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New York Transcatheter Valves, 2019

"Transcatheter Valve Therapies in Heart Failure; new perspectives for 2020"

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No relevant disclosures

Aortic Stenosis; a 50 yr journey

JAMA Cardiol. 2018;3(12):1141-1143

EDITORIAL

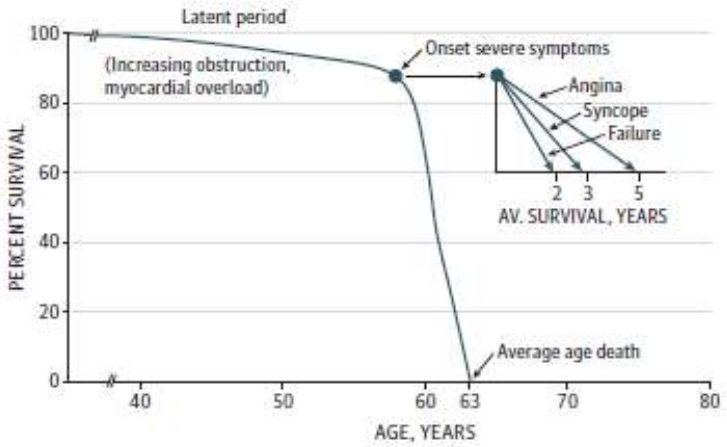
Aortic Stenosis—50 Years of Discovery

Robert O. Bonow, MD, MS; Patrick T. O'Gara, MD

Few images in medicine have had the influence or longevity of the iconic figure published by John Ross Jr, and Eugene Braunwald in their seminal 1968 article on the natural history of aortic stenosis (AS).[1] On its 50th anniversary, it is fitting to recognize the influence that this article—and this particular **Figure**—have had on the thought processes of generations of cardiologists throughout the world in their management of patients with AS. Indeed, it is unusual to attend a lecture on AS, whether presented to students or seasoned cardiovascular subspecialists, in which this figure is not shown. Their observations have also spawned decades of research associated with the natural history of the disease, including studies of valvular hemodynamics, left ventricular adaptation, imaging characteristics, mechanisms for disease progression, and the optimal timing of aortic valve replacement (AVR).

Ross and Braunwald emphasized "the grave prog-

Figure. Ross and Braunwald's Schematic of the Natural History of Aortic Stenosis



Aortic Stenosis, Volume: 137, Issue: 20, Pages: 2099-2100, DOI: (10.1161/CIRCULATIONAHA.118.033408)

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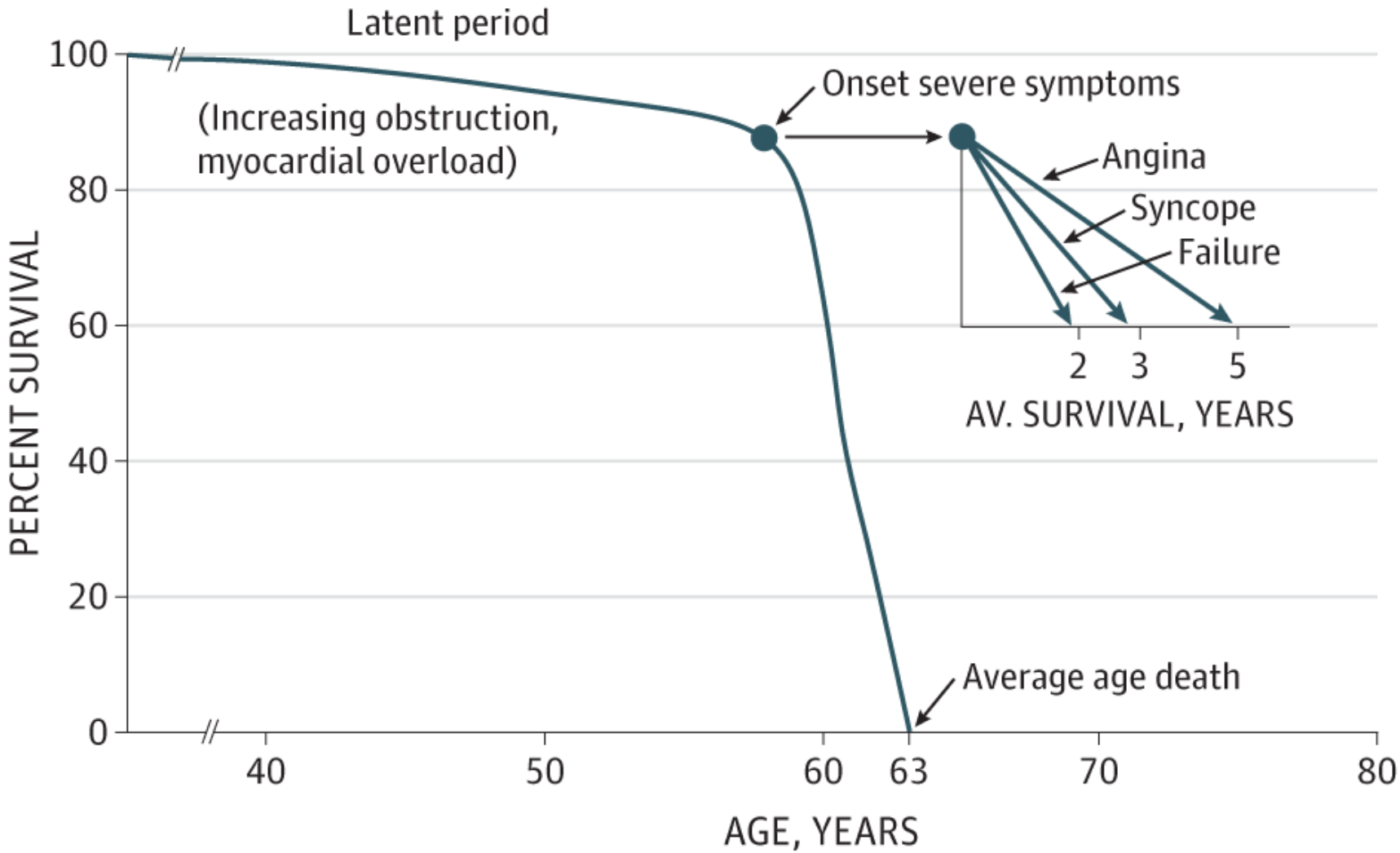
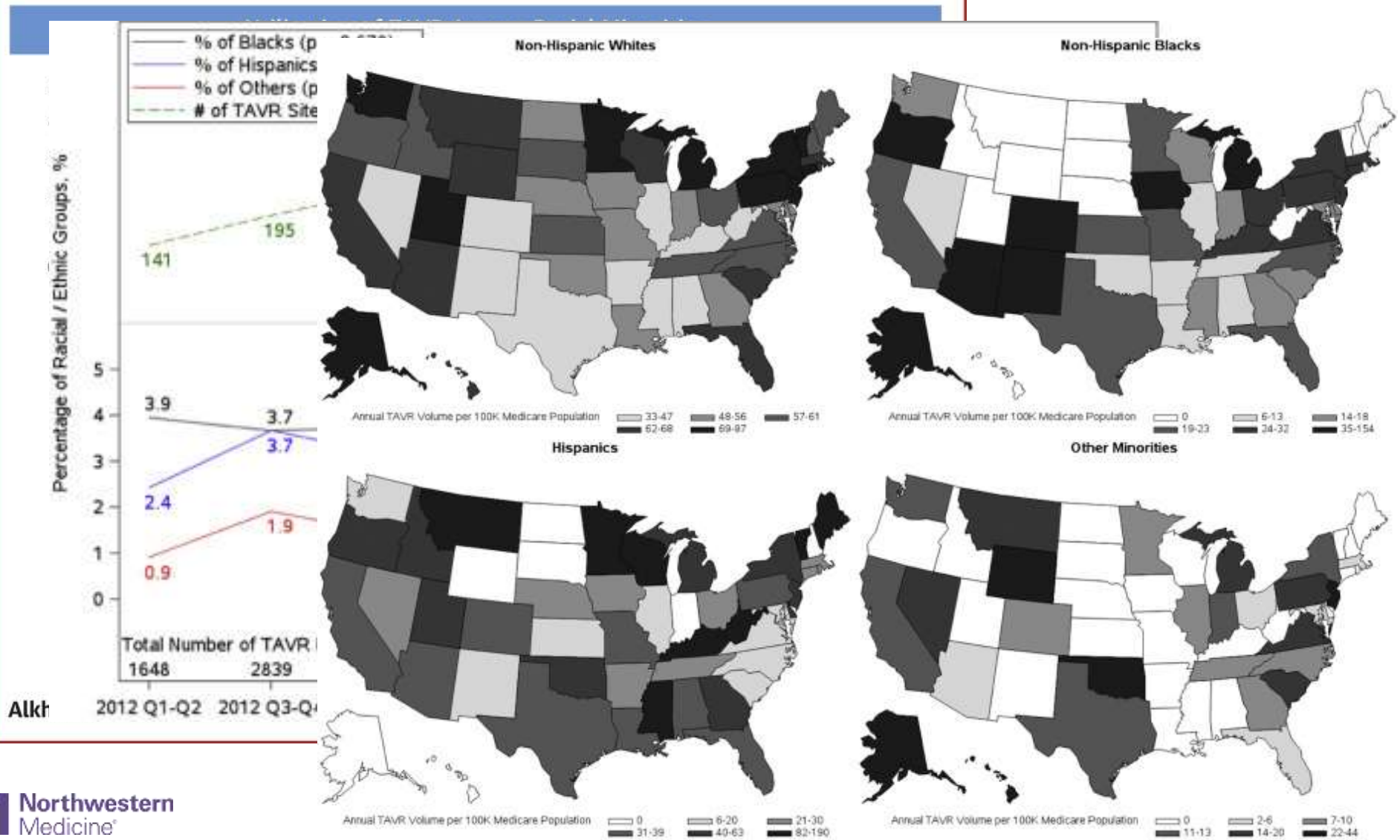


Aortic Stenosis, Volume: 137, Issue: 20, Pages: 2099-2100, DOI: (10.1161/CIRCULATIONAHA.118.033408)

CENTRAL ILLUSTRATION: Race-Stratified Differences in the Use and Outcomes of TAVR in the United States



