Heart Failure Update 2021: How to fix a broken heart

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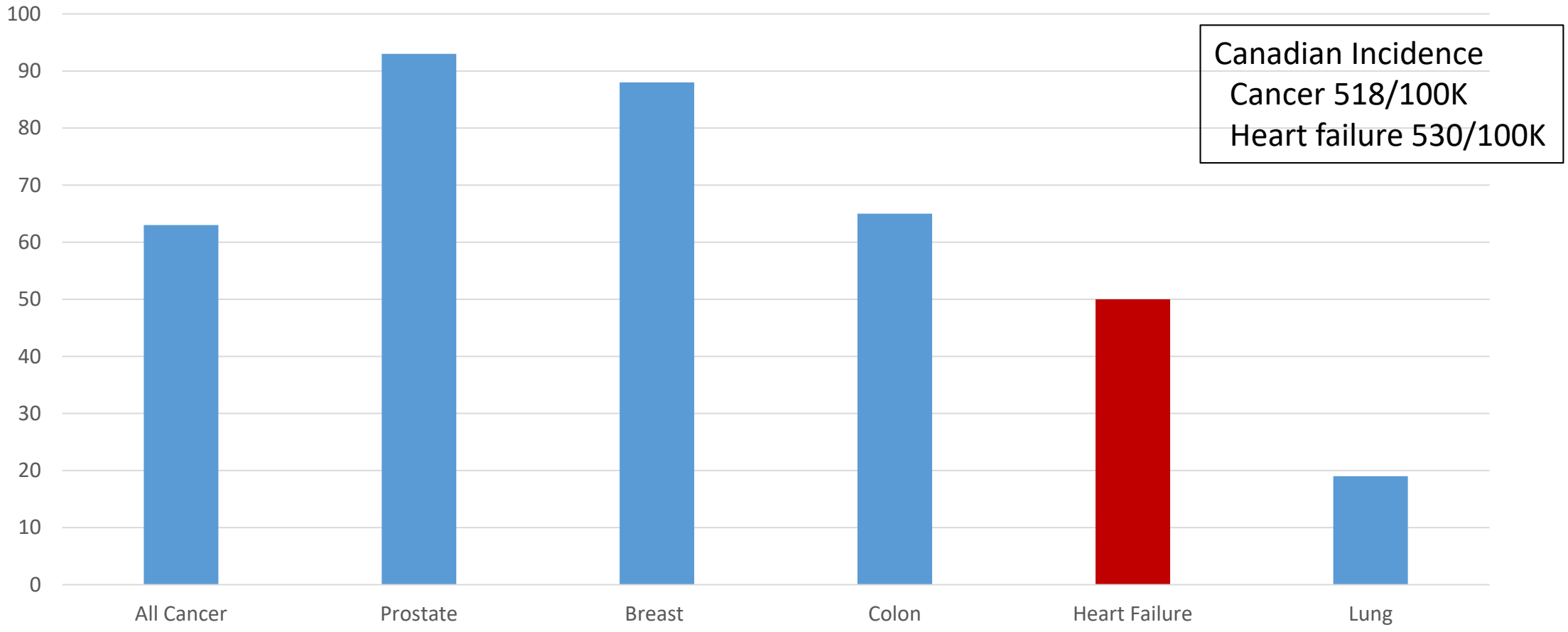
Objectives

- By the end of this presentation, you should be able to:
  - Discuss an approach to HF management

5 year survival



https://www.cancer.ca/~/media/cancer.ca/CW/cancer%20information/cancer%20101/Canadian%20cancer%20statistics/Canadian-Cancer-Statistics-2019-EN.pdf?la=en

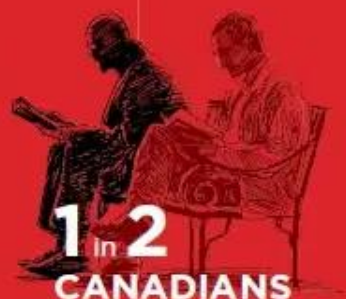
https://www.canada.ca/en/public-health/services/publications/diseases-conditions/report-heart-disease-Canada-2018.html

HEART FAILURE IS A GROWING EPIDEMIC

HEART FAILURE is on the **RISE** in **CANADA.**

600,000 CANADIANS are living with **HEART FAILURE.**

50,000 CANADIANS are diagnosed each year with **HEART FAILURE.**



1 in 2 CANADIANS has been touched by **HEART FAILURE.**

HEART FAILURE costs more than **$2.8 BILLION** per year.

HEART FAILURE COSTS EVERYONE

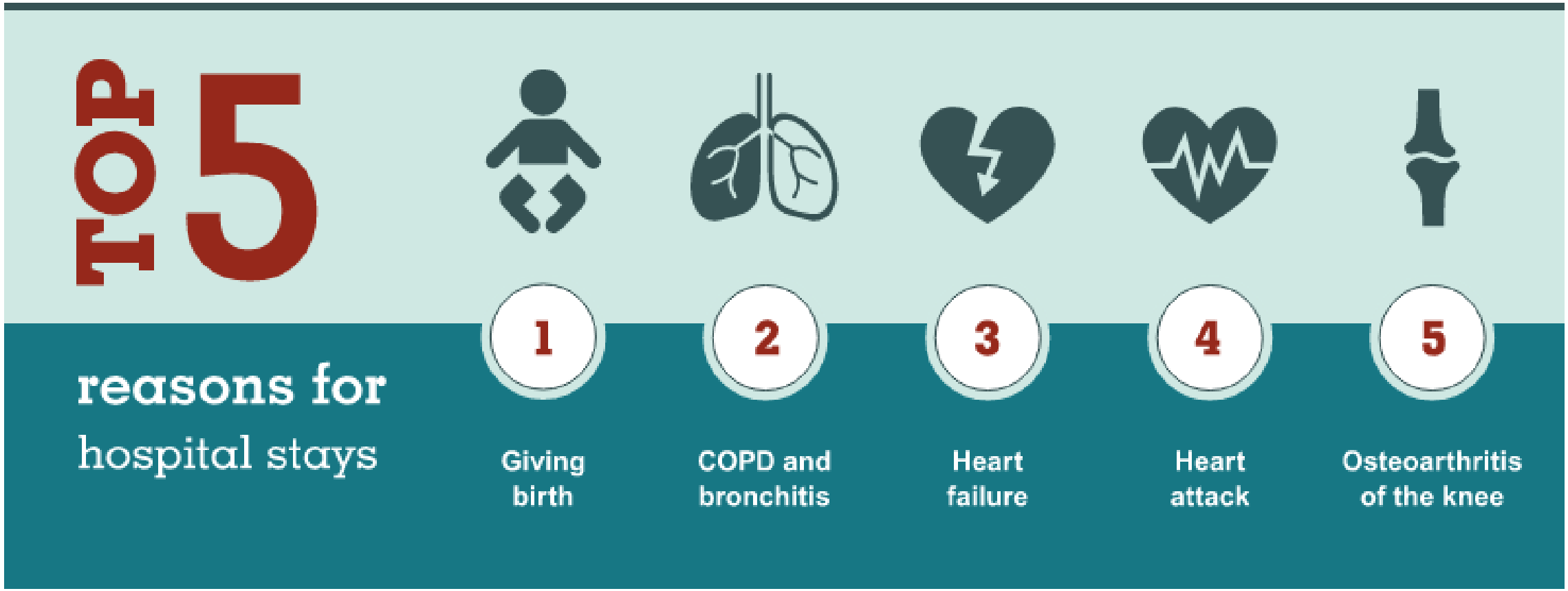
HEART FAILURE patients have **LONG** and **FREQUENT** hospital stays.

There is **NO CURE** for **HEART FAILURE.**

HEART FAILURE patients are **COMPLEX,** often managing other conditions.

HEART FAILURE patients experience **SHORTNESS OF BREATH,** exhaustion and swelling.

