NEW ERA FOR HEART FAILURE MANAGEMENT

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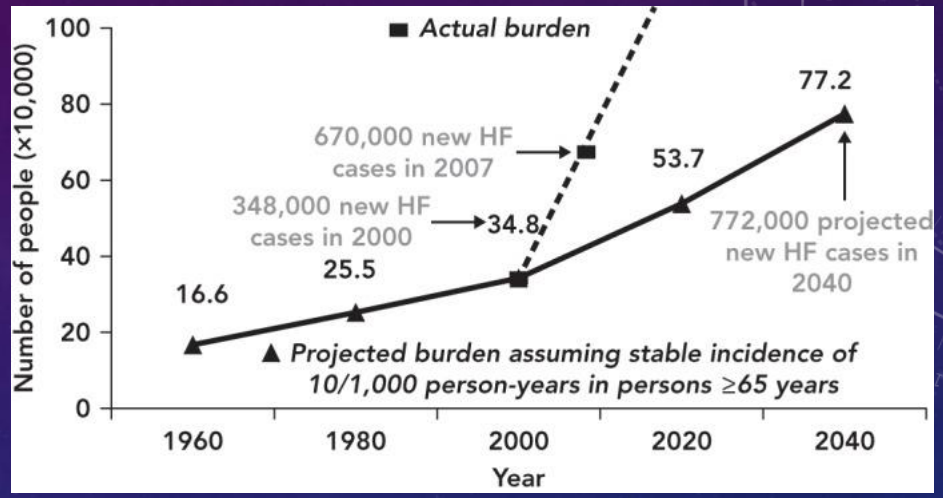
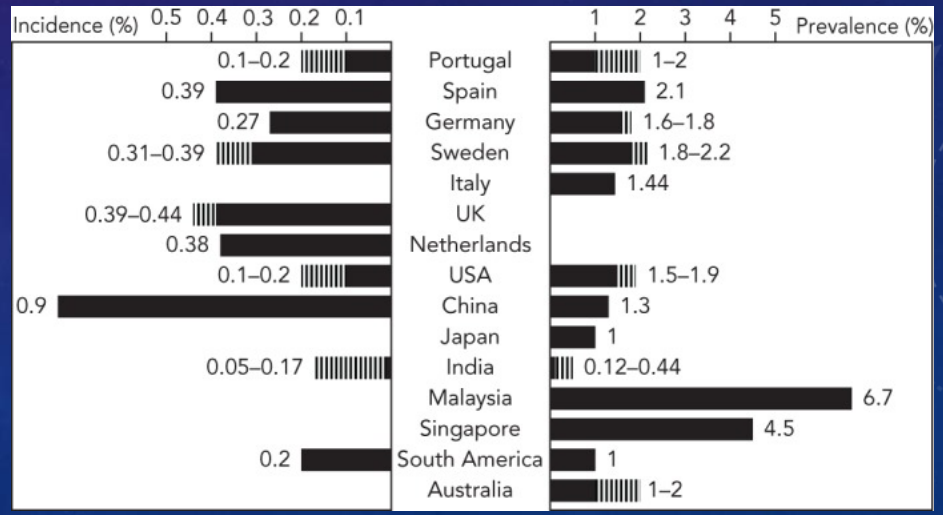
HEART FAILURE : STILL UNMET NEEDS IN CURRENT ERA

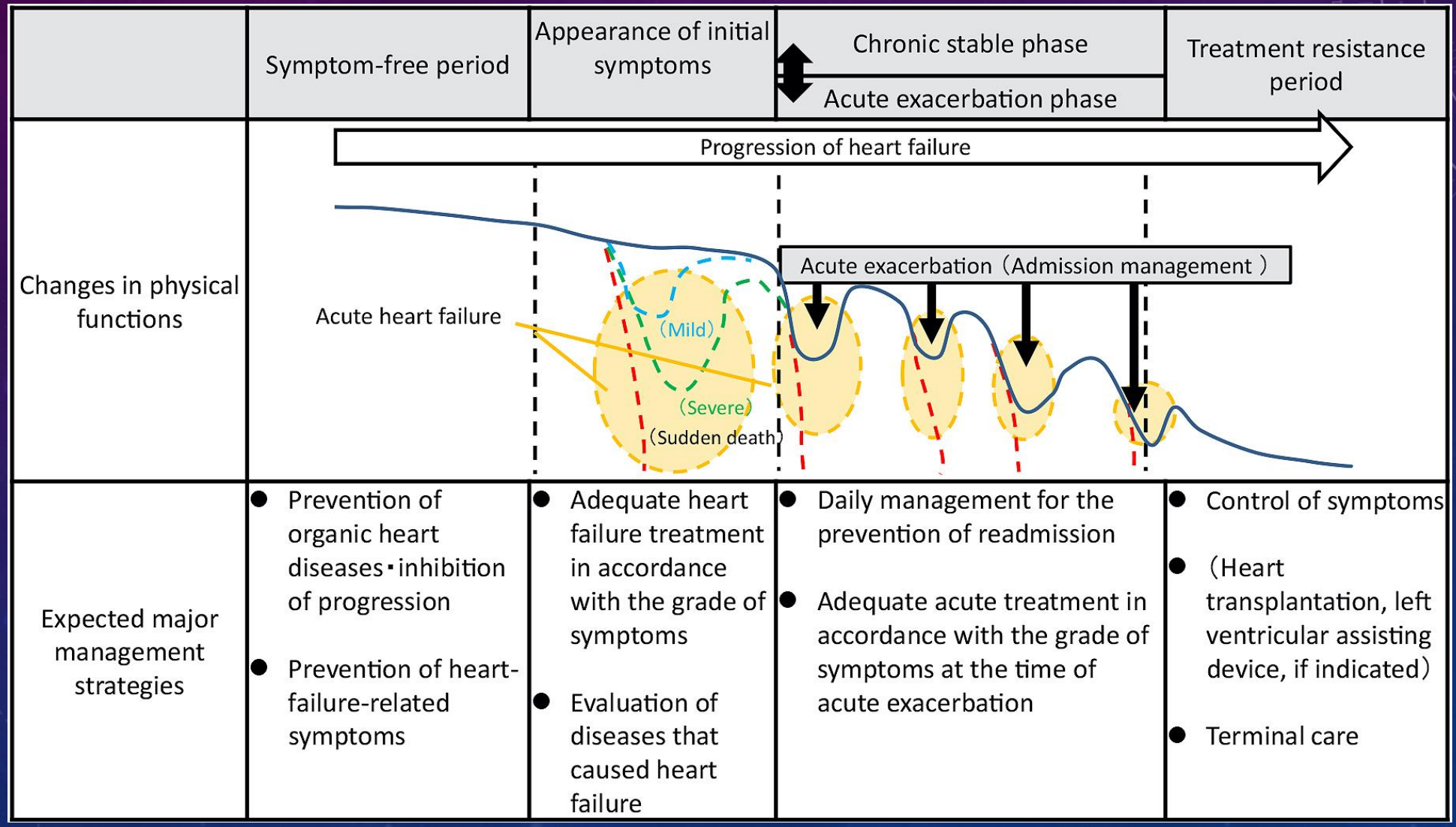
- Over past 4 decades, HF patients have derived substantial benefit from major advances in our understanding of pathophysiology of HF syndrome
  - Evolving treatment paradigms
  - new medications with novel mechanisms of actions
- **BUT** Unmet needs still:
- HF hospital discharges (index of population disease burden and economic impact) remain >1 million between 2000 and 2010
- Prevalence will increase aprox 50% between 2012-2030- >8 million people >18 yrs of age with HF
  - Aging population
  - Improved survival of AMI
  - HF survival increases at rate that exceed our impact to prevent development of HF



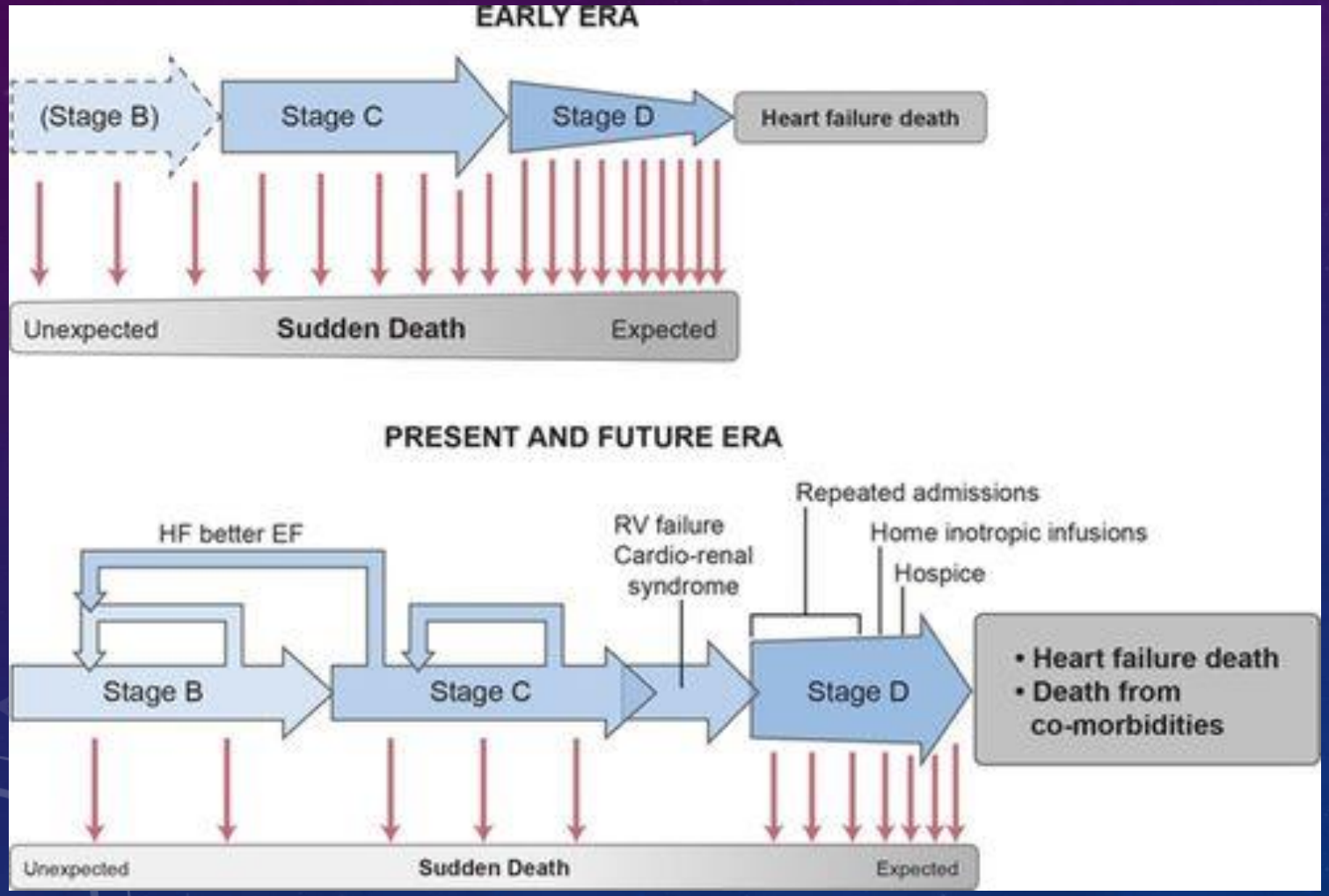


Cardiac Failure Review 2017;3(1):7-11

CLINICAL COURSE OF HEART FAILURE AND ITS MANAGEMENT



DURATION OF DISEASE STAGES IN EARLY ERA AND PRESENT/ FUTURE ERA



1. Patients in stage B and C may be stable for many years
2. Prolongation of life with anti HF therapies
3. Sudden death in previous era- occurred early in clinical syndrome , incurred with increasing frequency as HF progressed
4. RHF & cardiorenal syndrome herald progression to stage D HF with referral to palliative care

Circulation 2016;133:2671-2686

Heart failure diagnosed by the specialist

Offer diuretics for the relief of congestive symptoms and fluid retention

Heart failure with Preserved Ejection Fraction (HFPEF)

Heart failure with Reduced Ejection Fraction (HFREF)

Manage co-morbid conditions such as high blood pressure, atrial fibrilation ischaemic heart disease, and diabetes melitus in line with NICE guidance

First line:
Offer ACEi and BB
Offer an MRA if symptoms continue

All heart failure:
Offer a personalised, exercise-based cardiac rehabilitation programme, unless condition is unstable

Consider ARB if intolerant of ACEI

Consider hydralazine and nitrate if intolerant of ACEI and ARB

Specialist re-assessment

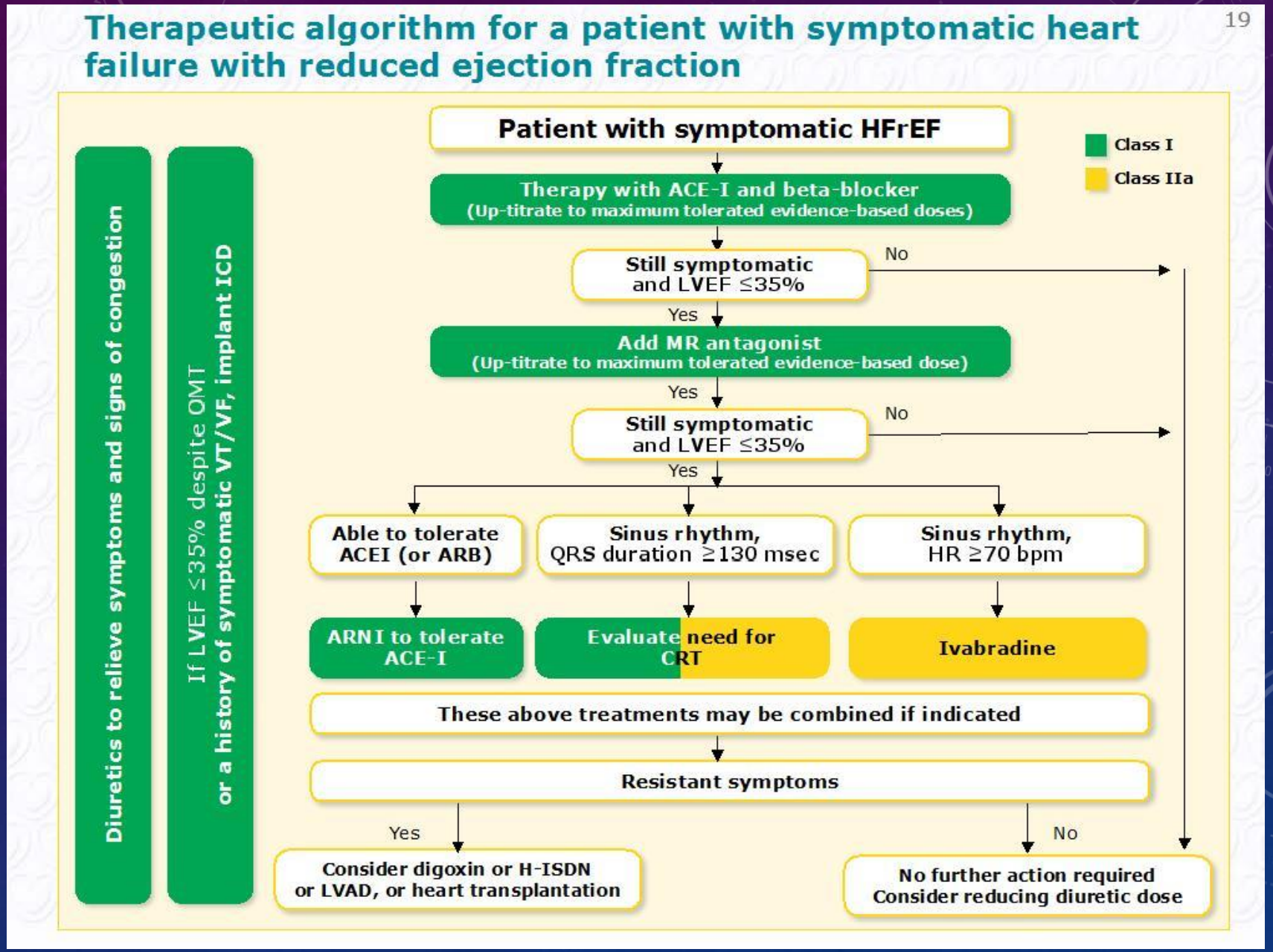
If symptoms persist despite optimal first line therapy, seek specialist advice and consider one or more of the following options

- Cardiac re-synchronisation therapy (CRT-P/D) **
- ICD**
- Replace ACEI (or ARB) with Sacubitril-Valsartan (if LVEF<35%) in accordance with TA388
- Add Ivabradine if in sinus rhythm, with a HR >75bpm and LVEF <35% in accordance with TA267
- Add Hydralazine and nitrate (especially if of African/ Caribbean descent)
- Digoxin for worsening HF*

*Please refer to CG180 for recommendation on the use of digoxin in patients with atrial fibrilation
** In accordance with TA314

Major advances:

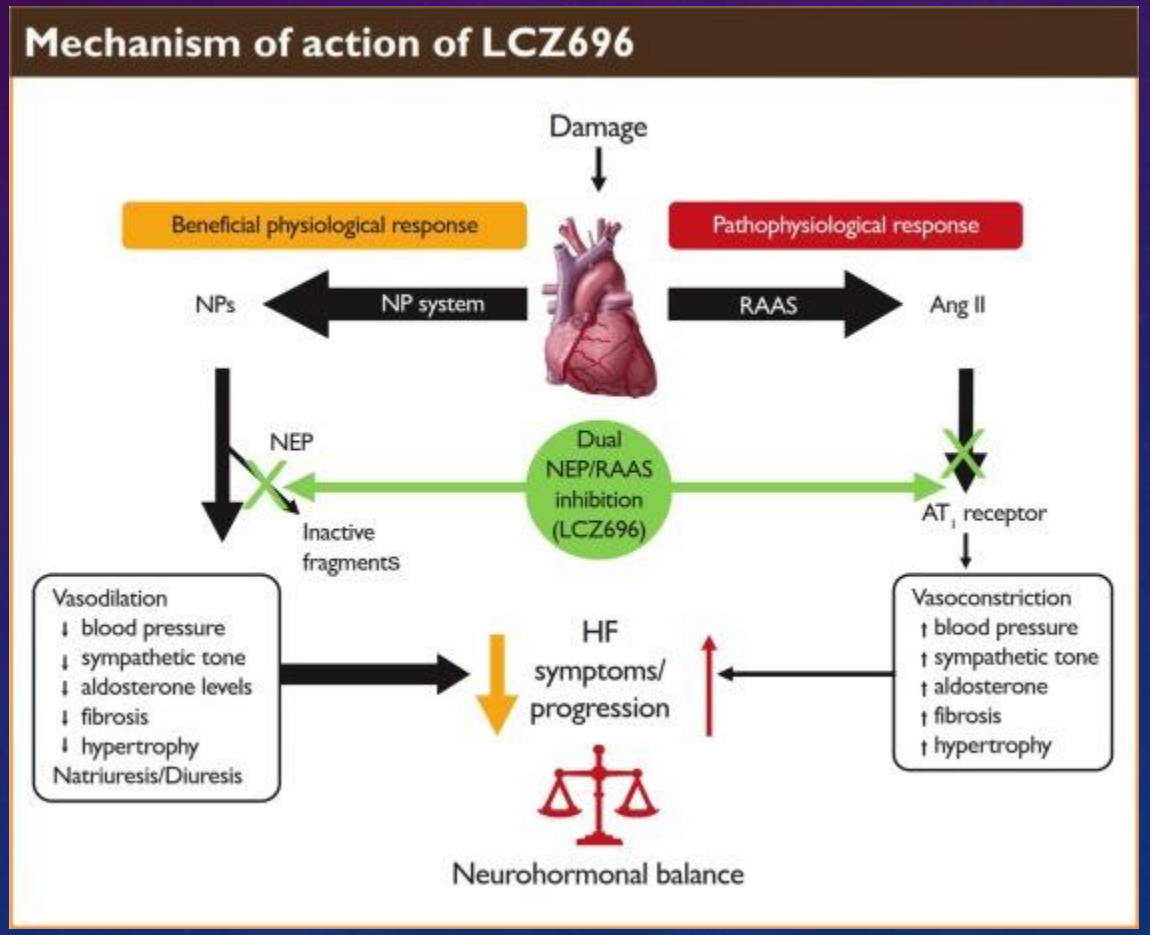
- Treatment based on large RCTs with subsequent incorporation of data into guidelines
- Then incorporated into systematic quality improvement efforts with landmark success