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Mechanisms of FMR in HFrEF

Review

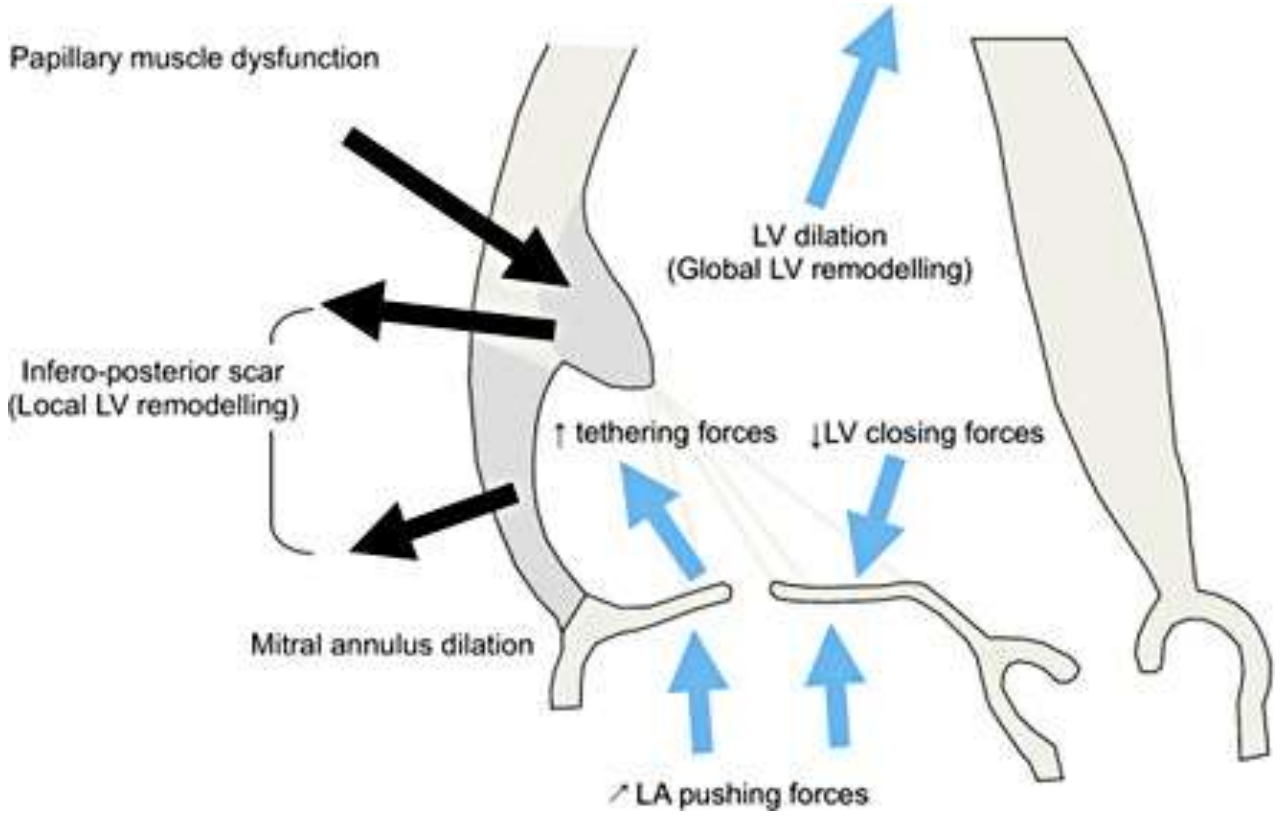
CARDIOLOGY

Cardiology 2013;125:110–117
DOI: 10.1159/000350356

Received: January 21, 2013
Accepted after revision: February 6, 2013
Published online: May 24, 2013

Secondary Mitral Regurgitation in Heart Failure with Reduced or Preserved Left Ventricular Ejection Fraction

Pierre Vladimir Ennezat[a] Sylvestre Maréchaux[b] Philippe Pibarot[c]
Thierry H. Le Jemtel[d]



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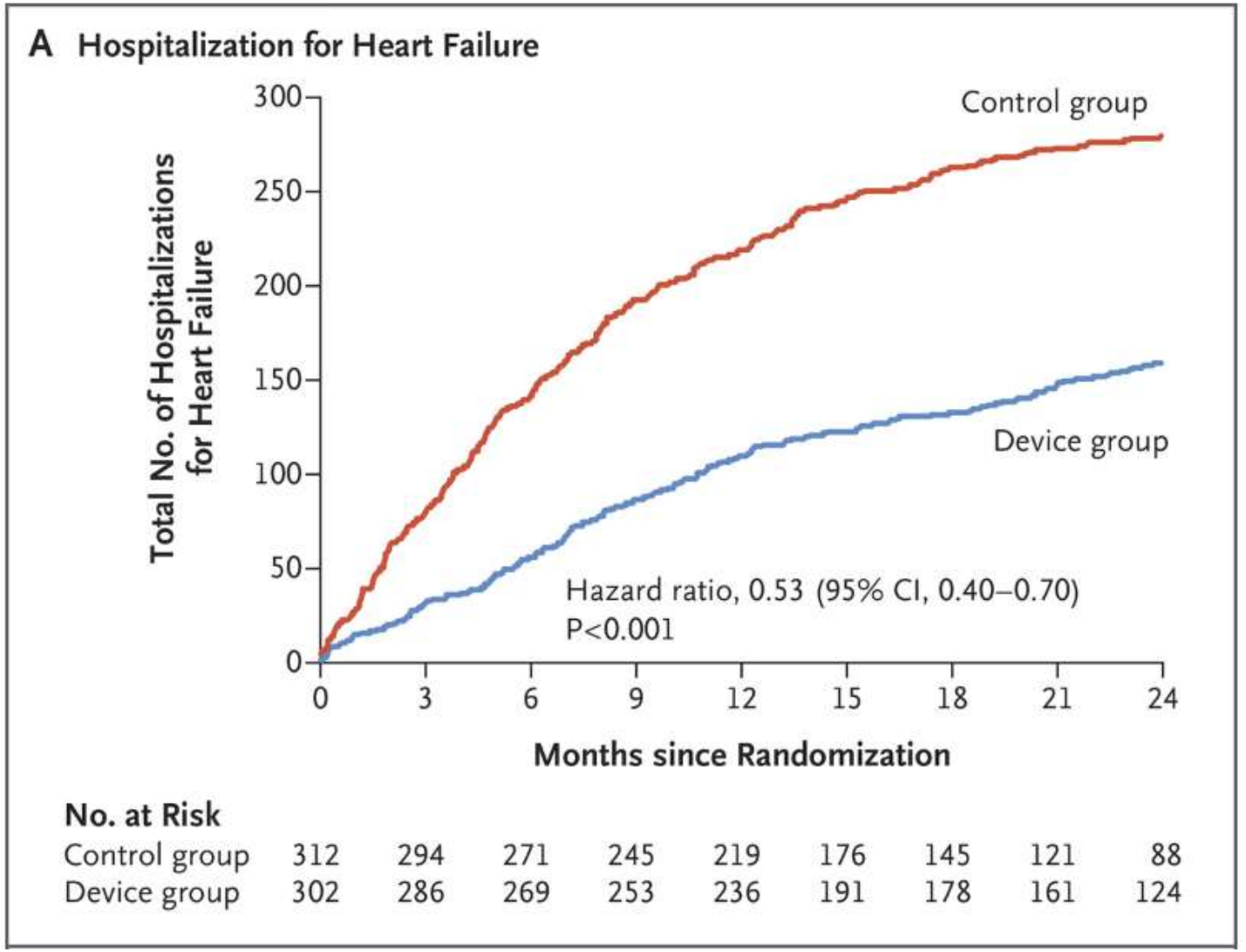
Primary Effectiveness and Safety End Points and Death.

Figure 1. Primary Effectiveness and Safety End Points and Death.



GW Stone et al. N Engl J Med 2018;379:2307-2318.

FDA Approval of tMVR, 03/2019

- "… The new indication, approved today, is for treatment of patients with normal mitral valves who develop heart failure symptoms and moderate-to-severe or severe mitral regurgitation because of diminished left heart function (commonly known as secondary or functional mitral regurgitation) ***despite being treated with optimal medical therapy.*** Optimal medical therapy includes combinations of different heart failure medications along with, in certain patients, cardiac resynchronization therapy and implantation of cardioverter defibrillators…"

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Characteristics of the Patients at Baseline.*

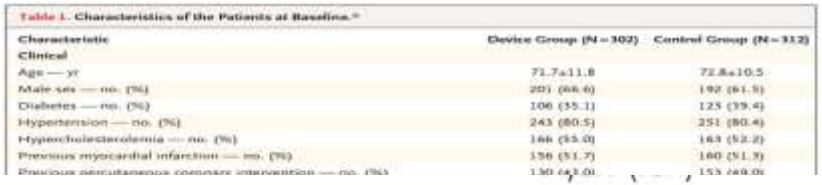


Table 1. Characteristics of the Patients at Baseline.*

Characteristic	Device Group (N = 302)	Control Group (N = 312)
Clinical		
Age — yr	71.7±11.8	72.8±10.5
Male sex — no. (%)	201 (66.6)	192 (61.5)
Diabetes — no. (%)	106 (35.1)	123 (39.4)
Hypertension — no. (%)	243 (80.5)	251 (80.4)
Hypercholesterolemia — no. (%)	166 (55.0)	163 (52.2)
Previous myocardial infarction — no. (%)	156 (51.7)	160 (51.3)
Previous percutaneous coronary intervention — no. (%)	130 (43.0)	153 (49.0)
Related to heart failure		
Cause of cardiomyopathy — no. (%)		
Ischemic	184 (60.9)	189 (60.6)
Nonischemic	118 (39.1)	123 (39.4)
NYHA class — no./total no. (%)		
I	1/302 (0.3)	0/311 (0)
II	129/302 (42.7)	110/311 (35.4)
III	154/302 (51.0)	168/311 (54.0)
IVa, ambulatory	18/302 (6.0)	33/311 (10.6)
Hospitalization for heart failure within previous 1 yr — no. (%)	176 (58.3)	175 (56.1)
Previous cardiac resynchronization therapy — no. (%)	115 (38.1)	109 (34.9)
Previous implantation of defibrillator — no. (%)	91 (30.1)	101 (32.4)
B-type natriuretic peptide level — pg/ml	1014.8±1086.0	1017.1±1212.8
N-terminal pro–B-type natriuretic peptide level — pg/ml	5174.3±6566.6	5943.9±8437.6
Mean — %	31.3±9.1	31.3±9.6
≤40% — no./total no. (%)	231/281 (82.2)	241/294 (82.0)
Right ventricular systolic pressure — mm Hg	44.0±13.4 (253)	44.6±14.0 (275)

* Plus–minus values are means ±SD. Data on B-type natriuretic peptide level were available for 208 patients in the device group and 205 patients in the control group; N-terminal pro–B-type natriuretic peptide level, 74 and 85, respectively; effective regurgitant orifice area, 289 and 302; left ventricular end-systolic dimension, 301 and 306; left ventricular end-diastolic dimension, 301 and 307; left ventricular end-systolic volume, end-diastolic volume, and ejection fraction, 281 and 294; and right ventricular systolic pressure, 253 and 275. There were no significant differences between the trial groups with regard to baseline characteristics. NYHA denotes New York Heart Association.
† The body-mass index is the weight in kilograms divided by the square of the height in meters.
‡ The mean creatinine clearance was calculated with the Cockcroft–Gault equation.
§ In accordance with World Health Organization criteria, anemia was defined as a hemoglobin level at initial presentation of less than 13 g per deciliter in men and less than 12 g per deciliter in women.
¶ Society of Thoracic Surgeons (STS) scores for the risk of death within 30 days after mitral-valve replacement range from 0.4 to 98.1%, with higher percentages indicating greater risk.
‖ Risk of surgery-related complications or death was determined by the central eligibility committee. High risk was defined as an STS score for the risk of death within 30 days after mitral-valve replacement of 8% or higher or the presence of features that portend an extremely high risk of operative stroke or death.