HEART FAILURE caregivers are often overwhelmed and **STRESSED.**



https://www.cihi.ca/en/hospital-stays-in-canada

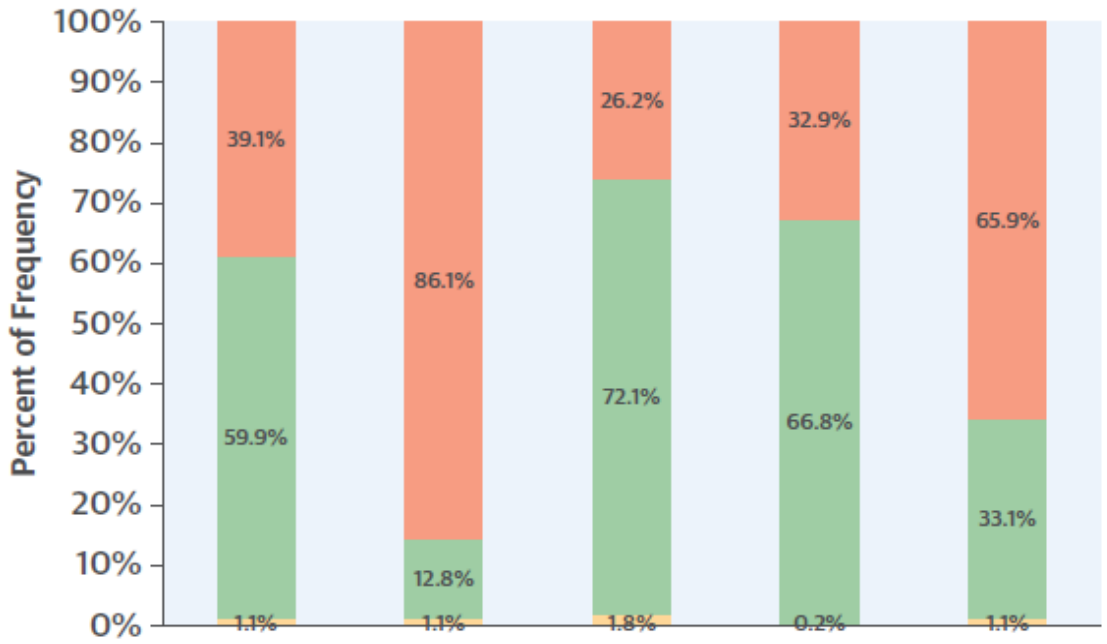
Timeline of HFrEF Pharmacotherapy

	1980	1990	2000	2010	2020
Hydralazine/ ISDN	VHeFT I (1986)		A-HeFT (2004)		
ACEi/ARB	CONSENSUS (1987)	SOLVD (1991) VHeFT II (1991) SAVE (1992) SOLVD-P (1992)	Val-Heft (2001) CHARM (2003) VALIANT (2003)		
BB		Carvedilol (1996) Merit-HF (1999) CIBIS II (1999)	COPERNICUS (2001) COMET (2003)		
Digoxin		DIG (1997)			
MRA		RALES (1999)	EMPHASIS-HF (2003) EPHESUS (2003)		
Ivabradine			BEAUTIFUL (2008)	SHIFT (2010)	
Sacubitril / Valsartan				PARADIGM-HF (2014) PIONEER-HF (2019)	
SGLT2i					DAPA-HF (2020) EMPEROR Reduced (2021)

The HF GDMT Care Gap

CENTRAL ILLUSTRATION Use and Dosing of Guideline-Directed Medical Therapy Among Patients With Chronic HFrEF in Contemporary U.S. Outpatient Practice

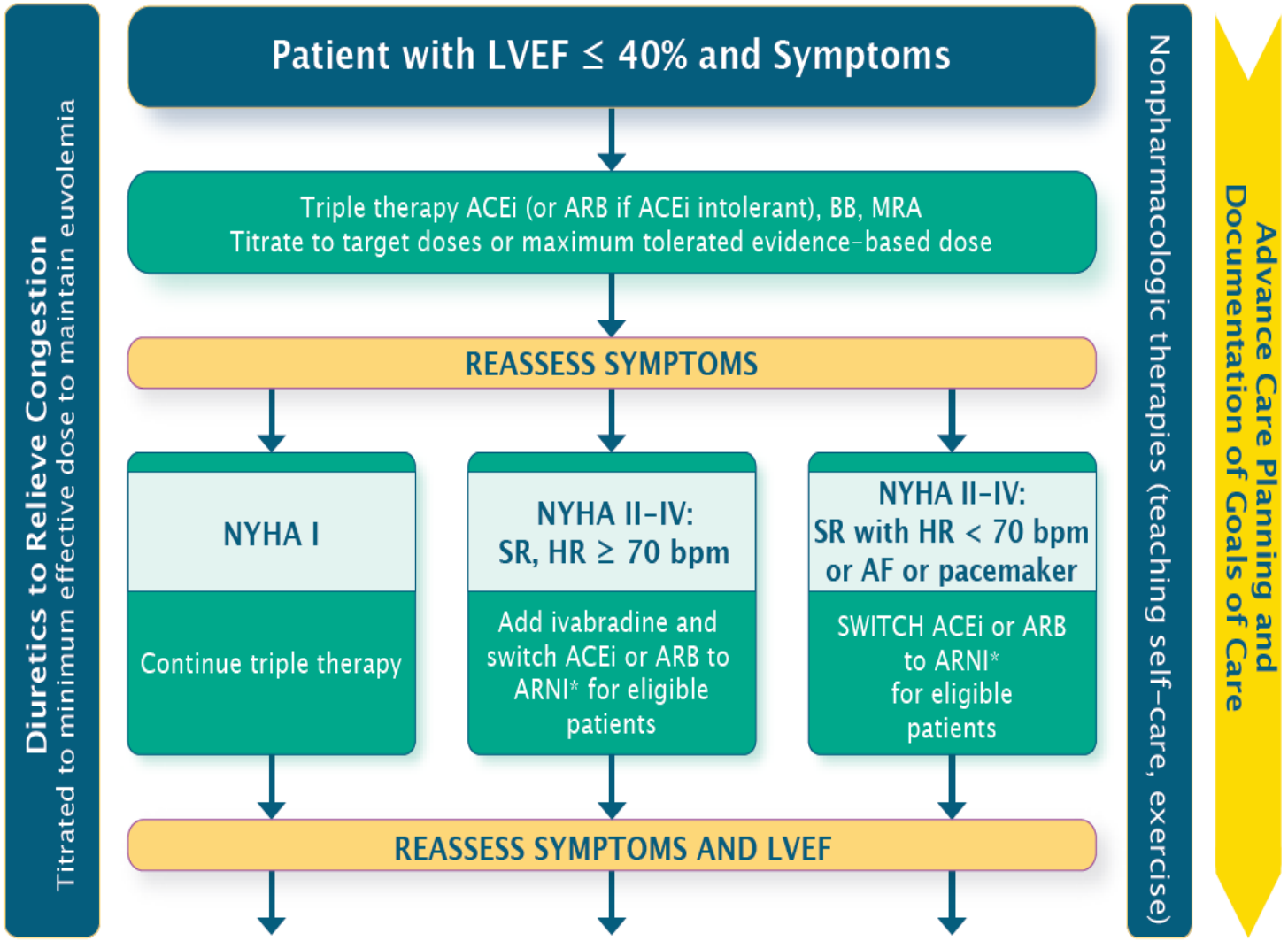
A



	ACEI/ARB	ARNI	ACEI/ARB/ ARNI	Beta-Blocker	MRA
Without Contraindication and Not Treated	1374	3029	920	1159	2317
Treated	2107	452	2536	2351	1163
With Contraindication	37	37	62	8	38