ESC Heart Failure Treatment Guidelines 2016

SACUBITRIL/ VALSARTAN

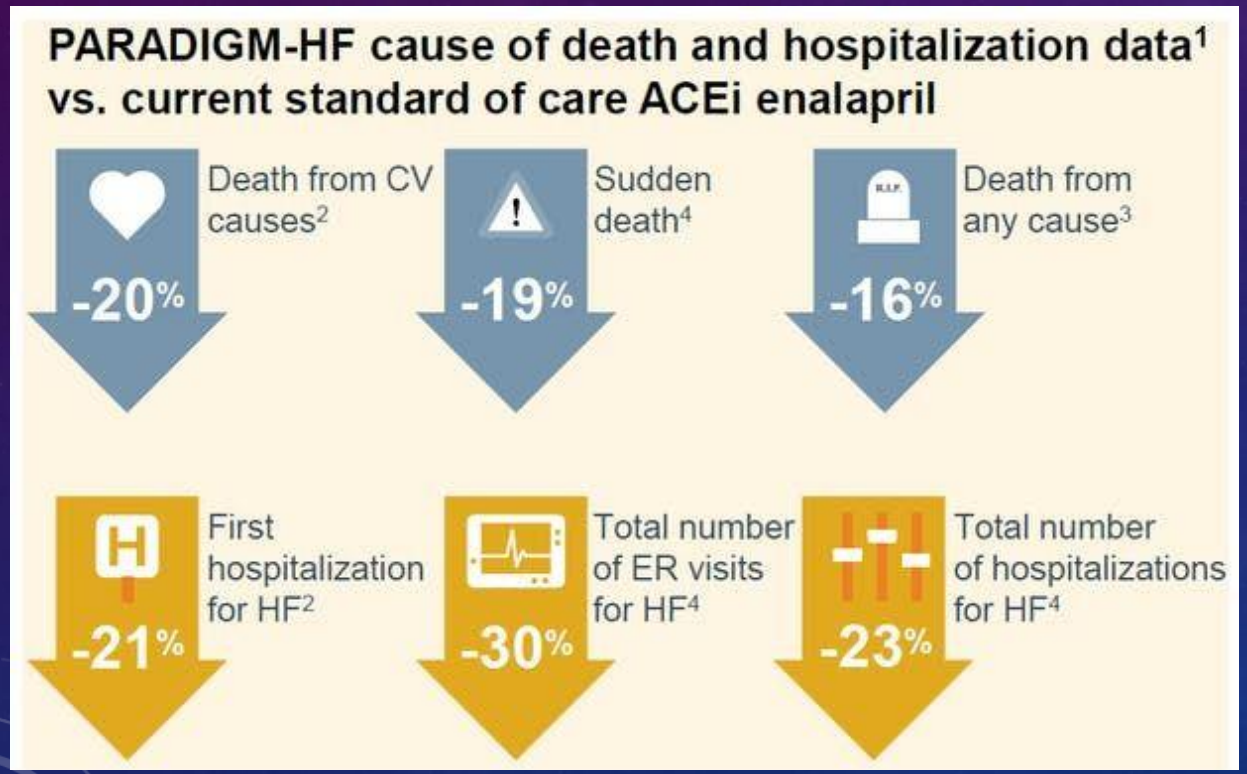
Neprilysin inhibitor (Sacubitril)

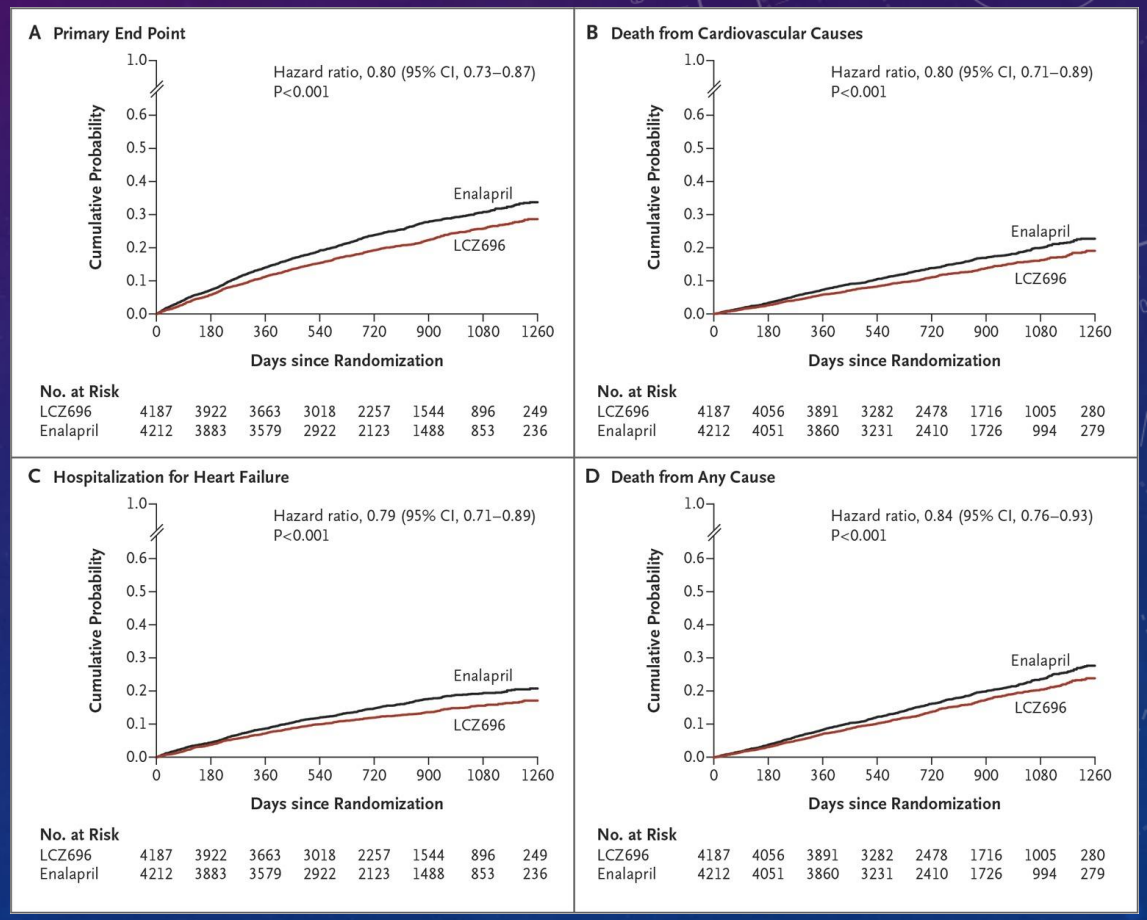


Angiotensin II Receptor Blocker (Valsartan)

PARADIGM-HF STUDY

Randomized 8442 pts with NYHA class II-IV HFrEF EF<40%
Trial stopped early after recruiting 25% pts at medican FU 27 mths

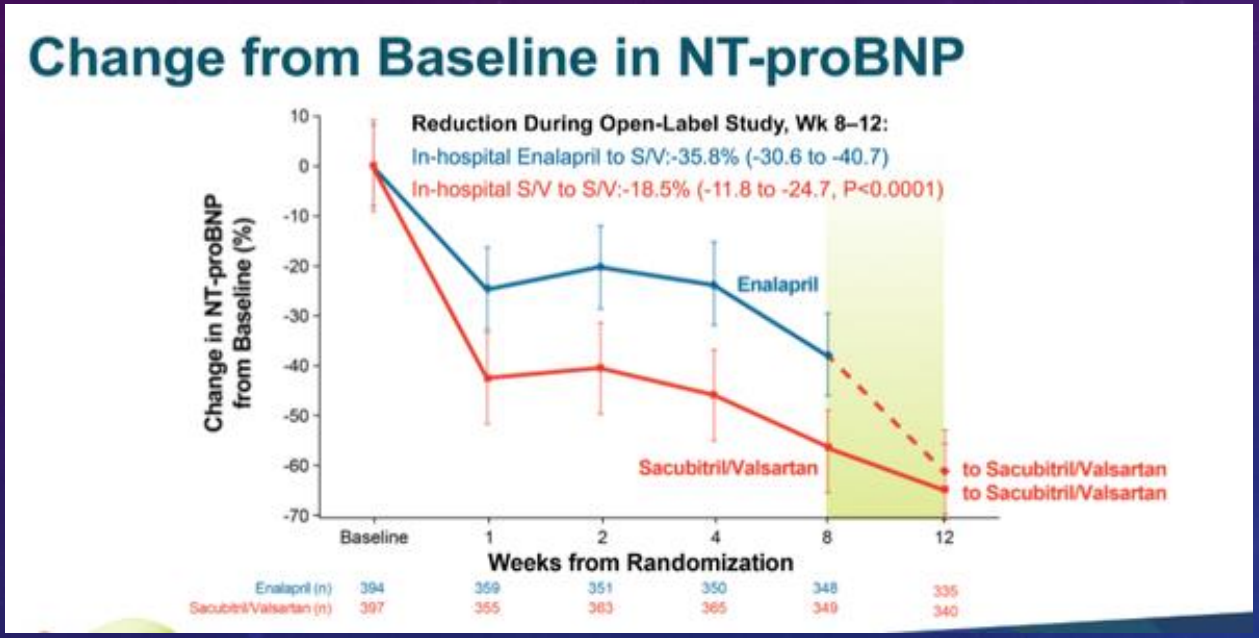


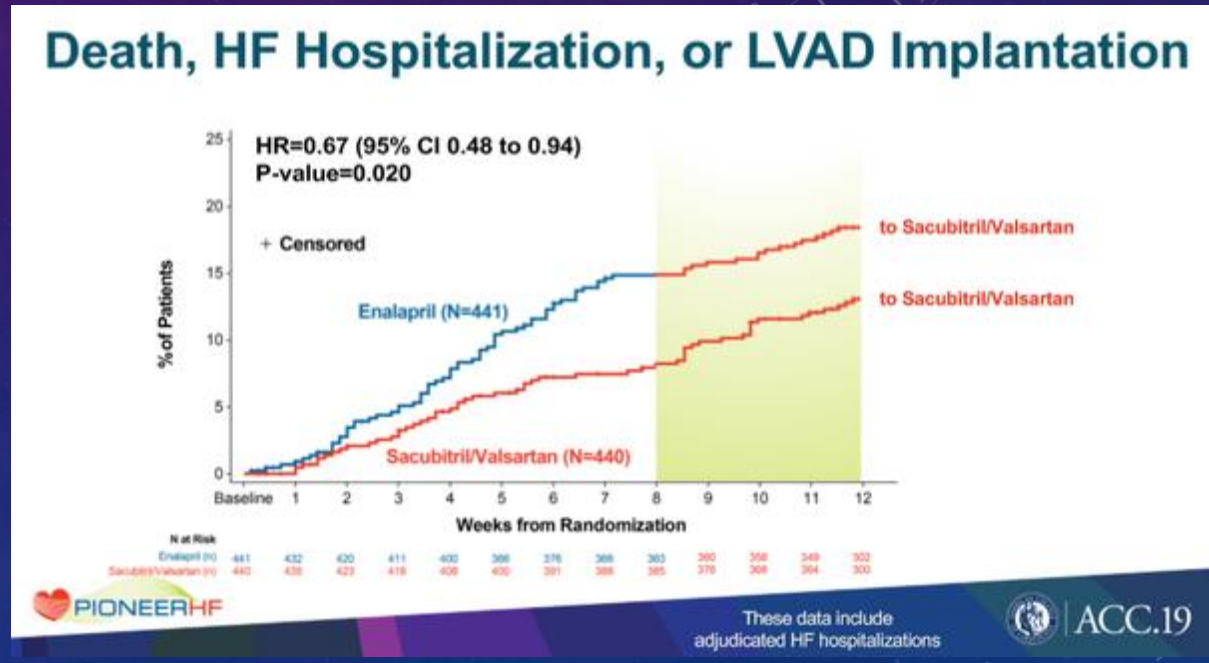


NEJM 2014;371:993-1004

PIONEER-HF STUDY
ANGIOTENSIN-NEPRILYSIN INHIBITION IN ACUTE DECOMPENSATED HEART FAILURE

NEJM 2019;380:539-48

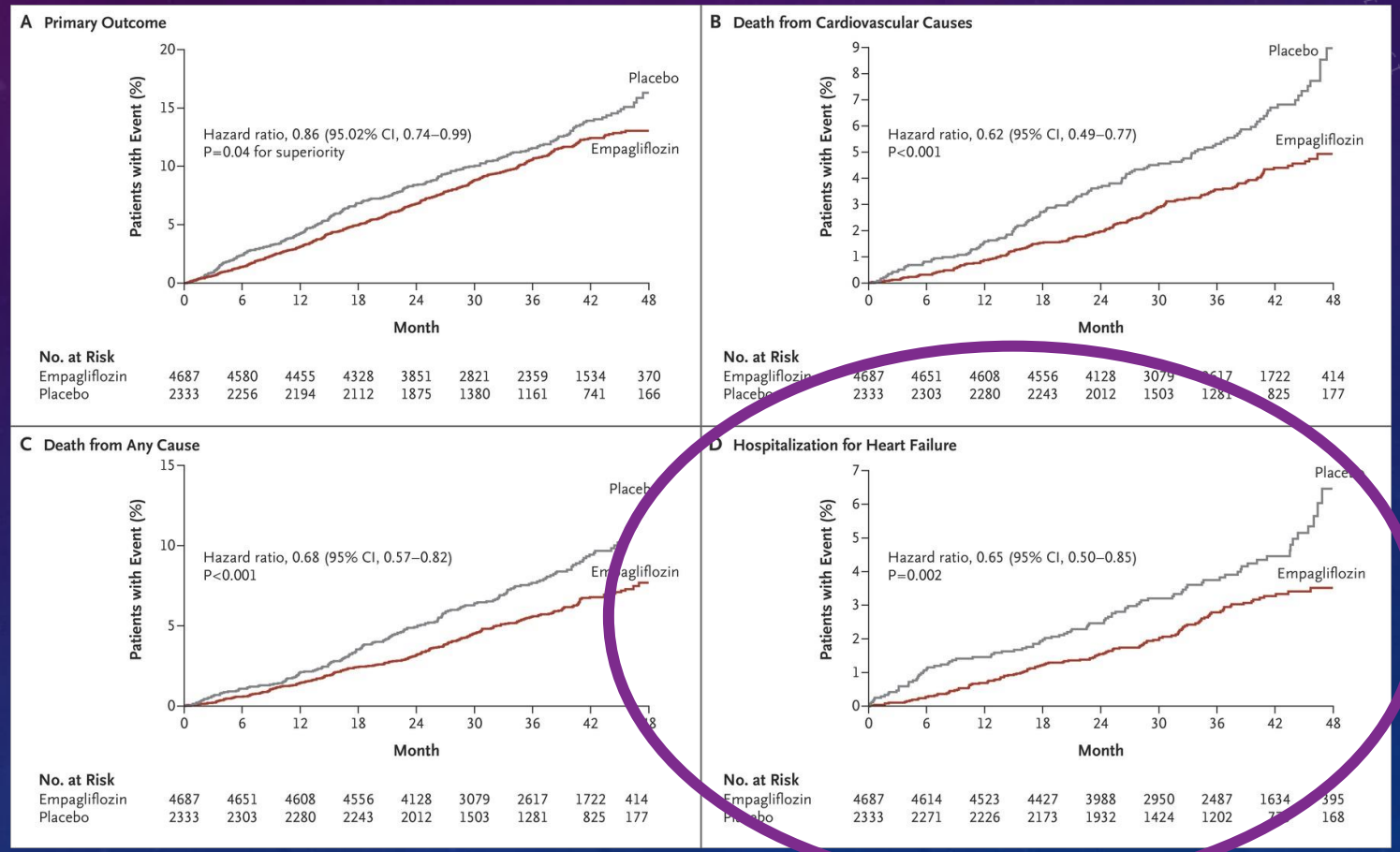




SODIUM-GLUCOSE CO-TRANSPORTER 2 INHIBITORS (SGLT2i)
A SERENDIPITOUS STORY IN HEART FAILURE (1)

EMPA-REG OUTCOME trial

- Randomized double-blind placebo controlled trial
- 7020 pts with type 2 DM at high CV risk/ established ASCVD