COAPT vs. MITRA-FR: MR, LV Volumes and Function

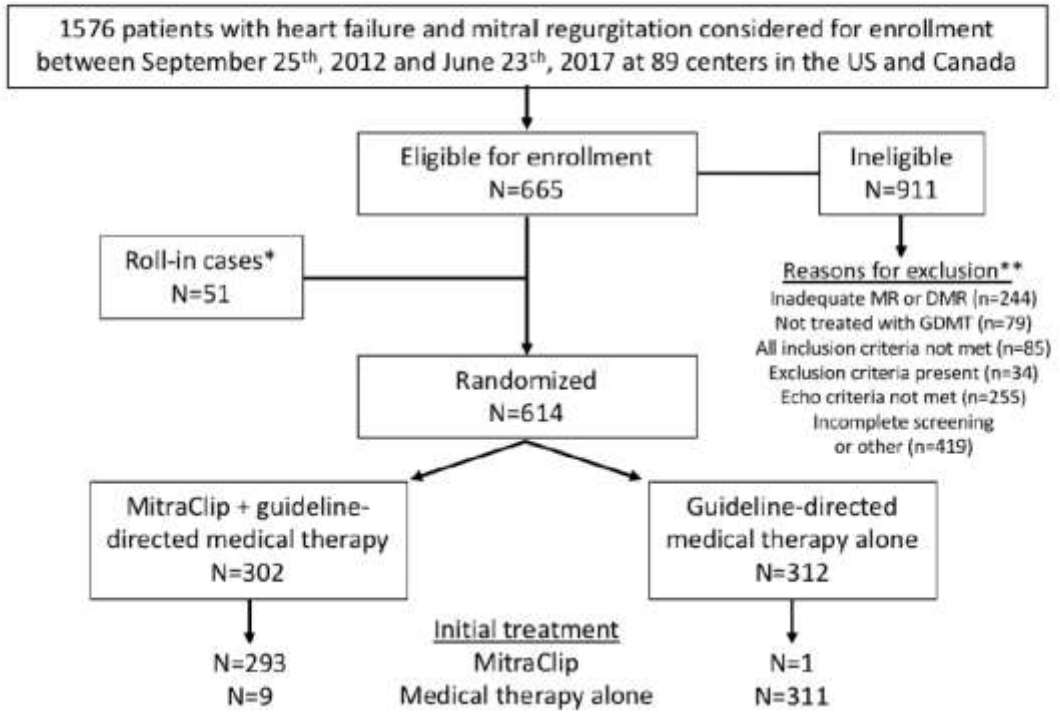
	COAPT (n=614)	MITRA-FR (n=304)
EROA, mm^2 (mean ± SD)	41 ± 15	31 ± 10
- <30 mm^2	14% (80/591)	52% (157/301)
- 30 – 40 mm^2	46% (270/591)	32% (95/301)
- >40 mm^2	41% (241/591)	16% (49/301)
LVEF, % (mean ± SD)	31 ± 9	33 ± 7
LVEDV, mL/m^2 (mean ± SD)	101 ± 34	135 ± 35

Obadia JF et al. NEJM. 2018 Aug 27. doi: 10.1056/NEJMoa1805374; Stone GW et al. NEJM. 2018 Sept 23.

Who was enrolled in COAPT?

Figure S2. CONSORT diagram of patient flow in the COAPT trial.

By protocol the primary endpoint was assessed at 24-month duration of follow-up, with all patients having a minimum of 12 months of follow-up. Patients were considered eligible for the 24-month follow-up visit if they reached the end of the follow-up window (731+30 days) at the time of database lock. All follow-up rates are presented for the intention-to-treat population.
*Enrolled at 34 sites by operators without prior or recent experience using the MitraClip device.
**Some patients had multiple exclusion criteria.



Inadequate MR: 15%

Insufficient GDMT:25%

No GDMT: 5%

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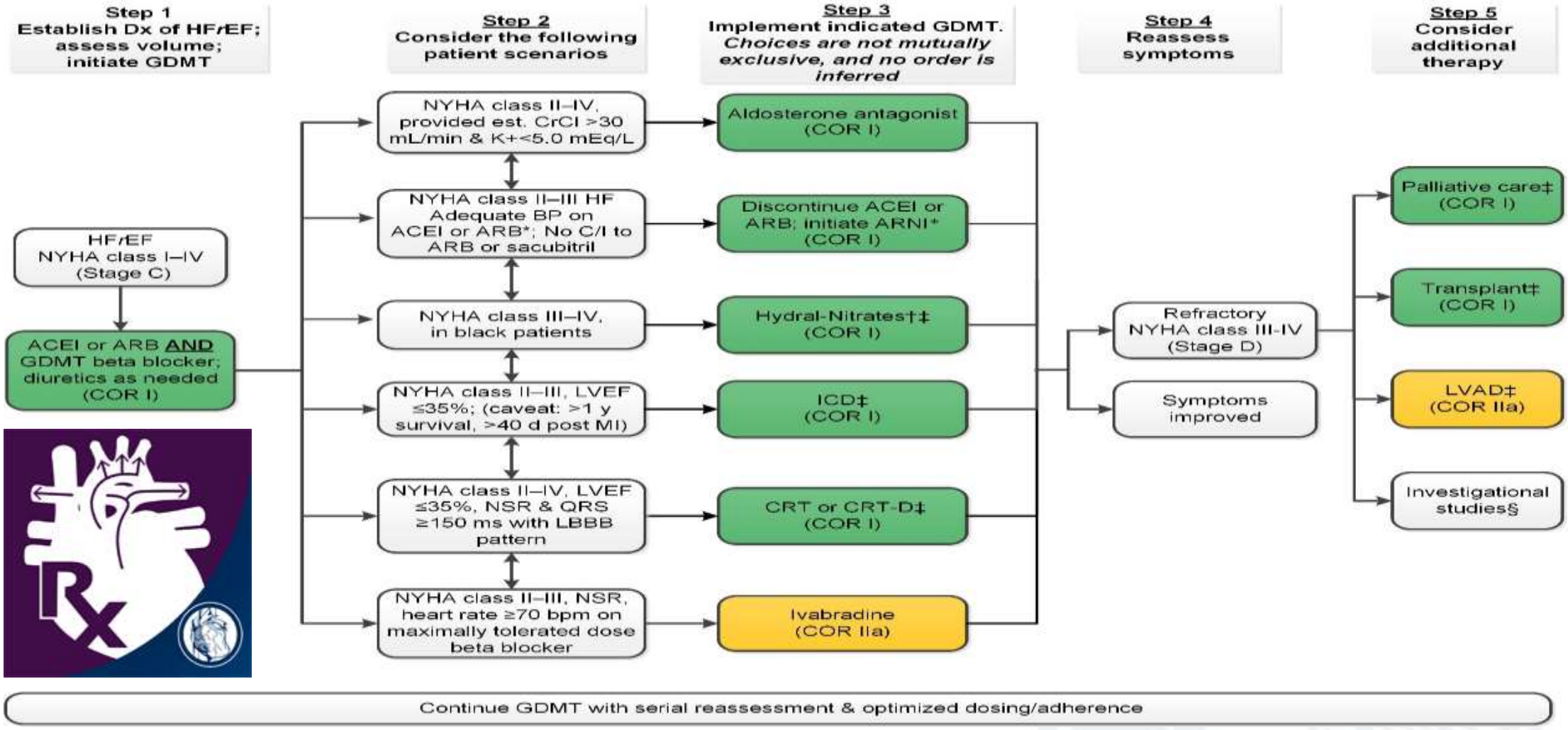
What constitutes GDMT?

Treatment of HFrEF Stage C and D



Yancy C, et al. JACC, 2016

†Hydral-Nitrates green box: The combination of ISDN/HYD with ARNI has not been robustly tested. BP response should be carefully monitored.
‡See 2013 HF guideline.
§Participation in investigational studies is also appropriate for stage C, NYHA class II and III HF.
ACEI indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor-blocker; ARNI, angiotensin receptor-neprilysin inhibitor; BP, blood pressure; bpm, beats per minute; C/I, contraindication; COR, Class of Recommendation; CrCl, creatinine clearance; CRT-D, cardiac resynchronization therapy–device; Dx, diagnosis; GDMT, guideline-directed management and therapy; HF, heart failure; HFrEF, heart failure with reduced ejection fraction; ICD, implantable cardioverter-defibrillator; ISDN/HYD, isosorbide dinitrate hydral-nitrates; K+, potassium; LBBB, left bundle-branch block; LVAD, left ventricular assist device; LVEF, left ventricular ejection fraction; MI, myocardial infarction; NSR, normal sinus rhythm; and NYHA, New York Heart Association.