J Am Coll Cardiol 2018;72:351-66

Guideline Overview:
2017 CCS HF Guidelines



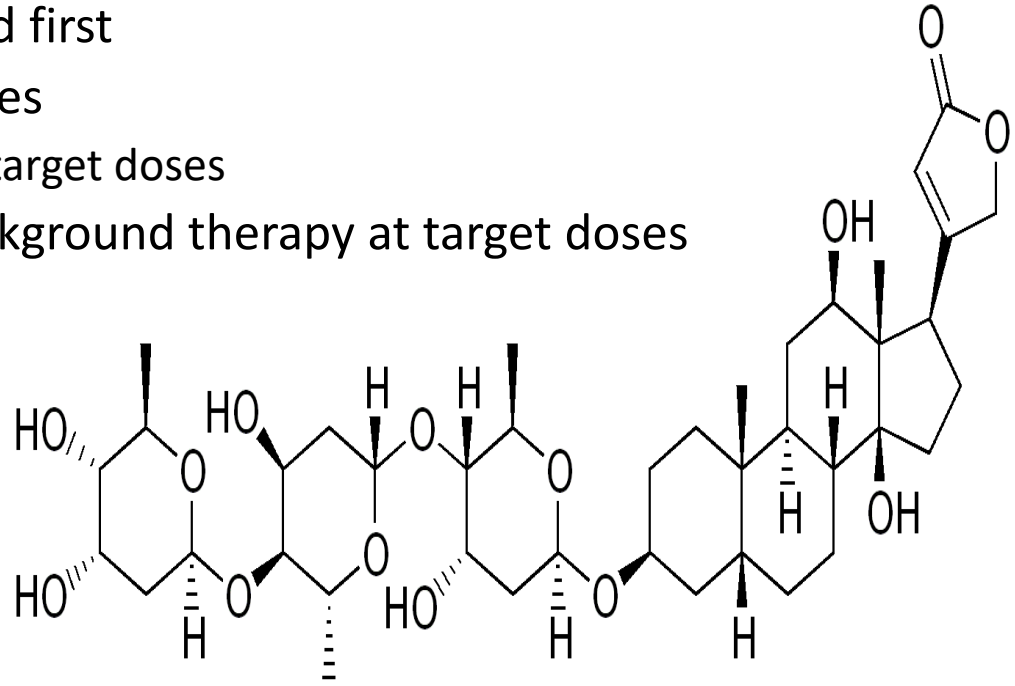
2020 Guidelines

8. **New.** We recommend SGLT2 inhibitors, such as dapagliflozin be used in patients with mild to moderate HF due to reduced LVEF (≤ 40%) and concomitant type 2 diabetes, to improve symptoms and quality of life and to reduce the risk of hospitalization and cardiovascular mortality (Strong Recommendation, High-Quality Evidence).
9. **New.** We recommend SGLT2 inhibitors, such as dapagliflozin be used in patients with mild to moderate HF due to reduced LVEF (≤ 40%) and without concomitant diabetes, to improve symptoms and quality of life and to reduce the risk of hospitalization and cardiovascular mortality (Conditional Recommendation, High-Quality Evidence).

Canadian Journal of Cardiology 2017 33, 1342-1433DOI: (10.1016/j.cjca.2017.08.022)

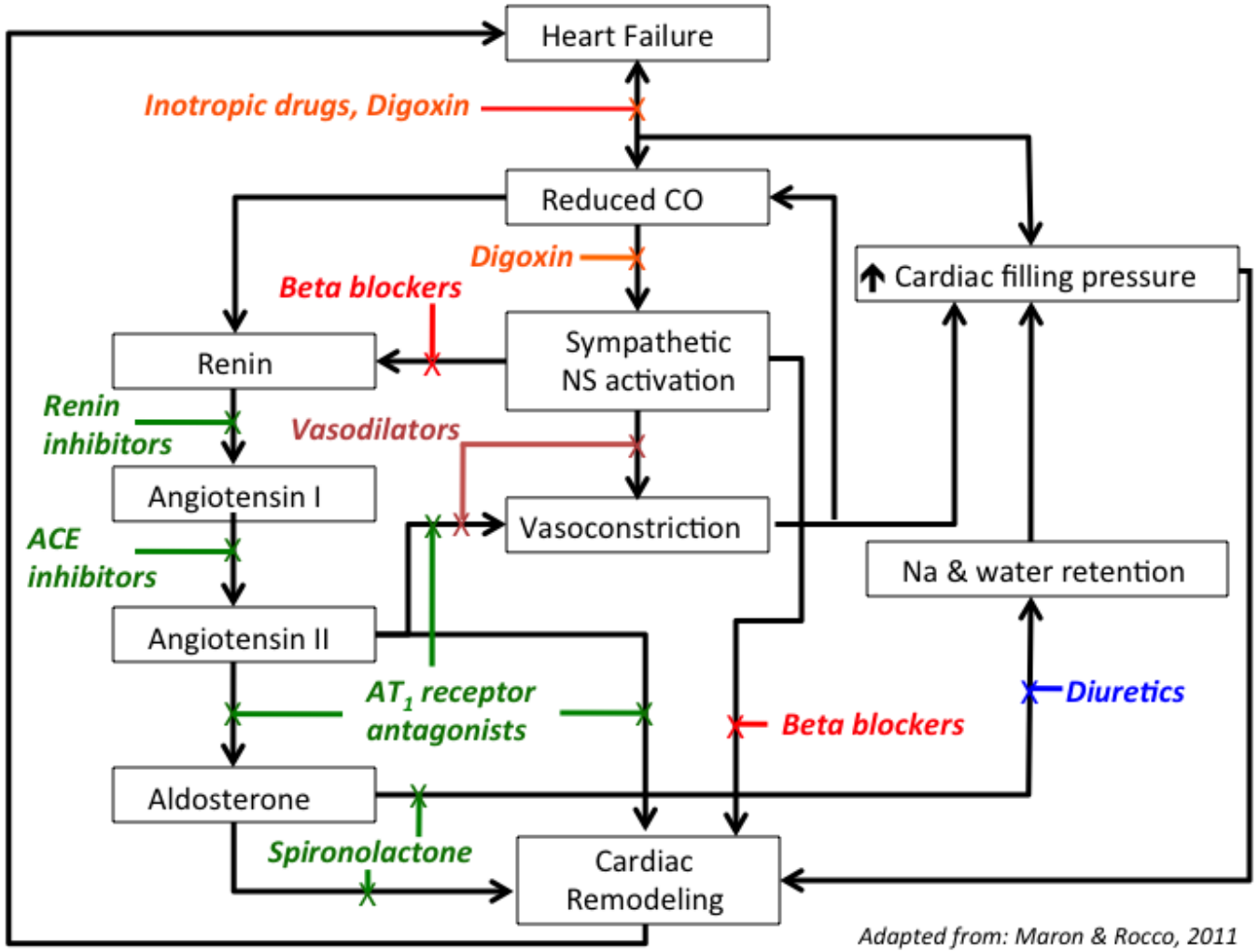
Stepped Approach Pitfall: Historical Precedent

- Precise sequence of clinical testing over 40 years
- Limitations
  - Assumes:
    - most effective / well tolerated drugs are developed first
    - Drug are only effective when titrated to target doses
      - Limited evidence to support significant value with target doses
    - Efficacy / safety of each class was tested on all background therapy at target doses



McMurrray JJV et al. 10/1161/CIRCULATIONAHA.120.052926

Stepped Approach Pitfall: Complex Pathophysiology



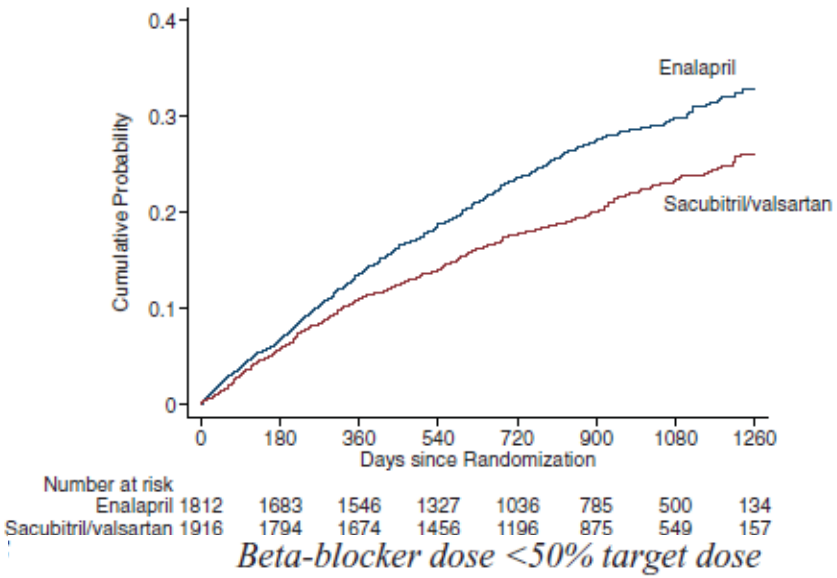
Stepped Approach Pitfalls: Magnitude of treatment effects

- Overlooks:
  - Magnitude of treatment benefits are independent of each other
  - Magnitude of adding a class is likely larger than up-titrating an existing drug