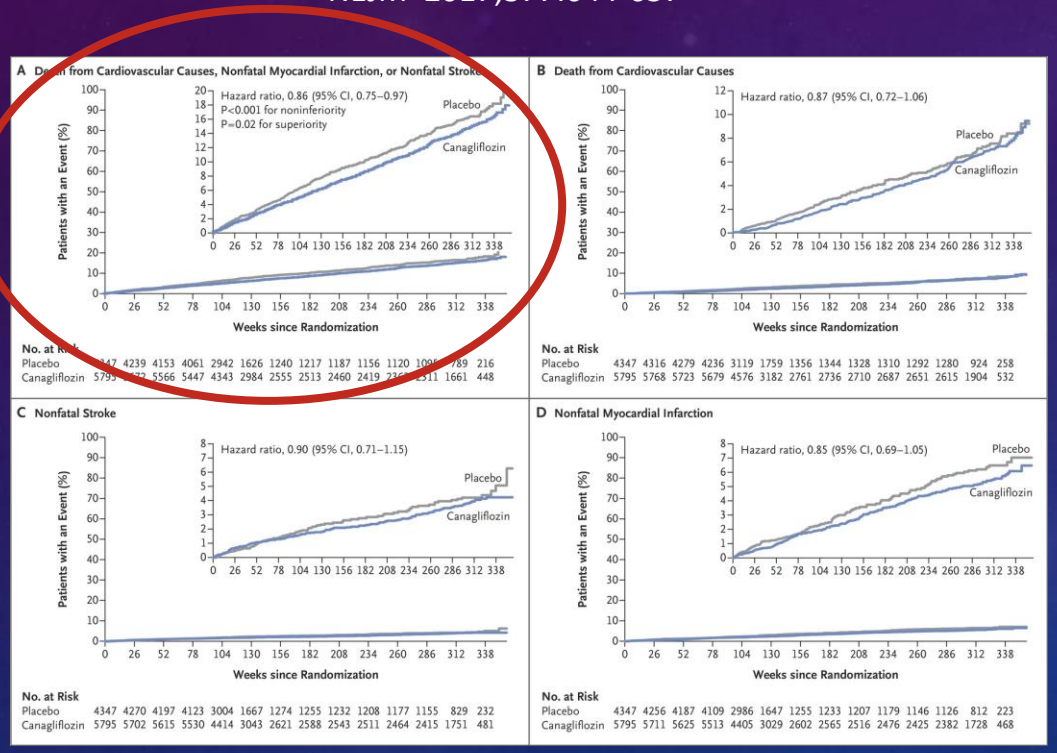
35% RRR

NEJM 2015;373:2117-2128

FURTHER STUDIES CONFIRMING BENEFITS OF HHF OR CV DEATH

CANVAS Program

NEJM 2017;377:644-657

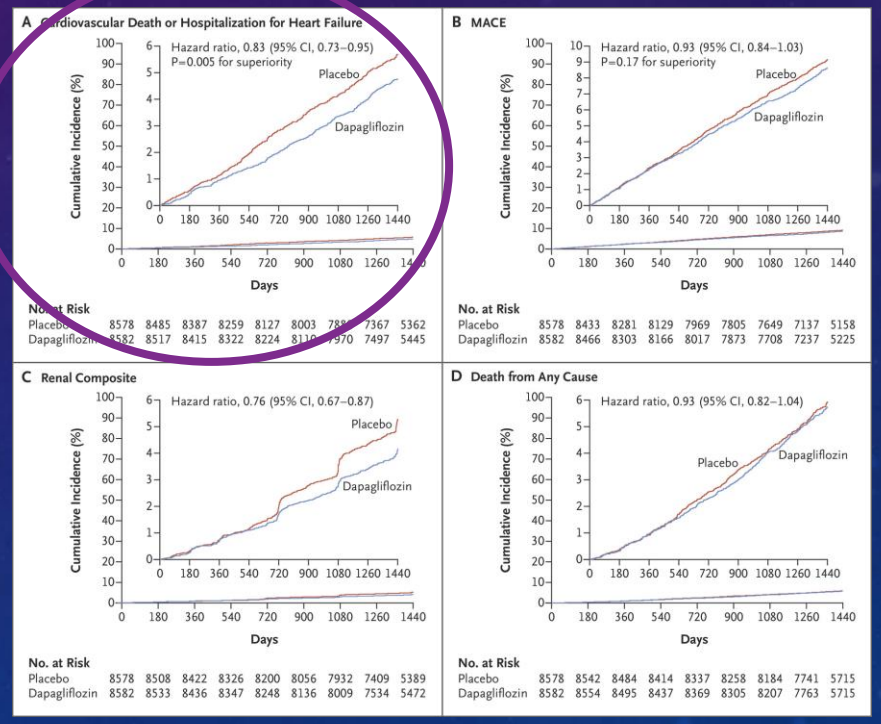


Canagliflozin

DECLARE-TIMI 58 Study

NEJM 2019:380:347-357

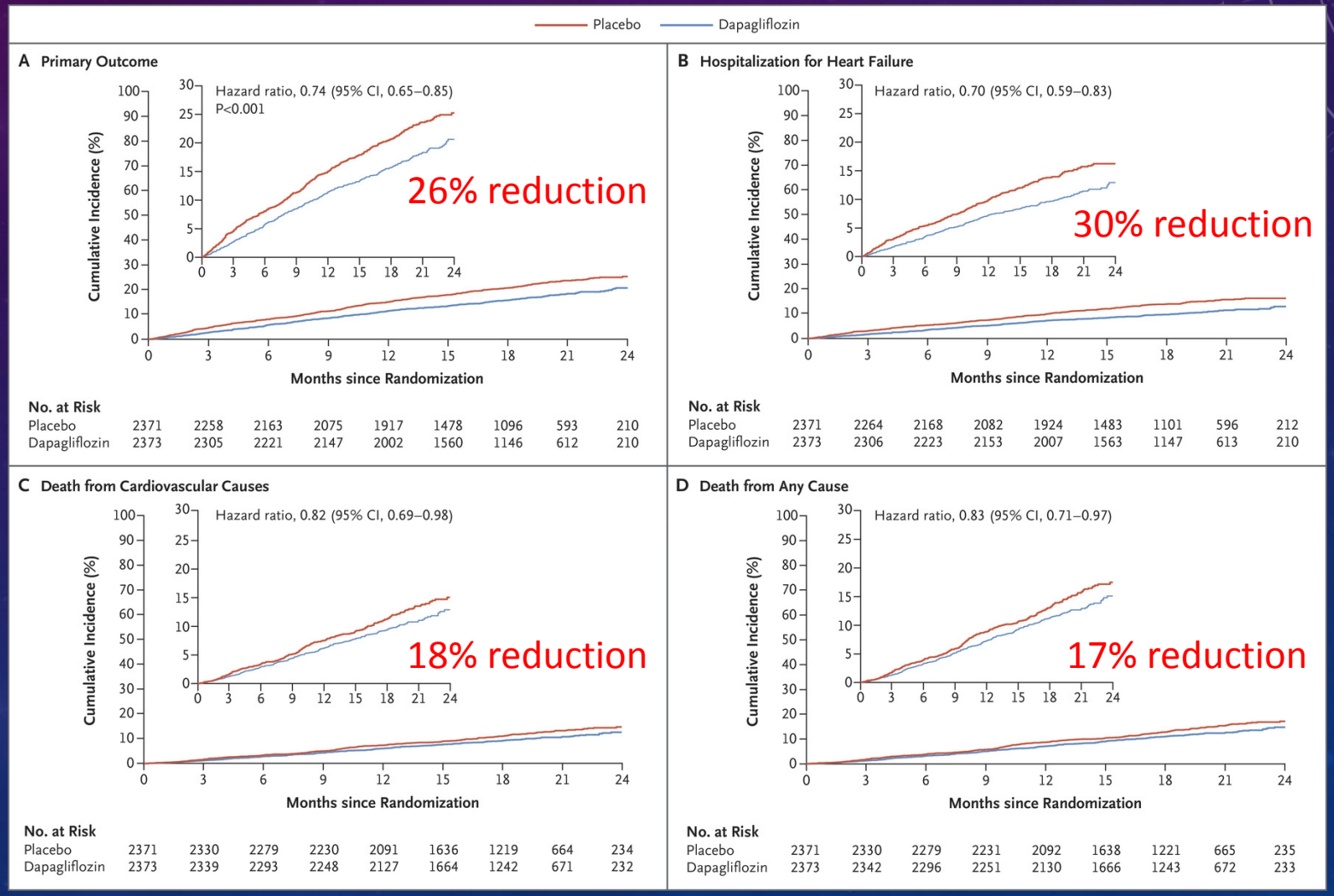
Non-inferiority

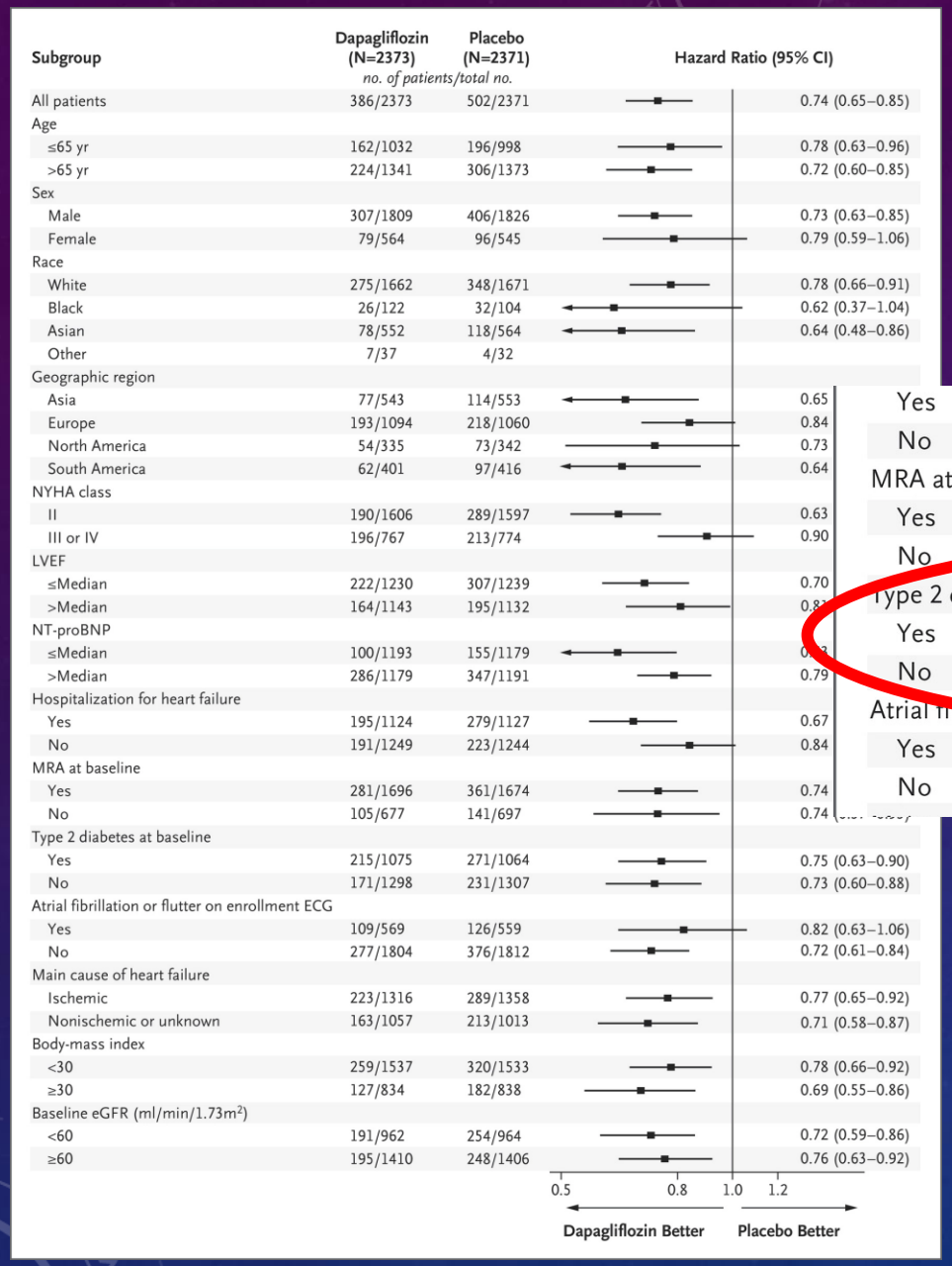


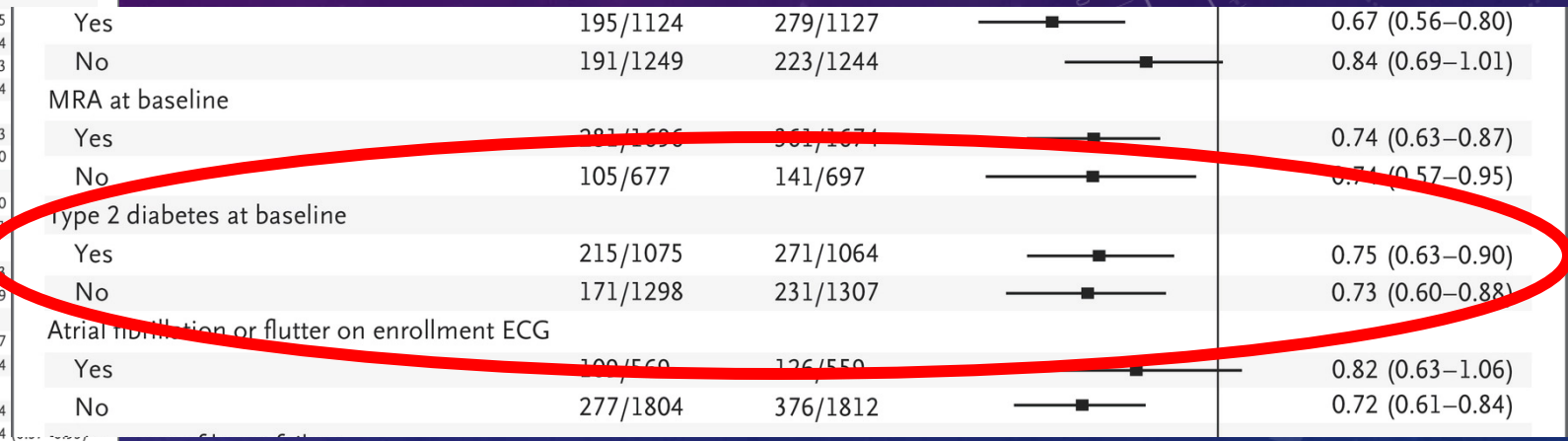
Dapagliflozin

DAPAGLIFLOZIN IN PATIENTS WITH HEART FAILURE AND REDUCED EJECTION FRACTION

- Phase 3, placebo-controlled trial
- 4744 pts- NYHA class II-IV
- Dapagliflozin vs placebo in addition to recommended therapy
- **With or without DM**

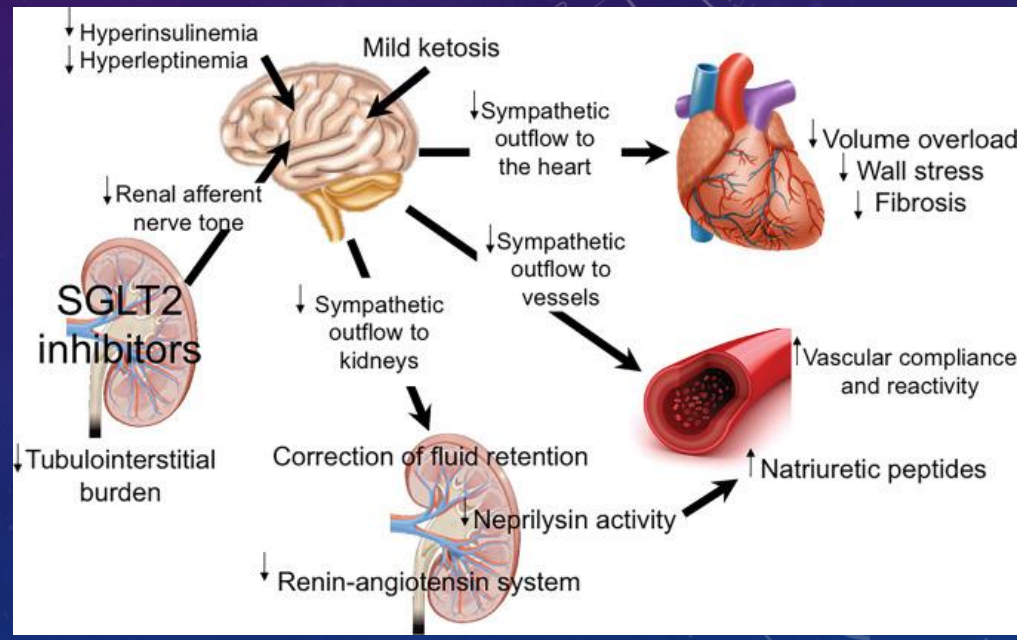



Subgroup
Dapagliflozin (N=2373)
Placebo (N=2371)
no. of patients/total no.
Hazard Ratio (95% CI)
All patients 386/2373 502/2371 0.74 (0.65–0.85)
Age
≤65 yr 162/1032 196/998 0.78 (0.63–0.96)
>65 yr 224/1341 306/1373 0.72 (0.60–0.85)
Sex
Male 307/1809 406/1826 0.73 (0.63–0.85)
Female 79/564 96/545 0.79 (0.59–1.06)
Race
White 275/1662 348/1671 0.78 (0.66–0.91)
Black 26/122 32/104 0.62 (0.37–1.04)
Asian 78/552 118/564 0.64 (0.48–0.86)
Other 7/37 4/32
Geographic region
Asia 77/543 114/553 0.65
Europe 193/1094 218/1060 0.84
North America 54/335 73/342 0.73
South America 62/401 97/416 0.64
NYHA class
II 190/1606 289/1597 0.63
III or IV 196/767 213/774 0.90
LVEF
≤Median 222/1230 307/1239 0.70
>Median 164/1143 195/1132
NT-proBNP
≤Median 100/1193 155/1179
>Median 286/1179 347/1191 0.79
Hospitalization for heart failure
Yes 195/1124 279/1127 0.67
No 191/1249 223/1244 0.84
MRA at baseline
Yes 281/1696 361/1674 0.74
No 105/677 141/697 0.74
Type 2 diabetes at baseline
Yes 215/1075 271/1064 0.75 (0.63–0.90)
No 171/1298 231/1307 0.73 (0.60–0.88)
Atrial fibrillation or flutter on enrollment ECG
Yes 109/569 126/559 0.82 (0.63–1.06)
No 277/1804 376/1812 0.72 (0.61–0.84)
Main cause of heart failure
Ischemic 223/1316 289/1358 0.77 (0.65–0.92)
Nonischemic or unknown 163/1057 213/1013 0.71 (0.58–0.87)
Body-mass index
<30 259/1537 320/1533 0.78 (0.66–0.92)
≥30 127/834 182/838 0.69 (0.55–0.86)
Baseline eGFR (ml/min/1.73m²)
<60 191/962 254/964 0.72 (0.59–0.86)
≥60 195/1410 248/1406 0.76 (0.63–0.92)
0.5
0.8
1.0
1.2
Dapagliflozin Better
Placebo Better


Yes 195/1124 279/1127 0.67 (0.56–0.80)
No 191/1249 223/1244 0.84 (0.69–1.01)
MRA at baseline
Yes 0.74 (0.63–0.87)
No 105/677 141/697
Type 2 diabetes at baseline
Yes 215/1075 271/1064 0.75 (0.63–0.90)
No 171/1298 231/1307 0.73 (0.60–0.88)
Yes 0.82 (0.63–1.06)
No 277/1804 376/1812 0.72 (0.61–0.84)

Rationale for exploring SGLT-2 inhibitors for the treatment of HF in patients without diabetes

- Diabetes and heart failure have similar pathophysiological features
  - Endothelial dysfunction
  - Insulin resistance
- Mechanistic effects of SGLT-2 inhibitors are seen in patients with and without diabetes
  - Diuretic effects
    - Natriuresis
    - Glucosuria
  - Metabolic effects
    - Increased glucagon
    - Increased ketone bodies
- CV benefits of SGLT-2 inhibitors are largely independent of glucose levels



CENTRAL ILLUSTRATION: Stepwise Approach to Prescription of SGLT2 inhibitors by Cardiologists

Patients with T2DM with or at High Risk for CV Disease, Already on Metformin

Below Individualized HbA1c Target:

Switch non-metformin oral therapies (e.g. sulfonylureas) to a SGLT2i

Above Individualized HbA1c Target:

Consider SGLT2i initiation

Drug Type

Canagliflozin, dapagliflozin, & empagliflozin with similar efficacy profile in reducing HF events

Starting Dose (once daily in AM)

- Canagliflozin (100mg)
- Dapagliflozin (5mg)
- Empagliflozin (10mg)
- Ertugliflozin (5mg)

Metformin+SGLT2i Combination Therapies

Consider to limit non-adherence and pill burden

Stable Hemodynamic and Clinical Status

Pre-Initiation eGFR must be above:

- 60 mL/min/1.73 m^2 (dapagliflozin, ertugliflozin)
- 45 mL/min/1.73 m^2 (canagliflozin, empagliflozin)

Anticipatory Guidance

Consider diuretic dose reduction

Patient Counseling

- Genital/perineal hygiene
- Orthostatic hypotension
- Regular foot exams
- Symptoms of DKA
- Avoid excessive alcohol