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GDMT- *a moving target?*

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The JAMA Network

From: **The Metabolodiuretic Promise of Sodium-Dependent Glucose Cotransporter 2 InhibitionThe Search for the Sweet Spot in Heart Failure**

JAMA Cardiol. 2017;2(9):939-940. doi:10.1001/jamacardio.2017.1891

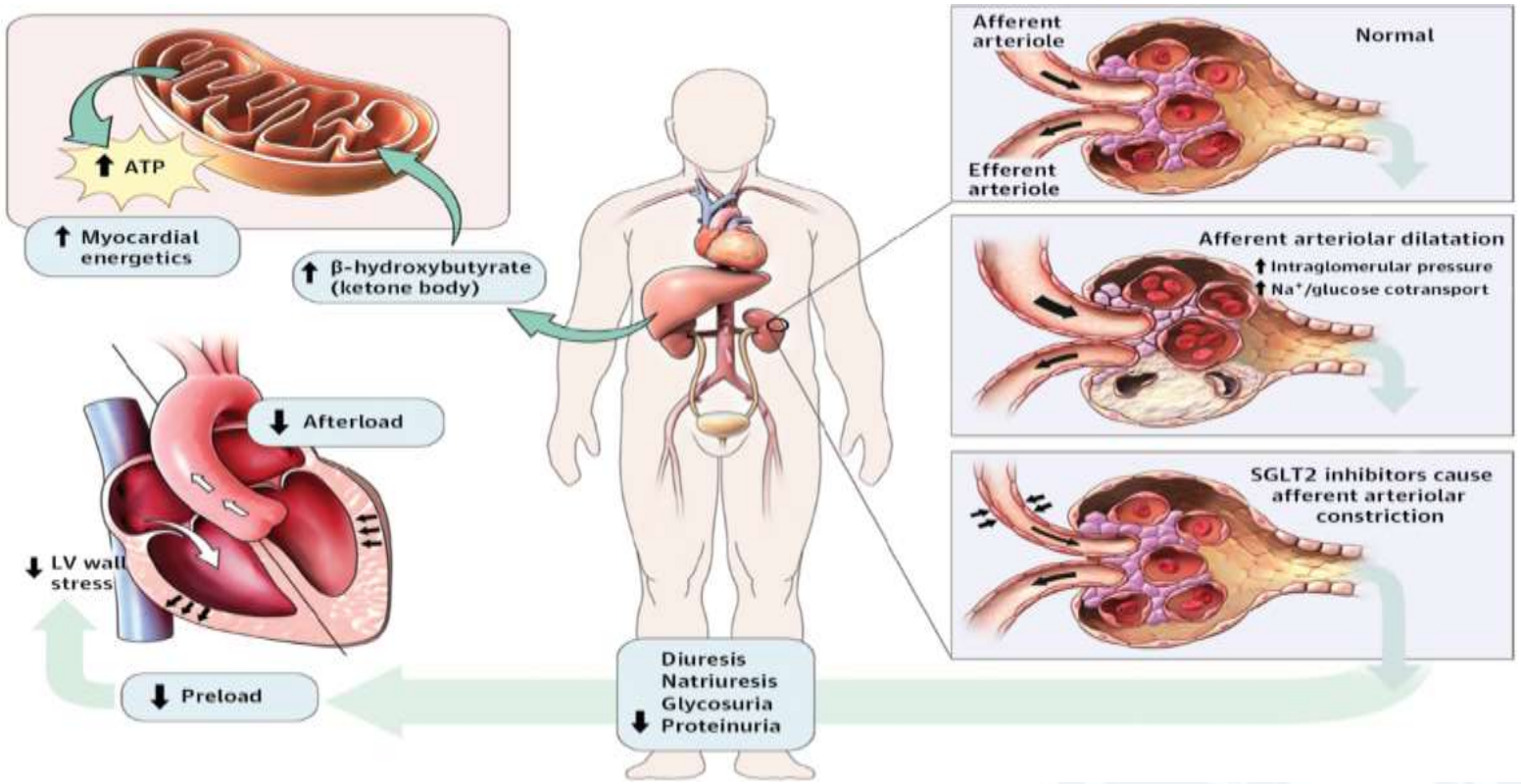
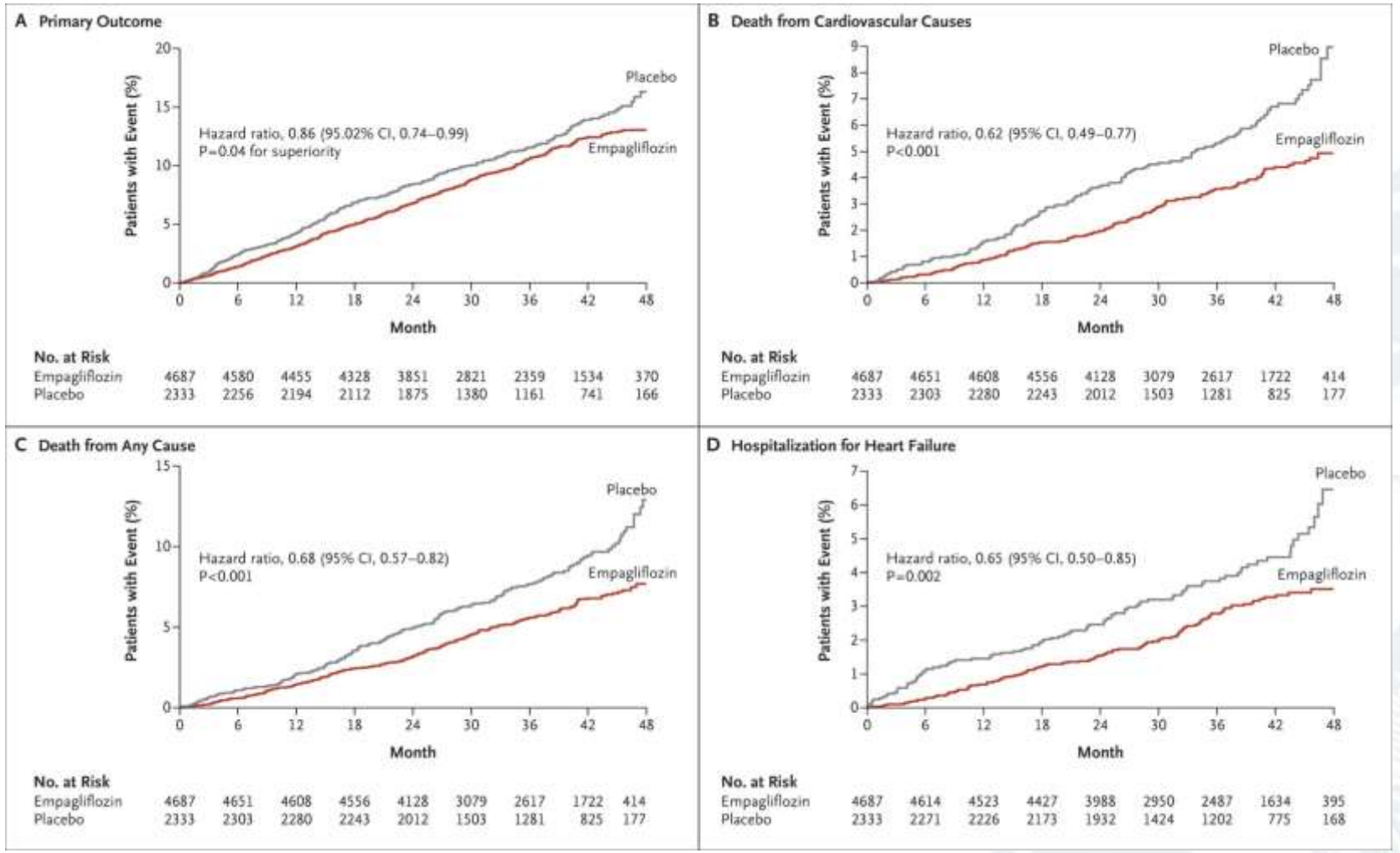


Figure Legend:

Proposed Mechanism of Cardiorenal Protection With Sodium-Dependent Glucose Cotransporter 2 (SGLT2) InhibitorsAt the level of the kidney, SGLT2 inhibition promotes glycosuria and natriuresis. It also promotes afferent arterioral constriction resulting in a decrease in intraglomerular pressure. A reduction in preload and resultant left ventricular (LV) wall stress improves overall LV filling conditions. Additionally, metabolic effects of SGLT2 inhibition to improve myocardial energetics and reduce afterload have also been proposed as cardioprotective mechanisms. ATP indicates adenosine triphosphate.

This figure was specifically commissioned for this article and has not been reproduced in any form in any media format. Figure created by M. Gail Rudakevich, BSc, MScBMC.

Cardiovascular Outcomes and Death from Any Cause.



The NEW ENGLAND JOURNAL of MEDICINE

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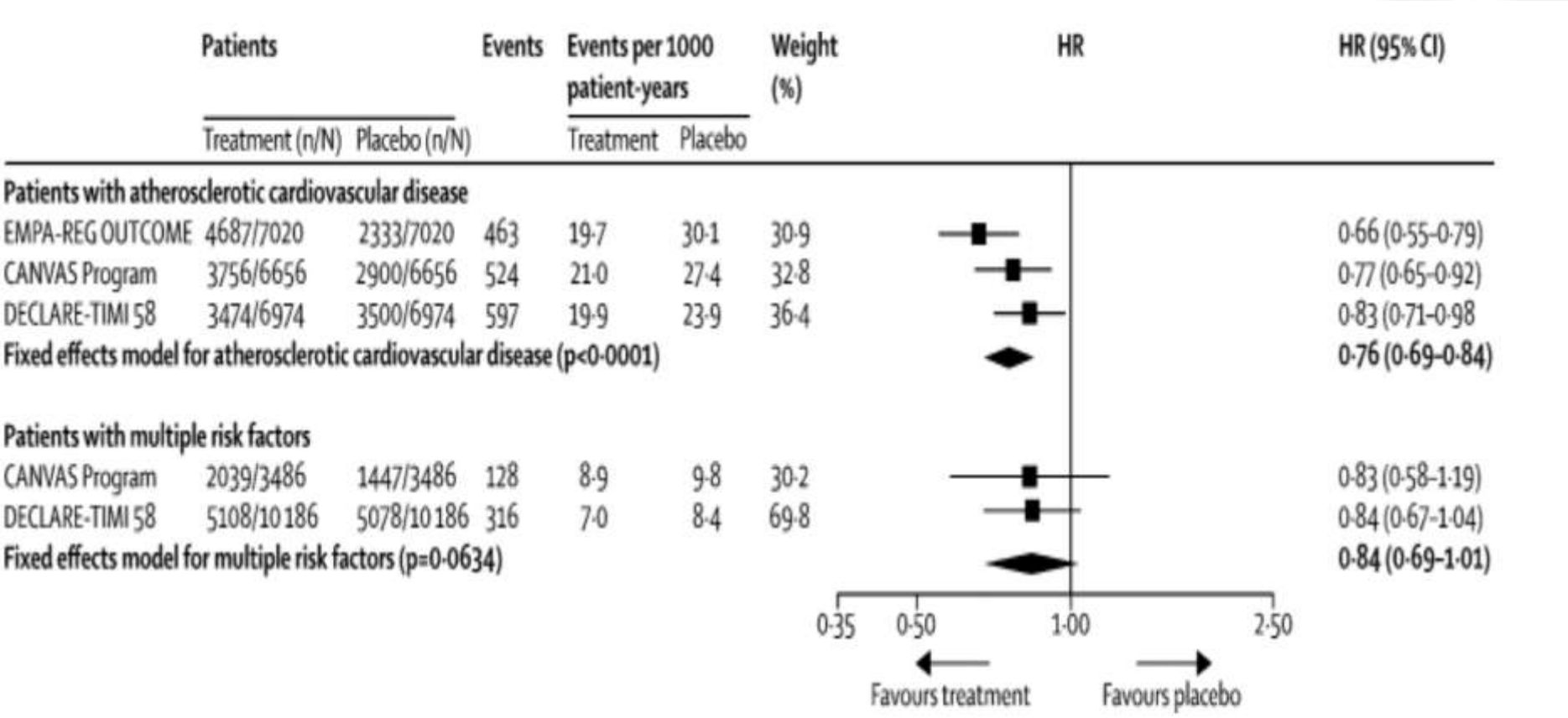
SGLT2 Inhibitors Reduce the Risk of Heart Failure Events in Type 2 Diabetes

Is the Mechanism of Benefit Through NHE-1 Inhibition?



