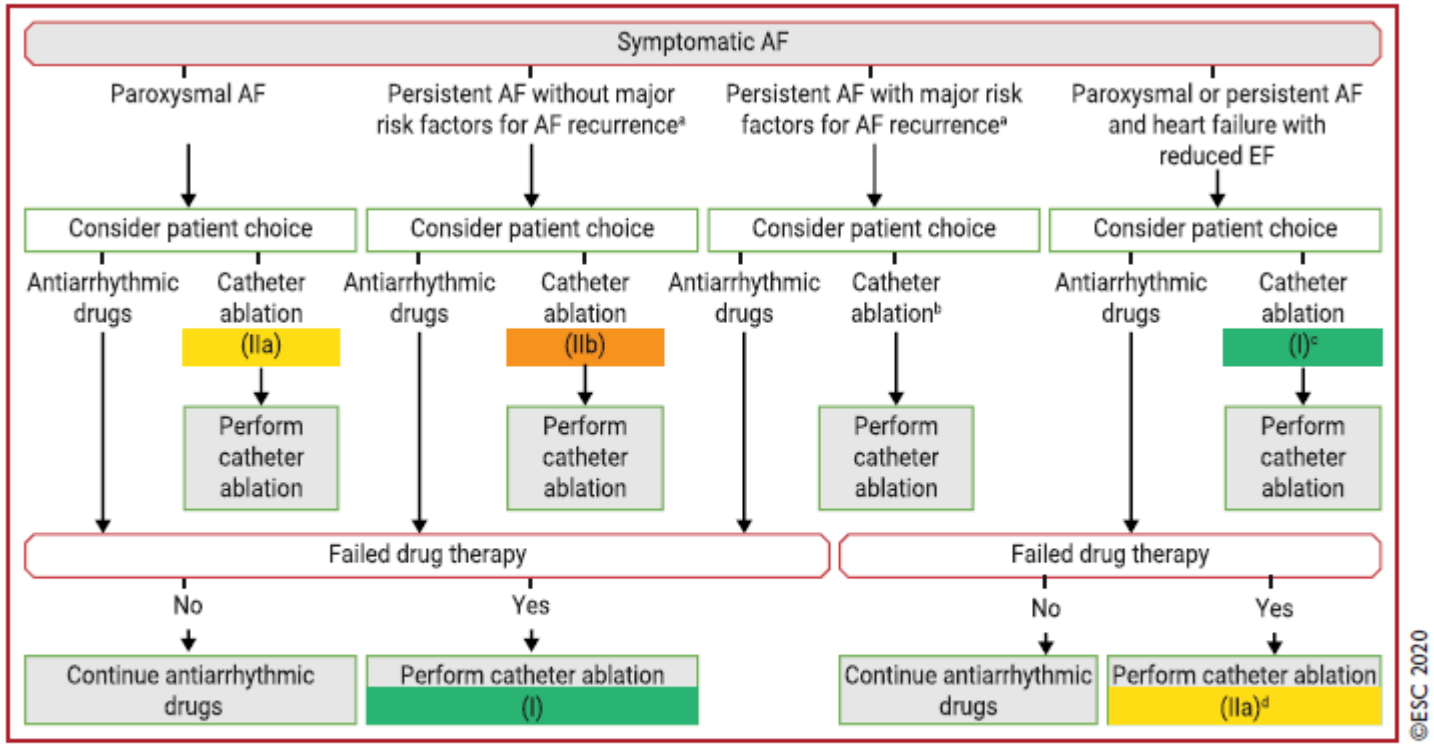


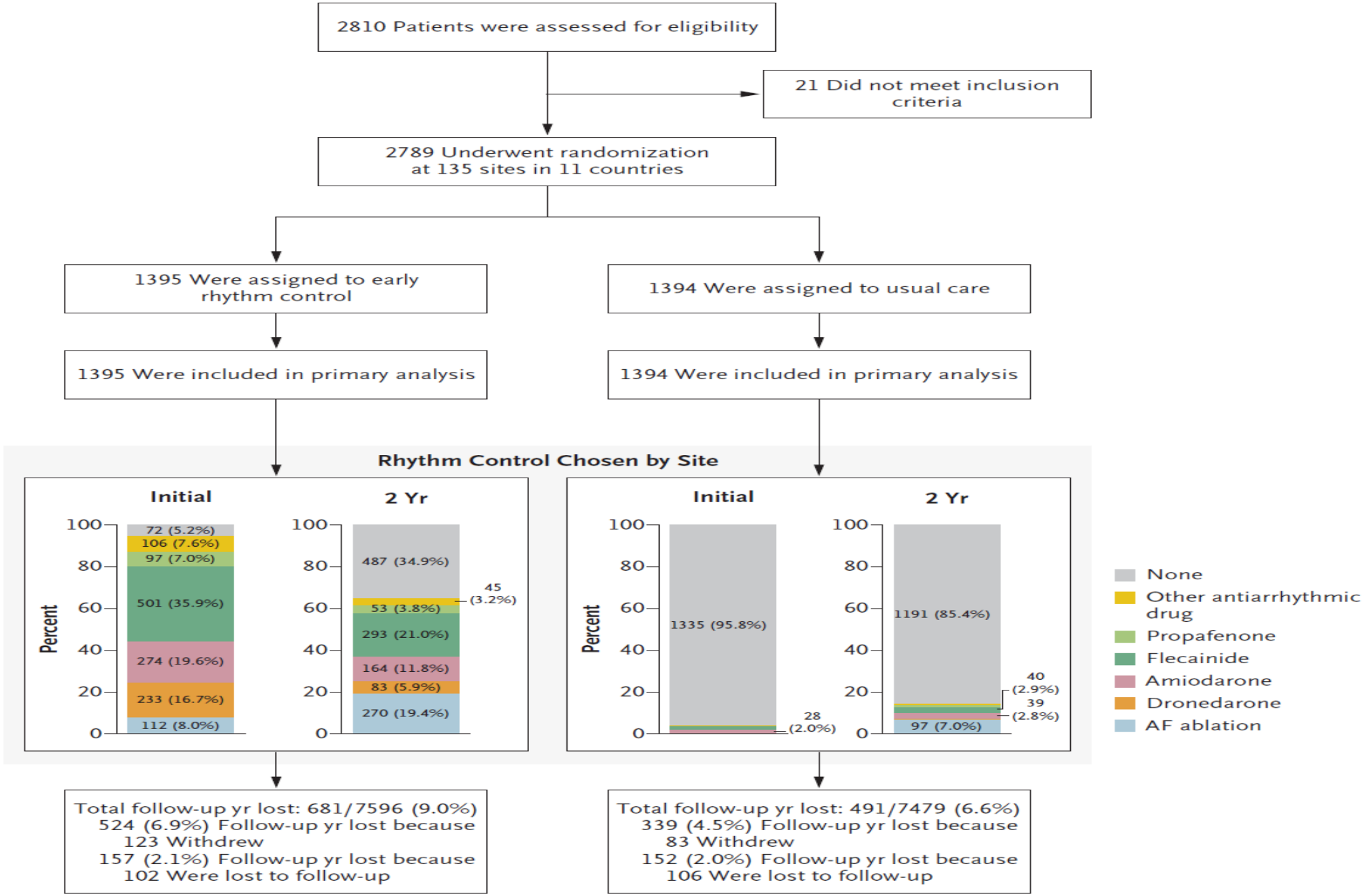
Figure 17 Indications for catheter ablation of symptomatic AF. The arrows from AAD to ablation indicate failed drug therapy. AAD = antiarrhythmic drug; AF = atrial fibrillation; EF = ejection fraction; LA = left atrial. [a]Significantly enlarged LA volume, advanced age, long AF duration, renal dysfunction, and other cardiovascular risk factors. [b]In rare individual circumstances, catheter ablation may be carefully considered as first-line therapy. [c]Recommended to reverse LV dysfunction when tachycardiomyopathy is highly probably. [d]To improve survival and reduce hospitalization.

Figure 18 Risk factors for AF contributing to the development of an abnormal substrate translating into poorer outcomes with rhythm control strategies. AF = atrial fibrillation; BMI = body mass index; CPAP = continuous positive airway pressure; HbA_{1C} = haemoglobin A1c; OSA = obstructive sleep apnoea. Several AF risk factors may contribute to the development of LA substrates and thus affect the outcome of AF catheter ablation, predisposing to a higher recurrence rate. Aggressive control of modifiable risk factors may reduce recurrence rate.

Gerhard Hindricks, Tatjana Potpara, Gregory Y H Lip et al, 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association of Cardio-Thoracic Surgery (EACTS): The Task Force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC) Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC, European Heart Journal, , ehaa612, https://doi.org/10.1093/eurheartj/ehaa612

The NEW ENGLAND JOURNAL of MEDICINE

Early Rhythm-Control Therapy in Patients with Atrial Fibrillation

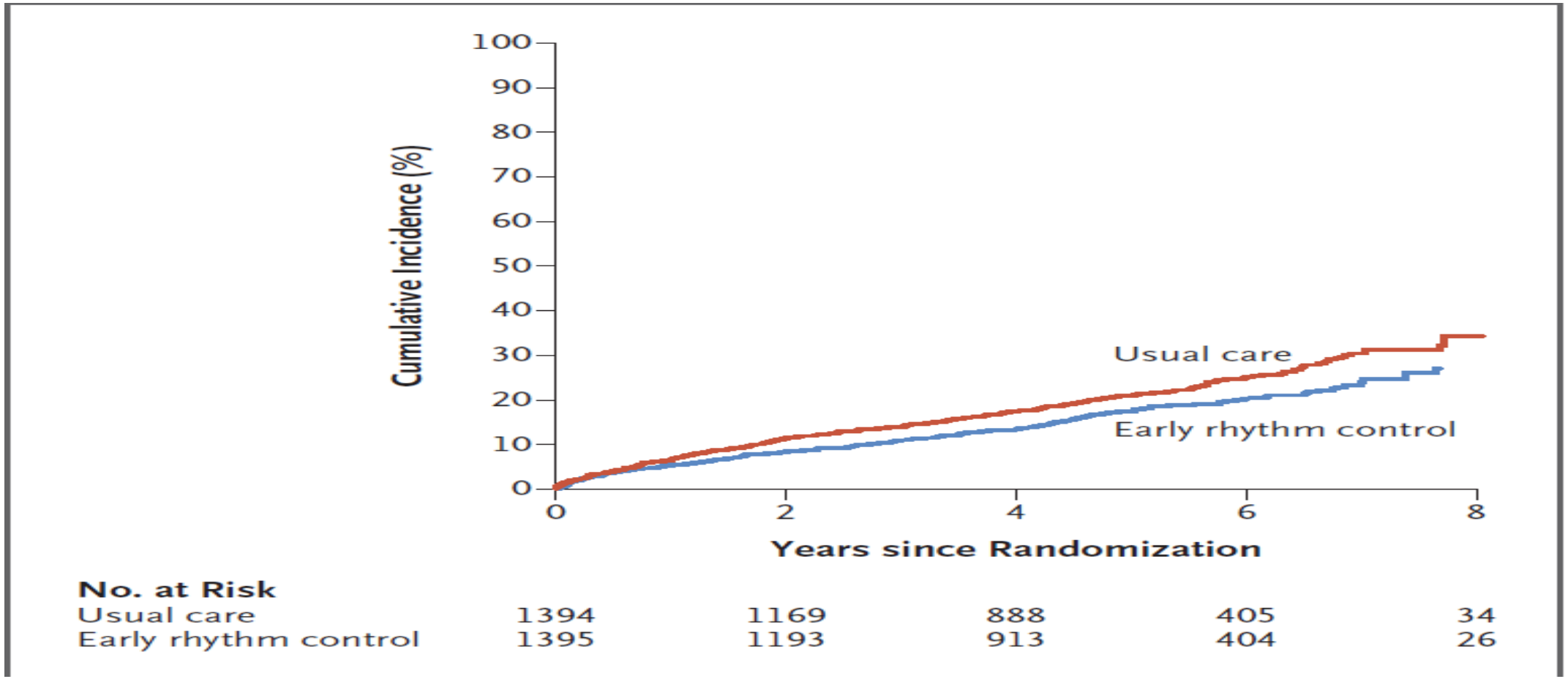

2810 Patients were assessed for eligibility
21 Did not meet inclusion criteria
2789 Underwent randomization at 135 sites in 11 countries
1395 Were assigned to early rhythm control
1394 Were assigned to usual care
1395 Were included in primary analysis
1394 Were included in primary analysis
Rhythm Control Chosen by Site
Initial
2 Yr
Percent
72 (5.2%)
106 (7.6%)
97 (7.0%)
501 (35.9%)
274 (19.6%)
233 (16.7%)
112 (8.0%)
487 (34.9%)
45 (3.2%)
53 (3.8%)
293 (21.0%)
164 (11.8%)
83 (5.9%)
270 (19.4%)
1335 (95.8%)
28 (2.0%)
1191 (85.4%)
40 (2.9%)
39 (2.8%)
97 (7.0%)
None
Other antiarrhythmic drug
Propafenone
Flecainide
Amiodarone
Dronedarone
AF ablation
Total follow-up yr lost: 681/7596 (9.0%)
524 (6.9%) Follow-up yr lost because
123 Withdrew
157 (2.1%) Follow-up yr lost because
102 Were lost to follow-up
Total follow-up yr lost: 491/7479 (6.6%)
339 (4.5%) Follow-up yr lost because
83 Withdrew
152 (2.0%) Follow-up yr lost because
106 Were lost to follow-up

Outcomes

Table 2. Efficacy Outcomes.*

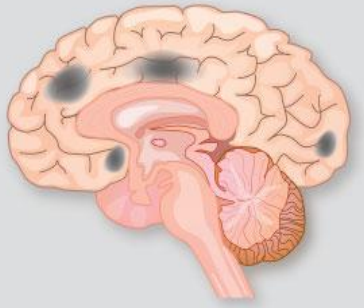
Outcome	Early Rhythm Control	Usual Care	Treatment Effect
First primary outcome — events/person-yr (incidence/100 person-yr)	249/6399 (3.9)	316/6332 (5.0)	0.79 (0.66 to 0.94)†
Components of first primary outcome — events/person-yr (incidence/100 person-yr)			
Death from cardiovascular causes	67/6915 (1.0)	94/6988 (1.3)	0.72 (0.52 to 0.98)‡
Stroke	40/6813 (0.6)	62/6856 (0.9)	0.65 (0.44 to 0.97)‡
Hospitalization with worsening of heart failure	139/6620 (2.1)	169/6558 (2.6)	0.81 (0.65 to 1.02)‡
Hospitalization with acute coronary syndrome	53/6762 (0.8)	65/6816 (1.0)	0.83 (0.58 to 1.19)‡
Second primary outcome — nights spent in hospital/yr	5.8±21.9	5.1±15.5	1.08 (0.92 to 1.28)§
Key secondary outcomes at 2 yr			
Change in left ventricular ejection fraction — %	1.5±9.8	0.8±9.8	0.23 (–0.46 to –0.91)¶
Change in EQ-5D score‖	–1.0±21.4	–2.7±22.3	1.07 (–0.68 to 2.82)¶
Change in SF-12 Mental Score**	0.7±10.6	1.6±10.1	–1.20 (–2.04 to –0.37)¶
Change in SF-12 Physical Score**	0.3±8.5	0.1±8.2	0.33 (–0.39 to 1.06)¶
Change in MoCA score	0.1±3.3	0.1±3.2	–0.14 (–0.39 to 0.12)¶
Sinus rhythm — no. of patients with feature/total no. (%)	921/1122 (82.1)	687/1135 (60.5)	3.13 (2.55 to 3.84)††
Asymptomatic — no. of patients with feature/total no. (%)‡‡	861/1159 (74.3)	850/1171 (72.6)	1.14 (0.93 to 1.40)††

Conclusions- Early rhythm-control therapy was associated with a lower risk of cardiovascular outcomes than usual care among patients with early atrial fibrillation and cardiovascular conditions



Brain Damage and Change in Cognitive Function in Patients with Atrial Fibrillation

BASELINE

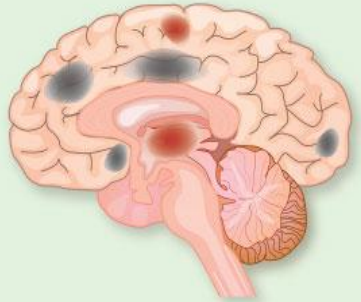


Patients with atrial fibrillation:

- n=1227
- Mean age : 71 years
- OAC: 90%
- History of stroke /TIA: 19%

Standardized brain MRI
&
Cognitive testing

2 YEAR FOLLOW-UP



New brain lesions:

- 2.3% new clinical stroke /TIA
- 5.5% new brain infarcts on MRI (88 % on OAC, 85 % silent)

Cognitive decline in patients with new overt or silent brain infarcts

Silent brain infarcts impact on cognitive function in atrial fibrillation

Incidence of Stroke is Directly Dependent on Diagnostic Methods Used and Traditional Stroke Symptoms Correlate Inconsistently with Infarcts on MRI

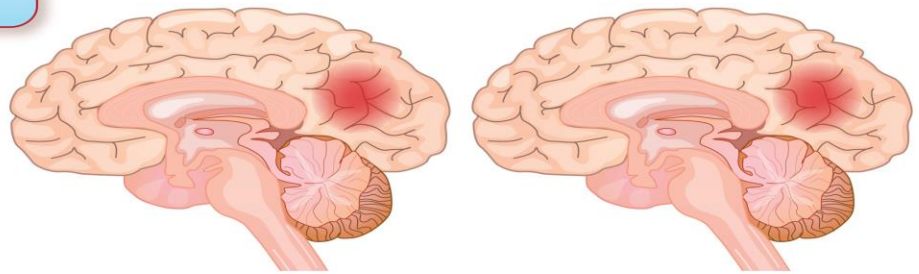
Different Viewpoints/Perspectives

Clinical Stroke/TIA Symptoms at 2 years → 2.3% Incidence

Brain MRI at 2 Years → 5.5% Incidence

2.4x Increase

Are "Silent" Strokes Really Silent?