McMurrray JJV et al. 10/1161/CIRCULATIONAHA.120.052926

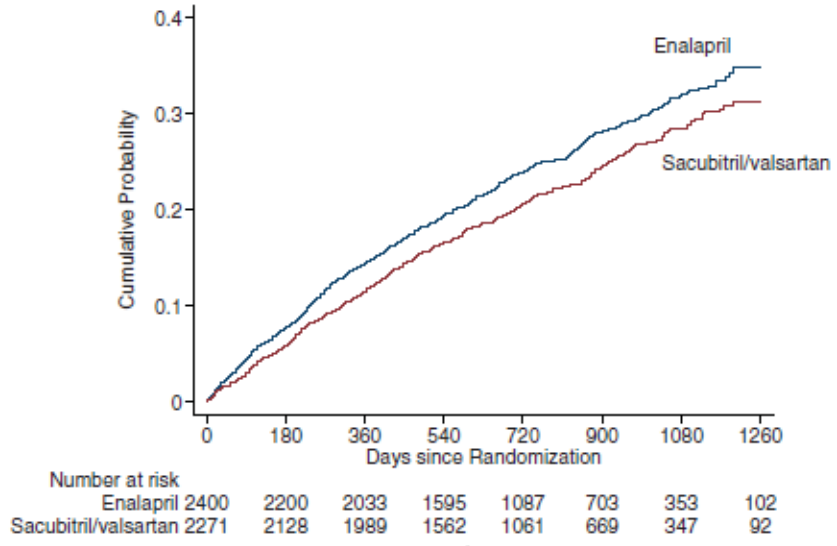
MRA

No mineralocorticoid receptor antagonist



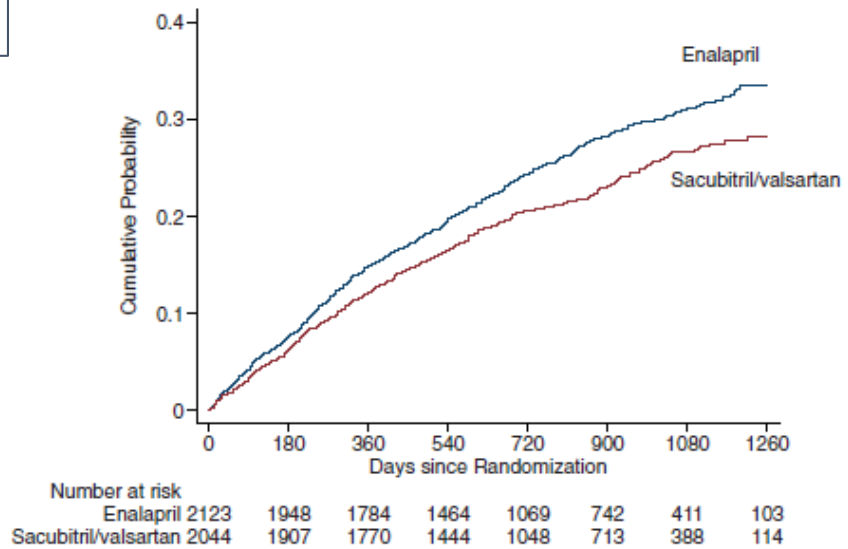
Beta-blocker dose <50% target dose

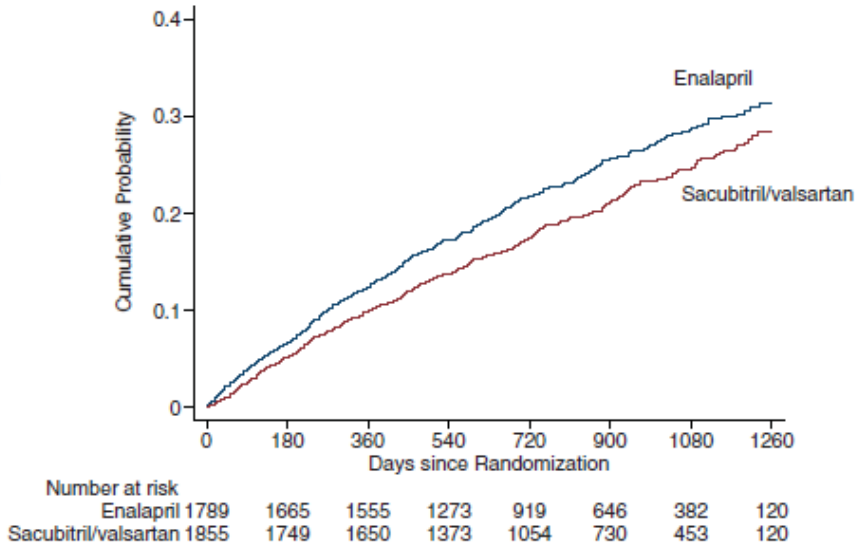
Mineralocorticoid receptor antagonist



Beta-blocker dose ≥50% target dose

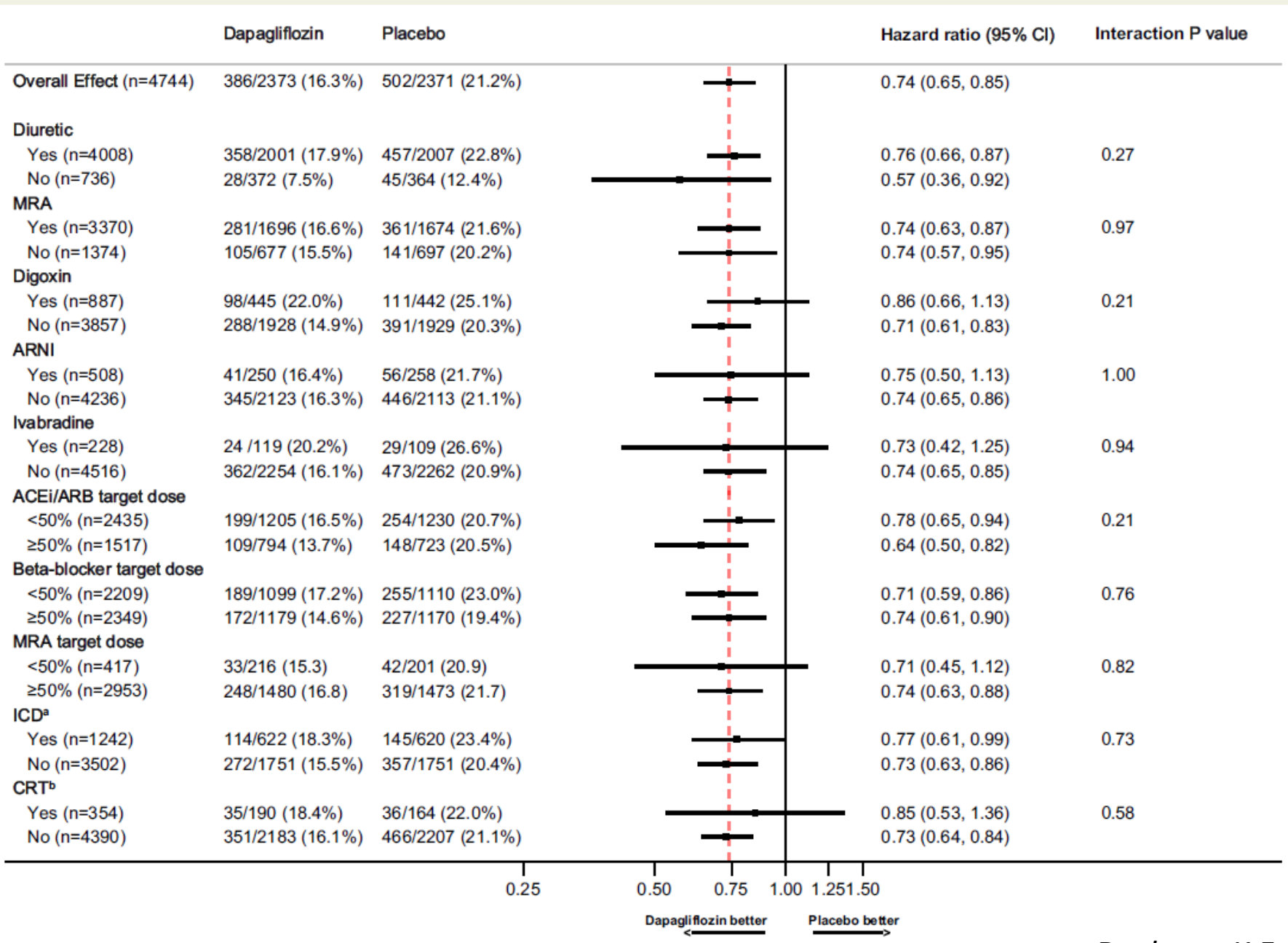
BB





PARADIGM-HF
Secondary analysis
Background therapy

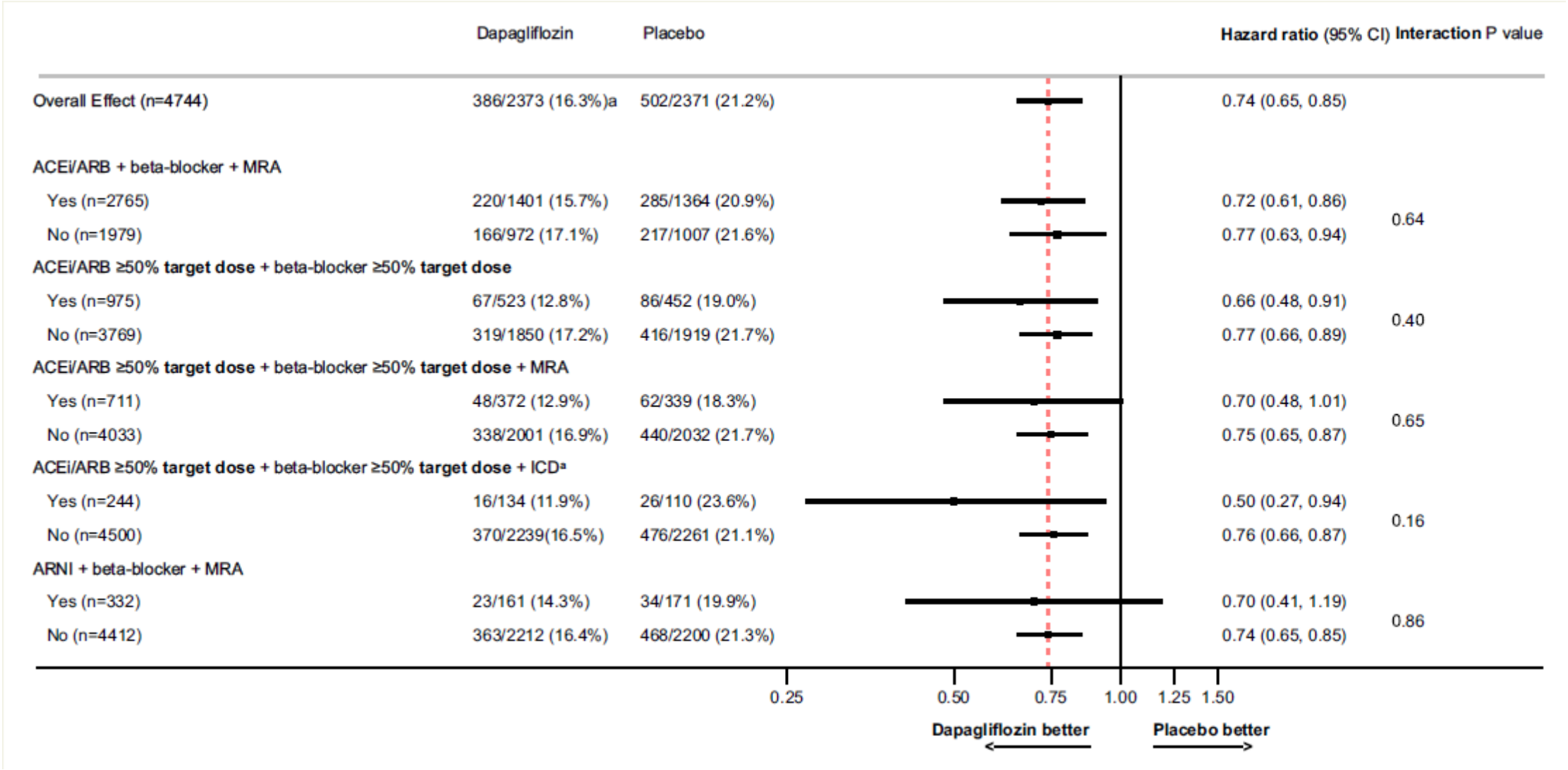
Okumura N, et al. Circ Heart Failure 2016;9:e003212