Lancet 2018 Nov (online)

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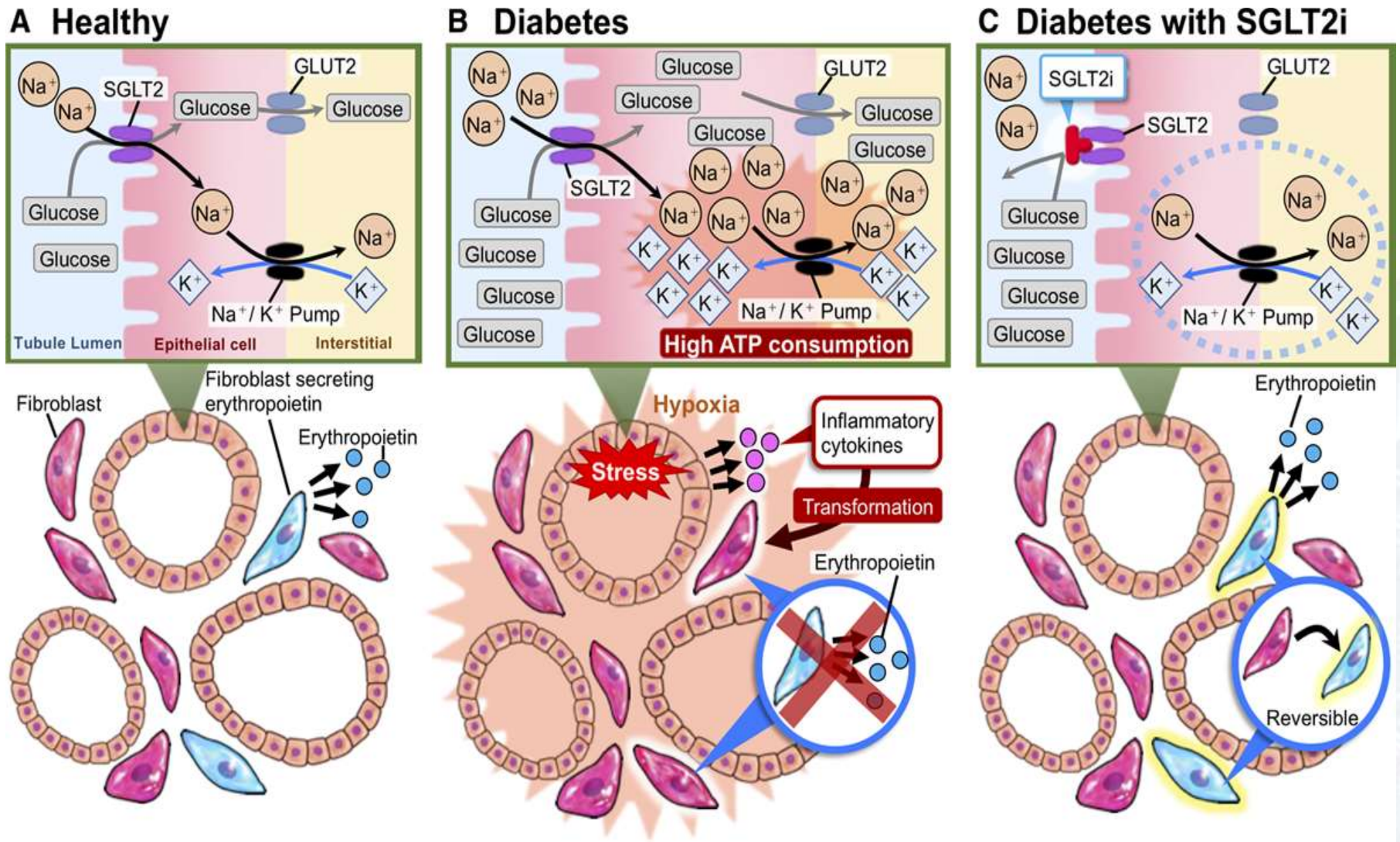
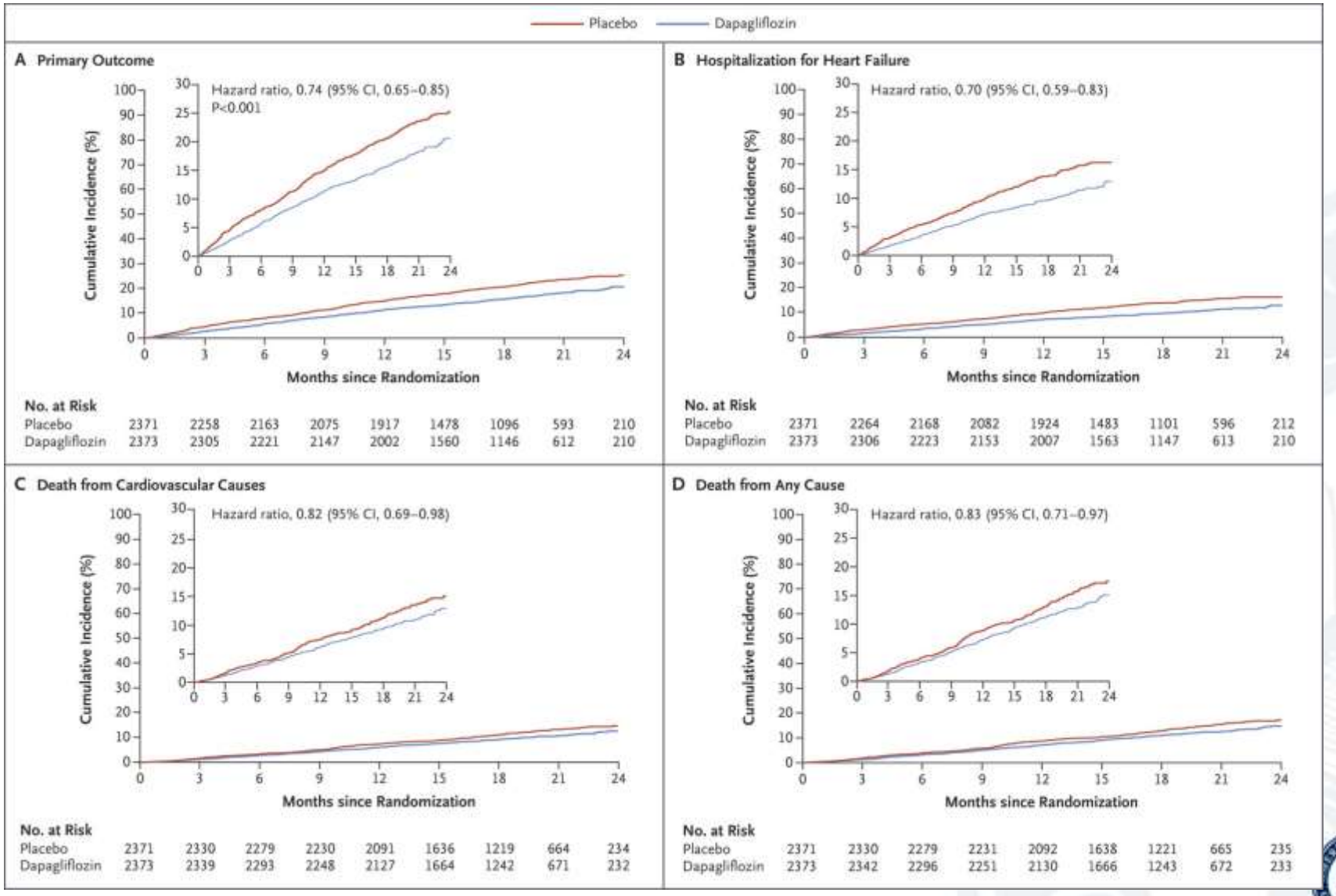


Possible Mechanism of Hematocrit Elevation by Sodium Glucose Cotransporter 2 Inhibitors and Associated Beneficial Renal and Cardiovascular Effects, Volume: 139, Issue: 17, Pages: 1985-1987, DOI: (10.1161/CIRCULATIONAHA.118.038881)

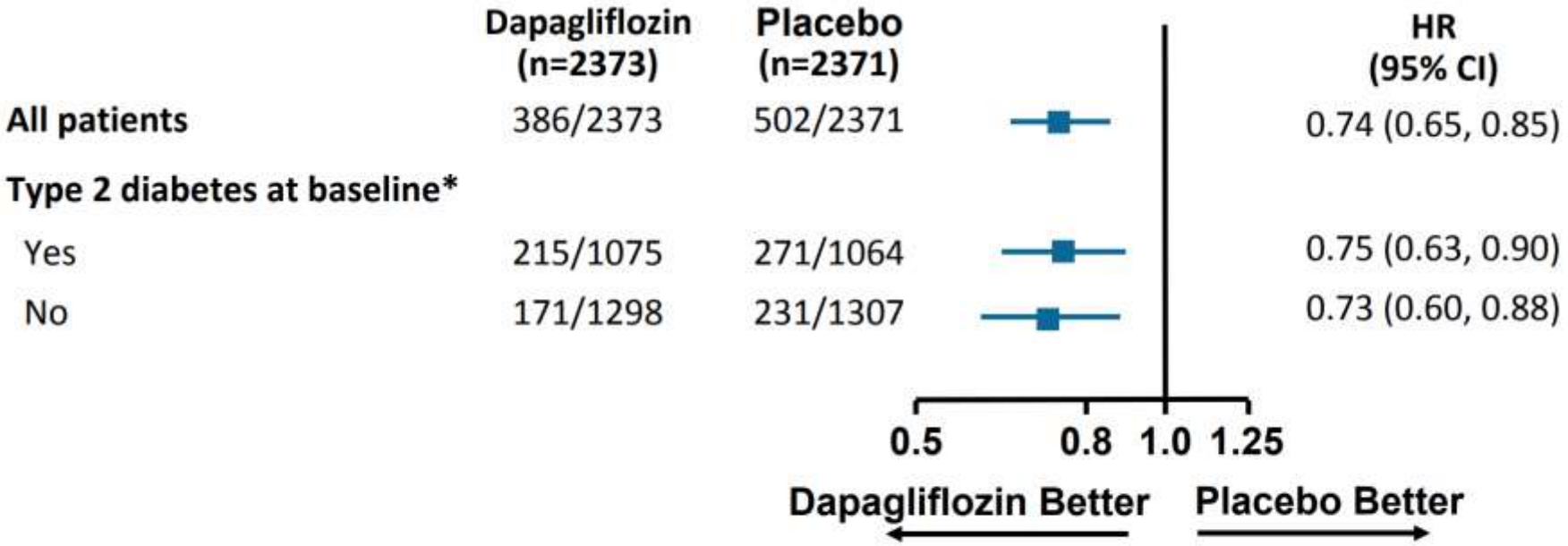
Cardiovascular Outcomes.