Traditional Clinical Symptoms

No Traditional Clinical Symptoms

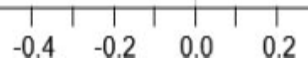
Deficiencies of cognitive operations, semantic memory, language production and mental flexibility are present with testing at 2 years

Brain Injury in Patients with Atrial Fibrillation

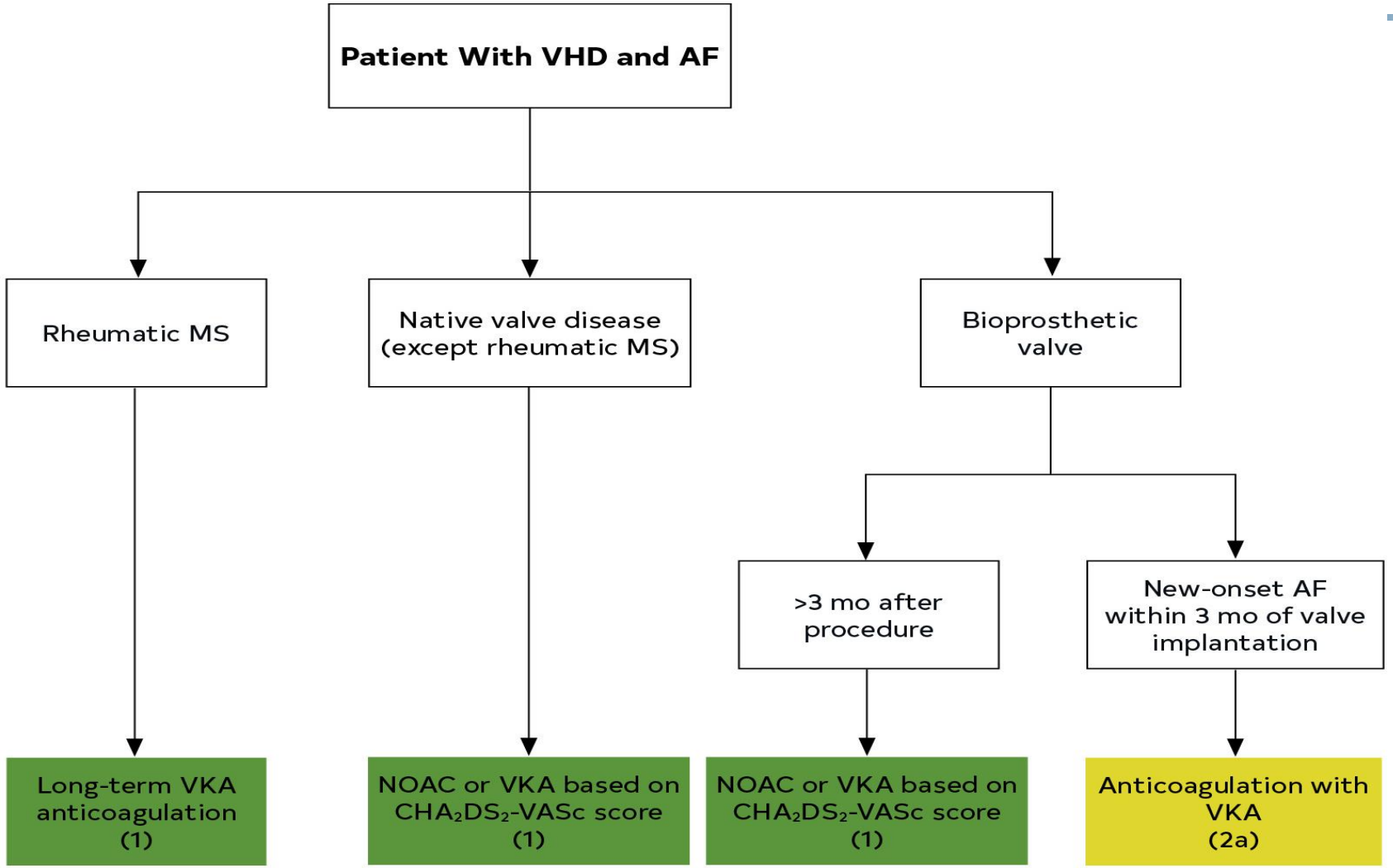
1. "Clinical" Stroke/TIA diagnosis significantly underestimated incidence
2. "Silent" Strokes is a misnomer and these infarcts impact function when targeted testing is used

Eur Heart J, ehab900, https://doi.org/10.1093/eurheartj/ehab900

Predictor	Estimate (95% CI)	p-value
Baseline CoCo score	−0·09 (−0·13; −0·05)	<0·001
Age; per 10 years	−0·08 (−0·11; −0·06)	<0·001
Female sex	0·01 (−0·03; 0·05)	0·682
Medium education	0·02 (−0·03; 0·07)	0·439
High education	0·04 (−0·01; 0·10)	0·129
New overt SNCI/LNCCI	−0·23 (−0·44; −0·01)	0·042
Volume of new overt SNCI/LNCCI	−0·01 (−0·09; 0·07)	0·829
New silent SNCI/LNCCI	−0·14 (−0·21; −0·06)	<0·001
Volume of new silent SNCI/LNCCI	0·01 (−0·04; 0·07)	0·654
New white matter lesions	−0·02 (−0·06; 0·02)	0·273
Volume of new white matter lesions	−0·01 (−0·04; 0·01)	0·317
New microbleeds	0·02 (−0·03; 0·07)	0·374



2020 ACC/AHA Guideline for the Management of Patients With Valvular Heart Disease

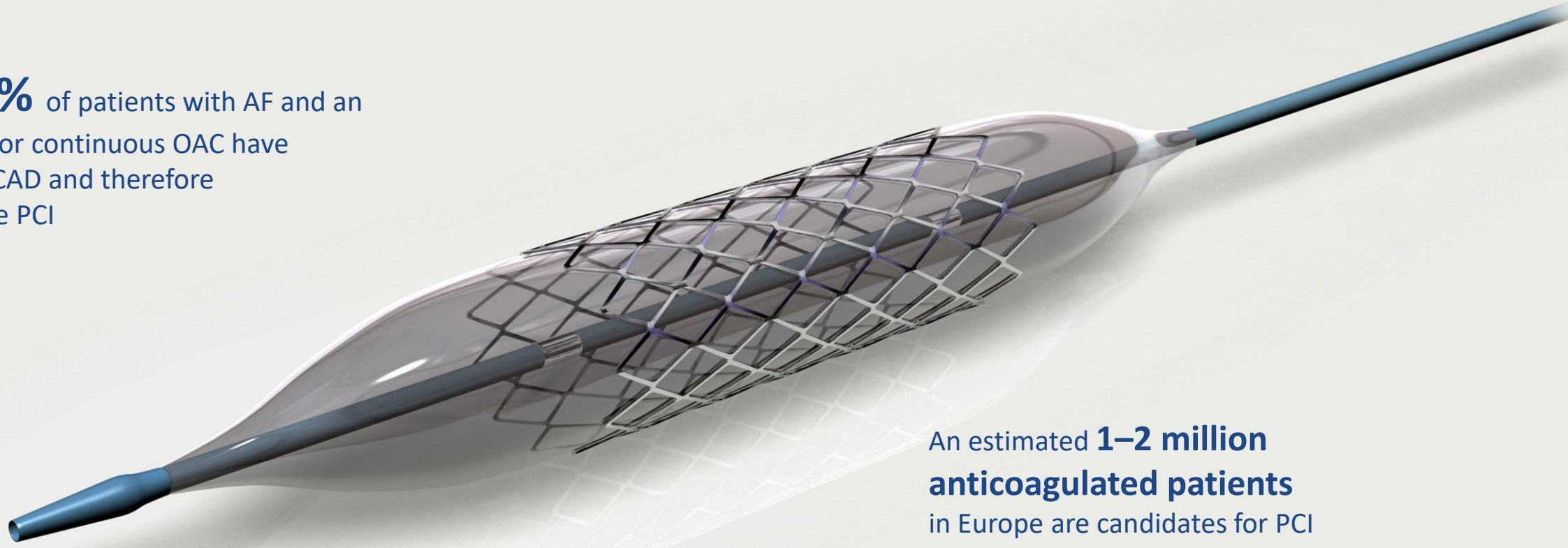


Subjects

- ✓Guidelines- Chest pain management.
- ✓New concept in Stable IHD & aggressive Lipid lowering treatment.
- ✓Atrial Fibrillation- A. changing the paradigm.
- ✓ B. Silent CVA in AF.
- Interventional Cardiology.
- Valvular Heart Diseases- what's new in the guidelines?
- Cardiomyopathies- A. HCM
  B. ATTR-CMP
- Heart Failure – The 2021 new guidelines.
  The role of SGLT2Inh.
- New frontiers – Tele- Med & AI
- The GOLDEN BULT in Cardiology

There is an unmet need in the management of patients with AF undergoing PCI

20–30% of patients with AF and an indication for continuous OAC have coexisting CAD and therefore may require PCI

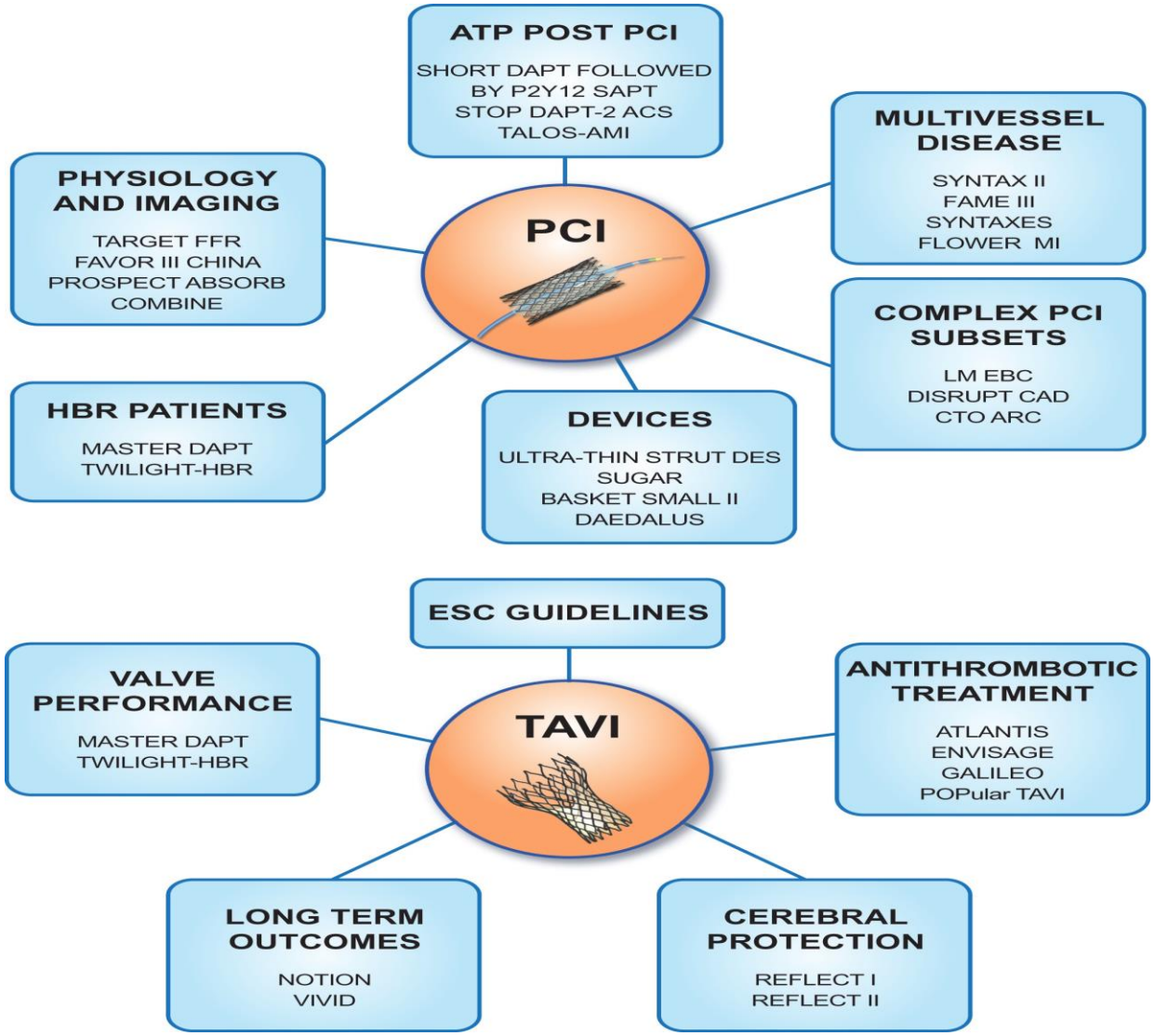


An estimated **1–2 million anticoagulated patients** in Europe are candidates for PCI procedures

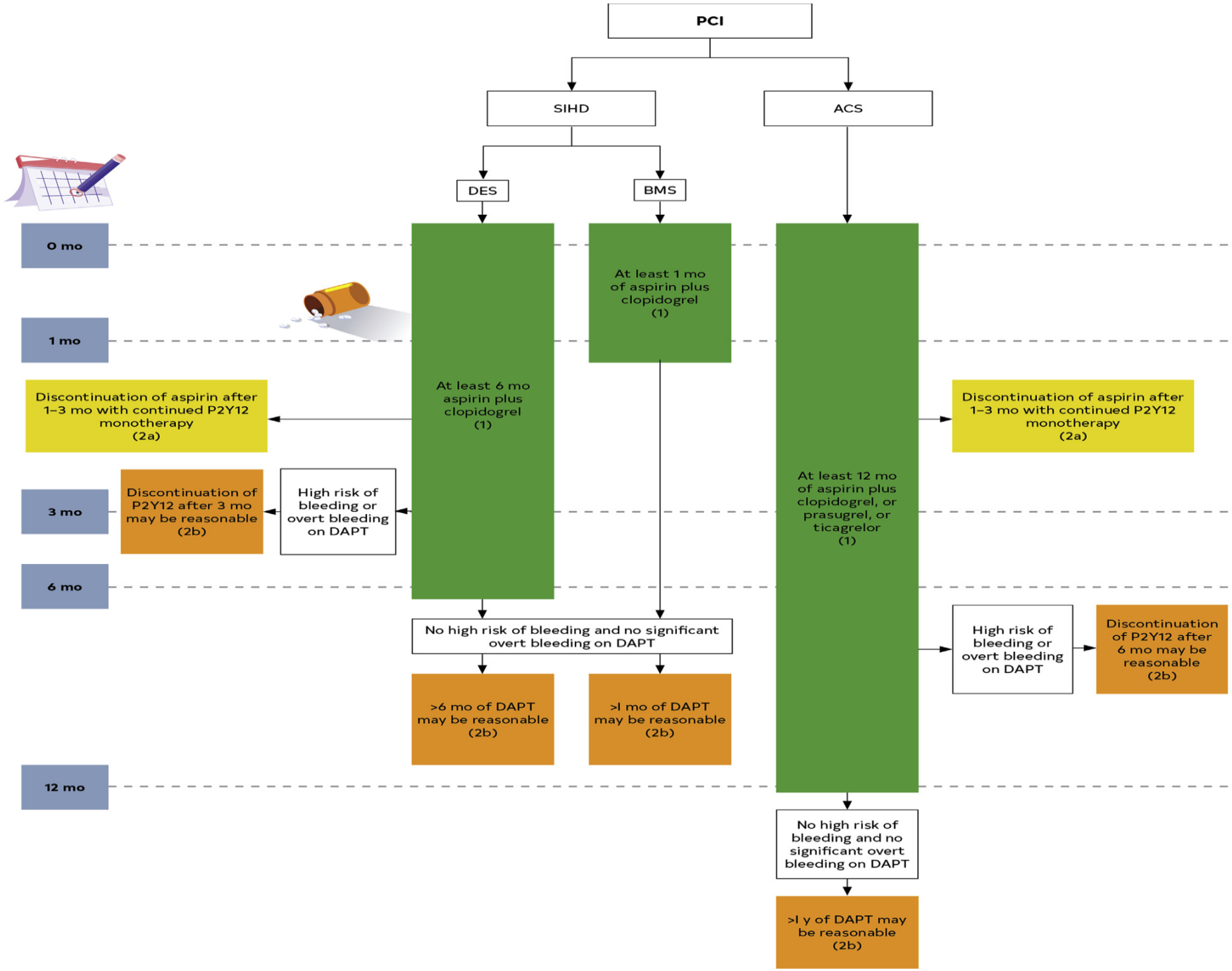
Stenting requires follow-up treatment with antiplatelets, which puts anticoagulated patients at **higher risk of bleeding**

CAD, coronary artery disease; PCI, percutaneous coronary intervention; Lip et al. Thromb Haemost 2010

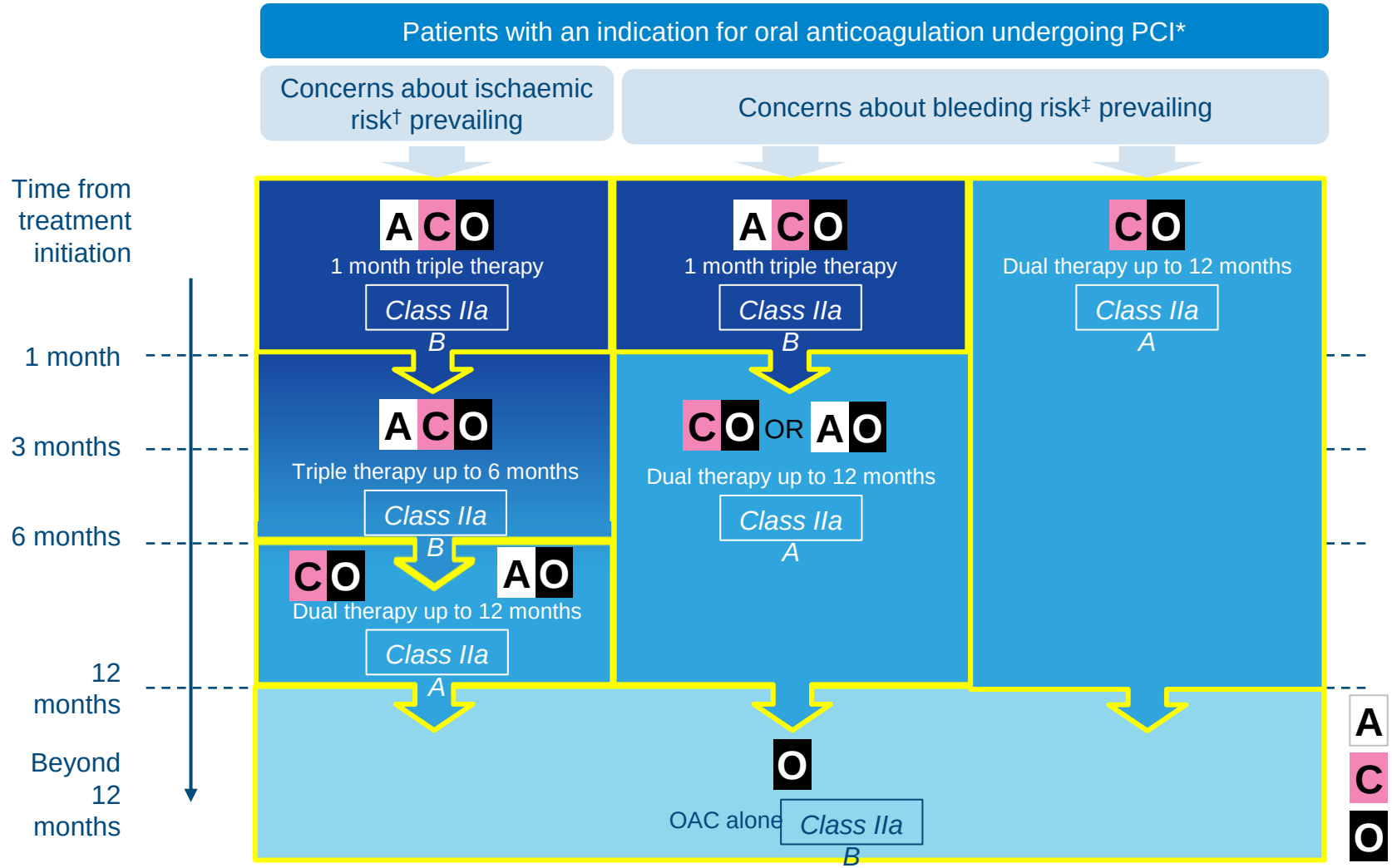
Interventional Cardiology 2021 summary



Eur Heart J, Volume 43, Issue 5, 1 February 2022, Pages 377–386


PCI
SIHD
ACS
DES
BMS
0 mo
1 mo
3 mo
6 mo
12 mo
At least 1 mo of aspirin plus clopidogrel (1)
At least 6 mo aspirin plus clopidogrel (1)
At least 12 mo of aspirin plus clopidogrel, or prasugrel, or ticagrelor (1)
Discontinuation of aspirin after 1–3 mo with continued P2Y12 monotherapy (2a)
Discontinuation of aspirin after 1–3 mo with continued P2Y12 monotherapy (2a)
High risk of bleeding or overt bleeding on DAPT
Discontinuation of P2Y12 after 3 mo may be reasonable (2b)
No high risk of bleeding and no significant overt bleeding on DAPT
High risk of bleeding or overt bleeding on DAPT
Discontinuation of P2Y12 after 6 mo may be reasonable (2b)
>6 mo of DAPT may be reasonable (2b)
>I mo of DAPT may be reasonable (2b)
No high risk of bleeding and no significant overt bleeding on DAPT
>I y of DAPT may be reasonable (2b)

ESC focused update recommends dual or triple therapy after PCI with stent depending on individual patient risk factors