DAPA-HF
Post-hoc analysis
Background therapy

Docherty K F et al. Eur Heat J 2020; 41:2379-92

Post-hoc: DAPA-HF Background Therapy



Docherty K F et al. Eur Heat J 2020; 41:2379-92

Comprehensive vs. Conventional Treatment

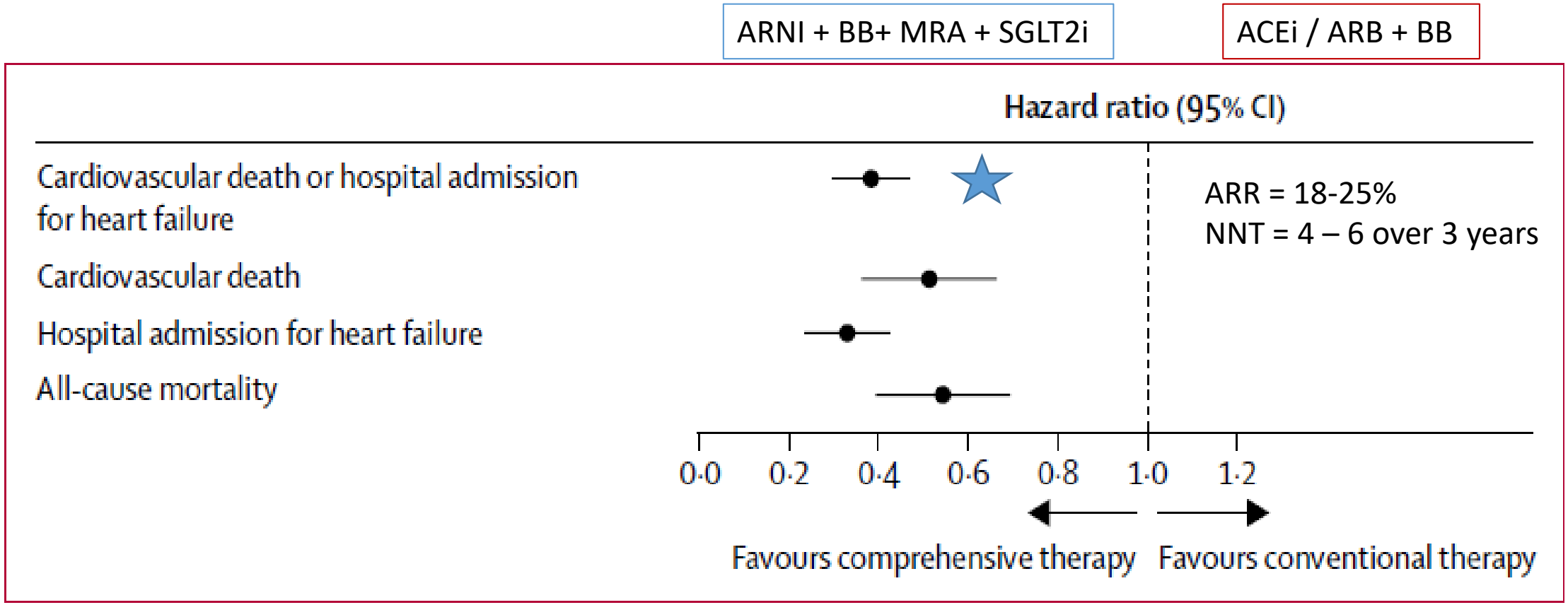


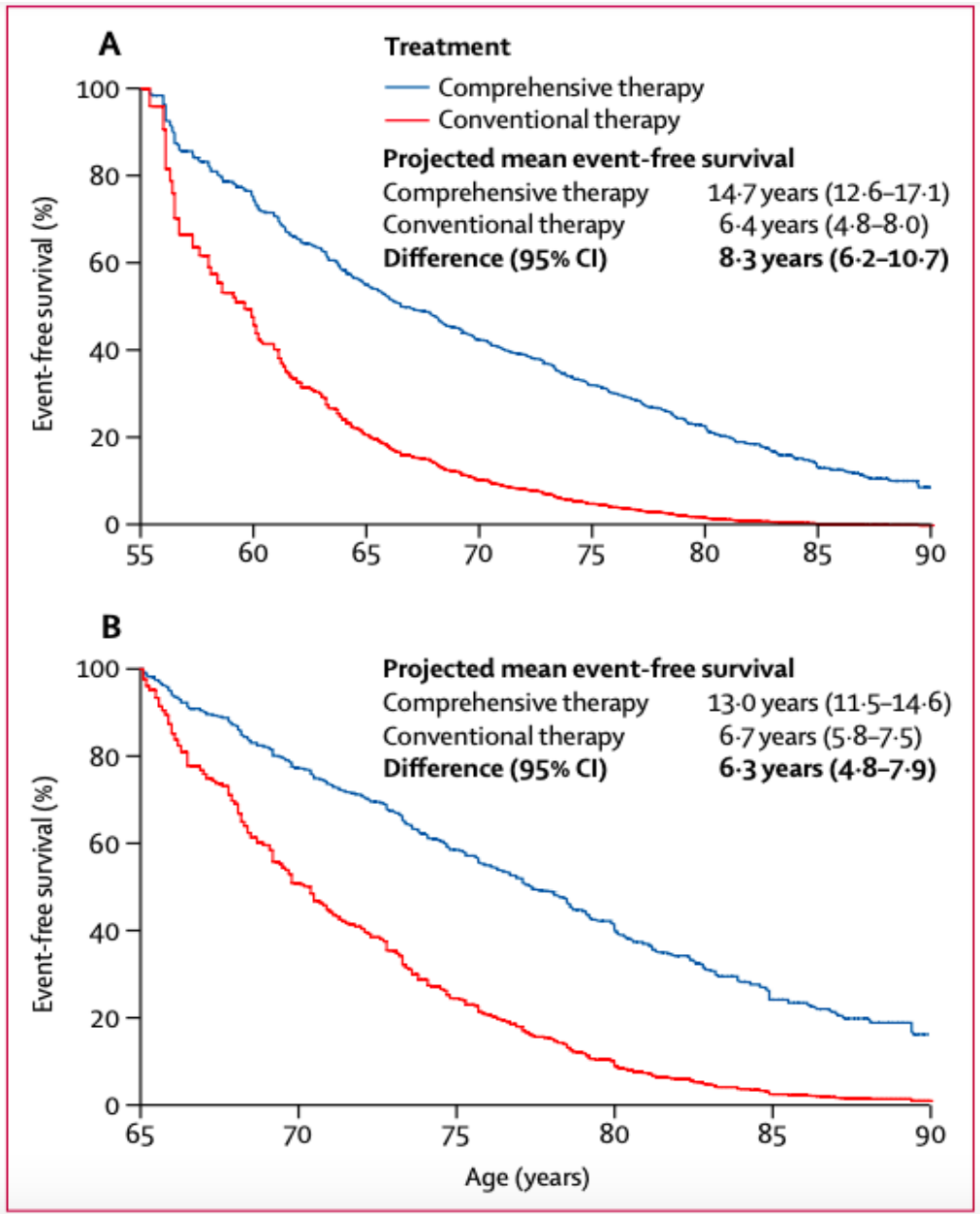
Figure 1: Estimation of relative treatment effects of comprehensive disease-modifying pharmacological therapy on key cardiovascular events

Vaduganathan M, et al. Lancet 2020; 396:121-128