Multidisciplinary Care

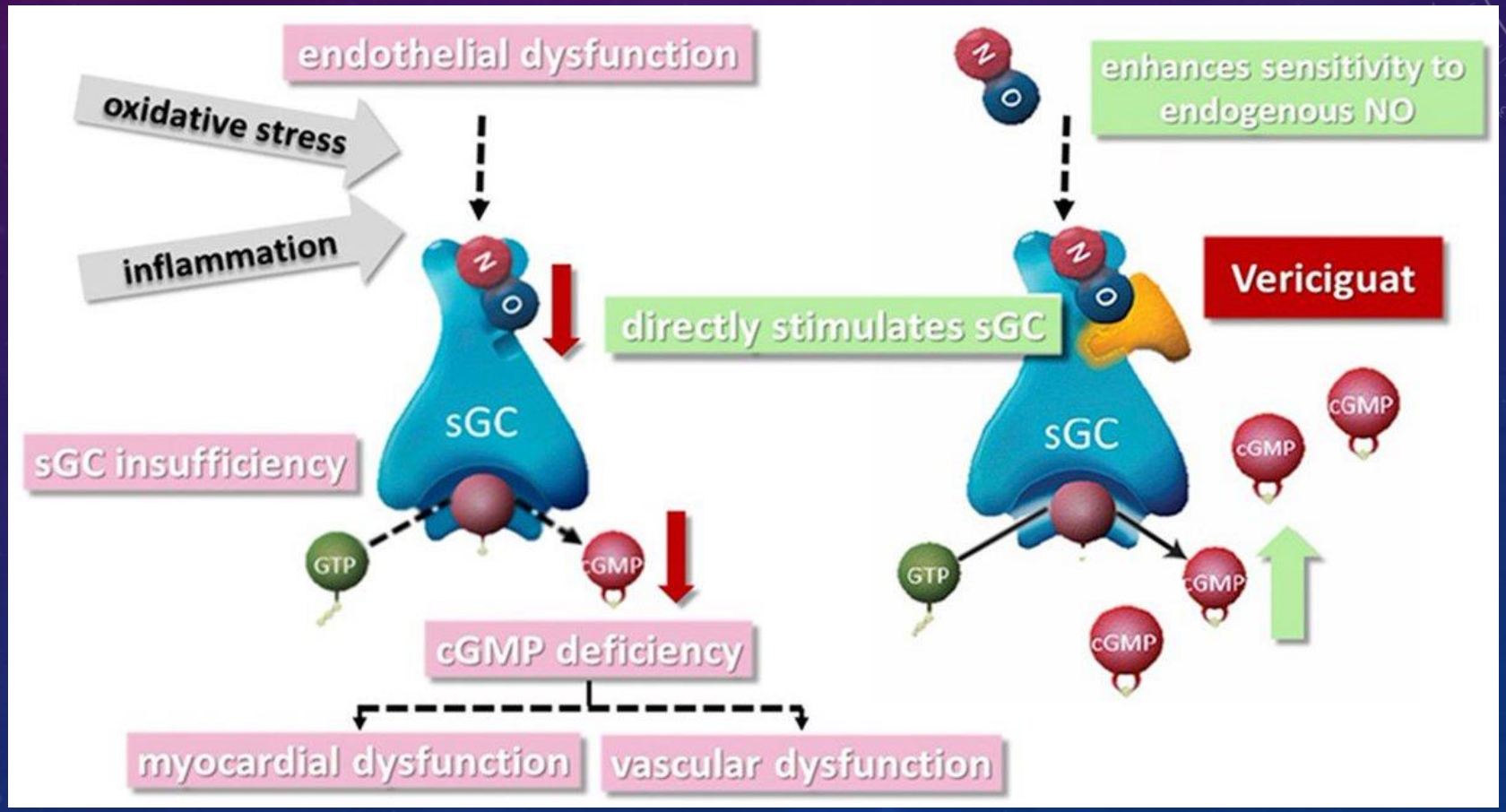
Close communication with other providers, including PCPs and endocrinologists

Follow-up and Monitoring

- Serial assessment of renal function, body weights, blood pressure, and symptoms
- Dose uptitration guided by need for glycemic control
- Ensure adherence to SGLT2i, other therapies, and therapeutic lifestyle
- Multidisciplinary care team follow-up

Vardeny, O. et al. J Am Coll Cardiol HF. 2019;7(2):169-72.

Soluble Guanylate Cyclase (sGC) STIMULATOR



THE VICTORIA TRIAL
STUDY RATIONALE AND BACKGROUND

Worsening HF is common despite GDMT

There is substantial risk of death or hospitalization after a worsening HF event

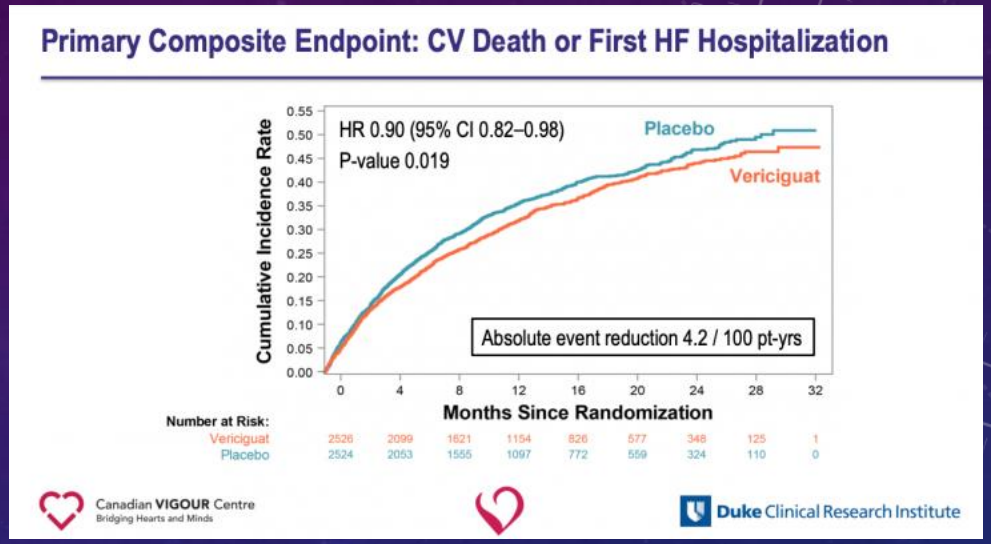
Vericiguat, a novel sGC stimulator, is a potential new therapy

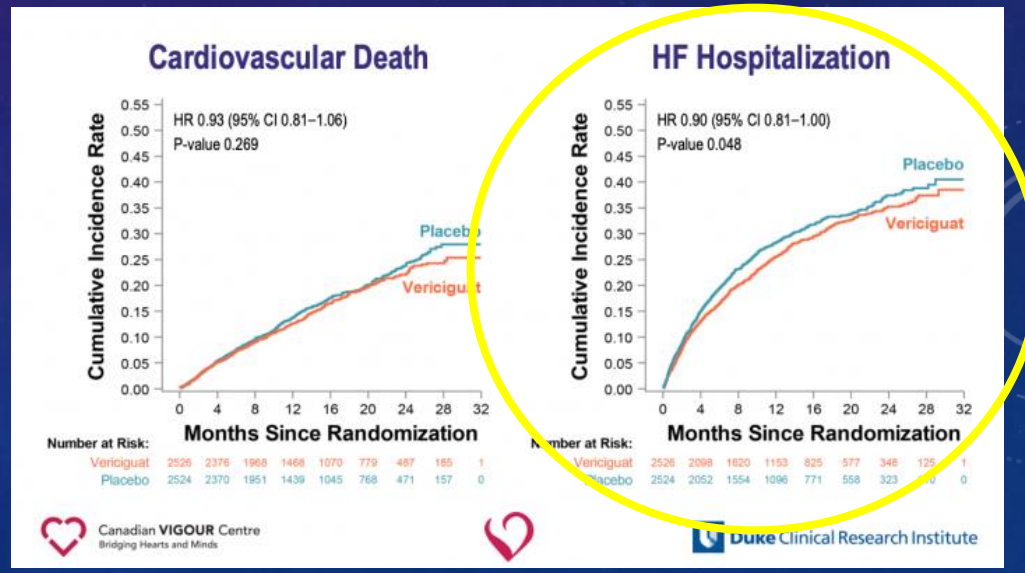
The Victoria trial assessed the efficacy and safety of vericiguat in patients with HFrEF after a recent worsening event

(randomized, placebi-controlled, parallel group, multi-center double-blind Phase 3 study)

VICTORIA

- Primary endpoint of CV death or HF hospitalization
  - -10% RRR
  - -4.2% ARR
- Driven by reduction in HF hospitalization
- Reduction in CV death did not reach statistical significance





"Another win in HFrEF treatment"
New physiologic target
New target population- worsening HF

VERICIGUAT SUCCESS IN HFrEF MAY NOT APPLY TO SICKEST AFTERALL: VICTORIA POST-HOC ANALYSIS

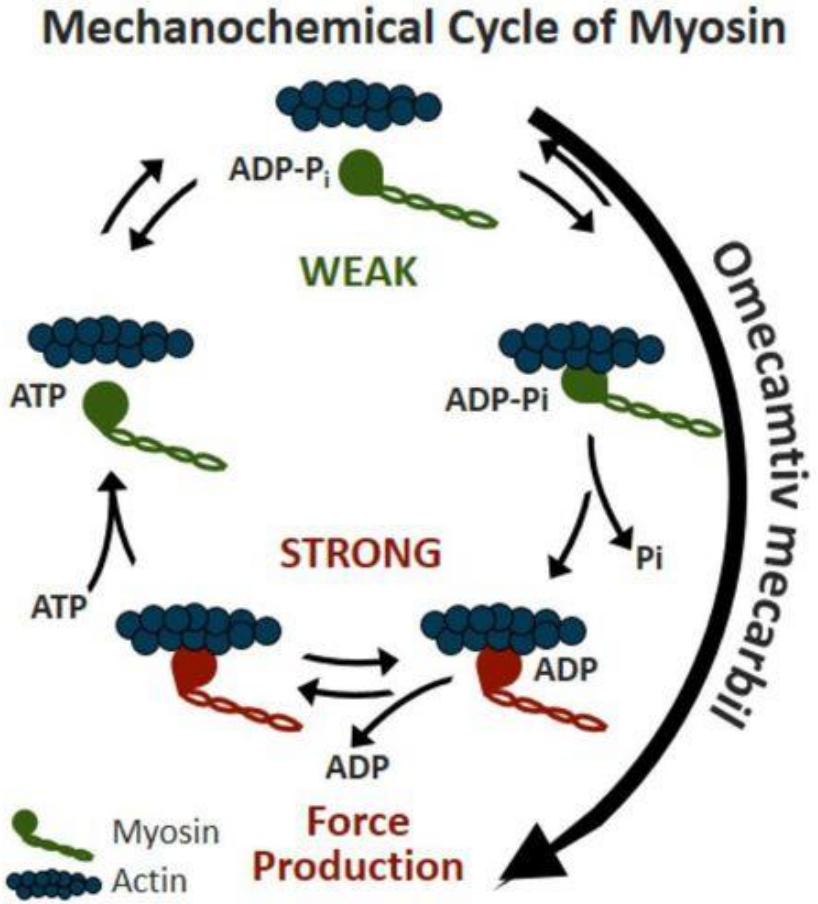
- Modest but significant clinical advantage in the 86% who had baseline NTproBNP levels 8000 pg/ml or lower
- Further amplified in pts with NTproBNP <4000 pg/ml
- Risk reduction in lowest NTproBNP reached **23%**
- **[DAPA HF 26% reduction; PARADIGM-HF 20% reduction]**
- **"demonstrated the potential upper limit of medication benefit in HFrEF population- subgroup identified the most advanced stage of disease and probably need for non-pharmacological treatment or palliative care"**

HR (95% CI) for outcomes by baseline NT-proBNP in Victoria

Endpoints	<4000 pg/ml (n=3100)	>4000 to 8000 pg/ml (n=1033)	>8000 pg/ml (n=672)
Primary endpoint	0.77 (0.68-0.88)	0.85 (0.76-0.95)	1.16 (0.94-1.41)
CV death	0.75 (0.6-0.94)	0.84 (0.71-0.99)	1.32 (1.01-1.71)
HF hospitalization	0.78 (0.67=0.9)	0.84 (0.75-0.95)	1.16 (0.94-1.41)

Presented HFA Discoveries Late Breaking Science Session June 19th 2020

Omecamtiv Mecarbil (OM) MOA Novel Selective Cardiac Myosin Activator



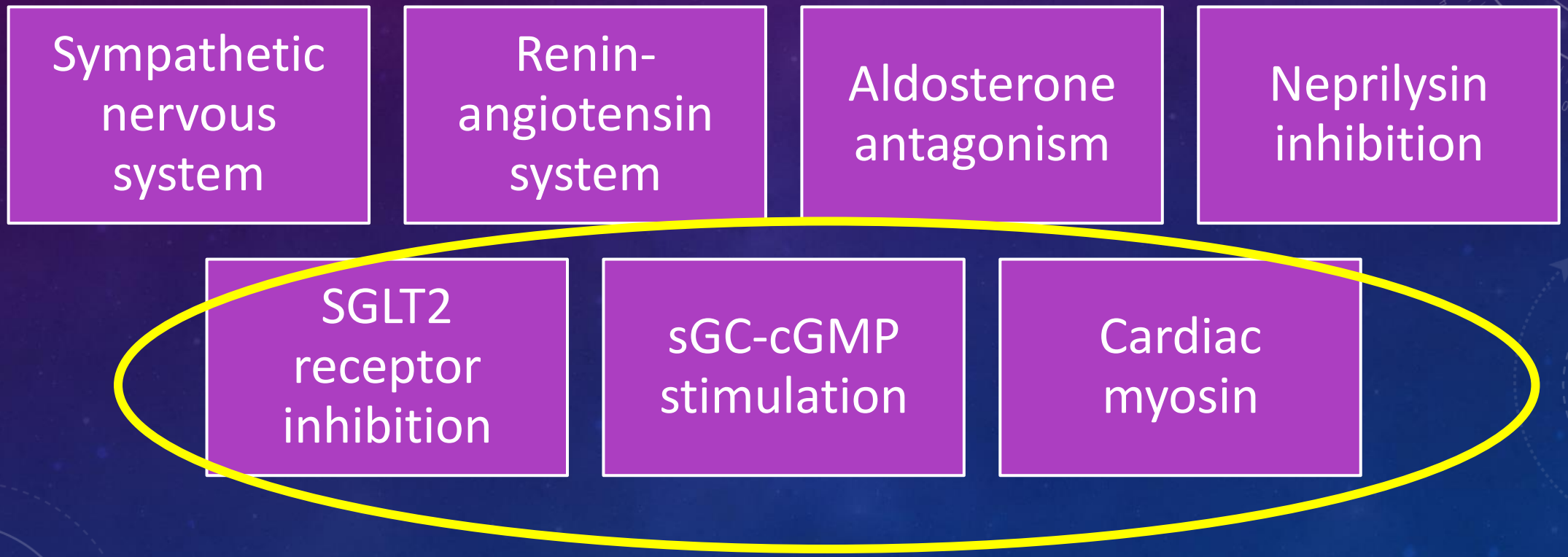
Omecamtiv mecarbil increases the entry rate of myosin into the tightly bound, force-producing state with actin

"More hands pulling on the rope"

Increases duration of systole
Increases stroke volume
No increase in myocyte calcium
No change in dP/dt_{max}
No increase in MVO_2

Malik FI, *et al. Science.* 2011; 331:1439-1443.

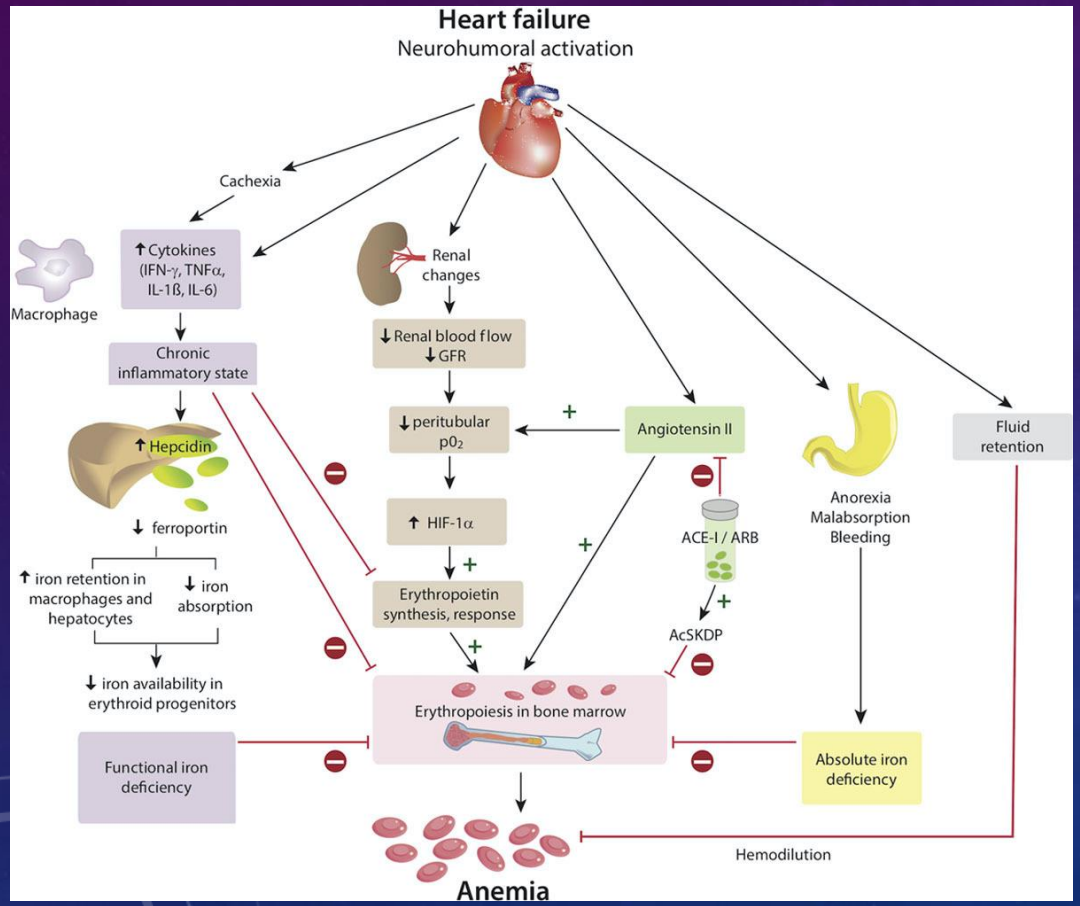
MANAGEMENT OF HFrEF IS BREAKING NEW GROUNDS
7 PARALLEL INDEPENDENT PATHWAYS IN HFrEF