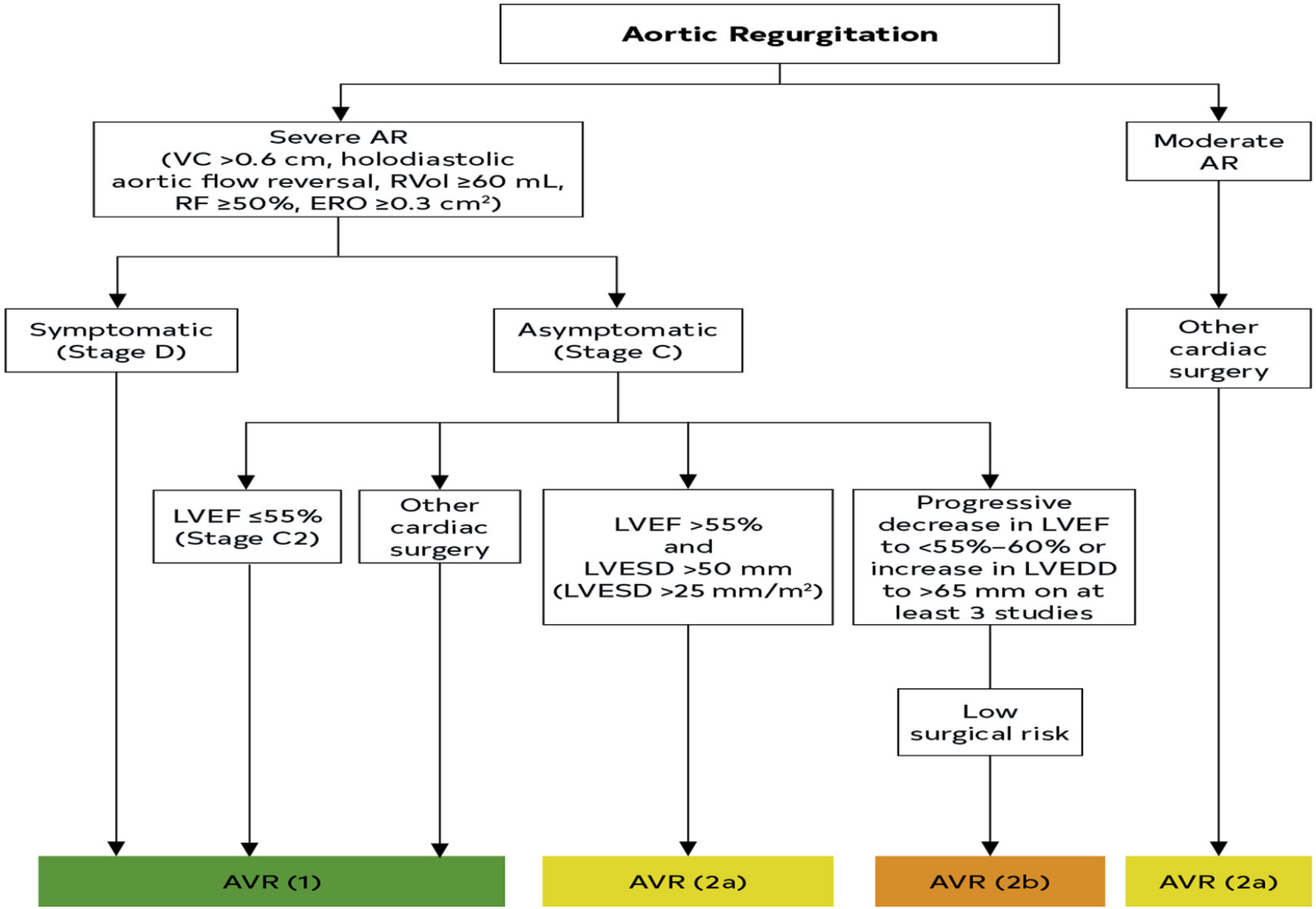


1. Peri-procedural administration of aspirin and clopidogrel during PCI is recommended irrespective of the treatment strategy; 2. High ischemic risk is considered as an acute clinical presentation or anatomical/procedural features which might increase the risk for myocardial infarction; 3. Bleeding risk can be estimated by HAS-BLED or ABC score. Valgimigli et al. Eur J Cardio-Thoracic Surgery 2017

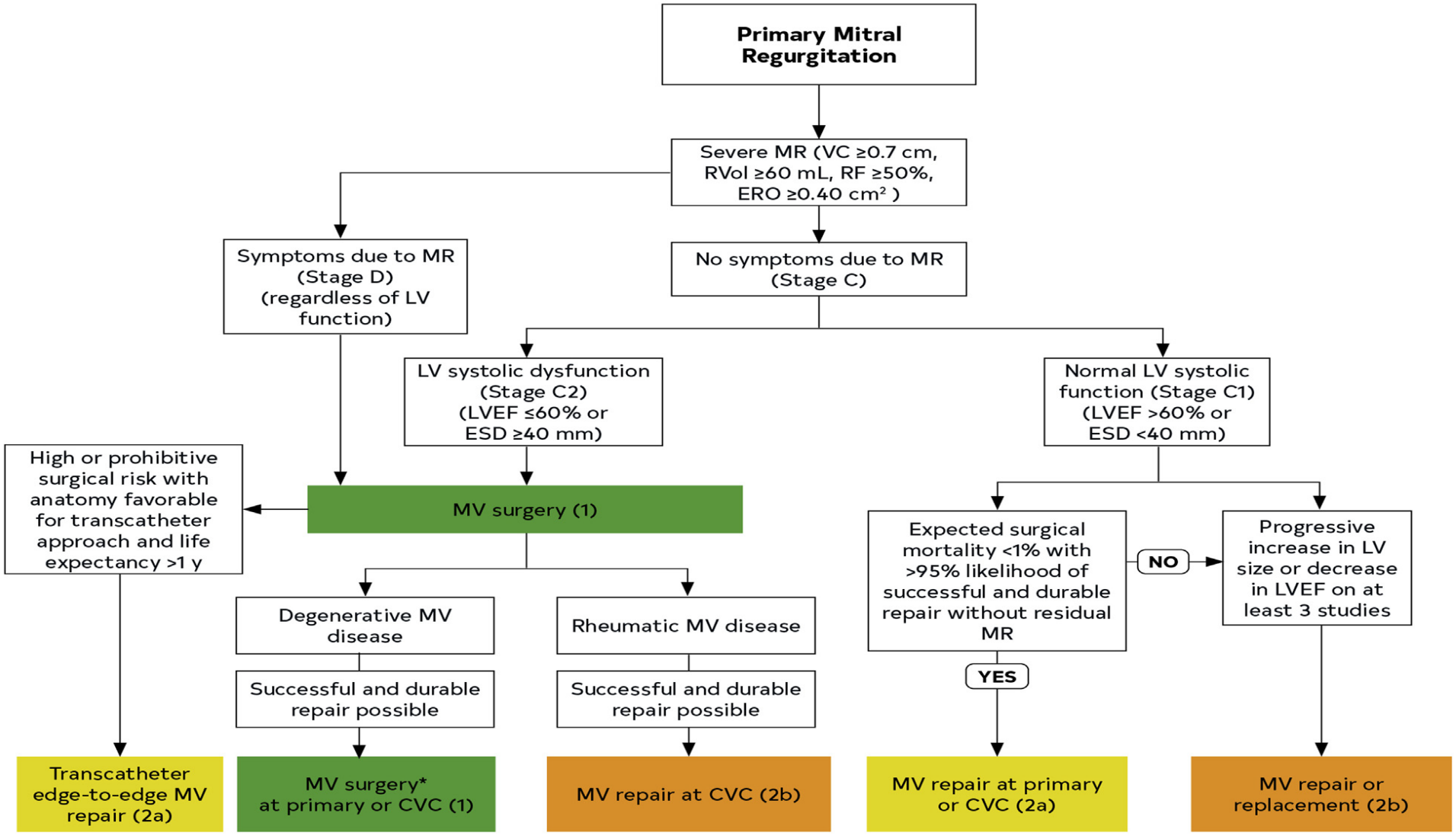
Subjects

- ✓Guidelines- Chest pain management.
- ✓New concept in Stable IHD & aggressive Lipid lowering treatment.
- ✓Atrial Fibrillation- A. changing the paradigm.
- ✓ B. Silent CVA in AF.
- ✓Interventional Cardiology.
- Valvular Heart Diseases- what's new in the guidelines?
- Cardiomyopathies- A. HCM
  B. ATTR-CMP
- Heart Failure – The 2021 new guidelines.
  The role of SGLT2Inh.
- New frontiers – Tele- Med & AI
- The GOLDEN BULT in Cardiology

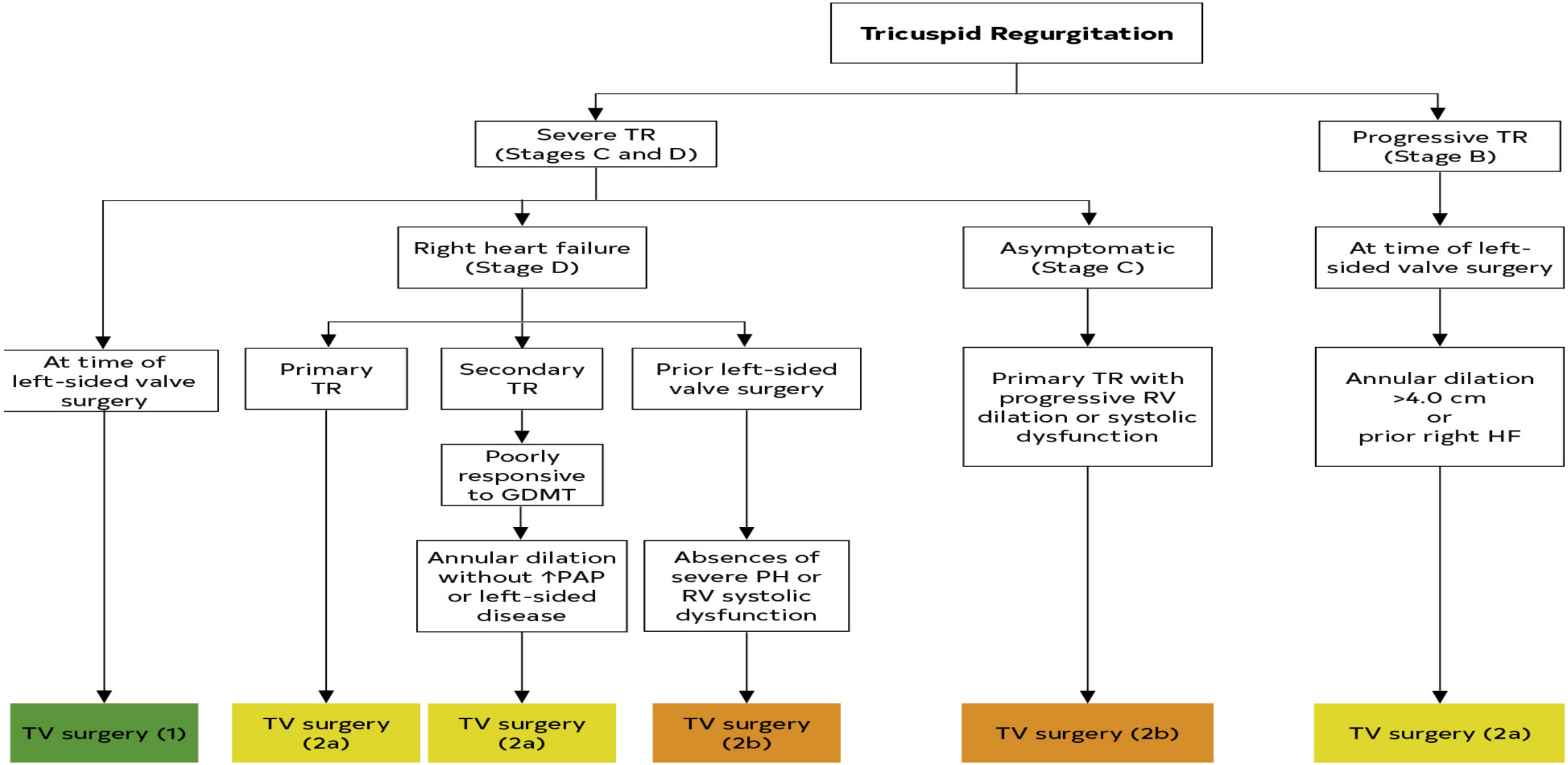
Timing of intervention for AR



Primary Mitral Regurgitation



Tricuspid Regurgitation



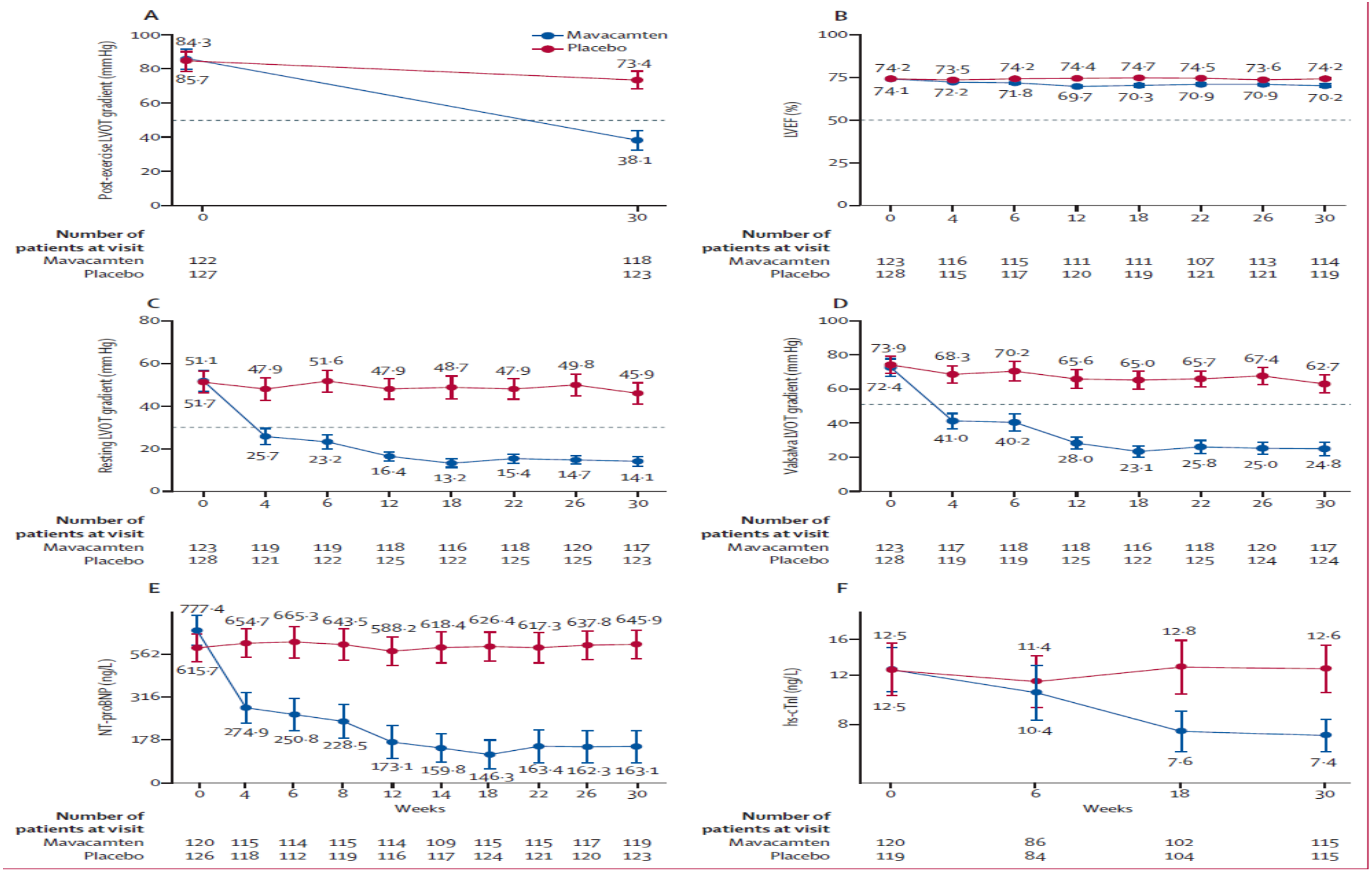
Subjects

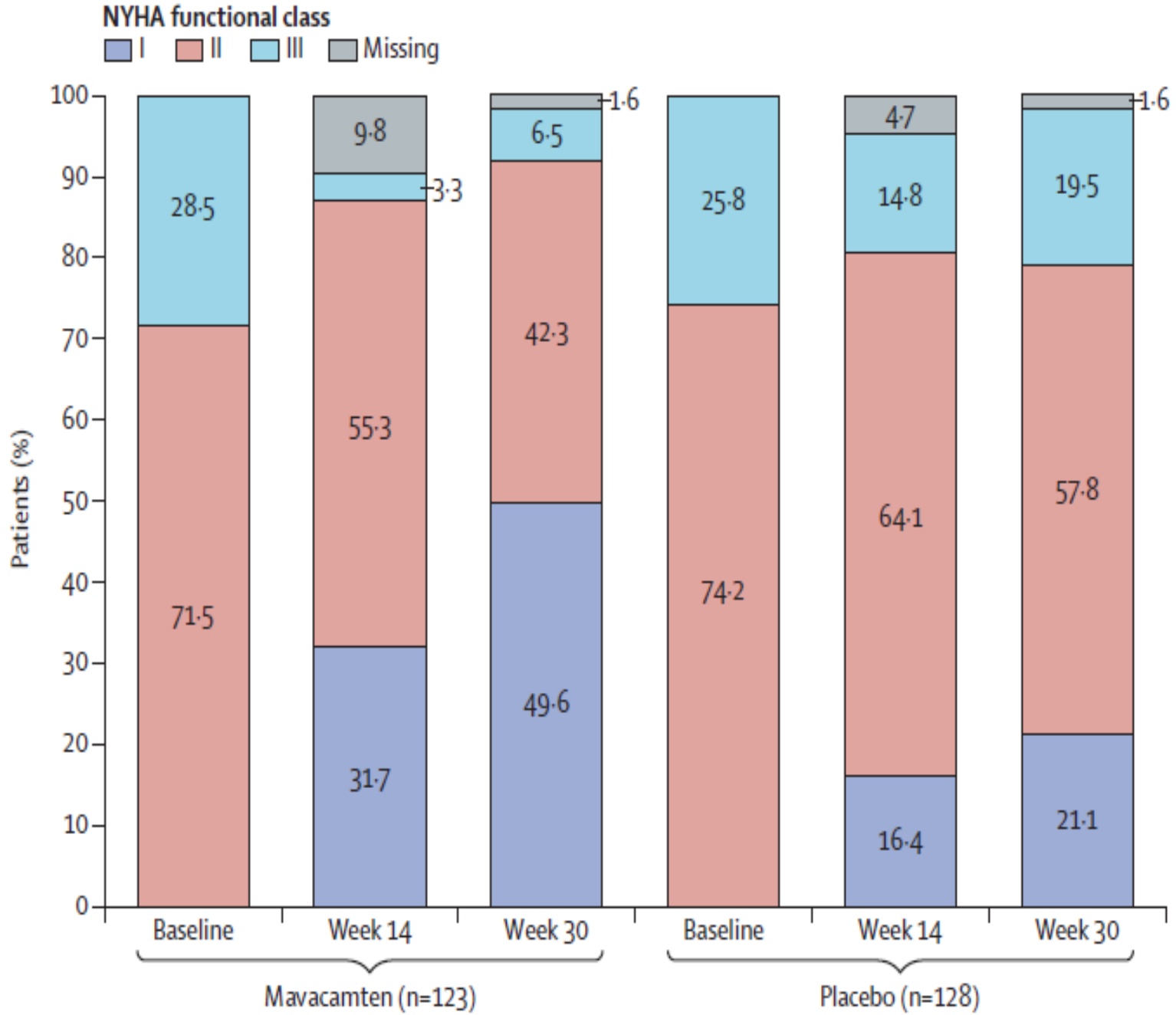
- ✓Guidelines- Chest pain management.
- ✓New concept in Stable IHD & aggressive Lipid lowering treatment.
- ✓Atrial Fibrillation- A. changing the paradigm.
- ✓ B. Silent CVA in AF.
- ✓Interventional Cardiology.
- ✓Valvular Heart Diseases- what's new in the guidelines?
- Cardiomyopathies- A. HCM
  B. ATTR-CMP
- Heart Failure – The 2021 new guidelines.
  The role of SGLT2Inh.
- New frontiers – Tele- Med & AI
- The GOLDEN BULT in Cardiology

Mavacamten for treatment of symptomatic obstructive hypertrophic cardiomyopathy (EXPLORER-HCM)

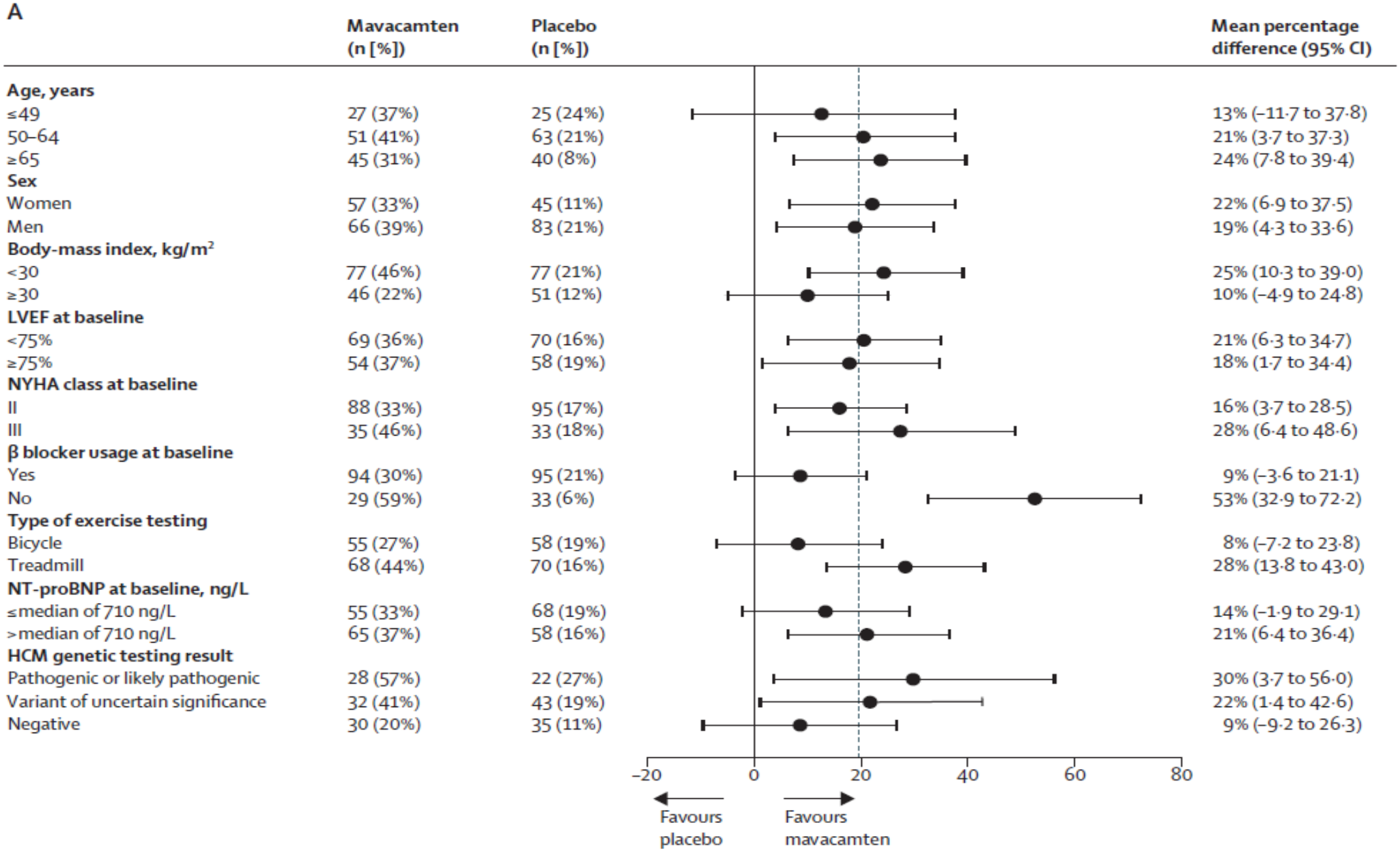
- Mavacamten is a first-in-class, small molecule, selective allosteric inhibitor of cardiac myosin ATPase specifically developed to target the underlying pathophysiology of hypertrophic cardiomyopathy by reducing actin–myosin cross-bridge formation, thereby reducing contractility and improving myocardial energetics.