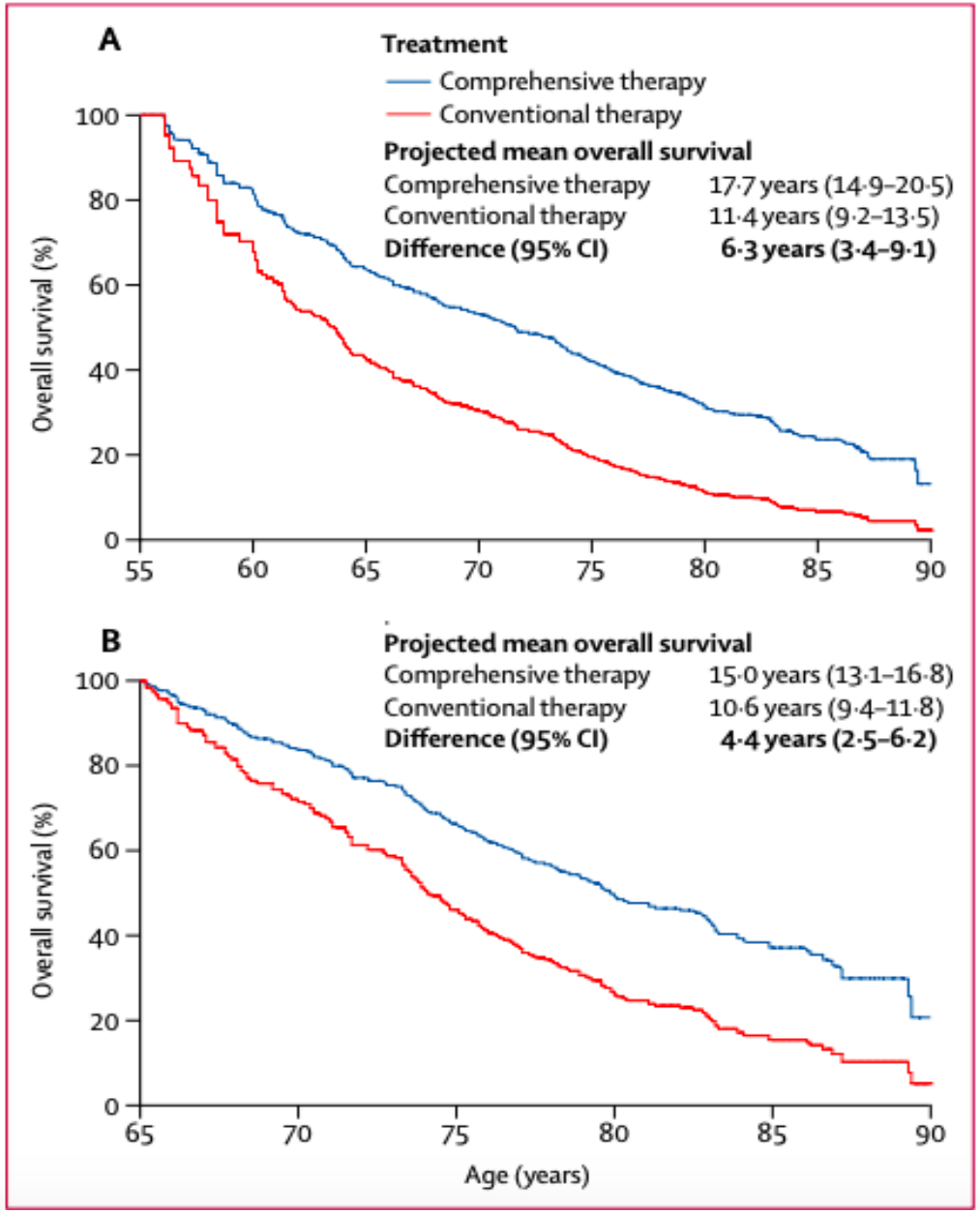
Comprehensive
- ARNI
- BB
- MRA
- SGLT2i

Conventional
- ACEi/ARB
- BB

Mean Event free survival



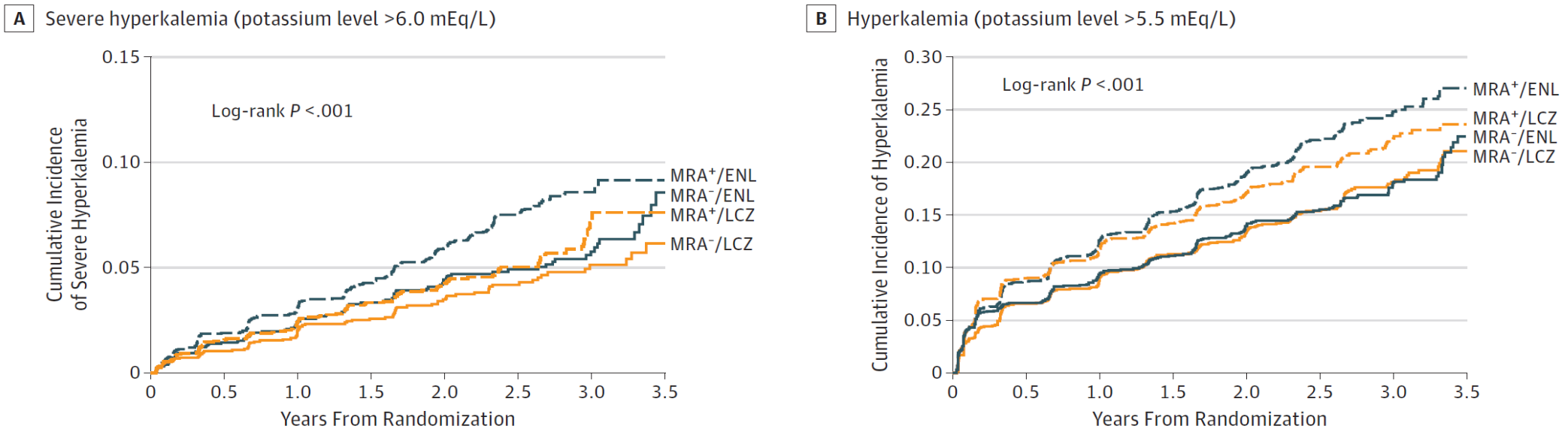
Mean Overall Survival



Vaduganathan M, et al. Lancet 2020; 396:121-128

Stepped Approach Pitfall:
Proper sequencing may improve safety / tolerability

Figure 3. Time to Development of Severe Hyperkalemia (A) and Hyperkalemia (B) According to Mineralocorticoid Receptor Antagonist (MRA) Use at Baseline and Treatment Assignment