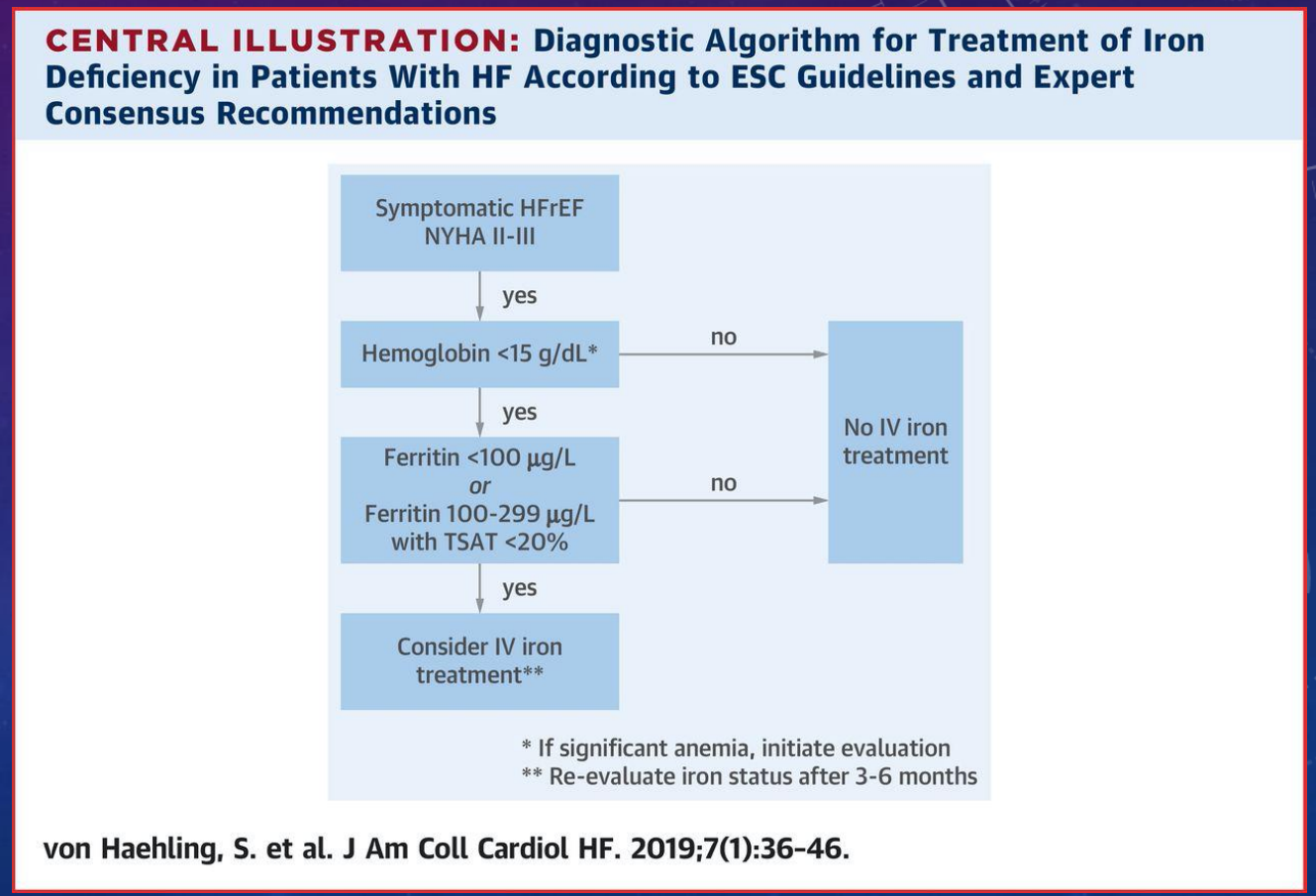
IRON DEFICIENCY IN HEART FAILURE

- Iron deficiency (ID) is common in patients with and without anemia with HFrEF
  - Estimated prevalence of over 50% in ambulatory patients
  - Risk factors: female sex, advanced HF, higher levels of NTproBNP and C reactive protein
- Associated with worse symptoms, quality of life and clinical outcomes of patients with HF across the whole spectrum of LVEF
- Definition of ID in heart failure differs from other conditions of chronic inflammation:
  - Ferritin <100 ug/L or ferritin of 100-299 ug/L with a transferrin saturation <20%
- Tremendous research effort into iron deficiency in HF patients:
    - Multiple placebo-controlled randomized clinical trials with IV iron in patients with NYHA class II-III HF with EF<45% who met criteria for iron deficiency, ***regardless of whether anemia was present***
    - Improved patient-reported outcomes and functional capacity

POTENTIAL MECHANISM INVOLVED IN PATHOGENESIS & DIAGNOSTIC ALGORITHM OF ANEMIA IN HEART FAILURE

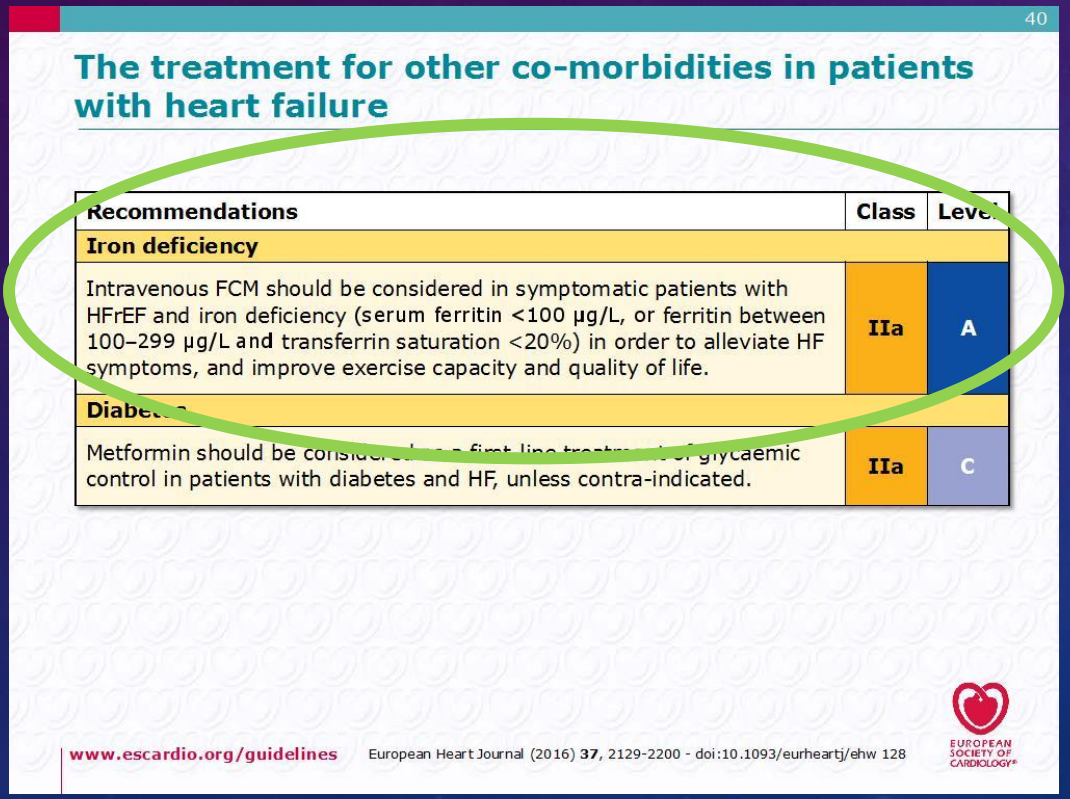


Circulation 2018; 138(1):80-98



TREATMENT OF IRON DEFICIENCY IN HF GUIDELINES INTRAVENOUS IRON IS PREFERRED ROUTE

ESC 2016 Guidelines for diagnosis and treatment of acute and chronic heart failure



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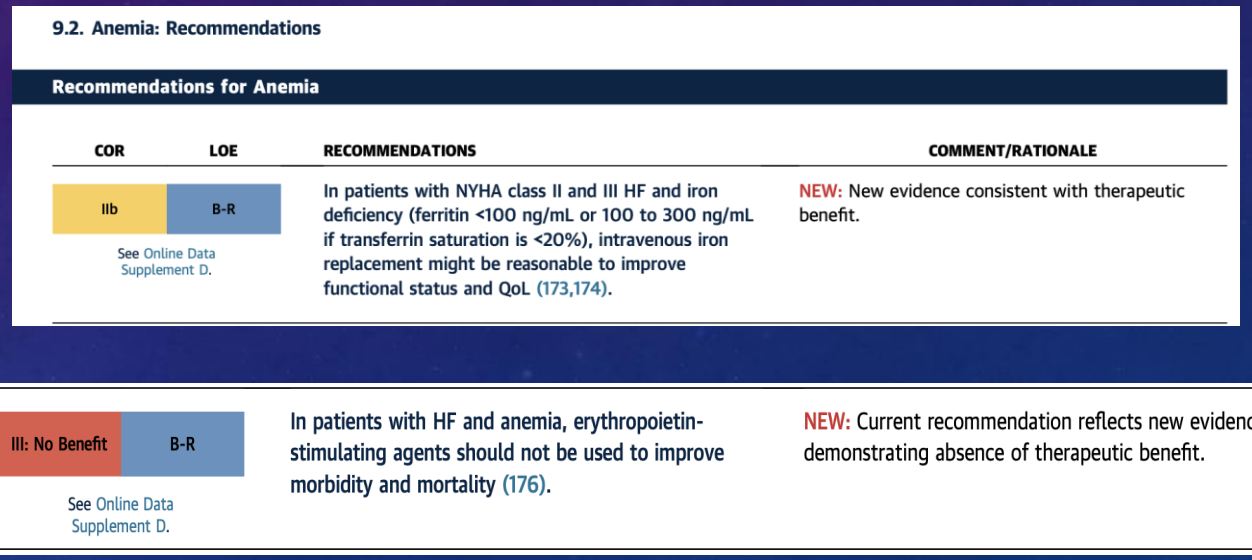
The treatment for other co-morbidities in patients with heart failure

Recommendations	Class	Level
Iron deficiency		
Intravenous FCM should be considered in symptomatic patients with HFrEF and iron deficiency (serum ferritin <100 µg/L, or ferritin between 100–299 µg/L and transferrin saturation <20%) in order to alleviate HF symptoms, and improve exercise capacity and quality of life.	IIa	A
Diabet		
Metformin should be consid[illegible] first-line treatm[illegible] glycaemic control in patients with diabetes and HF, unless contra-indicated.	IIa	C

www.escardio.org/guidelines European Heart Journal (2016) **37**, 2129-2200 - doi:10.1093/eurheartj/ehw 128

EUROPEAN SOCIETY OF CARDIOLOGY

2017 ACC/AHA HFSA focused update of 2013 ACCF/AHA guideline for management of heart failure



9.2. Anemia: Recommendations

Recommendations for Anemia

COR	LOE	RECOMMENDATIONS	COMMENT/RATIONALE
IIb	B-R	In patients with NYHA class II and III HF and iron deficiency (ferritin <100 ng/mL or 100 to 300 ng/mL if transferrin saturation is <20%), intravenous iron replacement might be reasonable to improve functional status and QoL (173,174).	NEW: New evidence consistent with therapeutic benefit.
		See Online Data Supplement D.	
III: No Benefit	B-R	In patients with HF and anemia, erythropoietin-stimulating agents should not be used to improve morbidity and mortality (176).	NEW: Current recommendation reflects new evidence demonstrating absence of therapeutic benefit.
		See Online Data Supplement D.	

1. IV iron sucrose (max dose 200mg per setting or
2. Ferric carboxymaltose (max dose 1000 mg /week)

The NEW ENGLAND JOURNAL of MEDICINE

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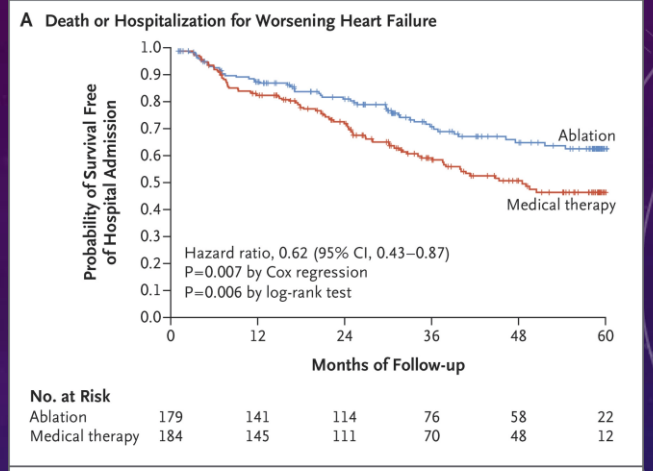
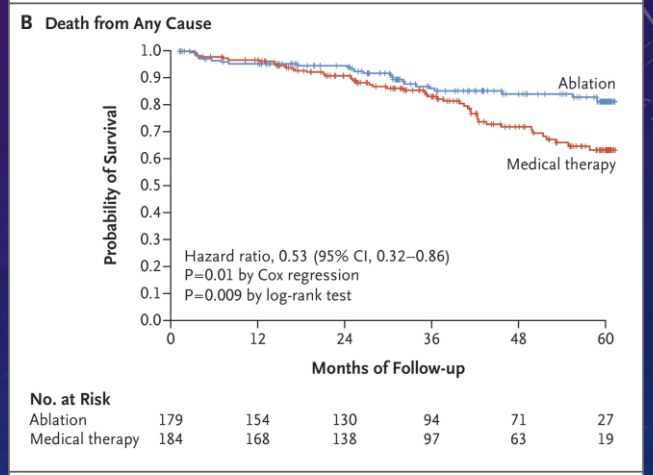
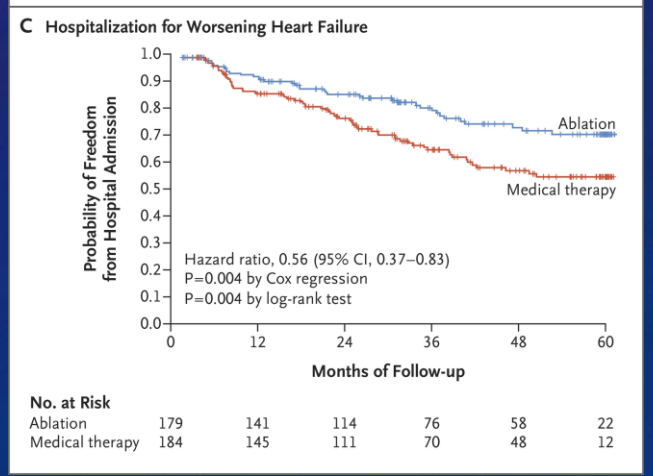
Catheter Ablation for Atrial Fibrillation with Heart Failure

Nassir F. Marrouche, M.D., Johannes Brachmann, M.D., Dietrich Andresen, M.D., Jürgen Siebels, M.D., Lucas Boersma, M.D., Luc Jordaens, M.D., Béla Merkely, M.D., Evgeny Pokushalov, M.D., Prashanthan Sanders, M.D., Jochen Proff, B.S., Heribert Schunkert, M.D., Hildegard Christ, M.D., Jürgen Vogt, M.D., and Dietmar Bänsch, M.D., for the CASTLE-AF Investigators*