- Grillo MP, Erve JCL, Dick R, et al. In vitro and in vivo pharmacokinetic characterization of mavacamten, a first-in-class small molecule allosteric modulator of beta cardiac myosin. *Xenobiotica* 2019; **49:** 718–33.
- Kawas RF, Anderson RL, Ingle SRB, Song Y, Sran AS, Rodriguez HM. A small-molecule modulator of cardiac myosin acts on multiple stages of the myosin chemomechanical cycle. *J Biol Chem* 2017; **292:** 16571–77.


A
Mavacamten
Placebo
Post-exercise LVOT gradient (mm Hg)
100
80
60
40
20
0
84·3
85·7
73·4
38·1
0
30
Number of patients at visit
Mavacamten 122 118
Placebo 127 123
B
LVEF (%)
100
75
50
25
0
74·2 73·5 74·2 74·4 74·7 74·5 73·6 74·2
74·1 72·2 71·8 69·7 70·3 70·9 70·9 70·2
0 4 6 12 18 22 26 30
Number of patients at visit
Mavacamten 123 116 115 111 111 107 113 114
Placebo 128 115 117 120 119 121 121 119
C
Resting LVOT gradient (mm Hg)
80
60
40
20
0
51·1 47·9 51·6 47·9 48·7 47·9 49·8 45·9
51·7 25·7 23·2 16·4 13·2 15·4 14·7 14·1
0 4 6 12 18 22 26 30
Number of patients at visit
Mavacamten 123 119 119 118 116 118 120 117
Placebo 128 121 122 125 122 125 125 123
D
Valsalva LVOT gradient (mm Hg)
100
80
60
40
20
0
73·9 68·3 70·2 65·6 65·0 65·7 67·4 62·7
72·4 41·0 40·2 28·0 23·1 25·8 25·0 24·8
0 4 6 12 18 22 26 30
Number of patients at visit
Mavacamten 123 117 118 118 116 118 120 117
Placebo 128 119 119 125 122 125 124 124
E
NT-proBNP (ng/L)
562
316
178
0
777·4 654·7 665·3 643·5 588·2 618·4 626·4 617·3 637·8 645·9
615·7 274·9 250·8 228·5 173·1 159·8 146·3 163·4 162·3 163·1
0 4 6 8 12 14 18 22 26 30
Weeks
Number of patients at visit
Mavacamten 120 115 114 115 114 109 115 115 117 119
Placebo 126 118 112 119 116 117 124 121 120 123
F
hs-cTnI (ng/L)
16
12
8
12·5 11·4 12·8 12·6
12·5 10·4 7·6 7·4
0 6 18 30
Weeks
Number of patients at visit
Mavacamten 120 86 102 115
Placebo 119 84 104 115


NYHA functional class
I
II
III
Missing
Patients (%)
100
90
80
70
60
50
40
30
20
10
0
28·5
71·5
9·8
3·3
55·3
31·7
6·5
1·6
42·3
49·6
25·8
74·2
4·7
14·8
64·1
16·4
19·5
1·6
57·8
21·1
Baseline
Week 14
Week 30
Baseline
Week 14
Week 30
Mavacamten (n=123)
Placebo (n=128)

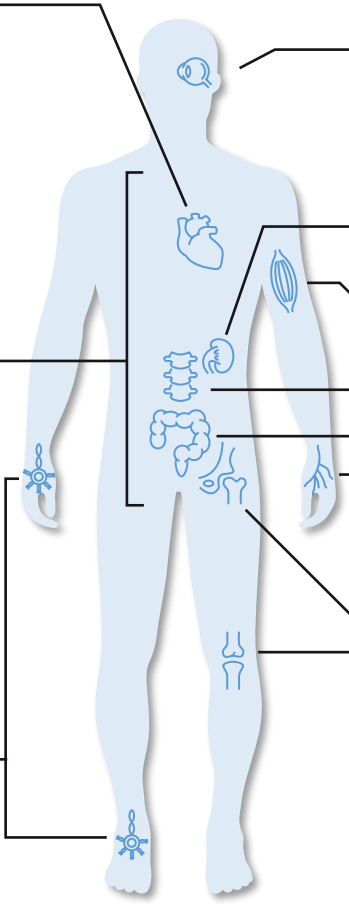
A


Mavacamten (n [%])
Placebo (n [%])
Mean percentage difference (95% CI)
Age, years
≤49 27 (37%) 25 (24%) 13% (–11·7 to 37·8)
50–64 51 (41%) 63 (21%) 21% (3·7 to 37·3)
≥65 45 (31%) 40 (8%) 24% (7·8 to 39·4)
Sex
Women 57 (33%) 45 (11%) 22% (6·9 to 37·5)
Men 66 (39%) 83 (21%) 19% (4·3 to 33·6)
Body-mass index, kg/m²
<30 77 (46%) 77 (21%) 25% (10·3 to 39·0)
≥30 46 (22%) 51 (12%) 10% (–4·9 to 24·8)
LVEF at baseline
<75% 69 (36%) 70 (16%) 21% (6·3 to 34·7)
≥75% 54 (37%) 58 (19%) 18% (1·7 to 34·4)
NYHA class at baseline
II 88 (33%) 95 (17%) 16% (3·7 to 28·5)
III 35 (46%) 33 (18%) 28% (6·4 to 48·6)
β blocker usage at baseline
Yes 94 (30%) 95 (21%) 9% (–3·6 to 21·1)
No 29 (59%) 33 (6%) 53% (32·9 to 72·2)
Type of exercise testing
Bicycle 55 (27%) 58 (19%) 8% (–7·2 to 23·8)
Treadmill 68 (44%) 70 (16%) 28% (13·8 to 43·0)
NT-proBNP at baseline, ng/L
≤median of 710 ng/L 55 (33%) 68 (19%) 14% (–1·9 to 29·1)
>median of 710 ng/L 65 (37%) 58 (16%) 21% (6·4 to 36·4)
HCM genetic testing result
Pathogenic or likely pathogenic 28 (57%) 22 (27%) 30% (3·7 to 56·0)
Variant of uncertain significance 32 (41%) 43 (19%) 22% (1·4 to 42·6)
Negative 30 (20%) 35 (11%) 9% (–9·2 to 26·3)
–20
0
20
40
60
80
Favours placebo
Favours mavacamten

Conclusions

In conclusion, in this first positive randomised phase 3 trial in patients with obstructive hypertrophic cardiomyopathy, mavacamten treatment improved functional capacity, LVOT gradient, symptoms, and key aspects of health status. The results of this pivotal trial highlight the benefits of disease-specific treatment in hypertrophic cardiomyopathy.

ATTR-CM Can Manifest in a Wide Range of Signs and Symptoms, Both Cardiac and Extracardiac[1-14]



CARDIOVASCULAR

- Heart failure (HF), especially with preserved ejection fraction
- Preponderance of right heart failure signs
- Echo showing increased left ventricular (LV) wall thickness
- Low QRS voltage relative to LV thickness
- Atrioventricular block with increased LV thickness
- Conduction abnormalities and arrhythmia, especially atrial fibrillation
- Intolerance to standard HF therapies
- Hypertrophic cardiomyopathy with infiltrative signs on magnetic resonance, such as apical sparing of longitudinal strain
- Aortic stenosis
- Mild increase in cardiac biomarkers

NERVOUS SYSTEM

AUTONOMIC

- Unexplained weight loss
- Orthostatic hypotension
- Sexual impotence
- Urinary retention and/or incontinence

PERIPHERAL

- Peripheral sensory motor dysfunction
- Muscle atrophy

OCULAR

- Vitreous opacity
- Glaucoma

RENAL

- Proteinuria
- Renal impairment
- Cardiorenal syndrome

MUSCULOSKELETAL/ORTHOPEDIC

- Biceps tendon rupture
- Lumbar spinal stenosis
- Carpal tunnel syndrome
- Hip/knee arthroplasty

GASTROINTESTINAL TRACT

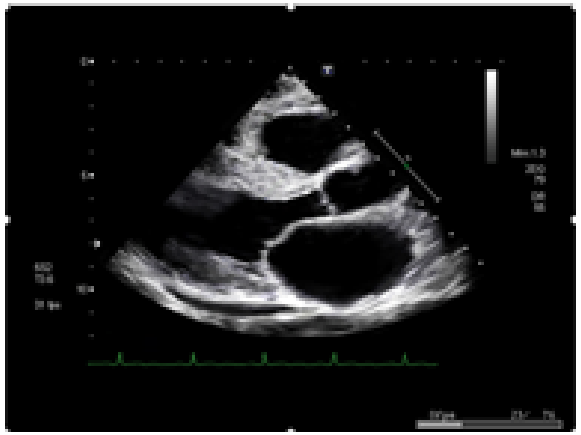
- Diarrhea and/or constipation
- Fecal incontinence
- Nausea and vomiting, and early satiety, leading to weight loss

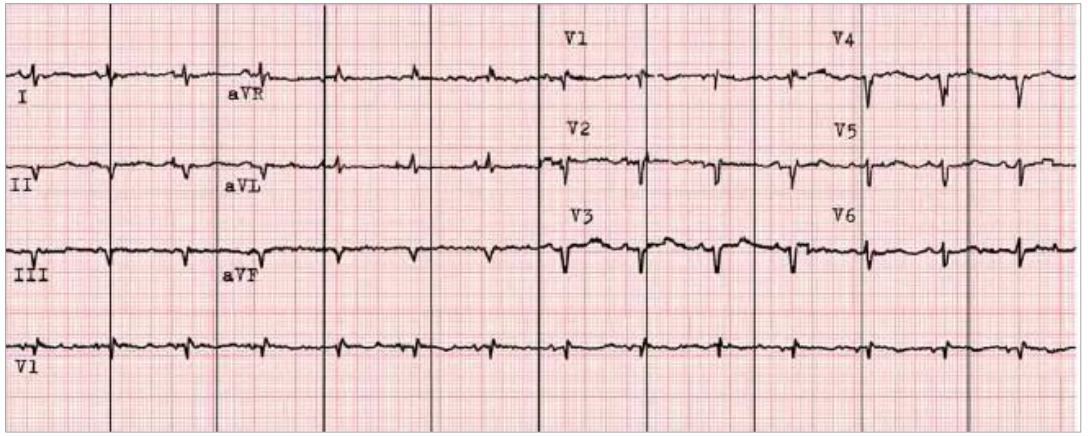
1. Nativi-Nicolau J, et al. *Curr Opin Cardiol*. 2018;33:571-579. 2. Narotsky DL, et al. *Can J Cardiol*. 2016;32:1166.e1-e10. 3. Maurer MS, et al. *Circulation*. 2017;135:1357-1377. 4. Brunjes DL, et al. *J Card Fail*. 2016;22:996-1003. 5. Siddiqi OK, Ruberg FL. *Trends Cardiovasc Med*. 2018;28:10-21. 6. Maurer MS, et al. *J Am Coll Cardiol*. 2016;63:161-172. 7. González-López E, et al. *Rev Esp Cardiol*. 2017;70:991-1004.
8. Reynolds MM, et al. *Am J Ophthalmol*. 2017;183:156-162. 9. Rubin J, et al. *Amyloid*. 2017;24:226-230. 10. Dang J, et al. *Mayo Clin Proc*. 2019;94:961-975. 11. Castano A, et al. *Eur Heart J*. 2017;38:2879-2887.
12. Gillmore JD, et al. *Eur Heart J*. 2018;39:2799-2806. 13. Treibel TA, et al. *Circ Cardiovasc Imaging*. 2016;9:54-63. 14. Obici L, Suhr OB. *Clin Auton Res*. 2019;29(Suppl 1):55-63.

Cardiac Clinical Clues

Electrocardiography

- Discordance between left ventricular wall thickness and QRS voltage[1]
- Pseudoinfarct pattern in up to 70% of cases[2]
- Arrhythmia and/or conduction disease[2,3]





Illustrative representations

Absence of low voltage does not rule out ATTR-CM as prevalence varies among ATTR-CM types.[4-8]

1. Ruberg FL, et al. *J Am Coll Cardiol.* 2019;73:2872-2892. 2. Maurer MS, et al. *Circulation.* 2017;135:1357-1377. 3. Huang J, et al. *Int Heart J.* 2015;56:522-526. 4. Cyrille NB, et al. *Am J Cardiol.* 2014;114:1089-1093 5. Connors LH, et al. *Circulation.* 2016;133:282-290. 6. Ng B, et al. *Arch Intern Med.* 2005;165:1425-1429. 7. Maurer MS, et al. *J Am Coll Cardiol.* 2016;68:161-172. 8. Quarta C, et al. *Circulation.* 2014;129:1840-1849.

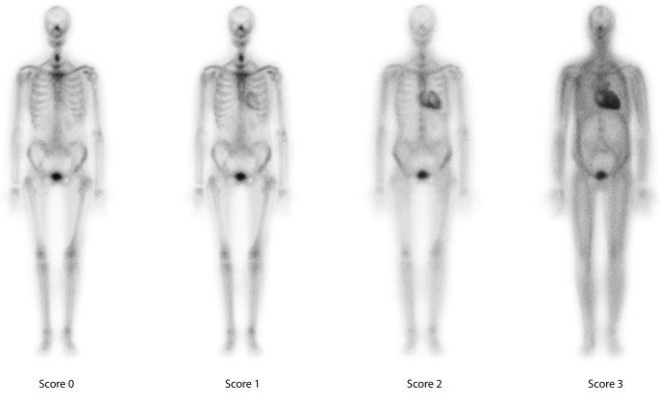
Nuclear Scintigraphy Is a Noninvasive, Widely Available Diagnostic Tool for ATTR-CM

Nuclear scintigraphy with ^{99m}Tc-labelled radiotracers is highly sensitive and specific to diagnose ATTR-CM when combined with testing for presence of monoclonal protein to rule out AL amyloidosis[1,2]

Three ^{99m}Tc-based bone radiotracers extensively studied for detecting amyloid deposition in the myocardium[3]

- **^{99m}Tc-PYP**
  pyrophosphate
- **^{99m}Tc-DPD**
  3,3-diphosphono-1,2-propanodicarboxylic acid
- **^{99m}Tc-HMDP**
  hydroxymethylene diphosphonate

Uptake of ^{99m}Tc-DPD in the Whole Body



Illustrative representation of ^{99m}Tc-DPD uptake developed in collaboration with Torbjörn Sundström, MD, PhD, Radiology/Nuclear Medicine, Umeå University Hospital, Sweden.

Criteria for Diagnosing ATTR-CM[4]

- ^{99m}Tc-PYP, DPD, HMDP myocardial uptake ≥ Grade 2
- AL amyloidosis ruled out
- Typical cardiac imaging features (echocardiography, CMR, PET)

LEARN MORE ABOUT INTERPRETATION OF ^{99M}TC-PYP/DPD/HMDP PLANAR AND SPECT UPTAKE

SPECT imaging is necessary in all cases of positive planar uptake to differentiate myocardial enhancement from blood pool[4]

To facilitate early diagnosis, scintigraphy should be more broadly considered in patients with the following[4]:

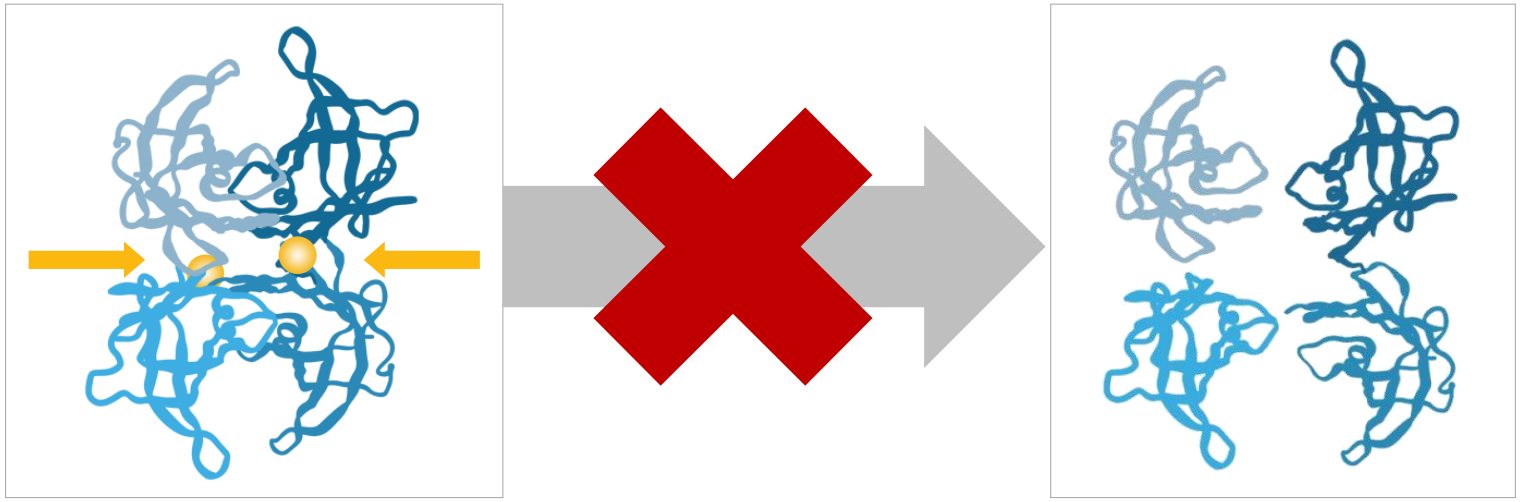
- Unexplained LV wall thickness
- HFpEF
- Familial history of amyloidosis
- Degenerative AS with low-flow gradient in elderly
- History of bilateral carpal tunnel syndrome

AL=immunoglobulin light chain amyloidosis; AS=aortic stenosis; CMR=cardiac magnetic resonance; HFpEF=heart failure with preserved ejection fraction; PET=positron emission tomography; Tc=technetium-labelled; LV=left ventricular.

1. Gillmore JD, et al. *Circulation*. 2016;133:2404-2412. 2. Bokhari S, et al. *Circ Cardiovasc Imaging*. 2013;6:195-201. 3. Rapezzi C, et al. *J Nucl Cardiol*. 2019;26:1638-1641. Dorbala S, et al. *J Nucl Cardiol*. 2019;26:2065-2123.