JJ McMurray et al. N Engl J Med 2019. DOI: 10.1056/NEJMoa1911303

DAPA-HF: Effect of Dapagliflozin in Heart Failure, With or Without Diabetes

Effect on Primary Endpoint of Cardiovascular Death and Serious Heart Failure Events



DAPA-HF: Effect of Dapagliflozin in Heart Failure, With or Without Diabetes

An inflection point in the care of patients with heart failure…

- Benefits seen in those with or without Diabetes
- Once a day therapy; single dose; no need for titration (N.B. low use of ARNI)
- No episodes of hypoglycemia or diabetic ketoacidosis
- Negligible incidence of amputations
- *NNT= 21; benefits seen even in those >75*
- Needs further validation; awaiting EMPEROR-REDUCED; candidate COR I/LOE A??
- Resolution of mechanism of action is needed

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Cell Metabolism
Volume 30, Issue 5, 5 November 2019, Pages 847-849

Preview

The DAI War aga

Deepak L. Bhatt [1]
Show more

https://doi.org/10.

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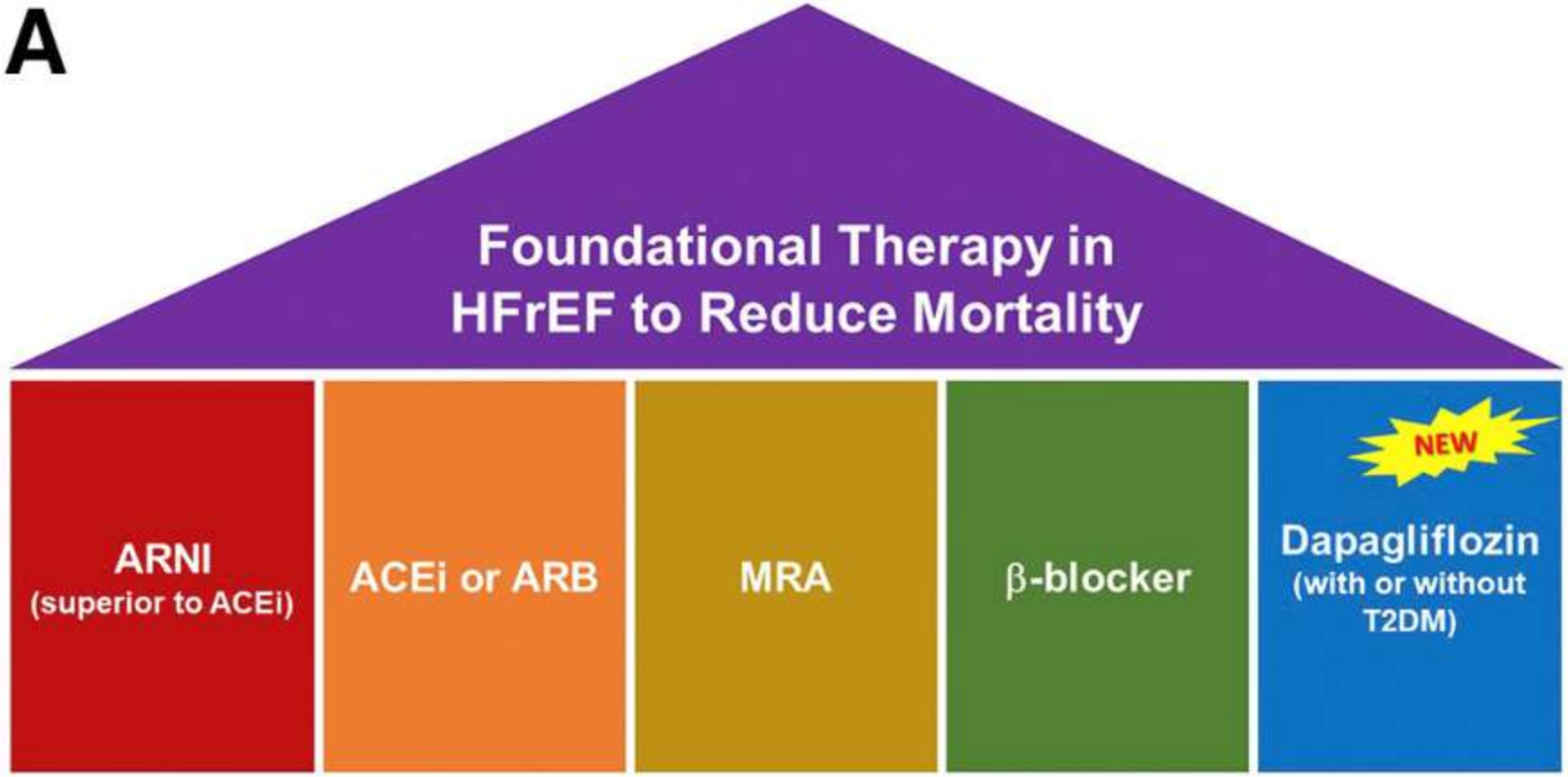

CARDIOLOGY

GDMT- *a challenging target?*

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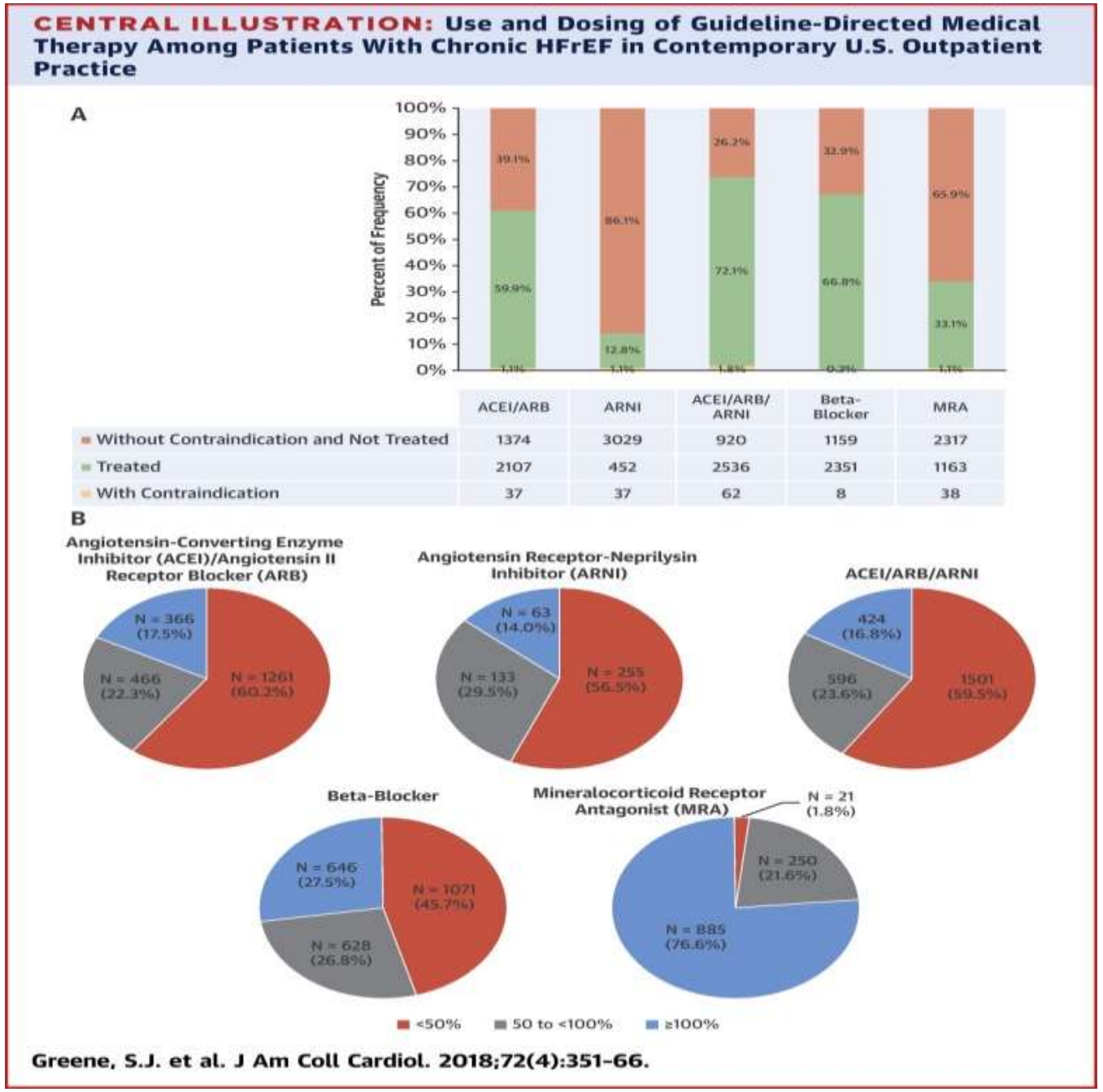
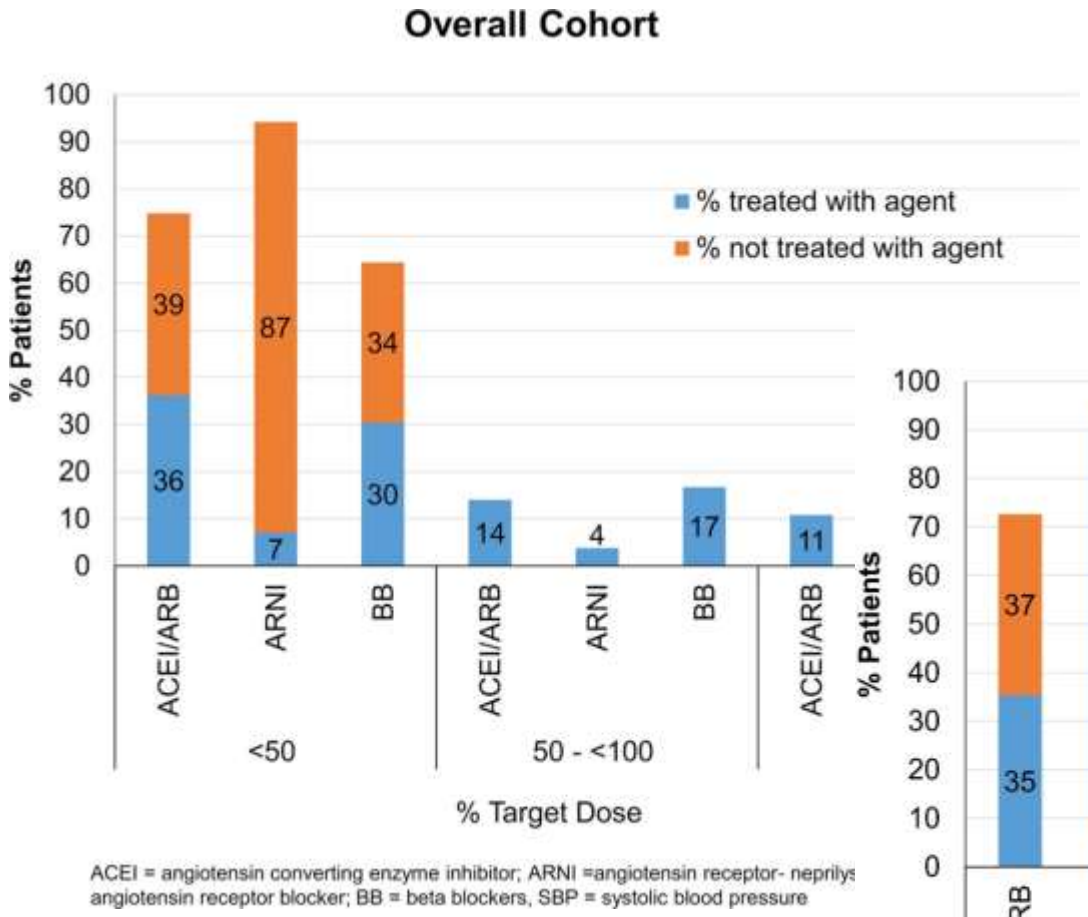
“Only 1% of eligible patients were simultaneously treated with target does of ACEI/ARB/ARNI, beta-blocker, and MRA therapy, and <25% of patients simultaneously received any dose of all 3 medications.”