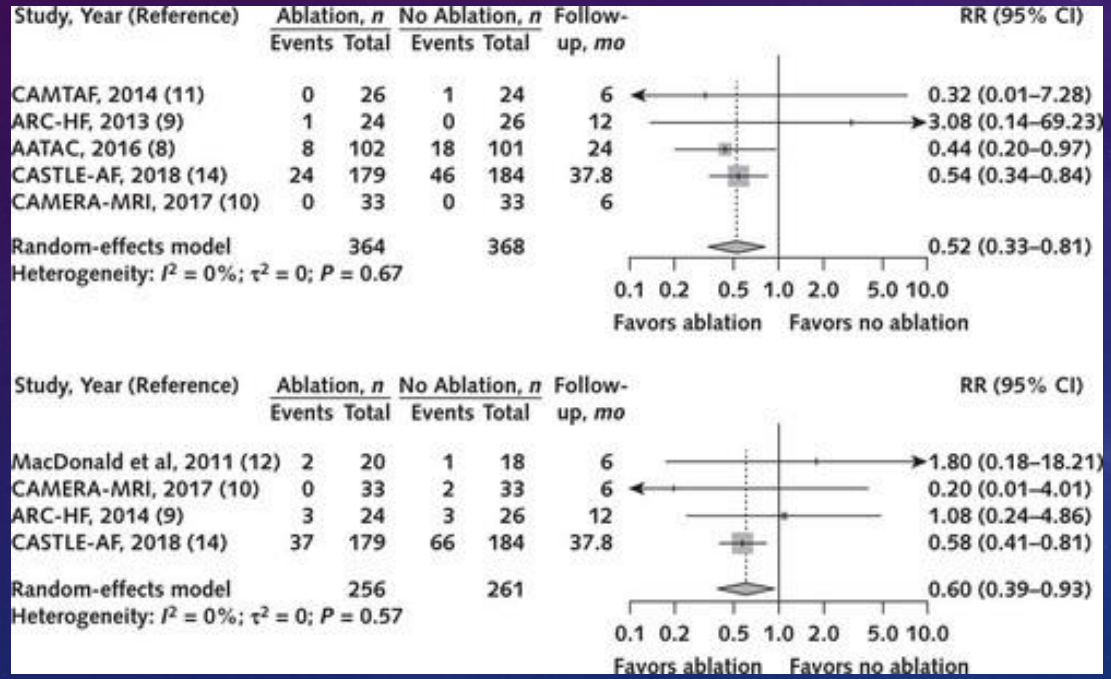


CATHETER ABLATION OF AF IN PATIENTS WITH HEART FAILURE

TURAGAM ET AL. ANNALS OF INTERNAL MEDICINE 2019; 170(1): 41-50

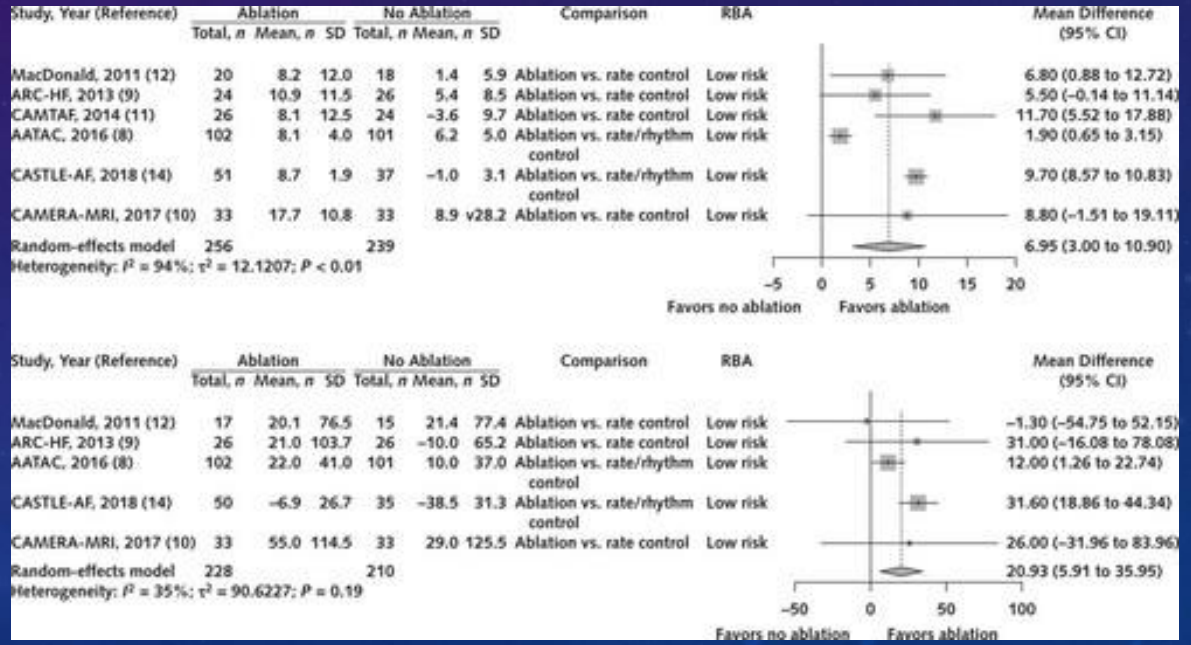
Decrease in All cause mortality and

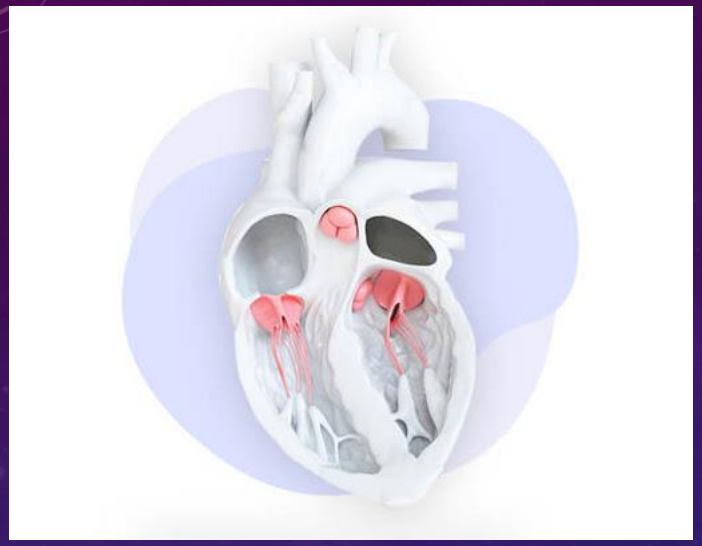
HF hospitalization



Improvement in LVEF and

6 minute walk test



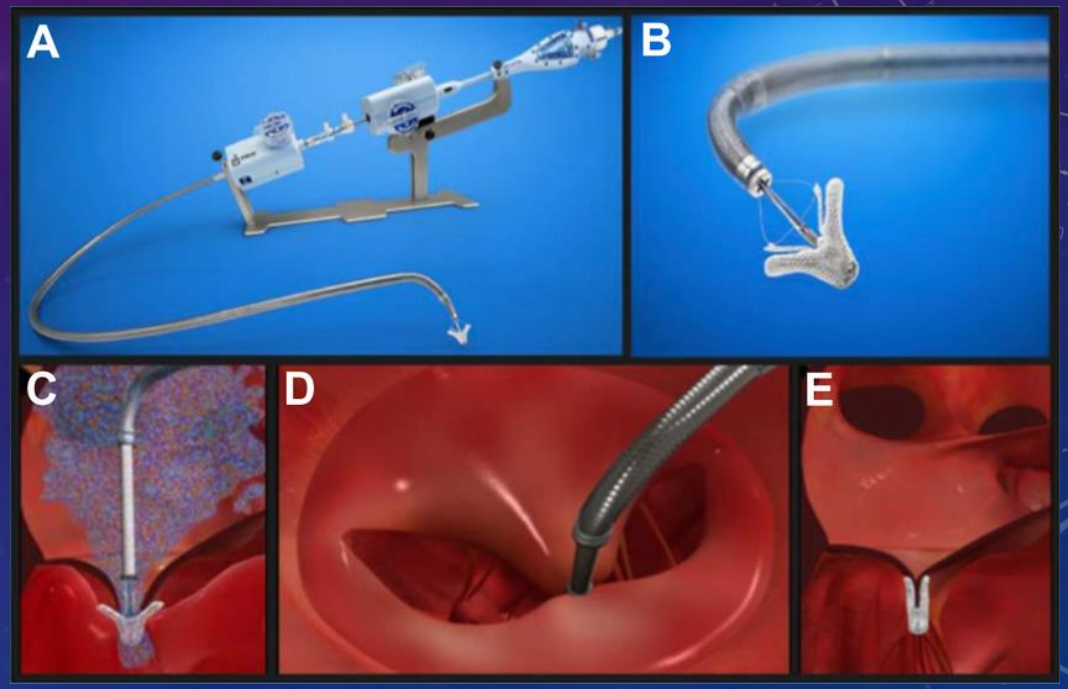


IN 2018, THE WORLD OF FUNCTIONAL MITRAL REGURGITATION CHANGED WITH THE PRESENTATION OF 2 TRIALS- *MITRA-FR* VS *COAPT*

PERCUTANEOUS MITRAL REPAIR

- Transcatheter mitral valve repair may be considered for severely symptomatic patients (**NYHA class III to IV**) with chronic severe **primary MR** (stage D) who have favorable anatomy for the repair procedure and a reasonable life expectancy but who have a **prohibitive surgical risk** because of severe comorbidities and remain severely symptomatic despite optimal GDMT for HF (IIB)

MitraClip

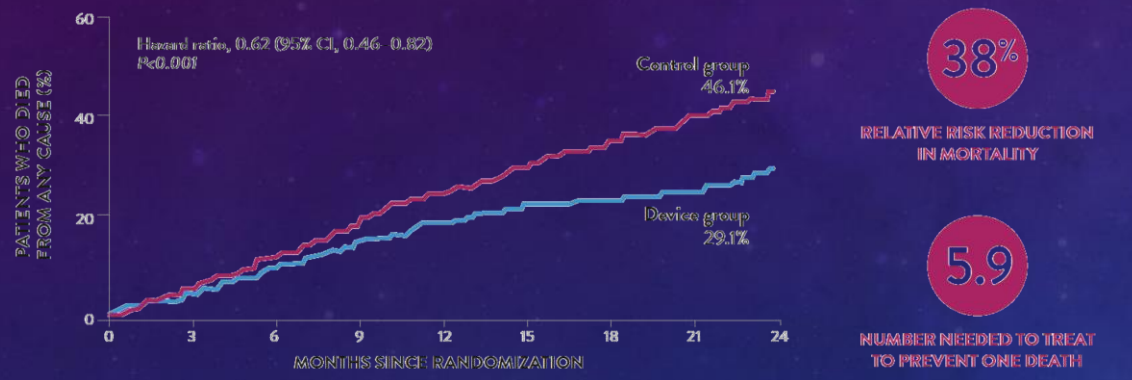


AHA/ACC Valvular Disease Guidelines 2014

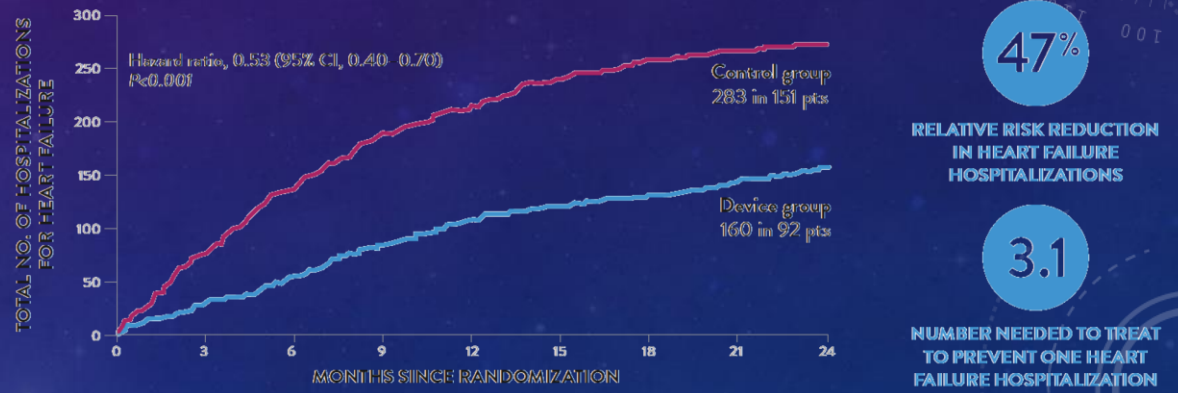
- 614 patients in US and Canada
- MR 3 or 4+ (EROA > 30, RV vol >45 ml)
- LVEF 20%-50% and LVESD <70mm
- Symptomatic after optimal HF treatment
- HF hospitalization within 12 mths and/or
  BNP >300pg/ml or
  NTproBNP >1500pg/ml

Randomized 1:1 MitraClip +GDMT vs GDMT alone

Stricter exclusion criteria



All cause mortality



Hospitalization for Heart Failure

* Additionally, all 10 secondary endpoints met statistical significance
In favor of MitraClip with GDMT over GDMT alone.

N Engl J Med 2018;379:2307- 2318

- 304 patients in France
- Inclusion:
  - EF 15-40%
  - No LVESD criteria
  - RV vol >30ml or EROA >20mm2 (actual mean EROA was 31)
  - Minimum of 1 hospitalization for HF within 12 mths preceding rndomization
- Primary outcome: all cause mortality + HF hospitalization at 12 months

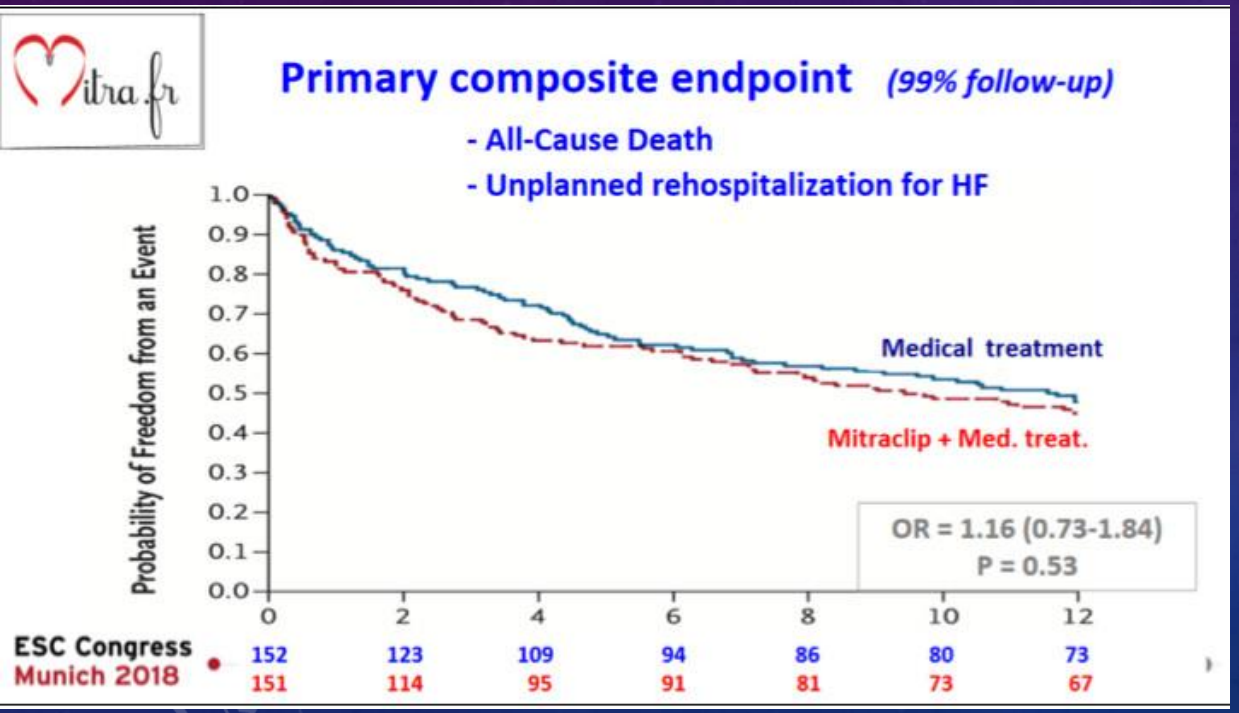


Table 3. Primary Outcome and Secondary Efficacy Outcomes at 12 Months (Intention-to-Treat Population).

Outcome	Intervention Group (N=152)	Control Group (N=152)	Hazard Ratio or Odds Ratio (95% CI)*	P Value†
Composite primary outcome: death from any cause or unplanned hospitalization for heart failure at 12 months — no. (%)	83 (54.6)	78 (51.3)	1.16 (0.73–1.84)	0.53
Secondary outcomes‡				
Death from any cause	37 (24.3)	34 (22.4)	1.11 (0.69–1.77)	
Cardiovascular death	33 (21.7)	31 (20.4)	1.09 (0.67–1.78)	
Unplanned hospitalization for heart failure	74 (48.7)	72 (47.4)	1.13 (0.81–1.56)	
Major adverse cardiovascular events§	86 (56.6)	78 (51.3)	1.22 (0.89–1.66)	

* Hazard ratios were calculated with the use of stratified Cox proportional-hazards models. The primary outcome was calculated with the use of a logistic-regression model and corresponds to an odds ratio. The 95% confidence intervals were not corrected for multiple testing; therefore, these intervals should not be used to infer definitive treatment effects.
† No P values other than that for the primary outcome are reported because no adjustment was made for multiple testing.
‡ The rates of the components of the composite primary outcome do not total the rates of the composite because patients could have more than one event.
§ This category is a composite of death, stroke, myocardial infarction, or unplanned hospitalization for heart failure.

WHY ARE THE COAPT RESULTS SO DIFFERENT FROM MITRA-FR?

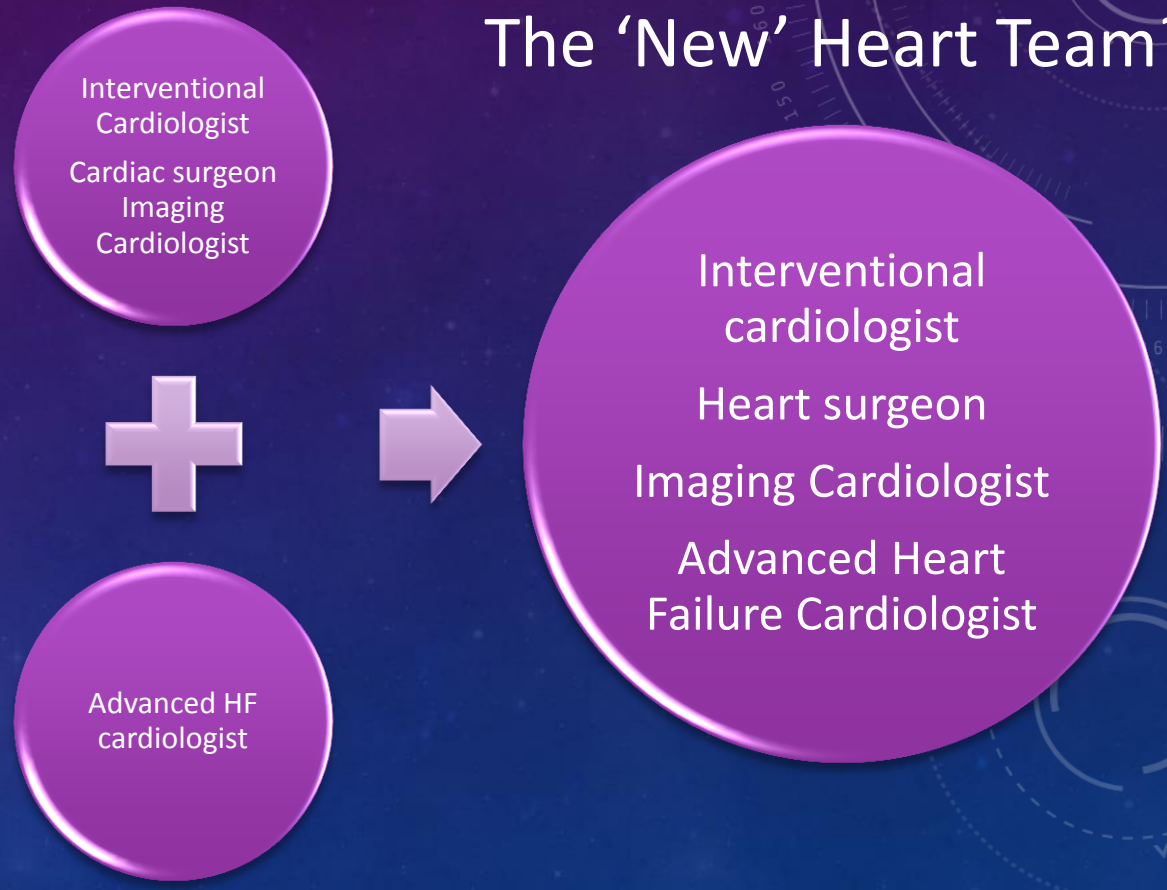
POSSIBLE REASONS

	MITRA-FR (n=304)	COAPT (n=614)
Severe MR entry criteria	Severe FMR by EU guidelines: EROA >20mm^2 or RV >30ml/beat	Severe FMR by US guidelines: EROA >30mm^2 or RV >45ml/beat
EROA	$31 \pm 10\ mm^2$	$41 \pm 15 mm^2$
LVEDV	$135 \pm 35\ ml/m^2$	$101 \pm 34\ ml/m^2$
GDMT at baseline and FU	Receiving HF meds at baseline- Allowed variable adjustment in each group during FU per "real world" practice	CEC confirmed pts were failing maximally tolerated GDMT at baseline- few major changes during follow-up
Acute results : No clip/ >3+ MR	9%/ 9%	5%/ 5%
Procedural complications	14.6%	8.5%
12 month MitraClip >3+ MR	17%	5%

FUNCTIONAL MR BEFORE AND AFTER COAPT

Before	After
MR is a risk marker	MR is a risk factor
MR= Color jet area	MR= EROA
Hugh LV volume is bad	Hugh LV volume is really bad
ACC/AHA IIB indication for surgery	ACC/AHA IIA indication for MitraClip?

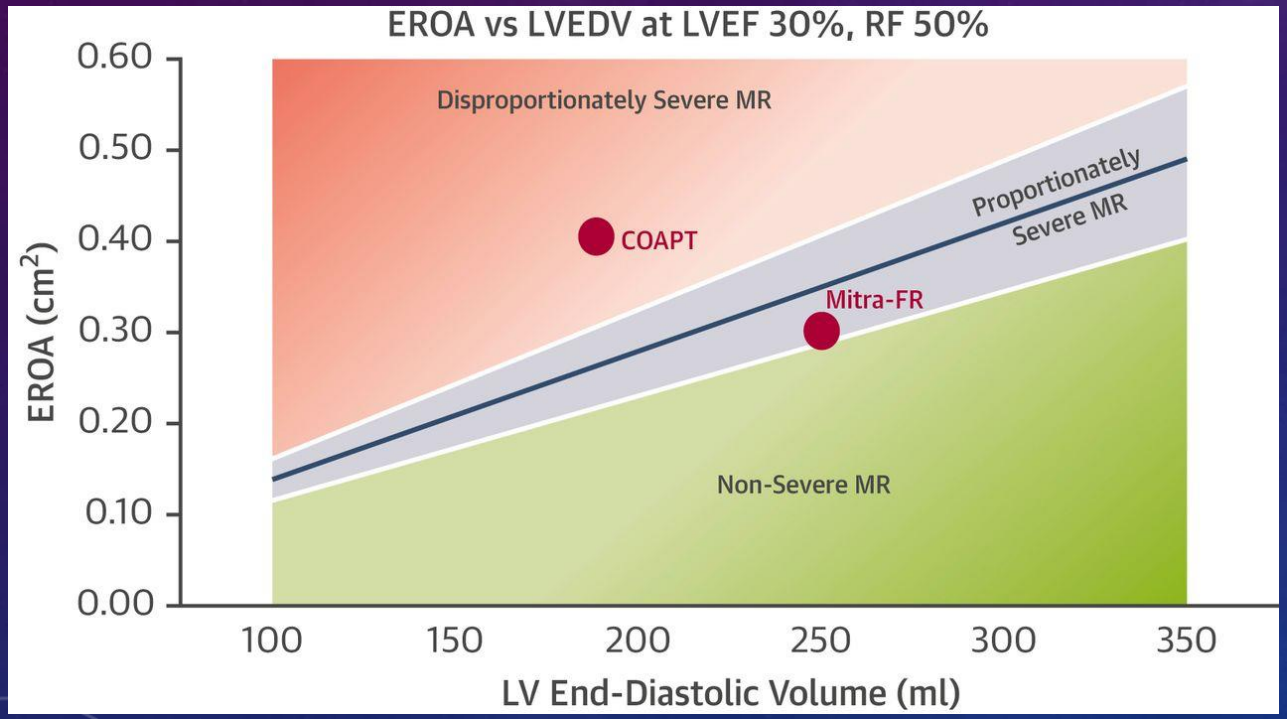
The 'New' Heart Team?