MECHANISM of ACTION

VYNDAMAX (tafamidis) Is a Selective Stabilizer of TTR[1,2]



Tafamidis stabilizes TTR to prevent dissociation into monomers, the rate-limiting step in the amyloidogenic process.[1,2]

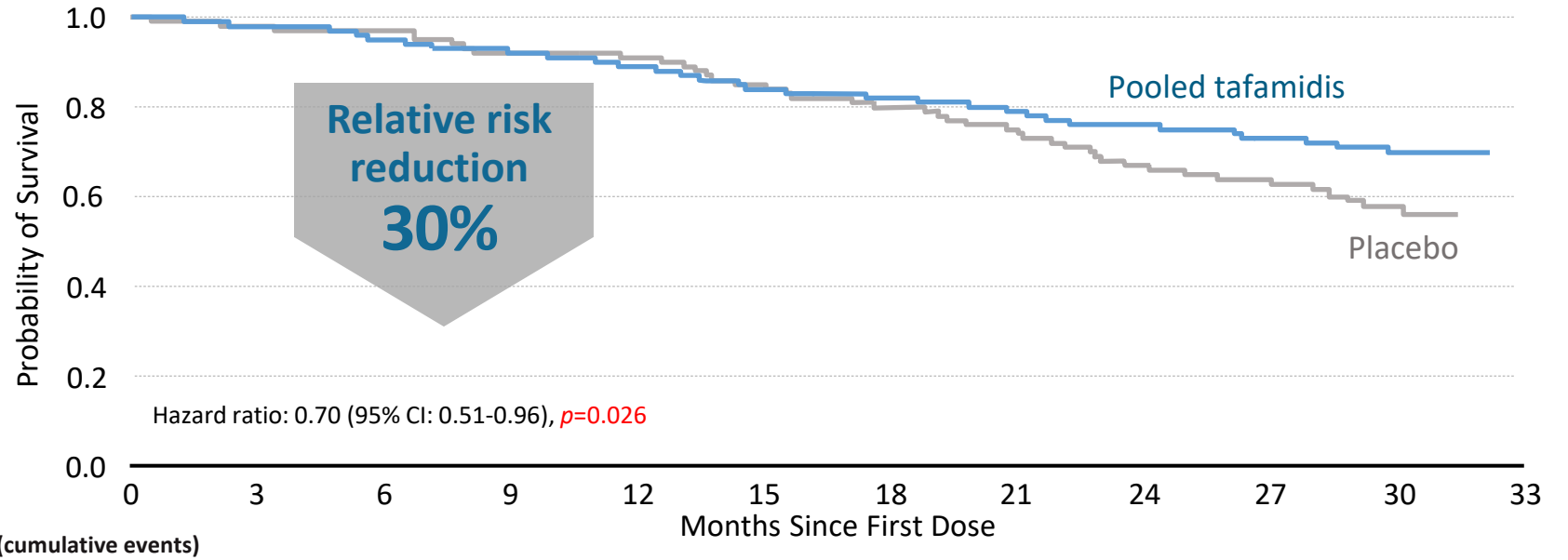
TTR=transthyretin.

1. Maurer MS, et al. *Circ Heart Fail*. 2017;10:e003815. 2. Bulawa CE, et al. *Proc Natl Acad Sci USA*. 2012;109:9629-9634.

*VYNDAMAX Significantly Reduced the Risk of All-Cause Mortality vs Placebo Over 30 Months

Individual Component of the Primary Analysis

All-cause Mortality at Month 30*[1,2]



No. at risk (cumulative events)

Pooled tafamidis	264 (0)	259 (5)	252 (12)	244 (20)	235 (29)	222 (42)	216 (48)	209 (55)	200 (64)	193 (71)	99 (78)	0 (78)
Placebo	177 (0)	173 (4)	171 (6)	163 (14)	161 (16)	150 (27)	141 (36)	131 (46)	118(59)	113(64)	51 (75)	0 (76)

Analysis not adjusted for multiplicity.

Number Needed to Treat: 7.5

~8 patients would need to be treated to prevent 1 death within 30 months.

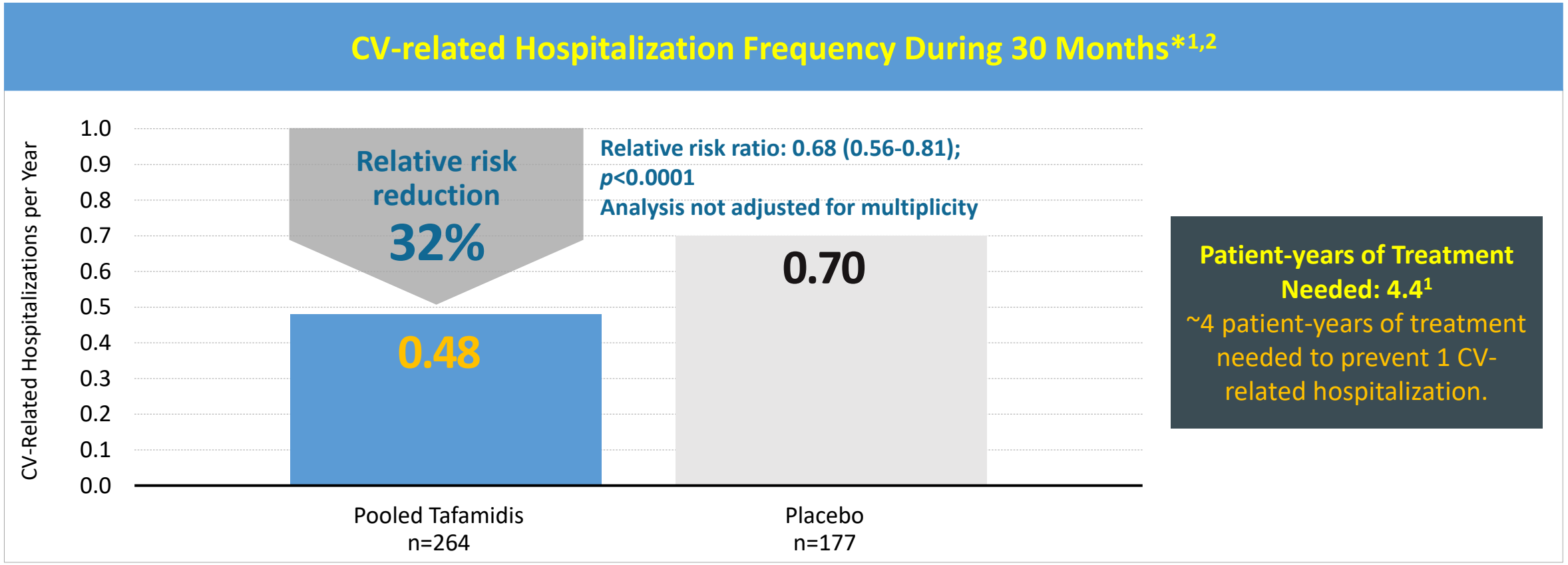
Chart and table adapted from Maurer MS, et al. *N Engl J Med*. 2018;379:1007-1016.

ATTR-CM=transthyretin amyloid cardiomyopathy.

*Heart transplantation, combined heart and liver transplantation, and cardiac mechanical assist device implantation are treated as equivalent to death in this analysis.[1] Analysis not adjusted for multiplicity. The components of the primary analysis, all-cause mortality, and CV-related hospitalizations, were evaluated individually. All-cause mortality was analyzed with the use of a Cox proportional hazards model, with treatment and the stratification factors treated as covariates.

VYNDAMAX Significantly Reduced the Risk of CV-Related Hospitalizations vs Placebo over 30 months[1,2]

Individual Component of the Primary Analysis



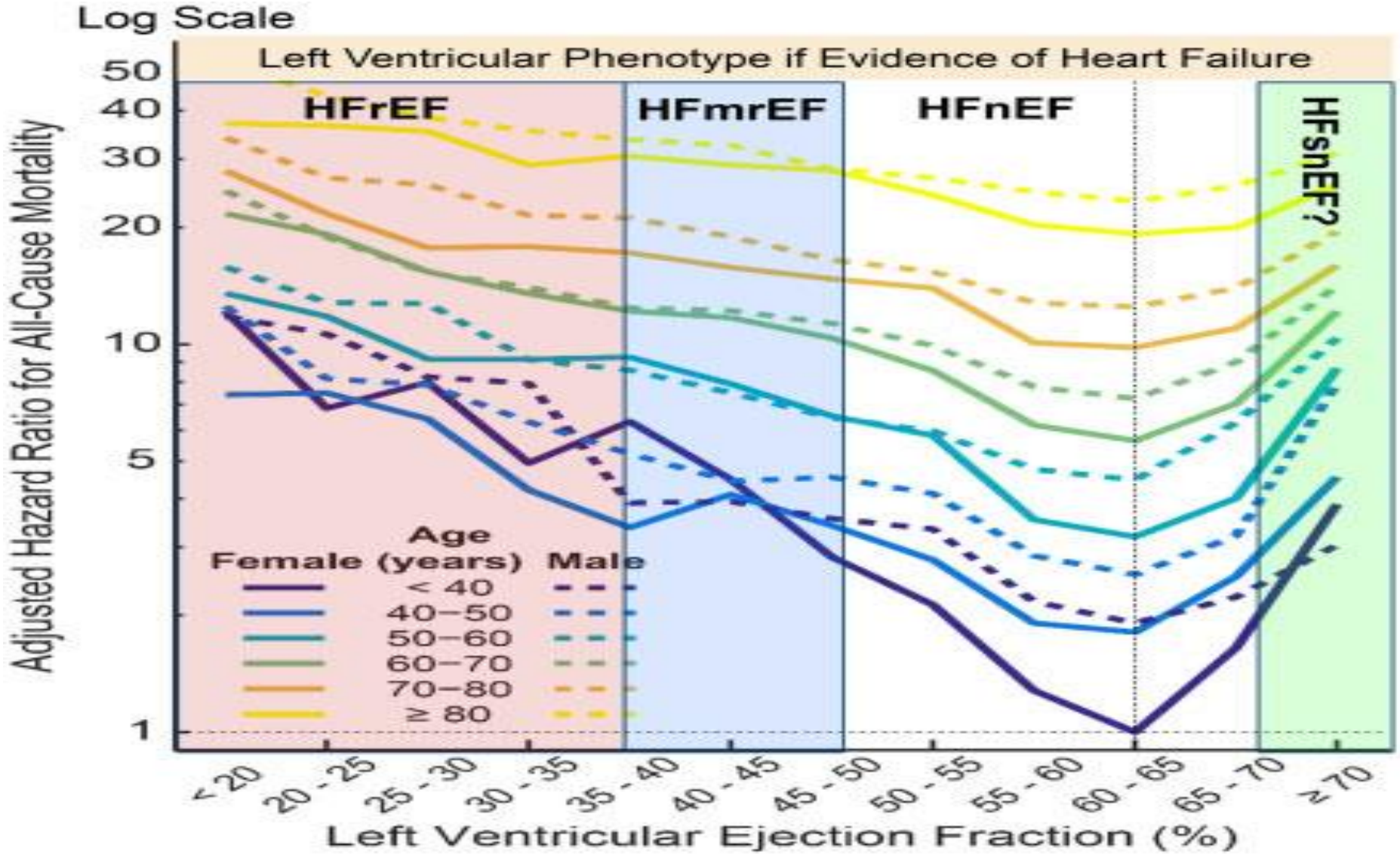
.

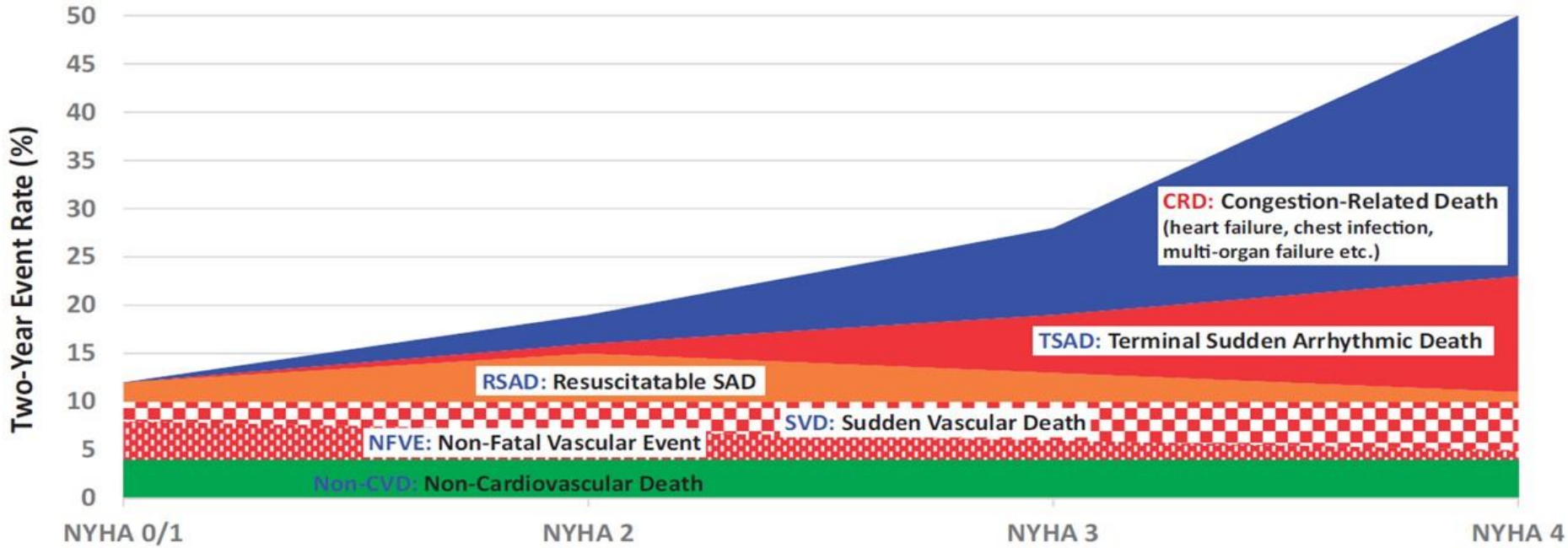
The components of the primary analysis, all-cause mortality, and CV-related hospitalizations, were evaluated individually. All-cause mortality was analyzed with the use of a Cox proportional hazards model, with treatment and the stratification factors treated as covariates. The CV-related hospitalization analysis was based on a Poisson regression model with treatment, transthyretin (TTR) status (hereditary and wild-type), New York Heart Association (NYHA) baseline class (NYHA classes I and II combined vs NYHA Class III), treatment by *TTR* genotype interaction, and treatment by NYHA baseline classification interaction terms as factors.[1]

CV=cardiovascular; NNT=number needed to treat.

Subjects

- ✓Guidelines- Chest pain management.
- ✓New concept in Stable IHD & aggressive Lipid lowering treatment.
- ✓Atrial Fibrillation- A. changing the paradigm.
- ✓ B. Silent CVA in AF.
- ✓Interventional Cardiology.
- ✓Valvular Heart Diseases- what's new in the guidelines?
- ✓Cardiomyopathies- A. HCM
- ✓ B. ATTR-CMP
- Heart Failure – The 2021 new guidelines.
  The role of SGLT2Inh.
- New frontiers – Tele- Med & AI
- The GOLDEN BULT in Cardiology

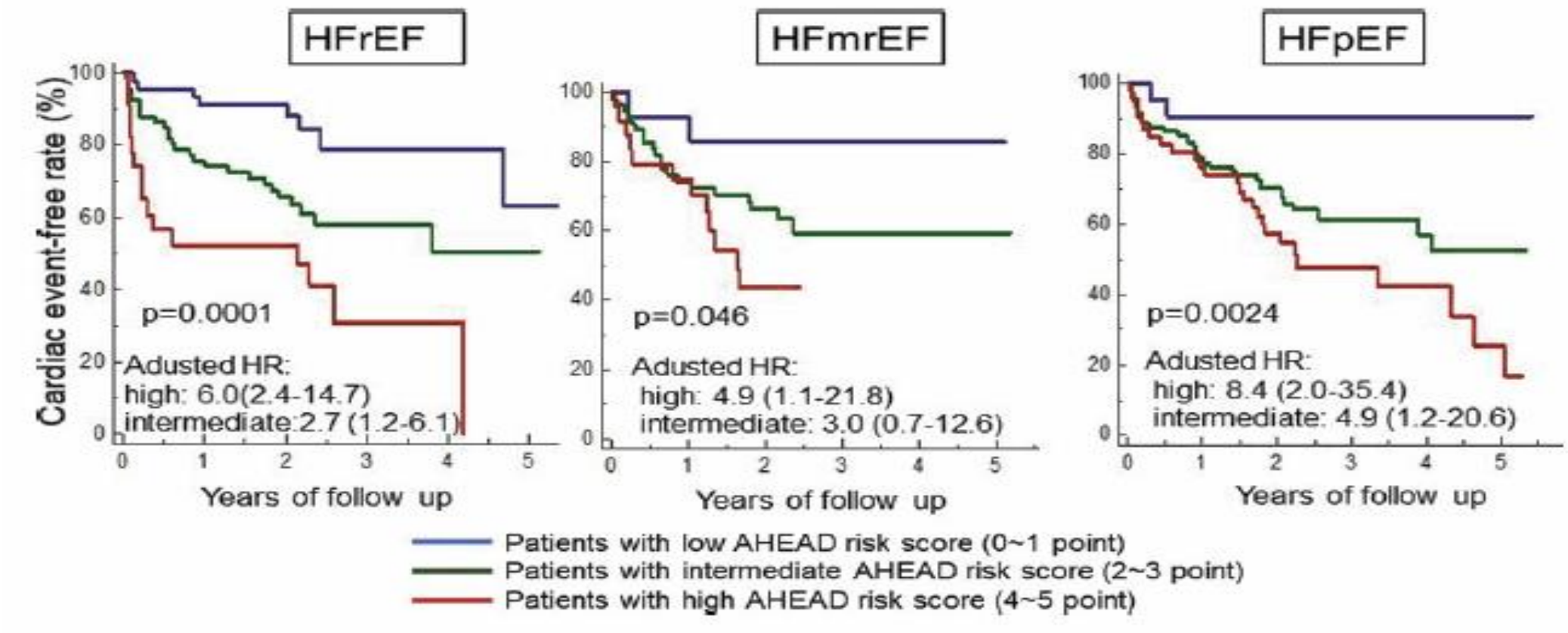

Log Scale
Left Ventricular Phenotype if Evidence of Heart Failure
HFrEF
HFmrEF
HFnEF
HFsnEF?
Adjusted Hazard Ratio for All-Cause Mortality
50
40
30
20
10
5
1
Age
Female (years) Male
< 40
40–50
50–60
60–70
70–80
≥ 80
< 20
20 - 25
25 - 30
30 - 35
35 - 40
40 - 45
45 - 50
50 - 55
55 - 60
60 - 65
65 - 70
≥ 70
Left Ventricular Ejection Fraction (%)



	NYHA 0/1		NYHA 2		NYHA 3		NYHA 4	
	Absolute Rate	% of Events	Absolute Rate	% of Events	Absolute Rate	% of Events	Absolute Rate	% of Events
CRD	0%	0%	3%	16%	9%	32%	27%	54%
TSAD	<1%	<1%	1%	5%	6%	21%	12%	24%
RSAD	2%	17%	5%	26%	3%	11%	1%	2%
SVD	2%	17%	3%	16%	4%	14%	5%	10%
NFVE	4%	33%	3%	16%	2%	7%	1%	2%
Non-CVD	4%	33%	4%	21%	4%	14%	4%	8%

AHEAD risk score

AHEAD (A: atrial fibrillation; H: hemoglobin; E: elderly; A: abnormal renal parameters; D: diabetes mellitus) risk score based on age and comorbidities has been reported as a useful long-term risk stratification score in acute decompensated heart failure (ADHF) patients