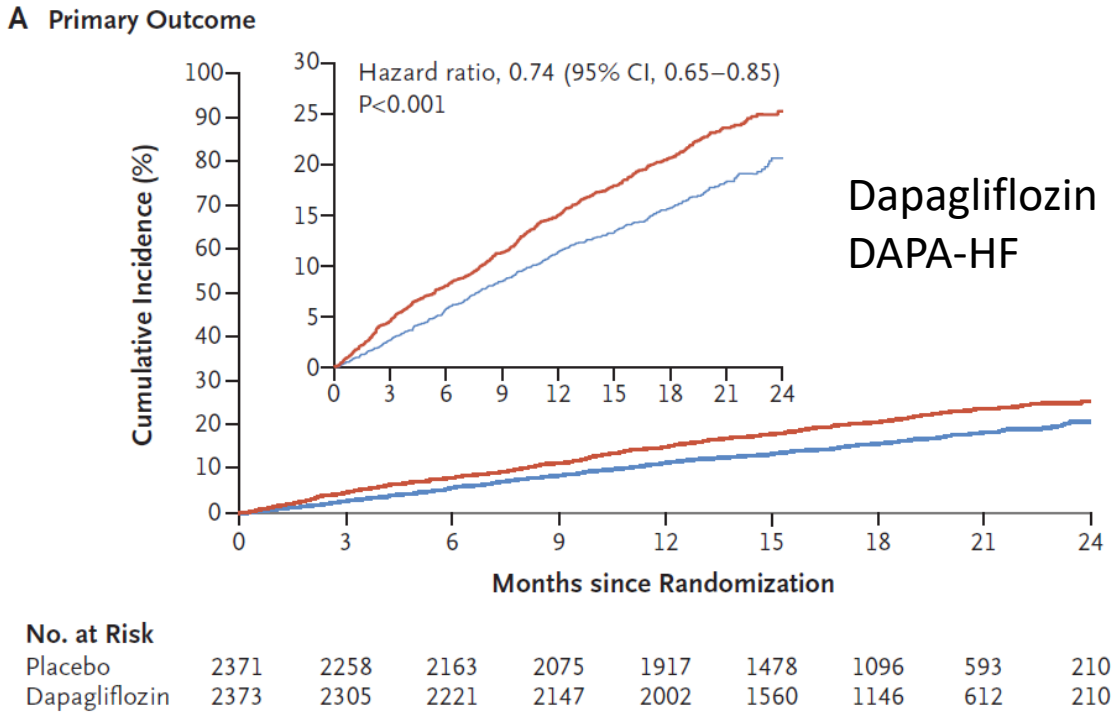


ENL indicates enalapril; and LCZ, sacubitril/valsartan.

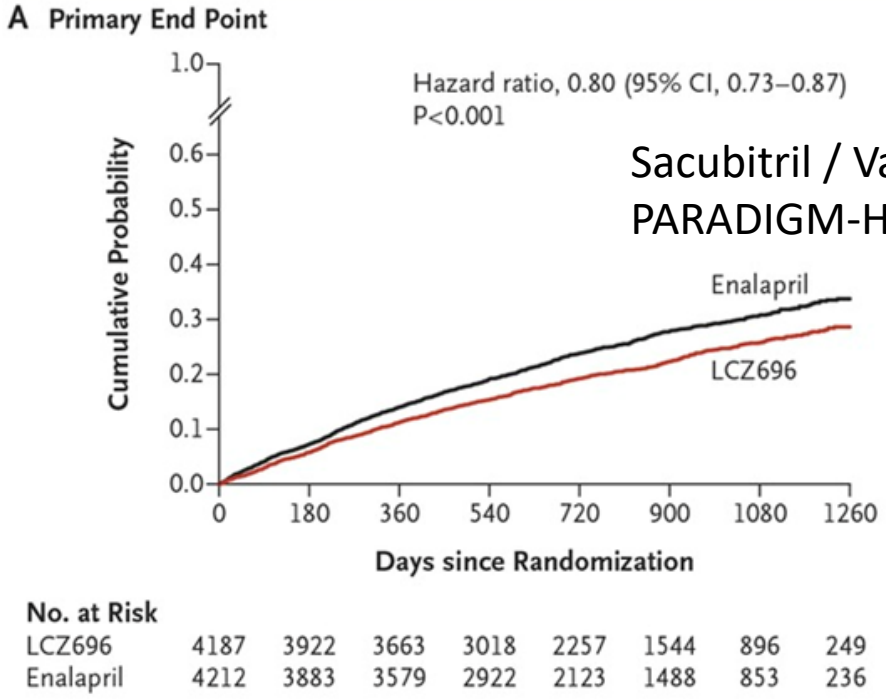
Desai AS, et al. JAMA Cardiol 2017;2:79-85

Stepped Approach Pitfalls: Delayed time to initiation of effective classes

- CCS: 6 mos
- Trials: benefits as early as 1-3 mos



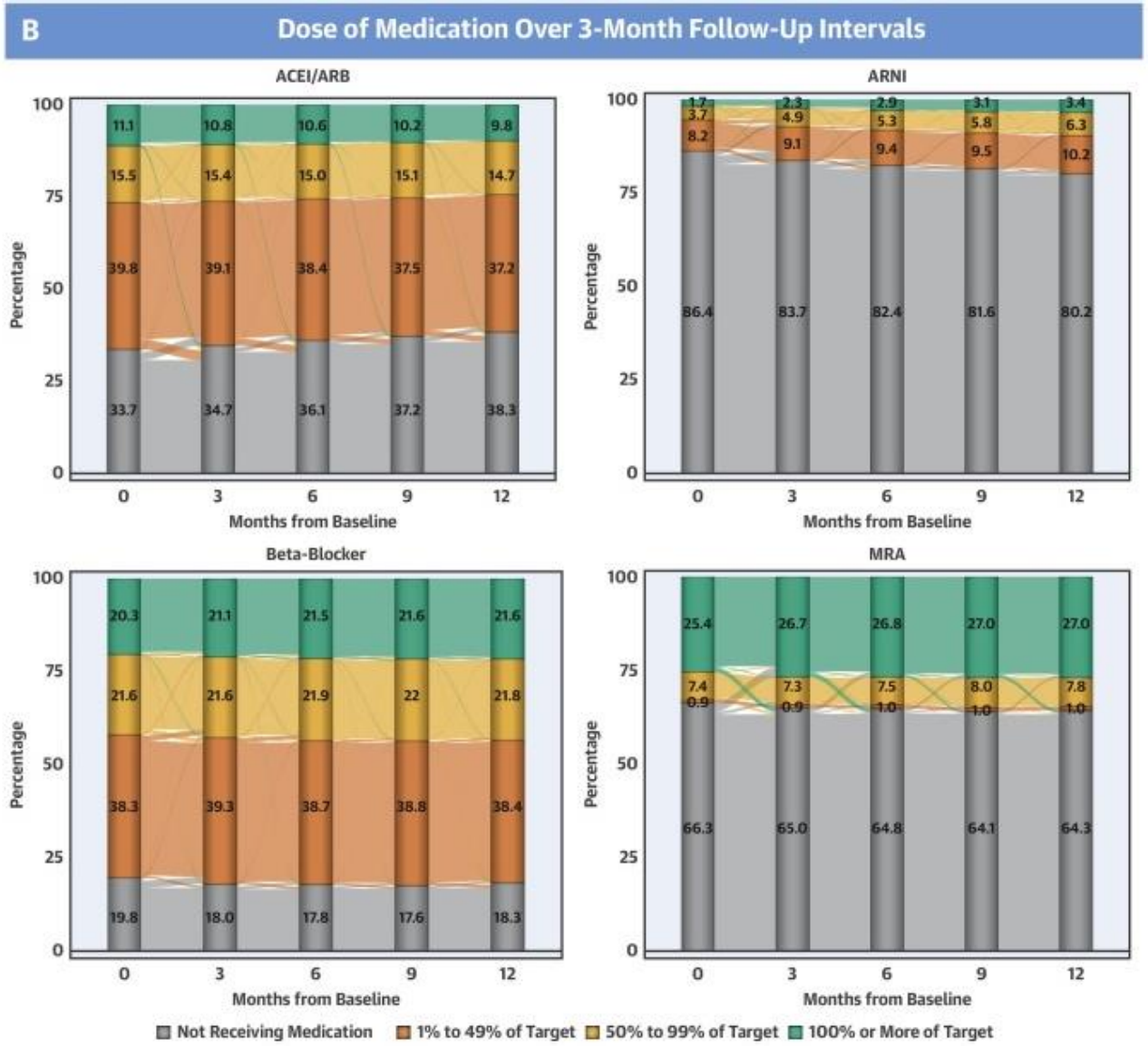
Dapagliflozin
DAPA-HF



Sacubitril / Valsartan
PARADIGM-HF

Stepped Approach Pitfalls: Human Resources

- Time and energy is required fo up-titration
  - Sub-optimal utilization
  - Sub-optimal doses



Greene, S.J. et al. J Am Coll Cardiol. 2019;73(19):2365-83.