Patient selection, medical treatment and procedural timing is key for success

Proportionate and Disproportionate Functional Mitral Regurgitation

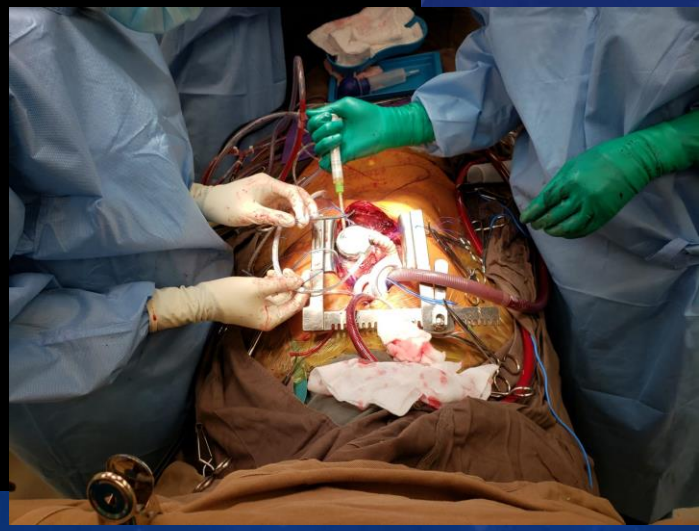
A New Conceptual Framework That Reconciles the Results of the MITRA-FR and COAPT Trials

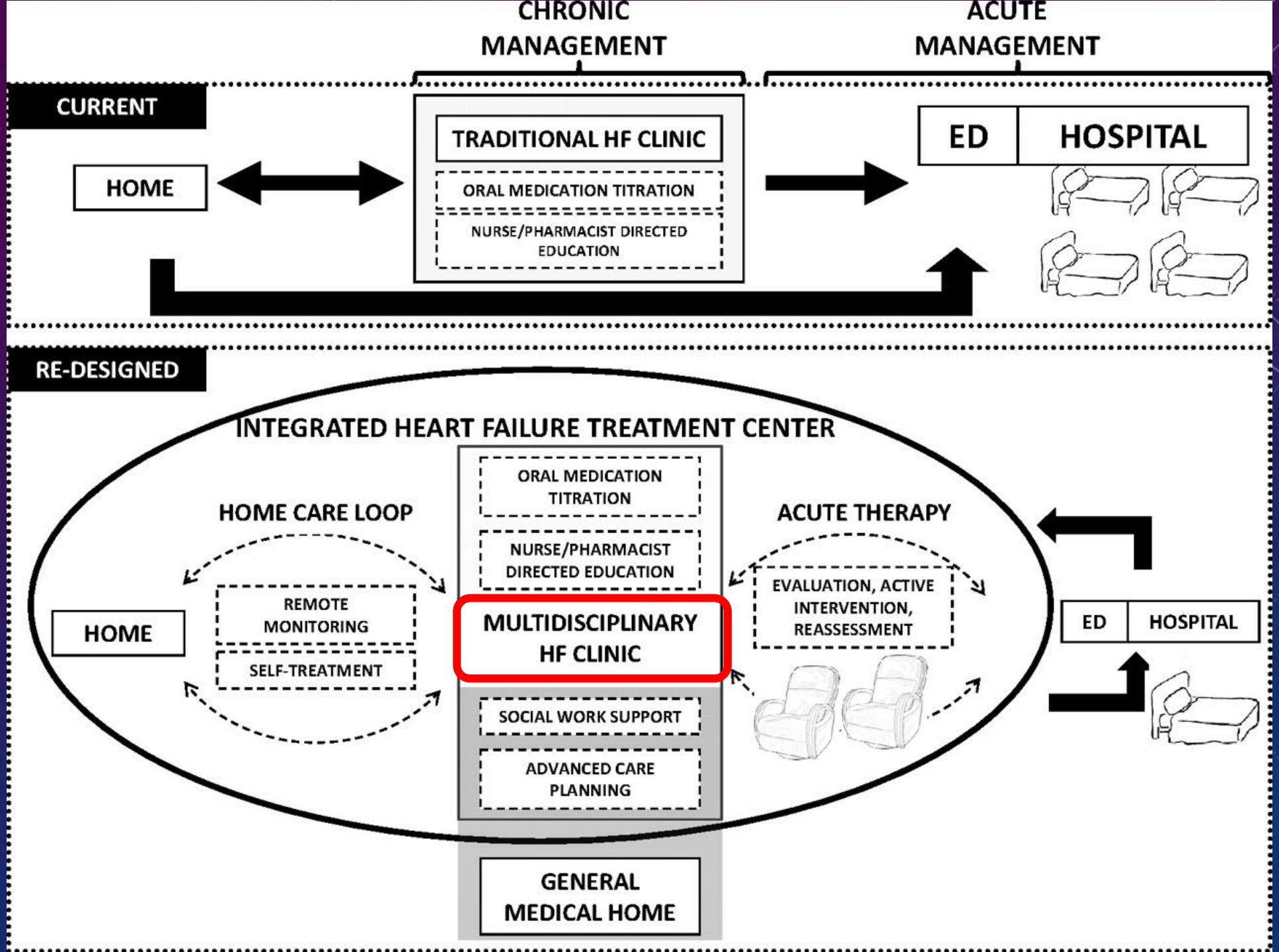


- Novel paradigm/ theory provides a strong pathophysiological basis for selecting patients for specialized interventions and explains the apparently discordant findings from randomized trials
- Concept:
- Characterization of MR as proportionate or disproportionate to LVEDV appears to be critical to the selection of an optimal treatment for patients with CHF and systolic dysfunction
- A patient with EROA/LVEDV ratio well below the line of proportionality has non severe MR and would not be expected to benefit from any intervention directed at mitral valve

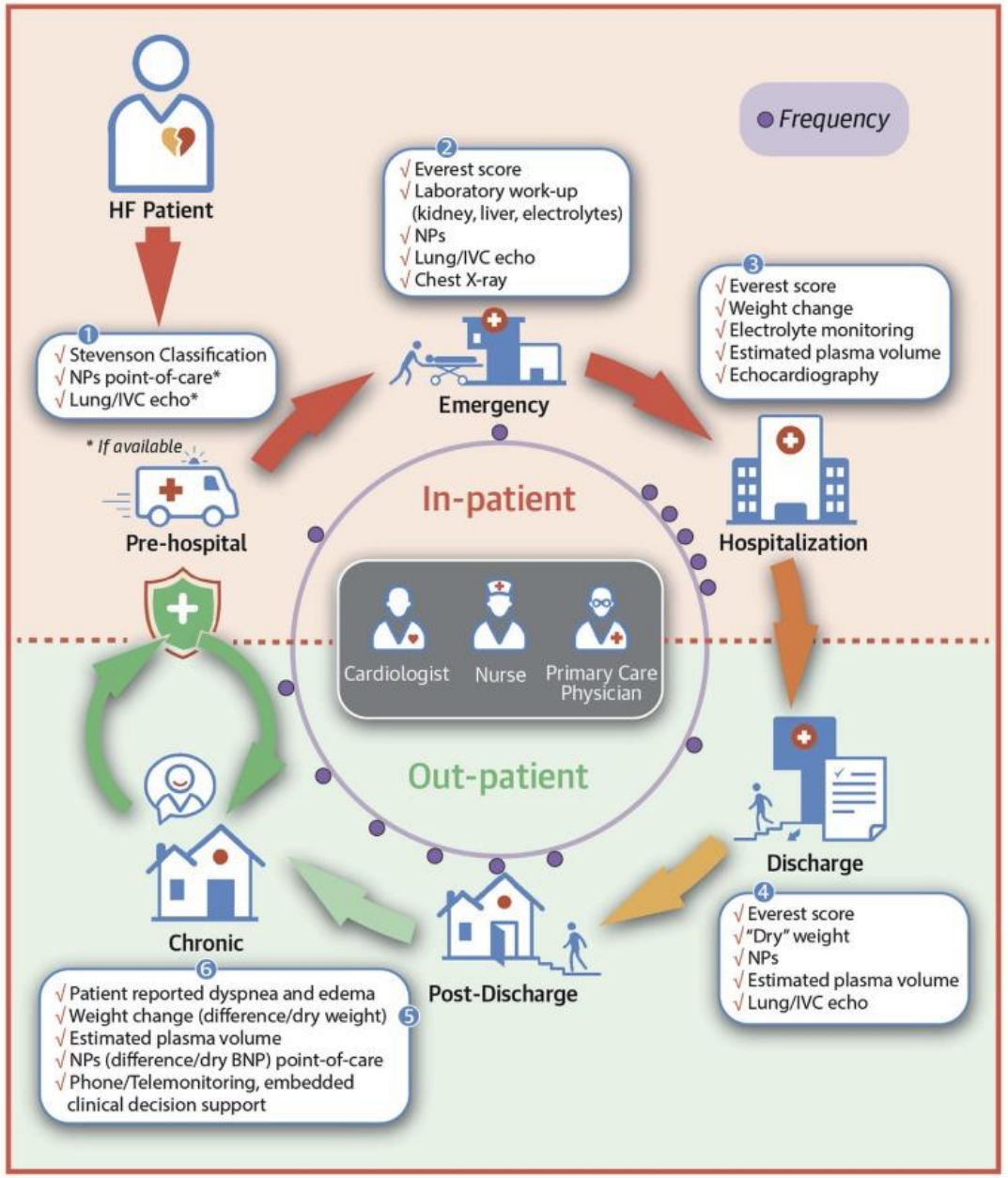
Grayburn P et al. JACC Img 2018

LEFT VENTRICULAR ASSIST DEVICE (LVAD)




CHRONIC MANAGEMENT
ACUTE MANAGEMENT
CURRENT
HOME
TRADITIONAL HF CLINIC
ORAL MEDICATION TITRATION
NURSE/PHARMACIST DIRECTED EDUCATION
ED
HOSPITAL
RE-DESIGNED
INTEGRATED HEART FAILURE TREATMENT CENTER
HOME CARE LOOP
HOME
REMOTE MONITORING
SELF-TREATMENT
ORAL MEDICATION TITRATION
NURSE/PHARMACIST DIRECTED EDUCATION
MULTIDISCIPLINARY HF CLINIC
SOCIAL WORK SUPPORT
ADVANCED CARE PLANNING
GENERAL MEDICAL HOME
ACUTE THERAPY
EVALUATION, ACTIVE INTERVENTION, REASSESSMENT
ED
HOSPITAL

CENTRAL ILLUSTRATION: Congestion Assessment in HF Patient Journey



Girerd, N. et al. J Am Coll Cardiol HF. 2018;6(4):273-85.

American Heart Association.
Rise Above Heart Failure®

Self-Check Plan for HF Management

Excellent – Keep Up the Good Work!

- ☐ No new or worsening shortness of breath
- ☐ Physical activity level is normal for you
- ☐ No new swelling, feet and legs look normal for you
- ☐ Weight check stable Weight: ____
- ☐ No sign of chest pain

GREAT! CONTINUE: Daily Weight Check · Meds as Directed · Low Sodium Eating · Follow-up Visits

Pay Attention – Use Caution!

- ☐ Dry, hacking cough
- ☐ Worsening shortness of breath with activity
- ☐ Increased swelling of legs, feet, and ankles
- ☐ Sudden weight gain of more than 2-3 lbs in a 24 hour period (or 5 lbs in a week)
- ☐ Discomfort or swelling in the abdomen
- ☐ Trouble Sleeping

CHECK IN! Your symptoms may indicate: A need to contact your doctor or provider · A need for a change in medications

Medical Alert – Warning!

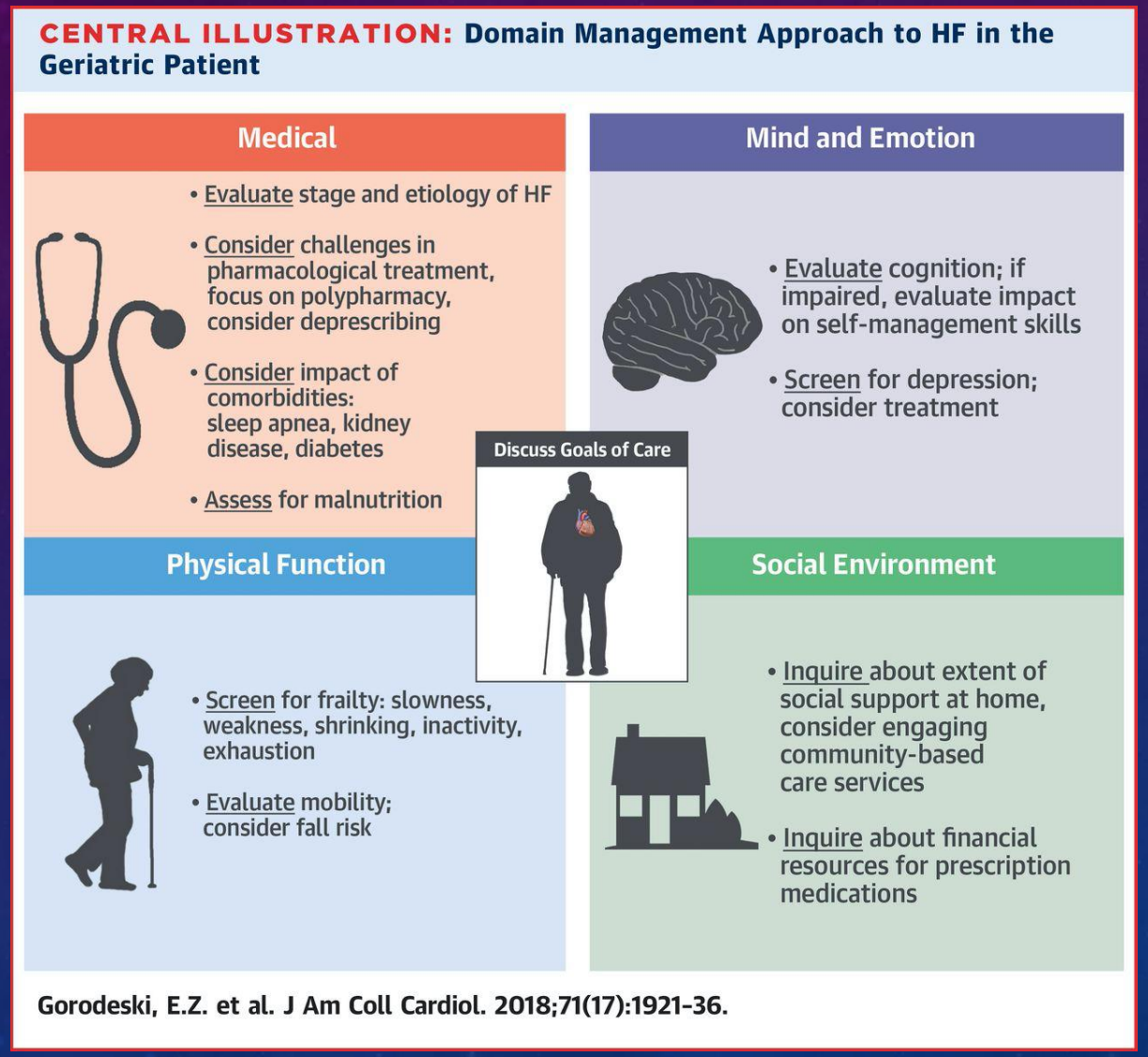
- ☐ Frequent dry, hacking cough
- ☐ Shortness of breath at rest
- ☐ Increased discomfort or swelling in the lower body
- ☐ Sudden weight gain of more than 2-3 lbs in a 24 hour period (or 5 lbs in a week)
- ☐ New or worsening dizziness, confusion, sadness or depression
- ☐ Loss of appetite
- ☐ Increased trouble sleeping; cannot lie flat