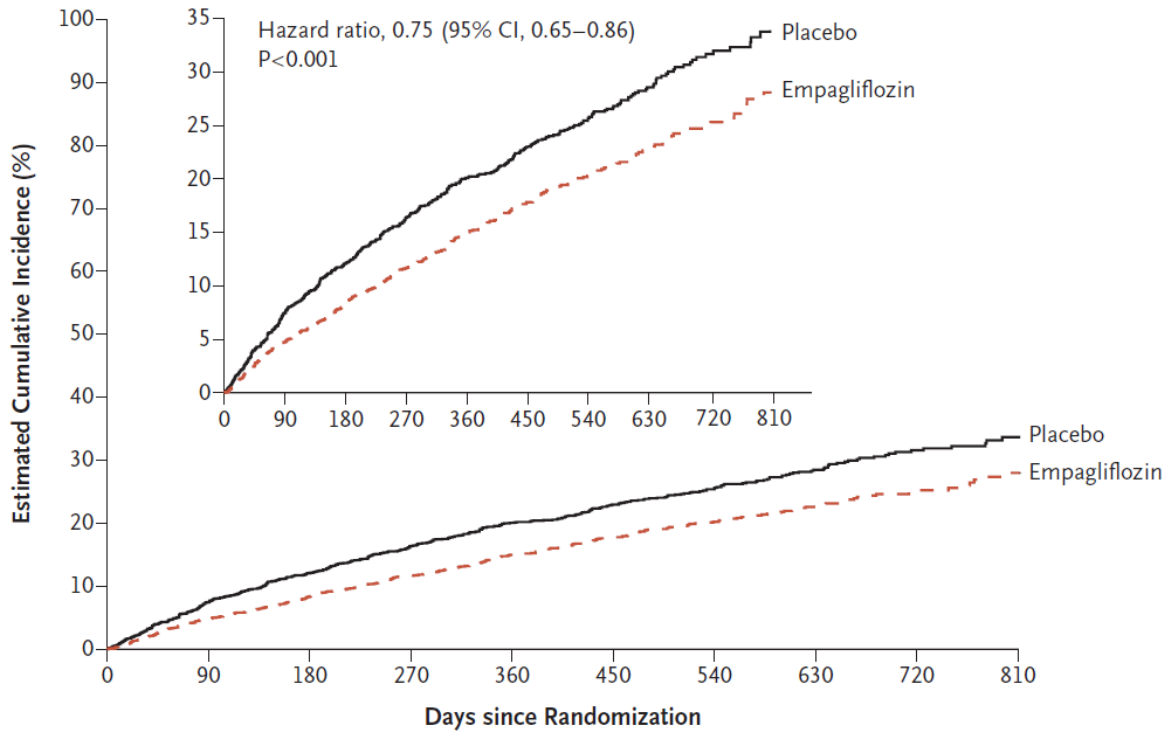


The NEW ENGLAND JOURNAL of MEDICINE

Cardiovascular and Renal Outcomes with Empagliflozin in Heart Failure

M. Packer, S.D. Anker, J. Butler, G. Filippatos, S.J. Pocock, P. Carson, J. Januzzi, S. Verma, H. Tsutsui, M. Brueckmann, W. Jamal, K. Kimura, J. Schnee, C. Zeller, D. Cotton, E. Bocchi, M. Böhm, D.-J. Choi, V. Chopra, E. Chuquiure, N. Giannetti, S. Janssens, J. Zhang, J.R. Gonzalez Juanatey, S. Kaul, H.-P. Brunner-La Rocca, B. Merkely, S.J. Nicholls, S. Perrone, I. Pina, P. Ponikowski, N. Sattar, M. Senni, M.-F. Seronde, J. Spinar, I. Squire, S. Taddei, C. Wanner, and F. Zannad, for the EMPEROR-Reduced Trial Investigators*

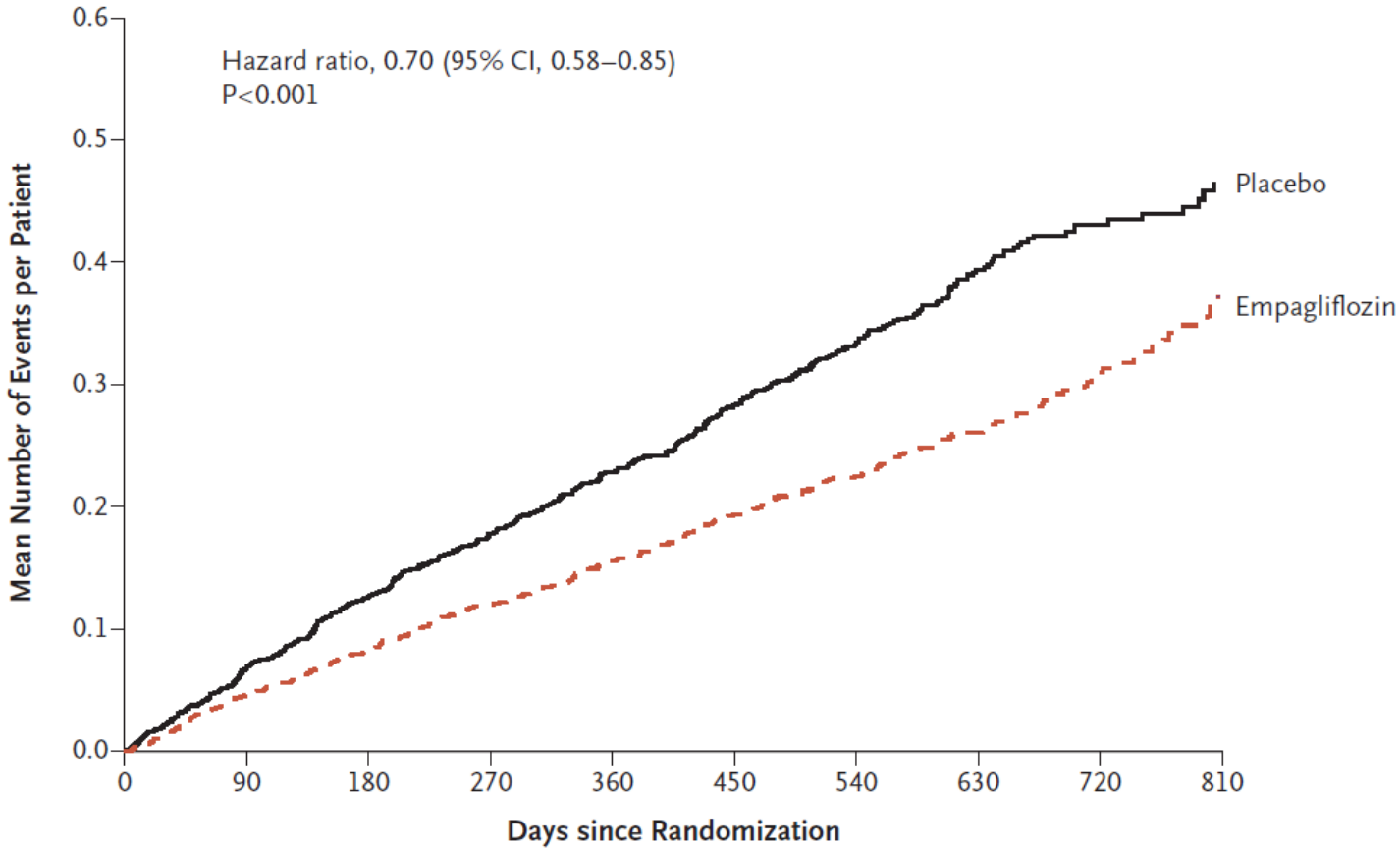
A **Primary Outcome**



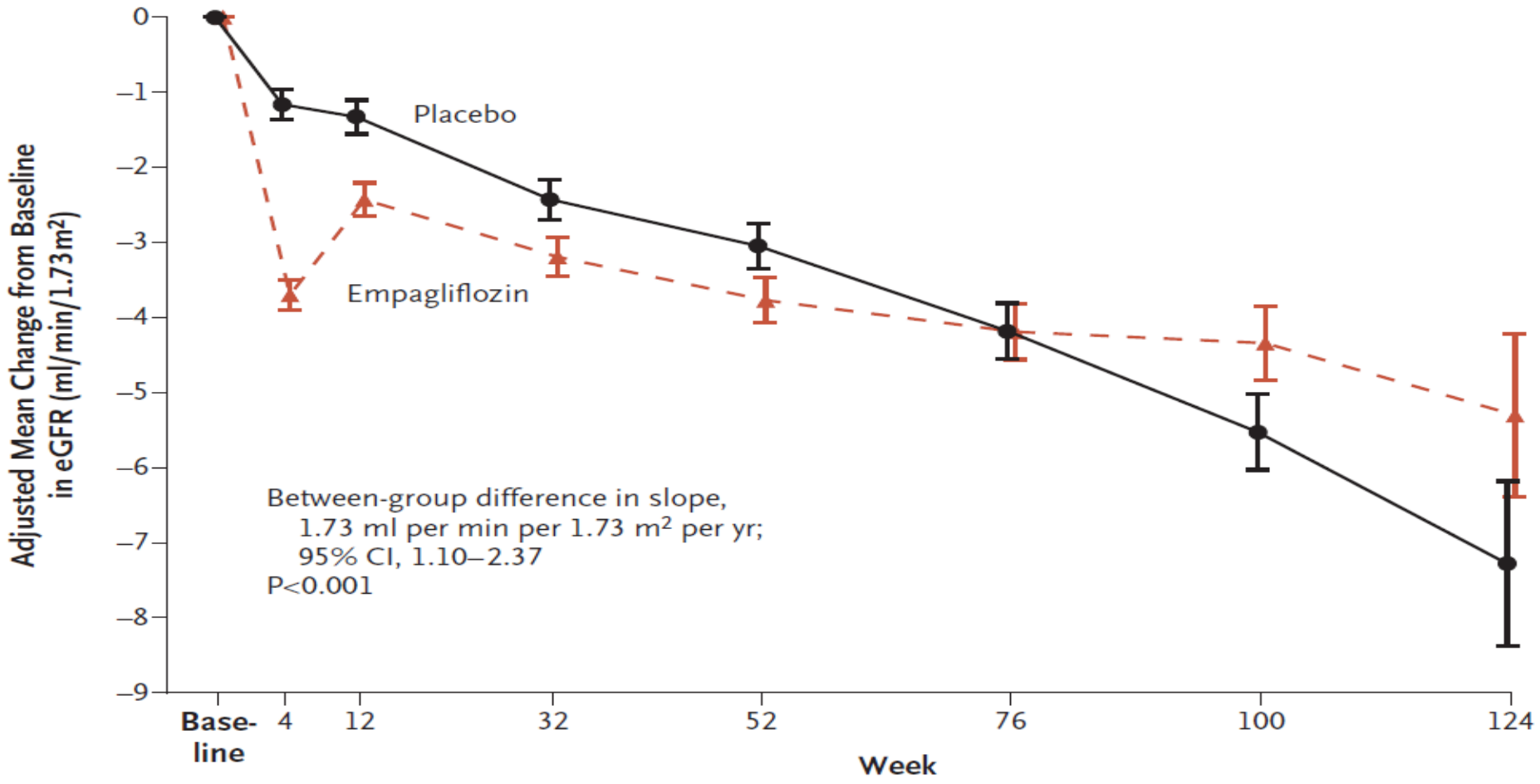
No. at Risk

Placebo	1867	1715	1612	1345	1108	854	611	410	224	109
Empagliflozin	1863	1763	1677	1424	1172	909	645	423	231	101

B First and Recurrent Hospitalizations for Heart Failure



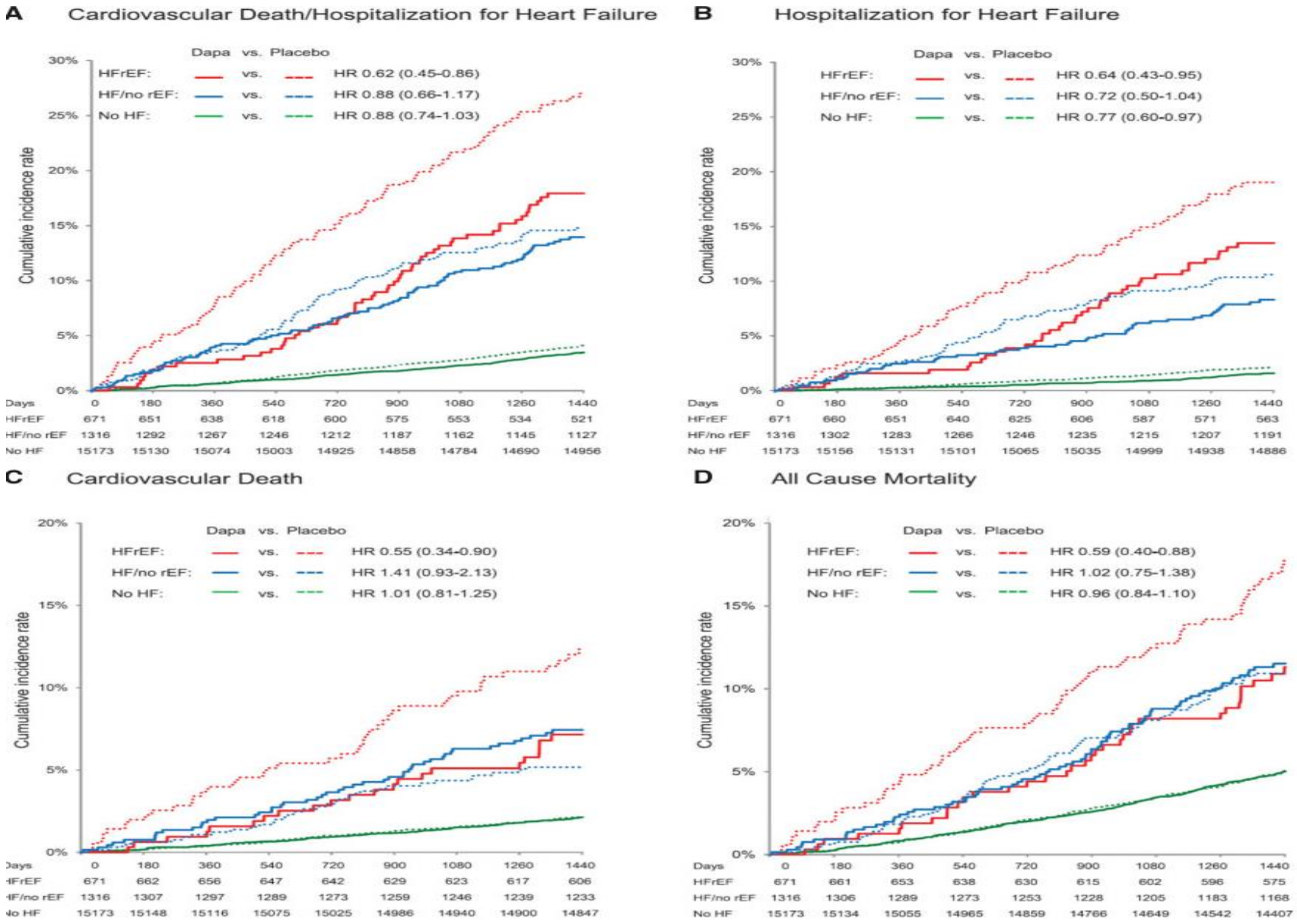
No. at Risk										
Placebo	1867	1820	1762	1526	1285	1017	732	497	275	135
Empagliflozin	1863	1826	1768	1532	1283	1008	732	495	272	118



No. at Risk								
Placebo	1792	1765	1683	1500	1146	745	343	76
Empagliflozin	1799	1782	1720	1554	1166	753	356	80

Figure 3. Changes in the Estimated Glomerular Filtration Rate.

Effect of dapagliflozin compared with placebo in type-2 diabetes mellitus in patients with heart failure with reduced ejection fraction, heart failure with preserved ejection fraction, or without heart failure.



SGLT2 inhibitors in patients with heart failure with reduced ejection fraction: a meta-analysis of the EMPEROR-Reduced and DAPA-HF trials

www.thelancet.com Published online August 30, 2020 https://doi.org/10.1016/S0140-6736(20)31824-9

	EMPEROR-Reduced		DAPA-HF	
	Empagliflozin	Placebo	Dapagliflozin	Placebo
Number of participants	1863	1867	2373	2371
Age, years	67·2 (10·8)	66·5 (11·2)	66·2 (11·0)	66·5 (10·8)
Sex				
Men	1426 (76·5%)	1411 (75·6%)	1809 (76·2%)	1826 (77·0%)
Women	437 (23·5%)	456 (24·4%)	564 (23·8%)	545 (23·0%)
NYHA functional classification				
II	1399 (75·1%)	1401 (75·0%)	1606 (67·7%)	1597 (67·4%)
III	455 (24·4%)	455 (24·4%)	747 (31·5%)	751 (31·7%)
IV	9 (0·5%)	11 (0·6%)	20 (0·8%)	23 (1·0%)
Mean LVEF, %	27·7 (6·0)	27·2 (6·1)	31·2 (6·7)	30·9 (6·9)
NT-pro BNP, pg/mL	1887 (1077–3429)	1926 (1153–3525)	1428 (857–2655)	1446 (857–2641)
Medical history				
Hospitalisation for heart failure*	577 (31·0%)	574 (30·7%)	1124 (47·4%)	1127 (47·5%)
Diabetes†	927 (49·8%)	929 (49·8%)	1075 (45·3%)	1064 (44·9%)
eGFR, mL/min per 1·73 m²‡	61·8 (21·7)	62·2 (21·5)	66·0 (19·6)	65·5 (19·3)
Heart failure medications				
ACE inhibitor	867 (46·5%)	836 (44·8%)	1332 (56·1%)	1329 (56·1%)
ARB	451 (24·2%)	457 (24·5%)	675 (28·4%)	632 (26·7%)
Mineralocorticoid receptor antagonist	1306 (70·1%)	1355 (72·6%)	1696 (71·5%)	1674 (70·6%)
ARNI	340 (18·3%)	387 (20·7%)	250 (10·5%)	258 (10·9%)
Device therapy				
ICD or CRT-D	578 (31·0%)	593 (31·8%)	622 (26·2%)	620 (26·1%)
CRT-D or CRT-P	220 (11·8%)	222 (11·9%)	190 (8·0%)	164 (6·9%)

A All-cause mortality

	Number with event/number of patients (%)		HR (95% CI)
	SGLT2 inhibitor	Placebo	
EMPEROR-Reduced	249/1863 (13·4%)	266/1867 (14·2%)	0·92 (0·77–1·10)
DAPA-HF	276/2373 (11·6%)	329/2371 (13·9%)	0·83 (0·71–0·97)
Total			**0·87 (0·77–0·98)**
Test for overall treatment effect p=0·018			
Test for heterogeneity of effect p=0·39			

B Cardiovascular death

	Number with event/number of patients (%)		HR (95% CI)
	SGLT2 inhibitor	Placebo	
EMPEROR-Reduced	187/1863 (10·0%)	202/1867 (10·8%)	0·92 (0·75–1·12)
DAPA-HF	227/2373 (9·6%)	273/2371 (11·5%)	0·82 (0·69–0·98)
Total			**0·86 (0·76–0·98)**
Test for overall treatment effect p=0·027			
Test for heterogeneity of effect p=0·40			

C First hospitalisation for heart failure or cardiovascular death

	Number with event/number of patients (%)		HR (95% CI)
	SGLT2 inhibitor	Placebo	
EMPEROR-Reduced	361/1863 (19·4%)	462/1867 (24·7%)	0·75 (0·65–0·86)
DAPA-HF	386/2373 (16·3%)	502/2371 (21·2%)	0·74 (0·65–0·85)
Total			**0·74 (0·68–0·82)**
Test for overall treatment effect p<0·0001			
Test for heterogeneity of effect p=0·89			

D First hospitalisation for heart failure

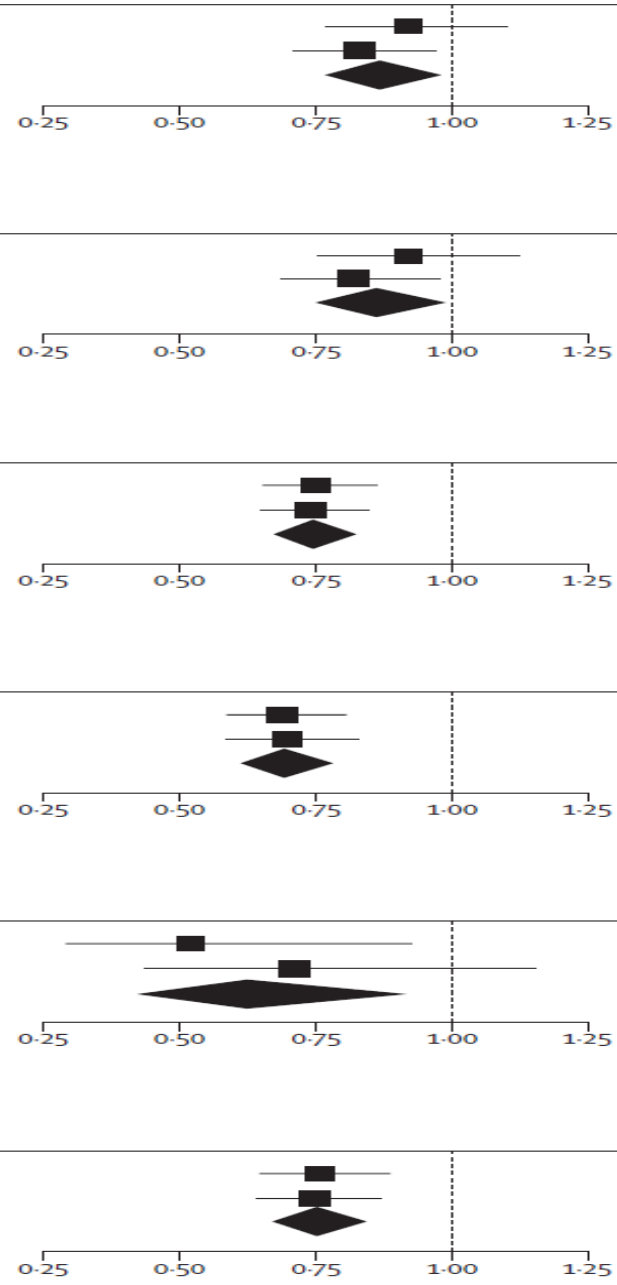
	Number with event/number of patients (%)		HR (95% CI)
	SGLT2 inhibitor	Placebo	
EMPEROR-Reduced	246/1863 (13·2%)	342/1867 (18·3%)	0·69 (0·59–0·81)
DAPA-HF	231/2373 (9·7%)	318/2371 (13·4%)	0·70 (0·59–0·83)
Total			**0·69 (0·62–0·78)**
Test for overall treatment effect p<0·0001			
Test for heterogeneity of effect p=0·90			