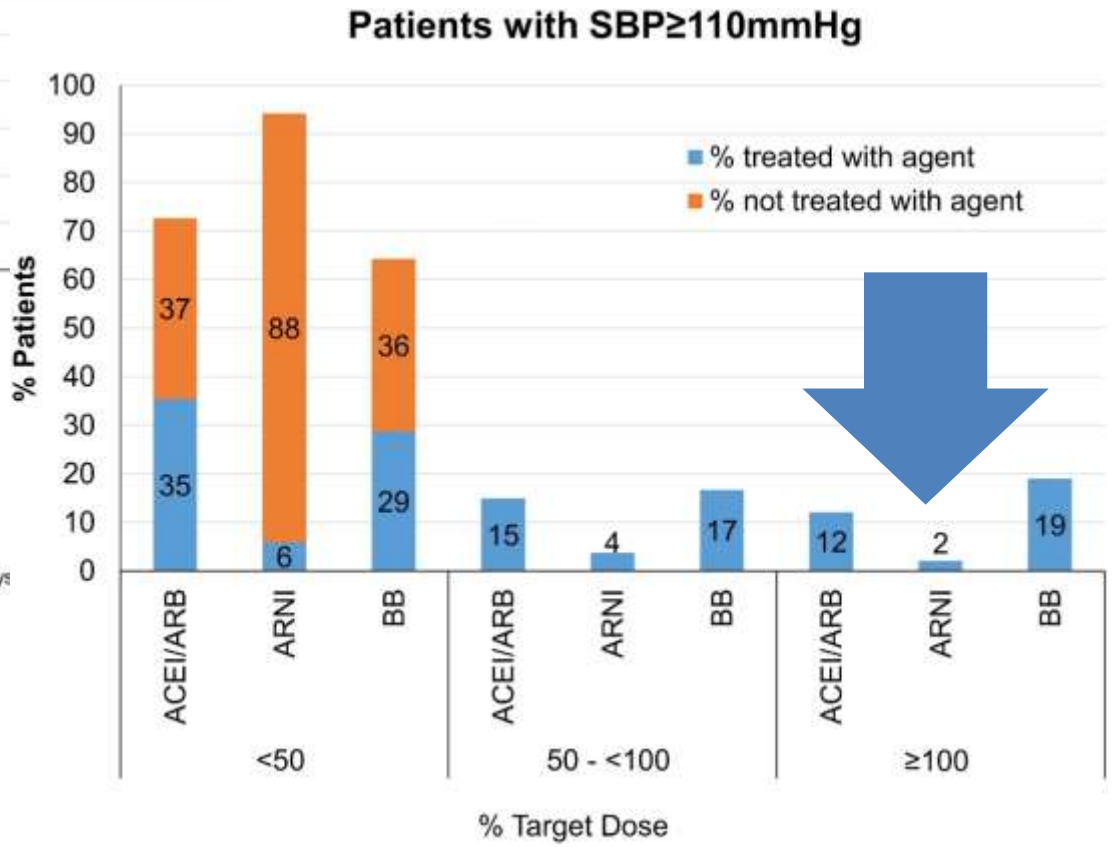


Greene, S.J. et al. J Am Coll Cardiol. 2018;72(4):351-66.

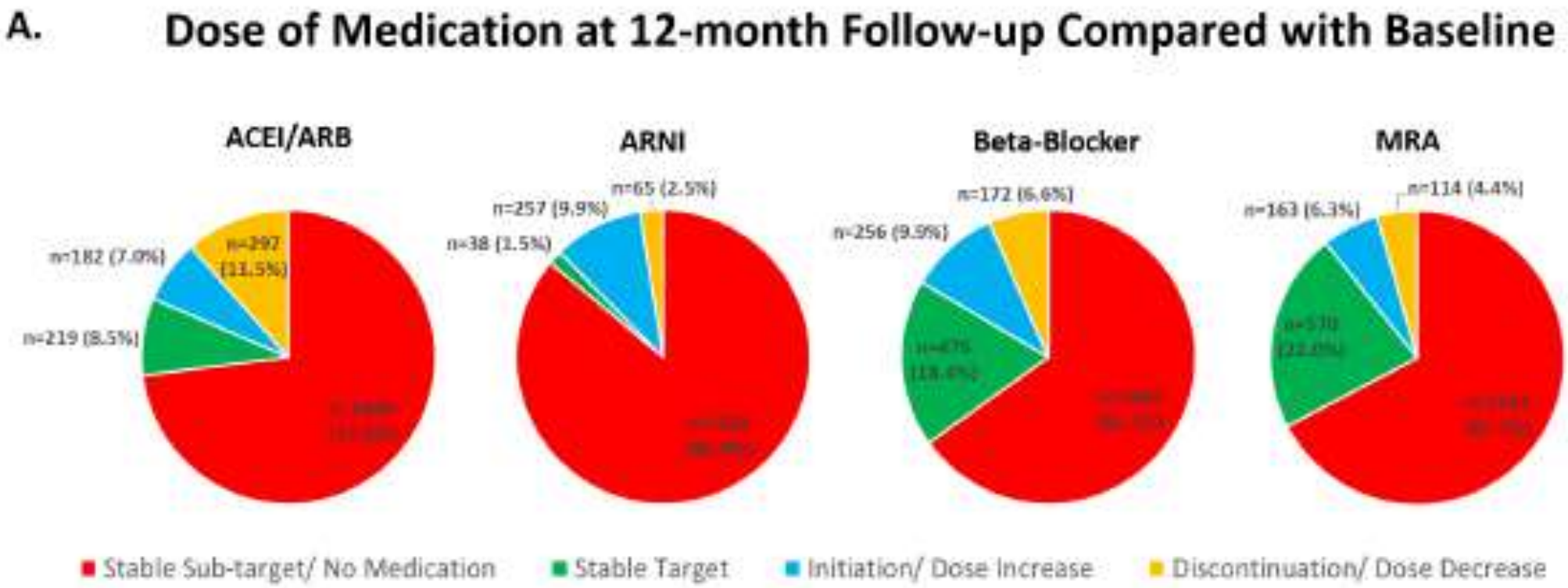
Target Doses of Heart Failure Medical Therapy and Blood Pressure: Insights From the CHAMP-HF Registry



ACEI = angiotensin converting enzyme inhibitor; ARNI =angiotensin receptor- neprilys
angiotensin receptor blocker; BB = beta blockers, SBP = systolic blood pressure



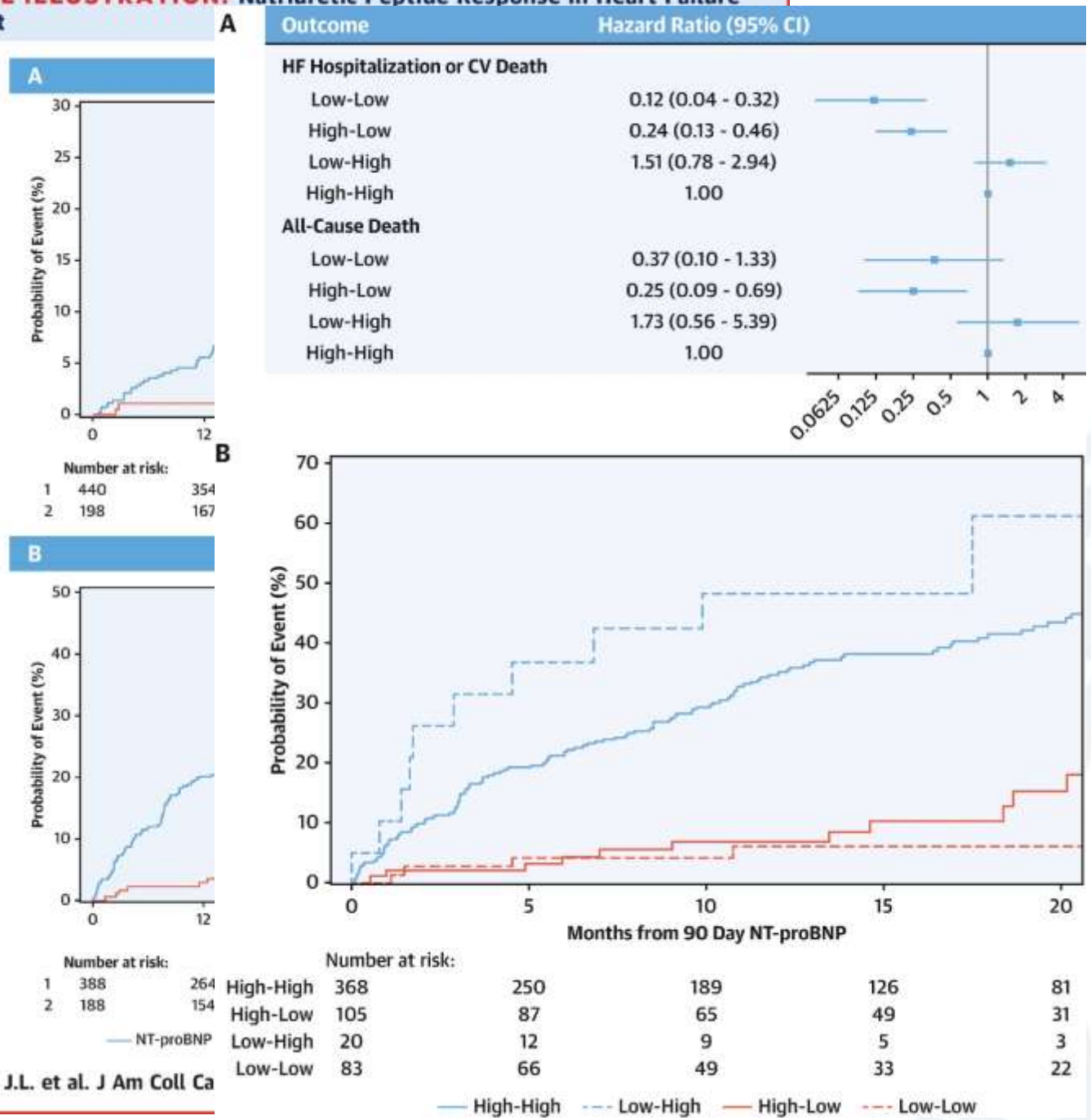
Longitudinal Titration of Medical Therapy for Heart Failure with Reduced Ejection



Greene, Fonarow, DeVore et al. JACC 2019

When is GDMT adequate?