Principles and Pathophysiologic Targets of HFrEF Pharmacotherapy

5 PATHWAYS

Modulation of five pathways shown to improve outcomes in the general HFrEF population

Angiotensin 2

Norepinephrine

Aldosterone

Neprilysin

SGLT

4 DRUGS

ARNI

May start with ACEi/ARB or ARNI in de novo. May use ACEi/ARB if cost or availability concerns.

Beta-blockers

Carvedilol, bisoprolol, metoprolol succinate

MRAs

SGLT2i

Dapagliflozin, Empagliflozin

3 OTHERS

Three additional pathways shown to improve outcomes in specific populations:

Ivabradine

NSR HR≥70 bpm

Hydralazine/nitrate

Self identified blacks

Vericiguat

Worsening HF

Omecamtiv Mecarbil

Tolerability, availability, costs, patient preference, and other consideration may impact choices, doses, and sequences of therapies – but pharmaco-pathophysiologic rationale suggests that **all attempts should be made to modulate all five pathways**.

Lam C, Butler J. Circulation 2020; 142(12):1129-31

New Approach = flexibility = individualization

The “Cluster Approach”

- Grouping classes:
  - Foundational
    - rapid improvement in CV morbidity and mortality
    - applicable to most patients
    - synergistic/additive effects irrespective of background therapy
  - Personalized
    - select population
    - lack of improvement in mortality
- Application:
  - Prioritize foundational therapies prior to optimization
  - Cluster medications (maximize safety, rapid initiation)
  - In-hospital initiation
  - Use medication titration protocols with multidisciplinary teams (pharmacists, NP) +/- remotely assisted titration

Miller RJ, Howlett JG, Fine NM. Canadian Journal of Cardiology (2021), doi: https:// doi.org/10.1016/j.cjca.2020.12.028.

Cluster Scheme

Initiation and Titration of Foundational Therapy for Heart Failure with LVEF < 40%

Red- Face to face visit with prescriber preferred | Blue- Either face to face or virtual visit with prescriber | Orange- Virtual visit with prescriber preferred

Cluster A: Diuretic & SGLTi	+	Cluster B: ARNi & MRA	+	Cluster C: Beta Blocker & SNI*

Encounter 1 (Usually face-to-face, up to 3 simultaneous medication initiations)

Start Preferred Cluster A Medication	Start Preferred Cluster B Medication	Start Preferred Cluster Medication*

1- 2 Weeks

Encounter 2 (whenever feasible, up to 3 simultaneous medication initiations)

Titrate Cluster A Medication	Start Second Cluster B Medication	Titrate Preferred Cluster C Medication*

1- 2 Weeks

Encounter 3 & ongoing (whenever feasible, up to 3 simultaneous medication titrations)

Diuretic titration as needed	Alternate Cluster B Medication Titration	Titrate Chosen C Medication Titration*

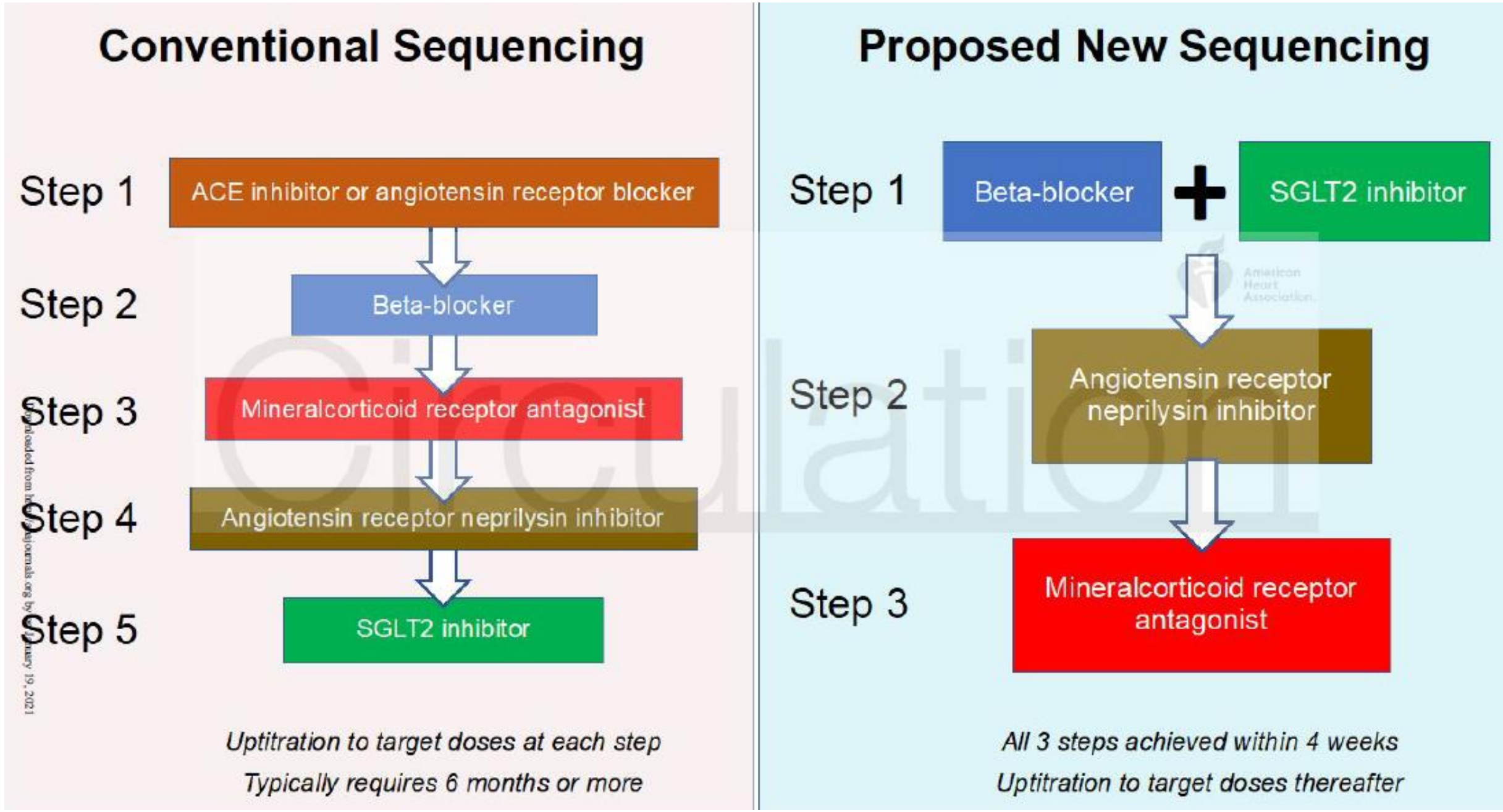
1- 2 Weeks

At Goal Foundational Therapy- Continue to actively manage as necessary

Addition of Personalized Therapies as dictated by clinical presentation and setting (see Table 2)

Recommended Total Time for Titration ≤ 12 weeks (3 months)

Miller RJ, Howlett JG, Fine NM. Canadian Journal of Cardiology (2021), doi: https:// doi.org/10.1016/j.cjca.2020.12.028.



McMurrray JJV et al. 10/1161/CIRCULATIONAHA.120.052926

Key Points

- HFrEF management is rapidly evolving
- New agents and their place in therapy require a new approach to increase application and save lives
- A multi-pathway approach should be prioritized over dose optimization
- Sequencing and optimization is flexible
- Focused early and efficient initiation will be key
- Barriers
  - Expertise / competency
  - Drug don’t work in those that don’t take them, especially with complex regimens
  - Universal access / coverage is necessary
  - Cost-effectiveness