E First kidney outcome composite

	Number with event/number of patients (%)		HR (95% CI)
	SGLT2 inhibitor	Placebo	
EMPEROR-Reduced	18/1863 (1·0%)	33/1867 (1·8%)	0·52 (0·29–0·92)
DAPA-HF	28/2373 (1·2%)	39/2371 (1·6%)	0·71 (0·44–1·16)
Total			**0·62 (0·43–0·90)**
Test for overall treatment effect p=0·013			
Test for heterogeneity of effect p=0·42			

F All (first and recurrent) hospitalisation for heart failure or cardiovascular death

	Number with event/number of patients (%)		RR (95% CI)
	SGLT2 inhibitor	Placebo	
EMPEROR-Reduced	575/1863 (30·9%)	753/1867 (40·3%)	0·76 (0·65–0·89)
DAPA-HF	567/2373 (23·9%)	742/2371 (31·3%)	0·75 (0·65–0·88)
Total			**0·75 (0·68–0·84)**
Test for overall treatment effect p<0·0001			
Test for heterogeneity of effect p=0·91			



A Diabetes status

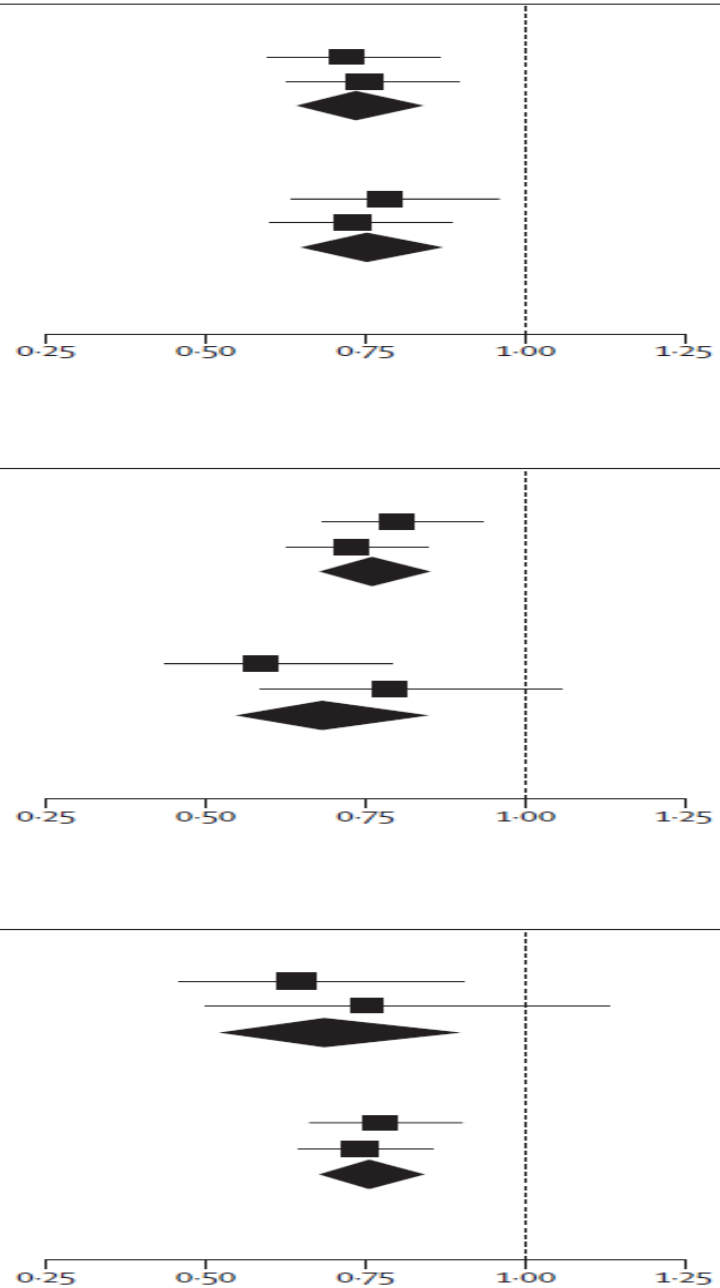
	Number with event/number of patients (%)		HR (95% CI)
	SGLT2 inhibitor	Placebo	
With diabetes			
EMPEROR-Reduced	200/927 (21·6%)	265/929 (28·5%)	0·72 (0·60–0·87)
DAPA-HF	215/1075 (20·0%)	271/1064 (25·5%)	0·75 (0·63–0·90)
Subtotal			**0·74 (0·65–0·84)**
Test for overall treatment effect p<0·0001			
Test for heterogeneity of effect p=0·76			
Without diabetes			
EMPEROR-Reduced	161/936 (17·2%)	197/938 (21·0%)	0·78 (0·64–0·97)
DAPA-HF	171/1298 (13·2%)	231/1307 (17·7%)	0·73 (0·60–0·88)
Subtotal			**0·75 (0·65–0·87)**
Test for overall treatment effect p<0·0001			
Test for heterogeneity of effect p=0·65			
Test for treatment by subgroup interaction p=0·81			

B Sex

	Number with event/number of patients (%)		HR (95% CI)
	SGLT2 inhibitor	Placebo	
Men			
EMPEROR-Reduced	294/1426 (20·6%)	353/1411 (25·0%)	0·80 (0·68–0·93)
DAPA-HF	307/1809 (17·0%)	406/1826 (22·2%)	0·73 (0·63–0·85)
Subtotal			**0·76 (0·68–0·85)**
Test for overall treatment effect p<0·0001			
Test for heterogeneity of effect p=0·41			
Women			
EMPEROR-Reduced	67/437 (15·3%)	109/456 (23·9%)	0·59 (0·44–0·80)
DAPA-HF	79/564 (14·0%)	96/545 (17·6%)	0·79 (0·59–1·06)
Subtotal			**0·68 (0·56–0·84)**
Test for overall treatment effect p=0·0004			
Test for heterogeneity of effect p=0·17			
Test for treatment by subgroup interaction p=0·37			

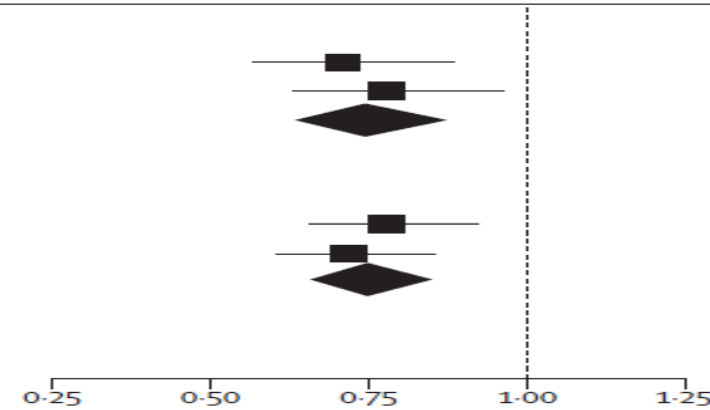
C Use of ARNI

	Number with event/number of patients (%)		HR (95% CI)
	SGLT2 inhibitor	Placebo	
Receiving ARNI			
EMPEROR-Reduced	51/340 (15·0)	93/387 (24·0)	0·64 (0·45–0·89)
DAPA-HF	41/250 (16·4)	56/258 (21·7)	0·75 (0·50–1·13)
Subtotal			**0·68 (0·53–0·89)**
Test for overall treatment effect p=0·0043			
Test for heterogeneity of effect p=0·56			
Not receiving ARNI			
EMPEROR-Reduced	310/1523 (20·4)	369/1480 (24·9)	0·77 (0·66–0·90)
DAPA-HF	345/2123 (16·3)	446/2113 (21·1)	0·74 (0·65–0·86)
Subtotal			**0·75 (0·68–0·84)**
Test for overall treatment effect p<0·0001			
Test for heterogeneity of effect p=0·71			
Test for treatment by subgroup interaction p=0·50			



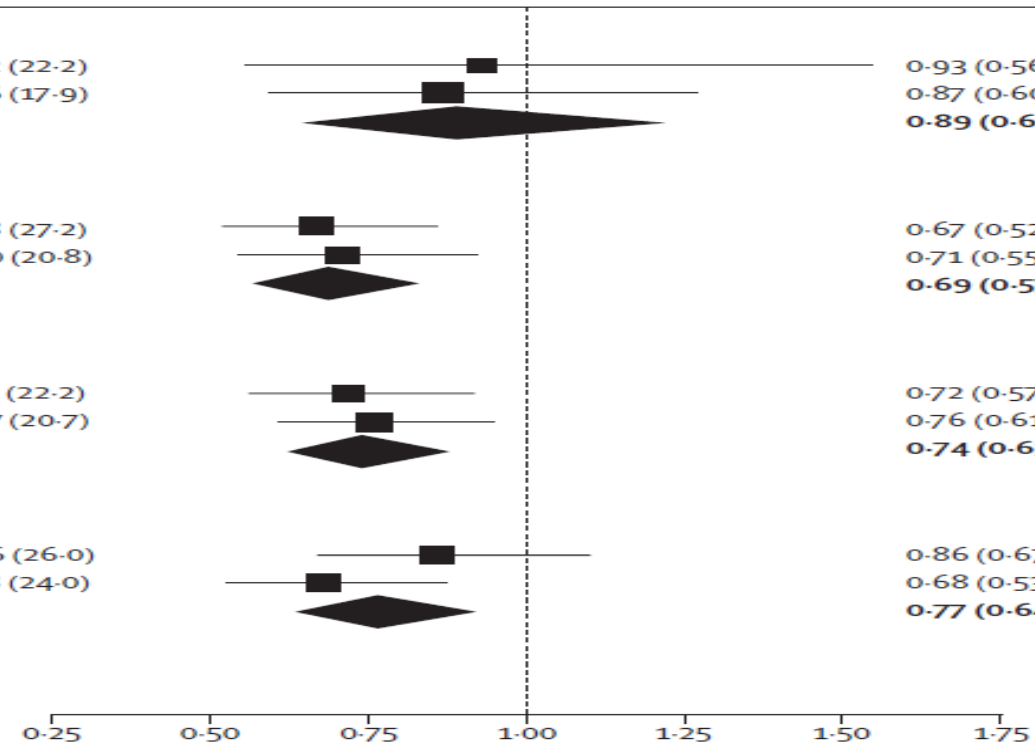
D Age (≤65 and >65 years)

	Number with event/number of patients (%)		HR (95% CI)
	SGLT2 inhibitor	Placebo	
Age ≤65 years			
EMPEROR-Reduced	128/675 (19·0)	193/740 (26·1)	0·71 (0·57–0·89)
DAPA-HF	162/1032 (15·7)	196/998 (19·6)	0·78 (0·63–0·96)
Subtotal			**0·75 (0·64–0·87)**
Test for overall treatment effect p=0·0002			
Test for heterogeneity of effect p=0·55			
Age >65 years			
EMPEROR-Reduced	233/1188 (19·6)	269/1127 (23·9)	0·78 (0·66–0·93)
DAPA-HF	224/1341 (16·7)	306/1373 (22·3)	0·72 (0·60–0·85)
Subtotal			**0·75 (0·66–0·85)**
Test for overall treatment effect p<0·0001			
Test for heterogeneity of effect p=0·52			
Test for treatment by subgroup interaction p=0·96			



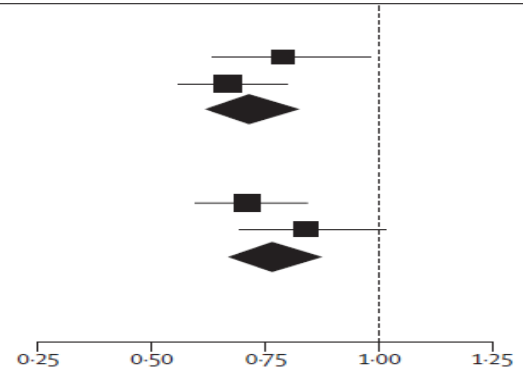
E Age (<55, 55–64, 65–74, and ≥75 years)

	Number with event/number of patients (%)		HR (95% CI)
	SGLT2 inhibitor	Placebo	
Age <55 years			
EMPEROR-Reduced	25/121 (20·7)	36/162 (22·2)	0·93 (0·56–1·55)
DAPA-HF	52/340 (15·3)	53/296 (17·9)	0·87 (0·60–1·28)
Subtotal			**0·89 (0·66–1·21)**
Test for overall treatment effect p=0·46			
Test for heterogeneity of effect p=0·84			
Age 55–64 years			
EMPEROR-Reduced	103/554 (18·6)	157/578 (27·2)	0·67 (0·52–0·86)
DAPA-HF	96/612 (15·7)	131/630 (20·8)	0·71 (0·55–0·93)
Subtotal			**0·69 (0·57–0·83)**
Test for overall treatment effect p<0·0001			
Test for heterogeneity of effect p=0·75			
Age 65–74 years			
EMPEROR-Reduced	118/685 (17·2)	140/631 (22·2)	0·72 (0·57–0·93)
DAPA-HF	135/830 (16·3)	184/887 (20·7)	0·76 (0·61–0·95)
Subtotal			**0·74 (0·63–0·87)**
Test for overall treatment effect p=0·0004			
Test for heterogeneity of effect p=0·75			
Age ≥75 years			
EMPEROR-Reduced	115/503 (22·9)	129/496 (26·0)	0·86 (0·67–1·10)
DAPA-HF	103/591 (17·4)	134/558 (24·0)	0·68 (0·53–0·88)
Subtotal			**0·77 (0·64–0·92)**
Test for overall treatment effect p=0·0033			
Test for heterogeneity of effect p=0·19			
Test for treatment by subgroup interaction p=0·54			



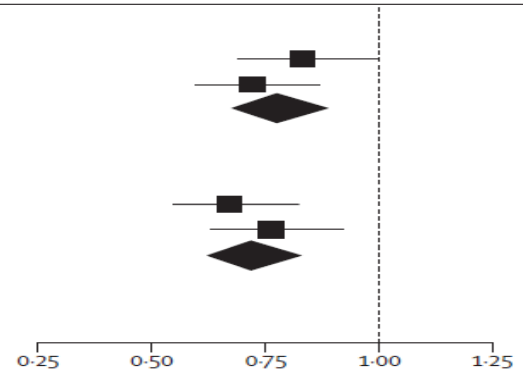
F History of hospitalisation for heart failure*

	Number with event/number of patients (%)		HR (95% CI)
	SGLT2 inhibitor	Placebo	
History of hospitalisation for heart failure			
EMPEROR-Reduced	153/577 (26·5)	177/574 (30·8)	0·79 (0·64–0·99)
DAPA-HF	195/1124 (17·3)	279/1127 (24·8)	0·67 (0·56–0·80)
Subtotal			**0·72 (0·62–0·82)**
Test for overall treatment effect p<0·0001			
Test for heterogeneity of effect p=0·25			
No history of hospitalisation for heart failure			
EMPEROR-Reduced	208/1286 (16·2)	285/1293 (22·0)	0·71 (0·60–0·85)
DAPA-HF	191/1249 (15·3)	223/1244 (17·9)	0·84 (0·69–1·01)
Subtotal			**0·77 (0·67–0·87)**
Test for overall treatment effect p<0·0001			
Test for heterogeneity of effect p=0·20			
Test for treatment by subgroup interaction p=0·48			



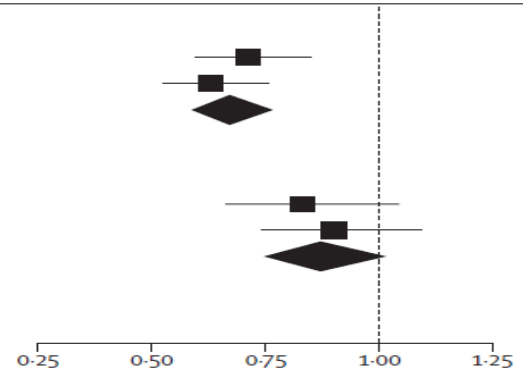
G eGFR

	Number with event/number of patients (%)		HR (95% CI)
	SGLT2 inhibitor	Placebo	
eGFR <60 mL/min per 1·73 m²			
EMPEROR-Reduced	202/893 (22·6)	237/906 (26·2)	0·83 (0·69–1·00)
DAPA-HF	191/962 (19·9)	254/964 (26·3)	0·72 (0·59–0·86)
Subtotal			**0·77 (0·68–0·88)**
Test for overall treatment effect p=0·0001			
Test for heterogeneity of effect p=0·29			
eGFR ≥60 mL/min per 1·73 m²			
EMPEROR-Reduced	159/969 (16·4)	224/960 (23·3)	0·67 (0·55–0·83)
DAPA-HF	195/1410 (13·8)	248/1406 (17·6)	0·76 (0·63–0·92)
Subtotal			**0·72 (0·62–0·82)**
Test for overall treatment effect p<0·0001			
Test for heterogeneity of effect p=0·38			
Test for treatment by subgroup interaction p=0·44			



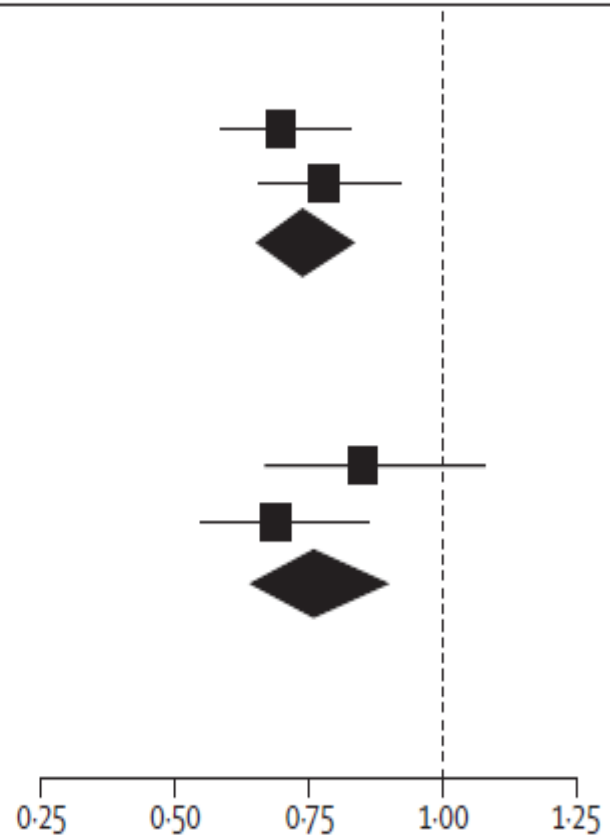
H NYHA functional class

	Number with event/number of patients (%)		HR (95% CI)
	SGLT2 inhibitor	Placebo	
NYHA class II			
EMPEROR-Reduced	220/1399 (15·7)	299/1401 (21·3)	0·71 (0·59–0·84)
DAPA-HF	190/1606 (11·8)	289/1597 (18·1)	0·63 (0·52–0·75)
Subtotal			**0·67 (0·59–0·76)**
Test for overall treatment effect p<0·0001			
Test for heterogeneity of effect p=0·36			
NYHA class III–IV			
EMPEROR-Reduced	141/464 (30·4)	163/466 (35·0)	0·83 (0·66–1·04)
DAPA-HF	196/767 (25·6)	213/774 (27·5)	0·90 (0·74–1·09)
Subtotal			**0·87 (0·75–1·01)**
Test for overall treatment effect p=0·064			
Test for heterogeneity of effect p=0·60			
Test for treatment by subgroup interaction p=0·0087			



K BMI

	Number with event/number of patients (%)		HR (95% CI)
	SGLT2 inhibitor	Placebo	
BMI: <30 kg/m²			
EMPEROR-Reduced	226/1263 (17·9)	322/1300 (24·8)	0·70 (0·59–0·83)
DAPA-HF	259/1537 (16·9)	320/1533 (20·9)	0·78 (0·66–0·92)
Subtotal			**0·74 (0·66–0·83)**
Test for overall treatment effect p<0·0001			
Test for heterogeneity of effect p=0·37			
BMI: ≥30 kg/m²			
EMPEROR-Reduced	135/600 (22·5)	140/567 (24·7)	0·85 (0·67–1·08)
DAPA-HF	127/834 (15·2)	182/838 (21·7)	0·69 (0·55–0·86)
Subtotal			**0·76 (0·65–0·90)**
Test for overall treatment effect p=0·001			
Test for heterogeneity of effect p=0·21			
Test for treatment by subgroup interaction p=0·79			