CENTRAL ILLUSTRATION: Natriuretic Peptide Response in Heart Failure Treatment



Januzzi, Jr., J.L. et al. J Am Coll Ca

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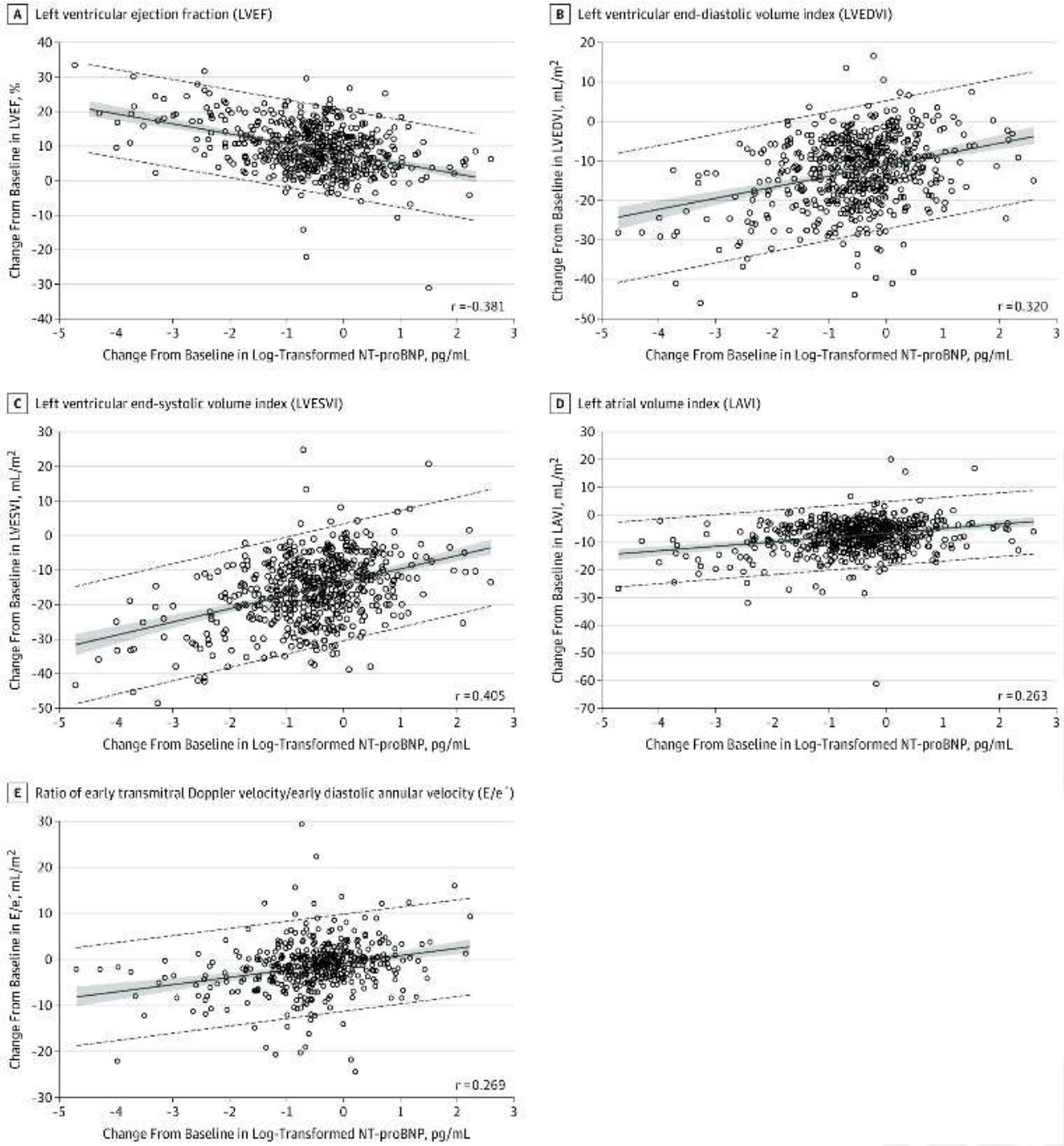

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Cumulative Impact of Evidence-Based Heart Failure with Reduced EF Medical Therapies

	Relative-risk	2 yr Mortality
None	- -	35%
ACEI or ARB	↓ 23%	27%
Beta Blocker	↓ 35%	18%
Aldosterone Ant	↓ 30%	13%
ARNI (replacing ACEI/ARB)	↓ 16%	10.9%
SGLT2 inhibitor	↓ 17%	9.1%

Cumulative risk reduction if all evidence-based medical therapies are used:
Relative risk reduction 74.0%, Absolute risk reduction: 25.9%, NNT = 3.9

Updated from Fonarow GC, et al. Am Heart J 2011;161:1024-1030 and Lancet 2008;372:1195-1196.


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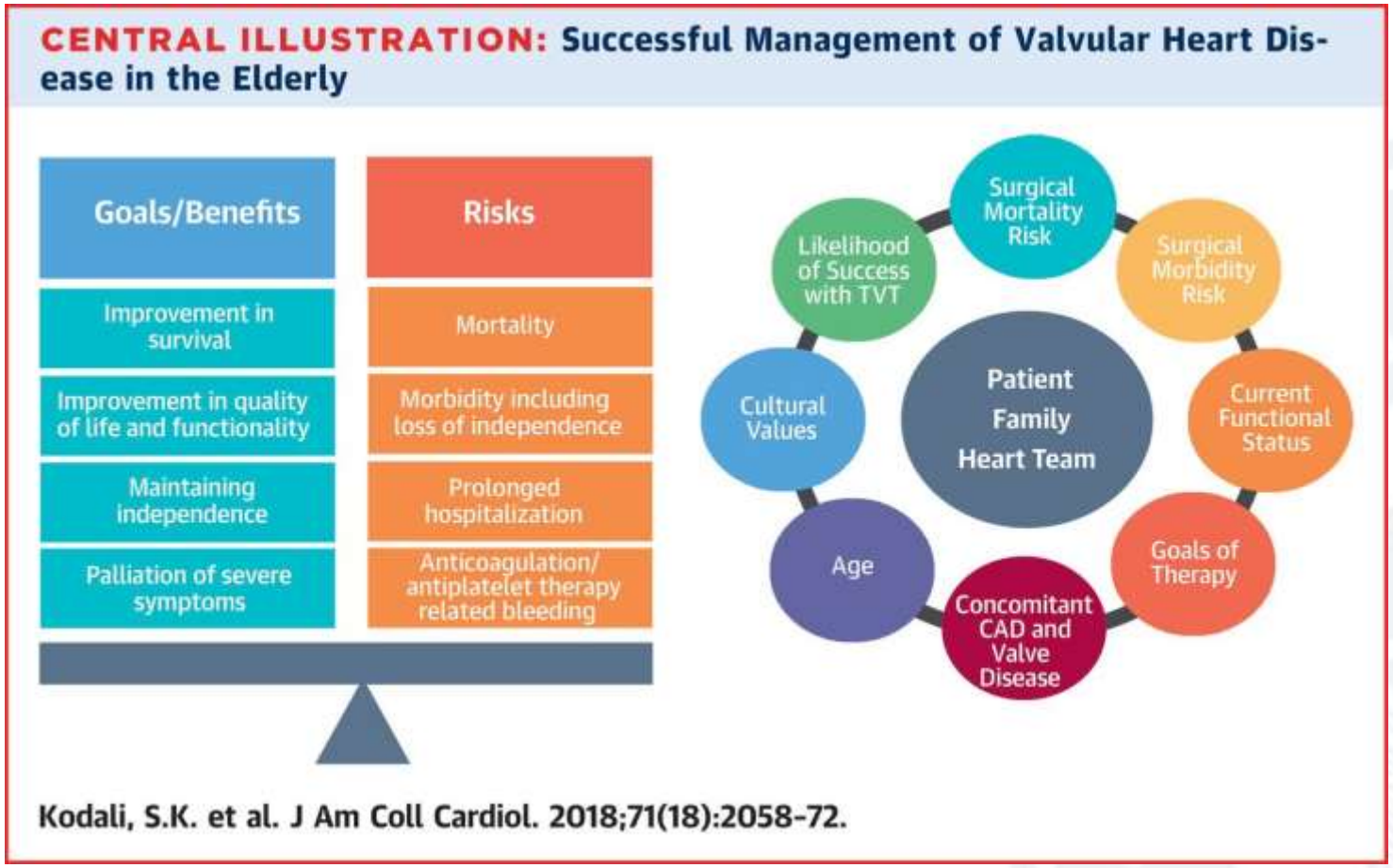
“Transcatheter Valve Therapies in Heart Failure; new perspectives for 2020”
Be aware of this…

Challenges in the attainment of GDMT for heart failure

- The complexity has increased
- Eight evidence based medical therapies, Four evidence based device therapies plus an array of disease management schemes & an indication for cardiac rehab
- Major challenges in drug titration, adherence- requires a team-based approach
- A call for more personalized therapy; Precision Medicine is needed to refine the choices of GDMT, especially regarding race, sex, age, co-morbidity
- Even with covered therapies, the aggregate cost of co-payments may be beyond the resources of many patients with heart failure

Successful valvular heart disease care requires team management



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“I have been impressed with the urgency of doing. Knowing is not enough; we must apply. Being willing is not enough; we must do.”
— Leonardo da Vinci