WARNING! You need to be evaluated right away. Call your physician or call 911

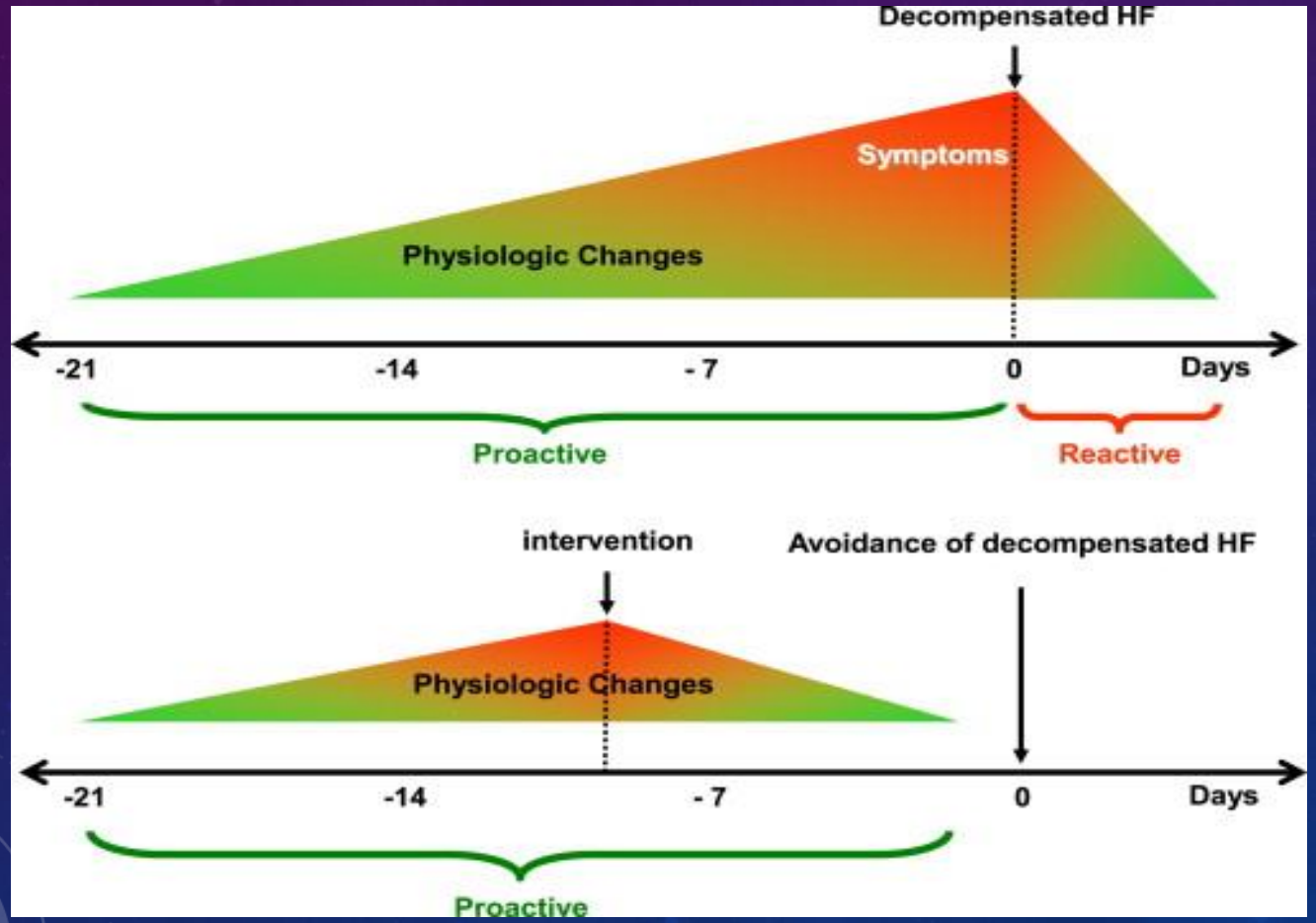
www.RiseAboveHF.org

3/19DS14555

DOMAIN MANAGEMENT APPROACH TO HEART FAILURE



HF INTERVENTION DURING EARLY PHYSIOLOGIC CHANGE: PROACTIVE VS REACTIVE



Hospital

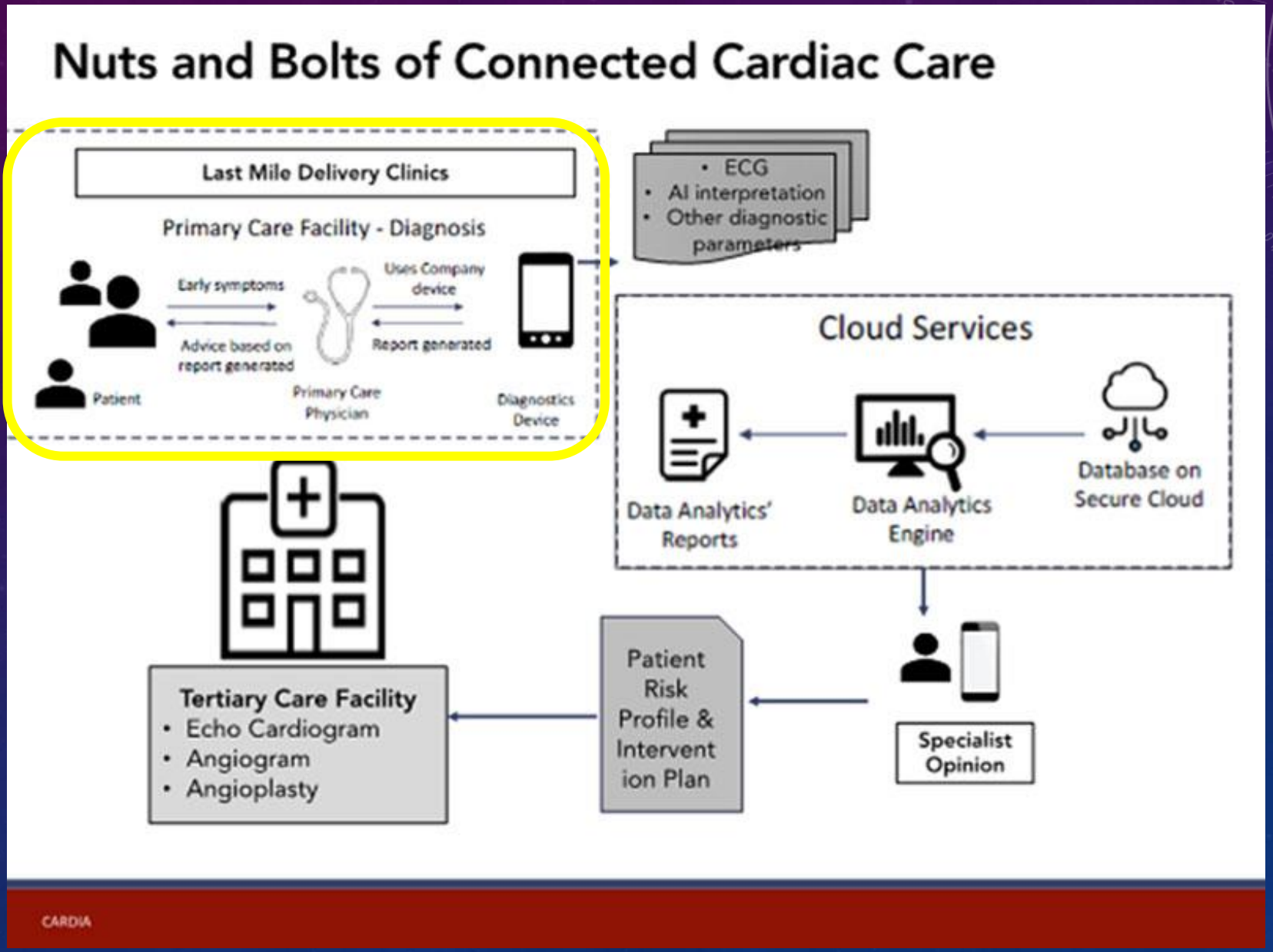
HF MANAGEMENT IN NEW ERA INTERNET OF THINGS (IoT)

- Models for the outpatient management of acutely decompensated heart failure have shown that ambulatory infusion of decompensated HF can reduce all-cause hospitalization at 30 days [1]
- Successful outpatient management of HF (***Proactive***):
  - Investment in home-based healthcare services
  - 24 hours telephone access for advice
  - Protocol for the management of electrolytes and changes in renal function

- One tools with immense potential to continue care – **TELEMEDICINE**
- Improve communication with patients
- Triage need for inpatient care or acute visits
- Monitor patients while they are in their communities

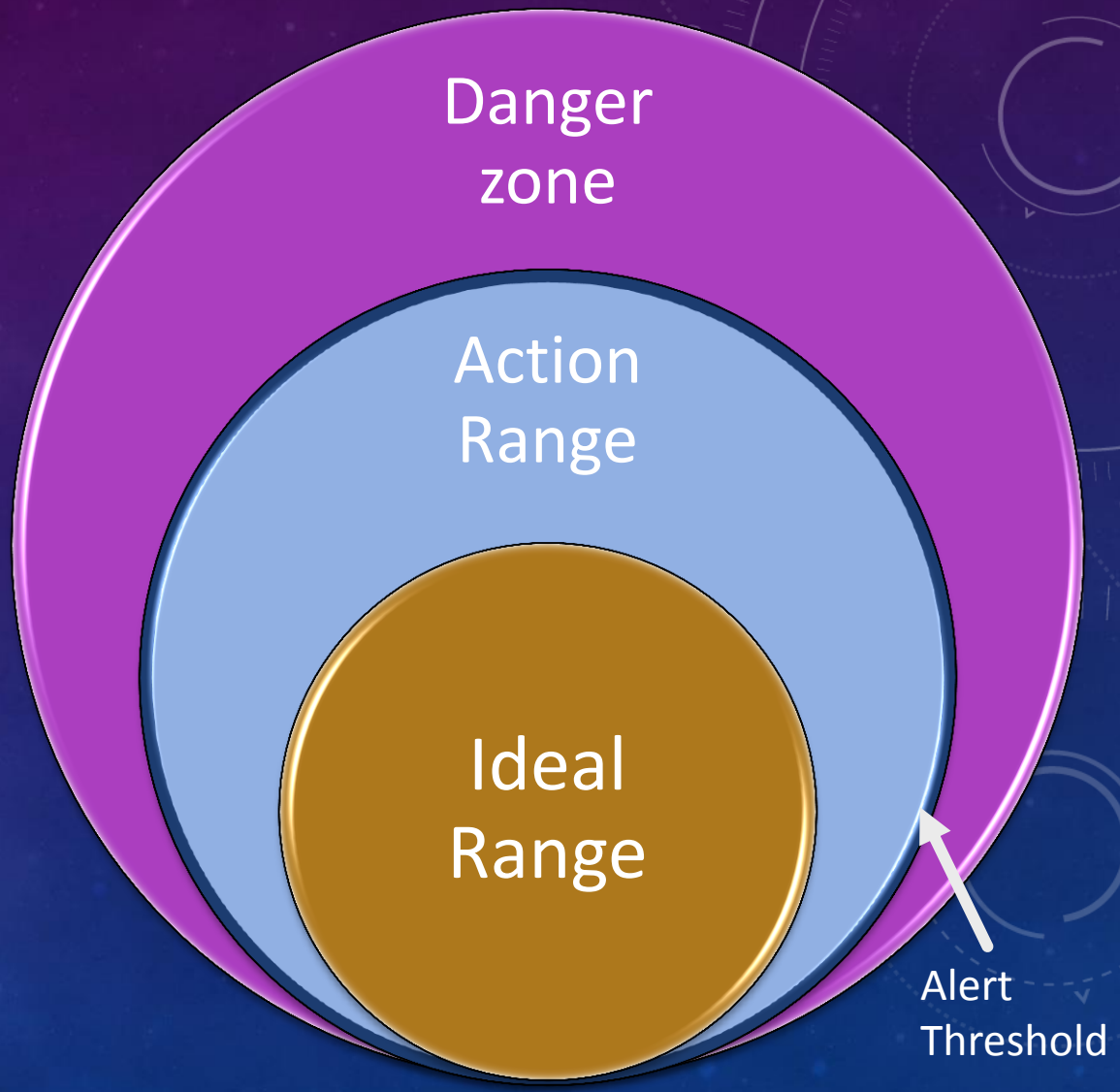
1. JACC Heart Failure 2016;4:1-8

CARDIAC CARE CONNECTED TECHNOLOGY PLATFORM

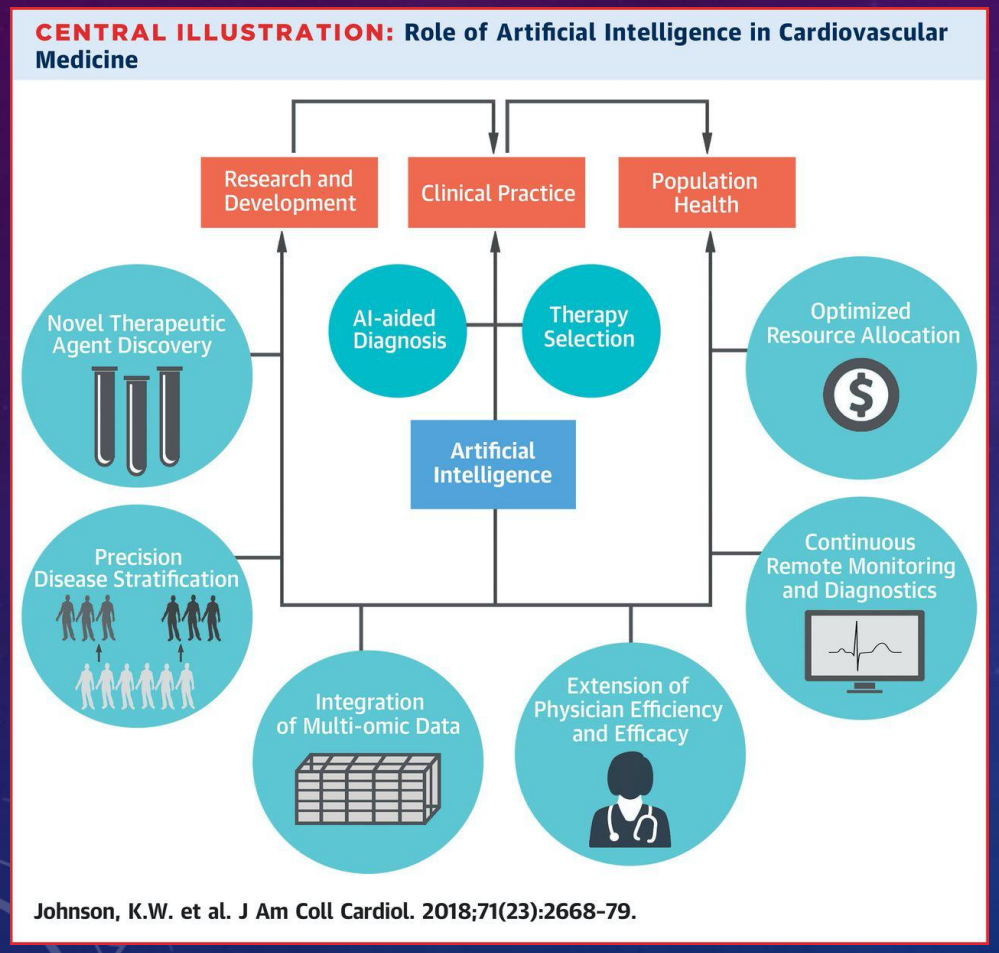


Telemonitoring for Heart Failure: Decision Support

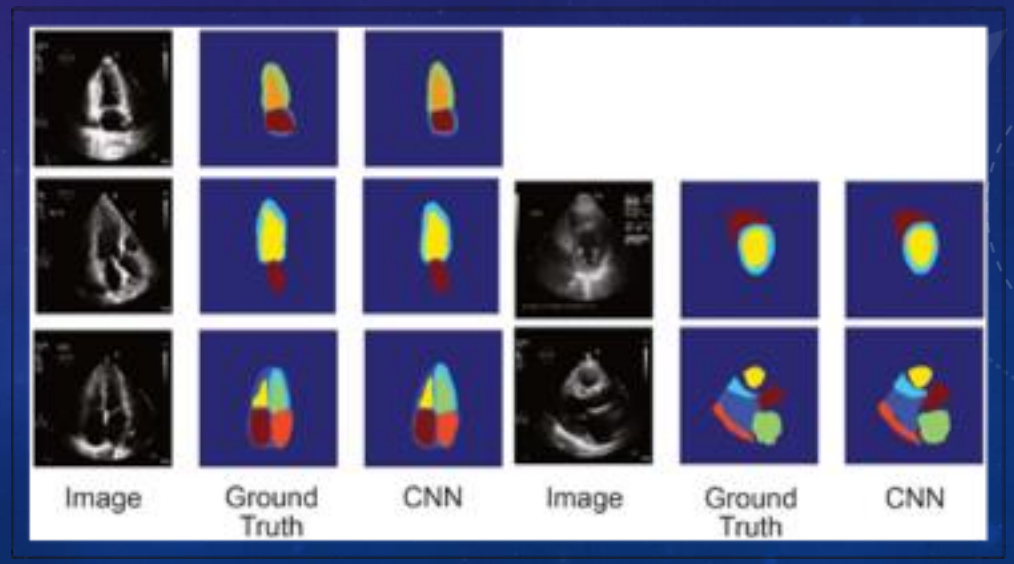
- For patients for health maintenance (majority)
  - Daily to maintain health envelope
  - Diet
  - Medications (principally diuretics)
- For Health Professionals for Alerts
  - “Traffic Lights” of risk status
  - Identify, prevent and manage crisis
  - Schedule tests
  - Alter care plan targets



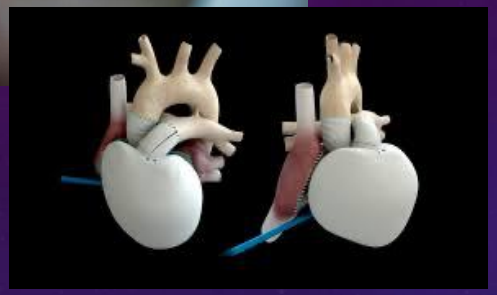
ARTIFICIAL INTELLIGENCE: THE FUTURE OF CARDIOLOGY

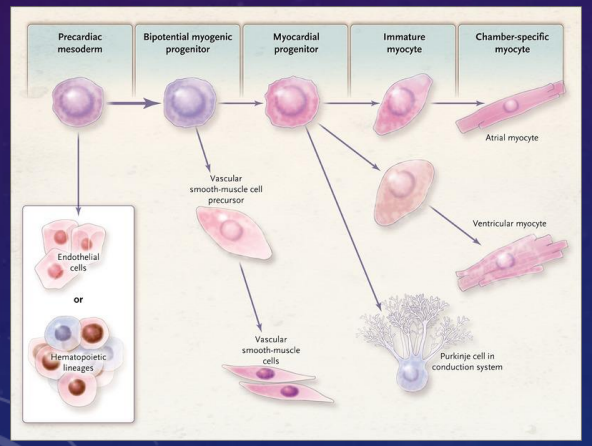


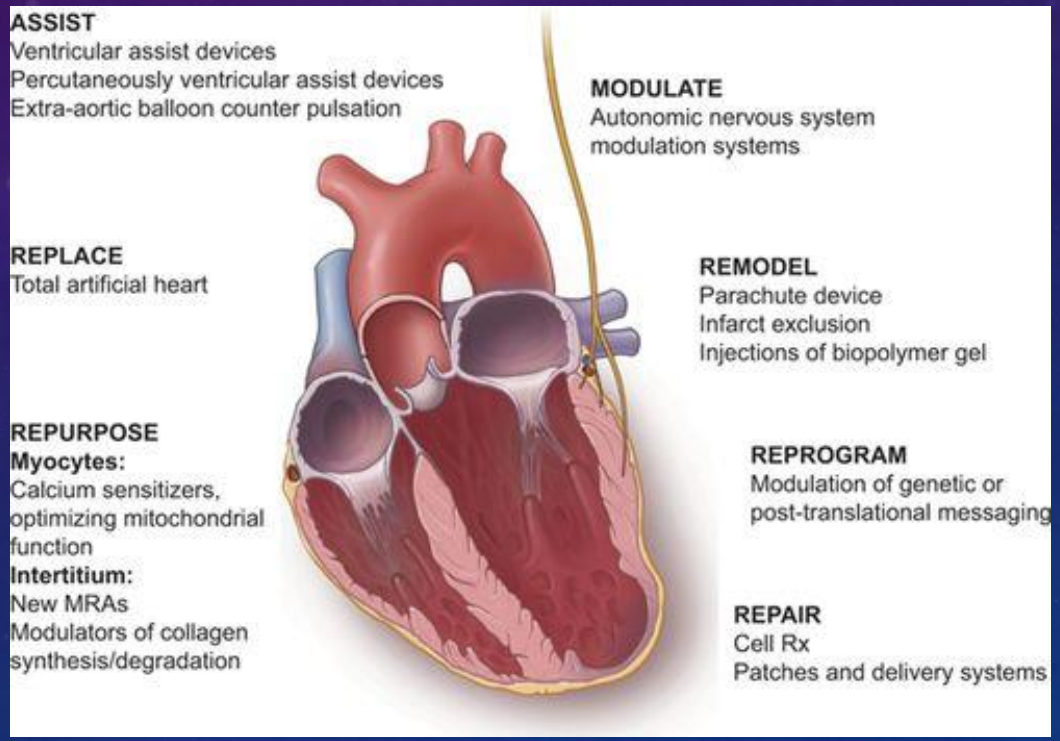
- "the theory and development of computer systems able to perform tasks normally requiring human intelligence"
- For example: automated predictions of cardiovascular disease risk score and HF diagnosis
- Automated method to interpret ECHO

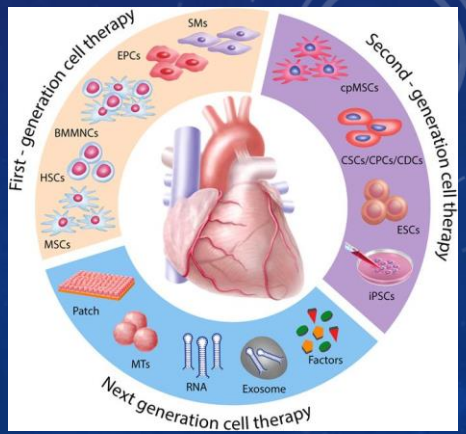


Circulation 2018;138:1623-1635









Circulation 2016;133:2671-2686

CONCLUSIONS

- Residual risk remains in heart failure due to inadequate GDMT implementation
- Targeting alternate parallel pathways may be associated with improved outcomes and modulation (eg SGLT2 inhibition, sGC-cGMP, cardiac myosin activation)
- Non pharmacological treatments play increasing important roles
- Physician and patient education, GDMT implementation and targeting all pathways and remote monitoring are important heart failure care.

5 IMAGINATIVE PREDICTIONS FOR TREATMENT OF HEART FAILURE IN 2028 BY DR MILTON PACKER

EUROPEAN HEART JOURNAL 2018;39 (1): 5-7

- 1. Heart failure with a preserved ejection fraction will be broken into distinct phenotypes. The most common phenotype – that associated with obesity- will be treated as a neurohormonal disorder
- 2. The next wave of new pharmacological agents for heart failure with a reduced ejection fraction will focus on drugs that induce the cellular housekeeping process of autophagy
- 3. Unless major changes take place in the pricing or uptake of new pharmaceuticals, drug development for heat failure will cease. The risks and expense of new drug development for these patients will exceed the likelihood of a meaningful return on investment.
- 4.Most patients with chronic heart failure will be managed by specialist practitioners who will not be cardiologists and may not be physicians
- 5. Cell- and gene-based treatments will fail, but because of advances in mechanical devices that provide effective circulatory support, no one with adequate financial resources will die of heart failure involuntarily

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THANK YOU!