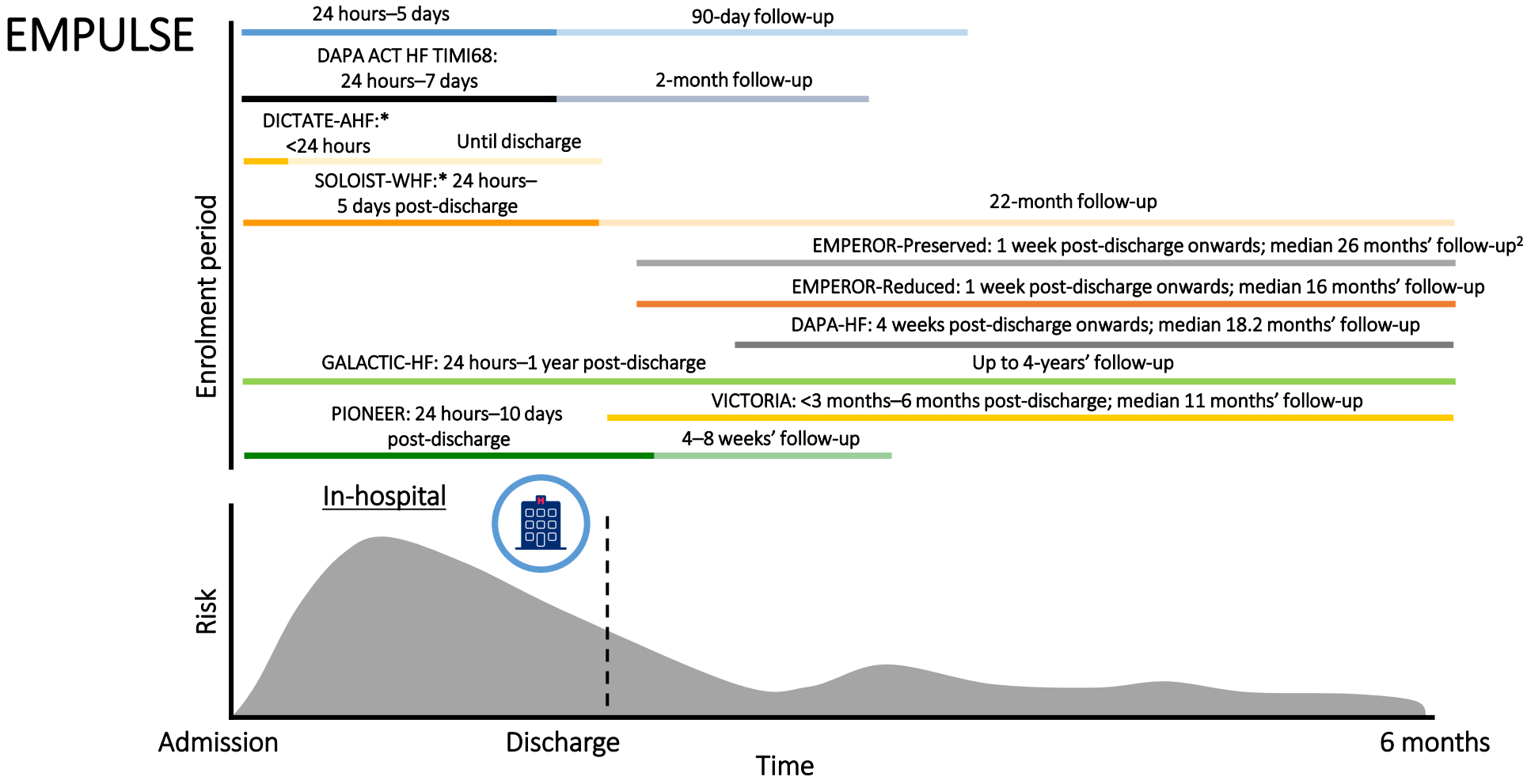
Adverse events

	EMPEROR-Reduced		DAPA-HF	
	Empagliflozin (n=1863)	Placebo (n=1867)	Dapagliflozin (n=2373)	Placebo (n=2371)
Serious adverse events	772 (41·4%)	896 (48·1%)	846 (35·7%)	951(40·2%)
Any renal adverse event	175 (9·4%)	192 (10·3%)	141 (6·0%)	158 (6·7%)
Volume depletion	197 (10·6%)	184 (9·9%)	170 (7·2%)	153 (6·5%)
Ketoacidosis	0	0	3 (0·1%)	0
Severe hypoglycaemic events	6 (0·3%)	7 (0·4%)	4 (0·2%)	4 (0·2%)
Bone fractures	45 (2·4%)	42 (2·3%)	48 (2·0%)	47 (2·0%)
Lower limb amputation	13 (0·7%)	10 (0·5%)	13 (0·5%)	12 (0·5%)
Fournier's Gangrene	1 (0·1%)	0	0	1 (0·1%)

conclusion

- **The effects of empagliflozin and dapagliflozin on hospitalizations for heart failure were consistent in the two independent trials and suggest that these agents also improve renal outcomes and reduce all-cause and cardiovascular death in patients with HFrEF.**

EMPULSE trial in Acute HF



*Only patients with type 2 diabetes.

1. Adapted from Tromp J *et al. Eur J Heart Fail.* 2021;23:826; 2. Anker S *et al. N Engl J Med.* 2021;385:1451.

EMPULSE: Conclusions

Patients hospitalized for acute HF treated with empagliflozin were **36% more likely to experience a clinical benefit*** versus patients on placebo

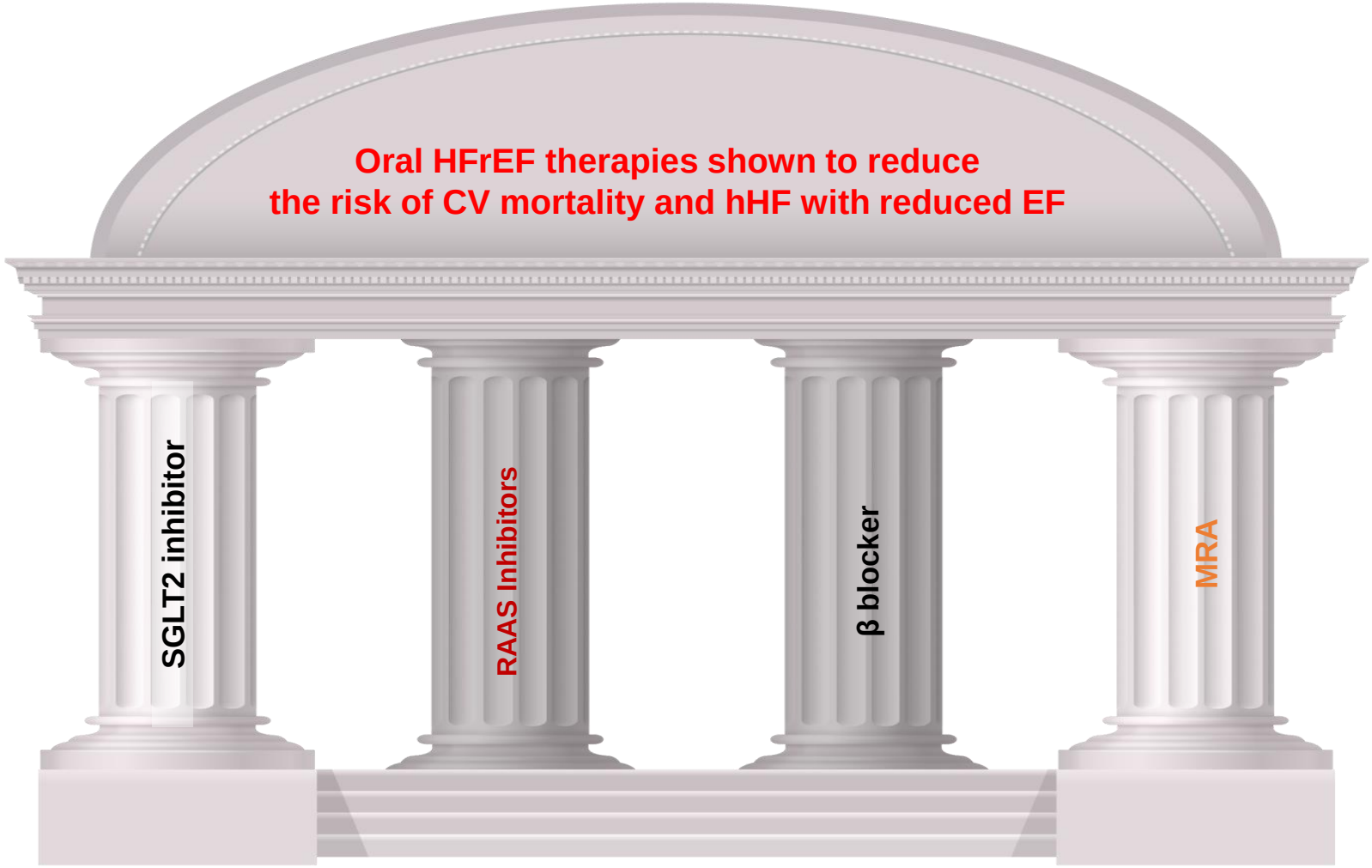
The clinical benefits were **consistent in patients with HFrEF or HFpEF**, and **in patients with de novo or decompensated chronic heart failure**

Empagliflozin was **well tolerated**, with overall safety data consistent with previous studies

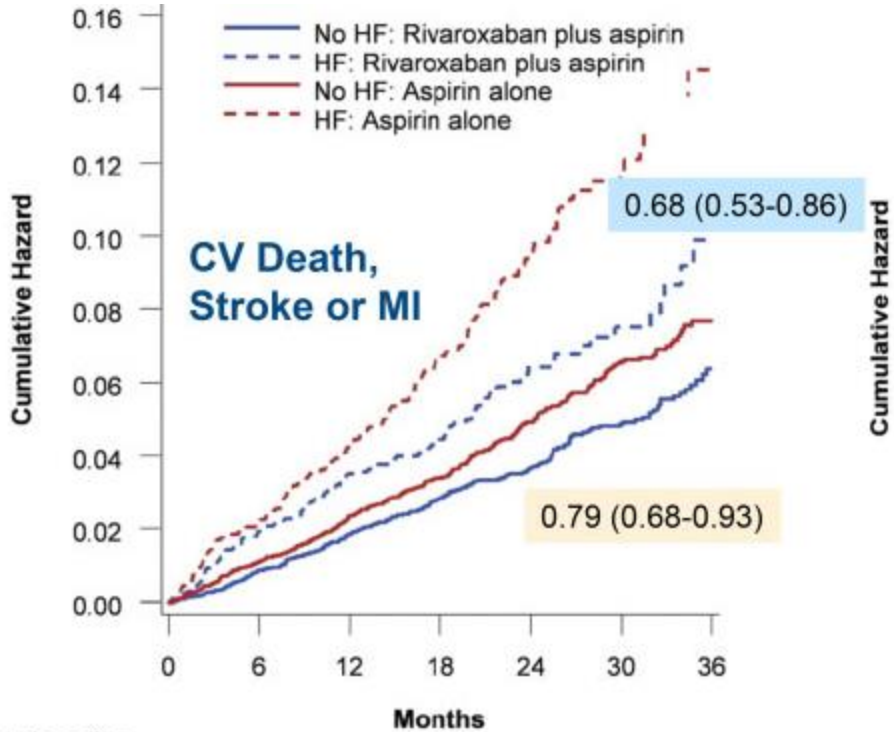
*Evaluated with a win ratio based on a composite of death, number of HFEs (including HHFs, urgent HF visits and unplanned outpatient visits), time to first HFE and change from baseline in KCCQ-TSS after 90 days of treatment. HF, heart failure; HFE, heart failure event; HHF, hospitalization for heart failure; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; KCCQ-TSS, Kansas City Cardiomyopathy Questionnaire Total Symptom Score.

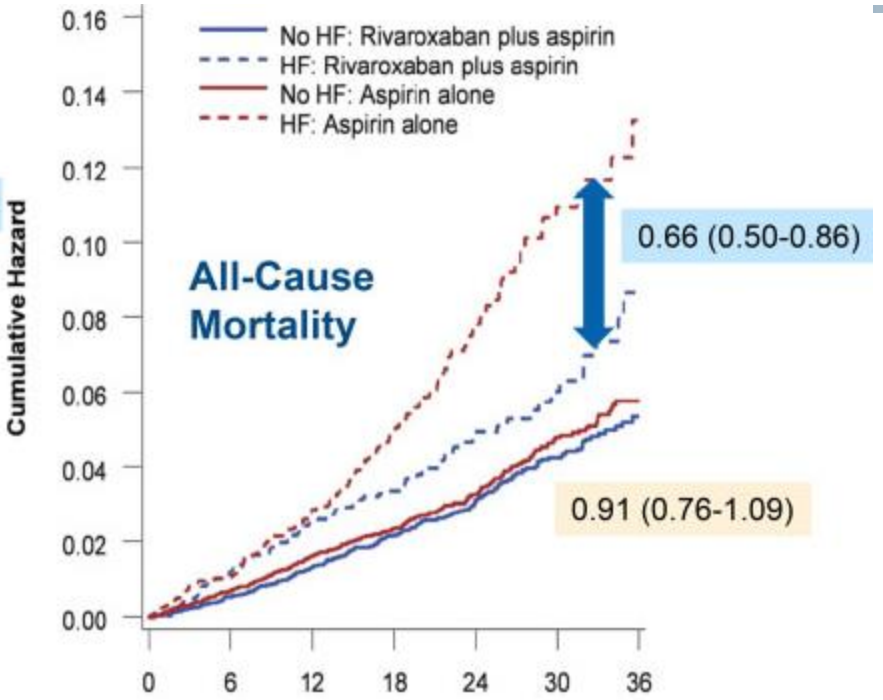
Voors AA et al. *Nat Med*. 2022; https://doi.org/10.1038/s41591-021-01659-1

Bases on ESC/EHFA Guidelines June 2021 we currently have Four major pillars in CHF treatment



CIHD &PAD +/- HF (driven from COMPASS)





No. at Risk							
No heart failure at baseline							
Rivaroxaban plus aspirin	7189	7103	6285	5071	3224	1855	557
Aspirin alone	7147	7045	6202	4978	3224	1837	582
Heart failure at baseline							
Rivaroxaban plus aspirin	1963	1922	1613	1218	687	355	101
Aspirin alone	1979	1936	1596	1179	636	330	86

Greenberg B, et al. Association of rivaroxaban with thromboembolic events in patients with heart failure, coronary disease, and sinus rhythm:

a post hoc analysis of the COMMANDER HF trial. JAMA Cardiol 2019;4:515.

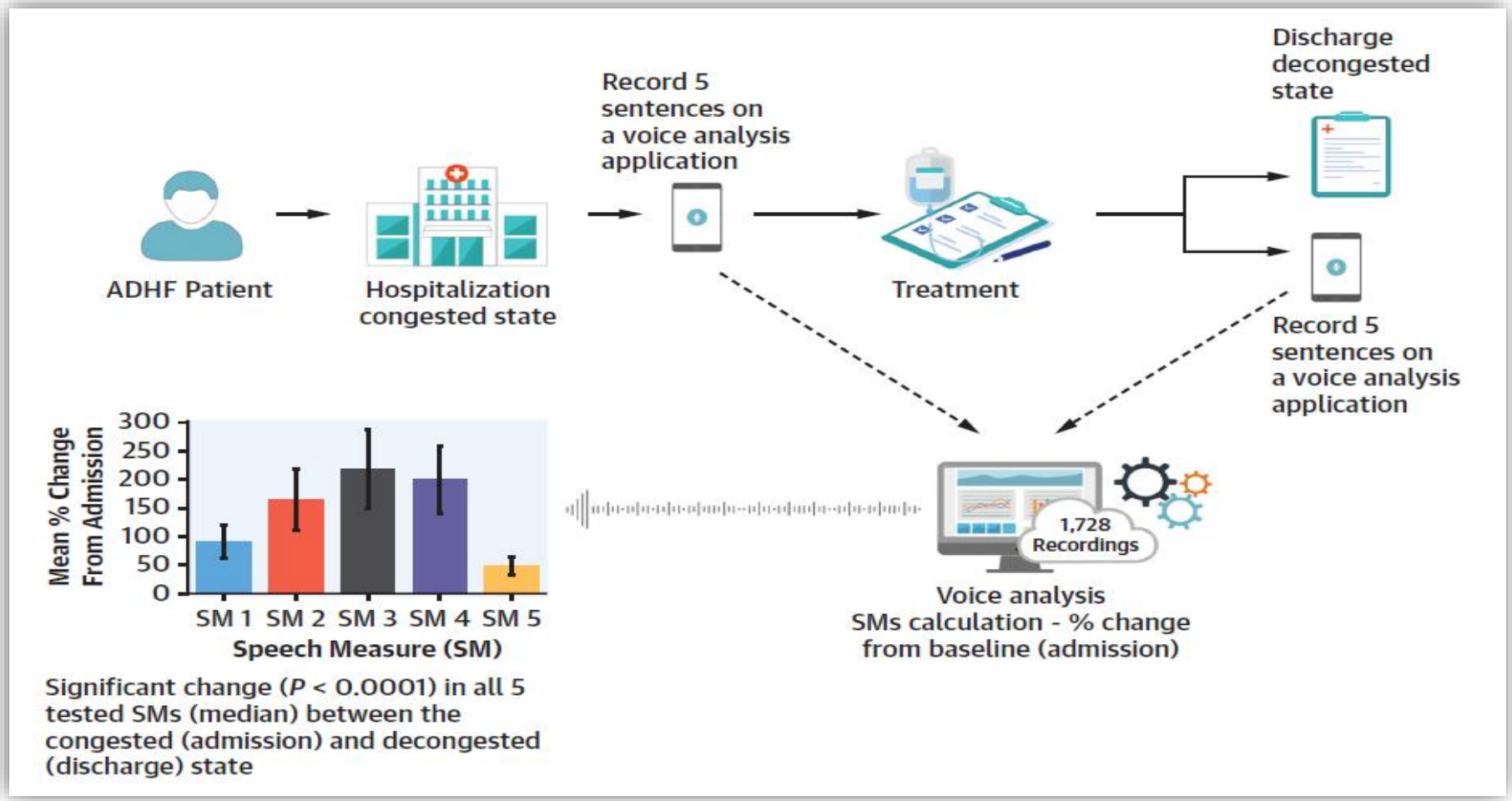
Subjects

- ✓Guidelines- Chest pain management.
- ✓New concept in Stable IHD & aggressive Lipid lowering treatment.
- ✓Atrial Fibrillation- A. changing the paradigm.
- ✓ B. Silent CVA in AF.
- ✓Interventional Cardiology.
- ✓Valvular Heart Diseases- what's new in the guidelines?
- ✓Cardiomyopathies- A. HCM
- ✓ B. ATTR-CMP
- ✓Heart Failure – The 2021 new guidelines.
- ✓ The role of SGLT2Inh.
- New frontiers – Tele- Med & AI
- The GOLDEN BULT in Cardiology

Speech Analysis in Heart Failure

Remote Speech Analysis in the Evaluation of Hospitalized Patients With Acute Decompensated Heart Failure

Offer Amir, MD, William T. Abraham, MD, Zaher S. Azzam, MD, Gidon Berger, MD, Stefan D. Anker, MD, PHD,
Sean P. Pinney, MD, Daniel Burkhoff, MD, PHD, Ilan D. Shallom, PHD, Chaim Lotan, MD, Elazer R. Edelman, MD, PHD



JACC: HEART FAILURE VOL. 10, NO. 1, 2022 JANUARY 2022:41–49

Heart Transplant

Subjects

- ✓Guidelines- Chest pain management.
- ✓New concept in Stable IHD & aggressive Lipid lowering treatment.
- ✓Atrial Fibrillation- A. changing the paradigm.
- ✓ B. Silent CVA in AF.
- ✓Interventional Cardiology.
- ✓Valvular Heart Diseases- what's new in the guidelines?
- ✓Cardiomyopaties- A. HCM
- ✓ B. ATTR-CMP
- ✓Heart Failure – The 2021 new guidelines.
- ✓ The role of SGLT2Inh.
- ✓New frontiers – Tele- Med & AI
- The GOLDEN BULT in Cardiology


BOOM!

New generation of artificial heart- by end of 2022


1
April
fool's day

מצוינות מהמעלה הראשונה !!!

לשאלות או קבלת המצגת
ניתן לפנות אליי בוואצאפ

דורון מנחמי
052-2313820