Updates in Heart Failure Pharmacology and Overview of MHI Chronic Heart Failure Assessment and Management Program (CHAMP)

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Disclosures

- None

Objectives

- Explain the implications of a heart failure (HF) diagnosis
- Describe the rationale for guideline directed medical therapy (GDMT) in HFrEF and the four pillars of HFrEF medical therapy
- Understand AHMHI program for HF management: CHAMP

Heart Failure in the United States

6.7 MILLION ADULTS
in the U.S. have heart failure

Expected to increase to 8.5 million by 2030

Lifetime risk of HF has increased to 24%. 1 in 4 persons will develop HF in their lifetime

After cancer,
HF is the leading cause of death

Higher incidence and prevalence in Black individuals

Mortality rates have been increasing since 2012

$70 BILLION total projected heart failure medical costs by 2030.

50% of the costs
are attributed to hospitalization

Bozkurt, B, *et al. J Card Fail* 2023

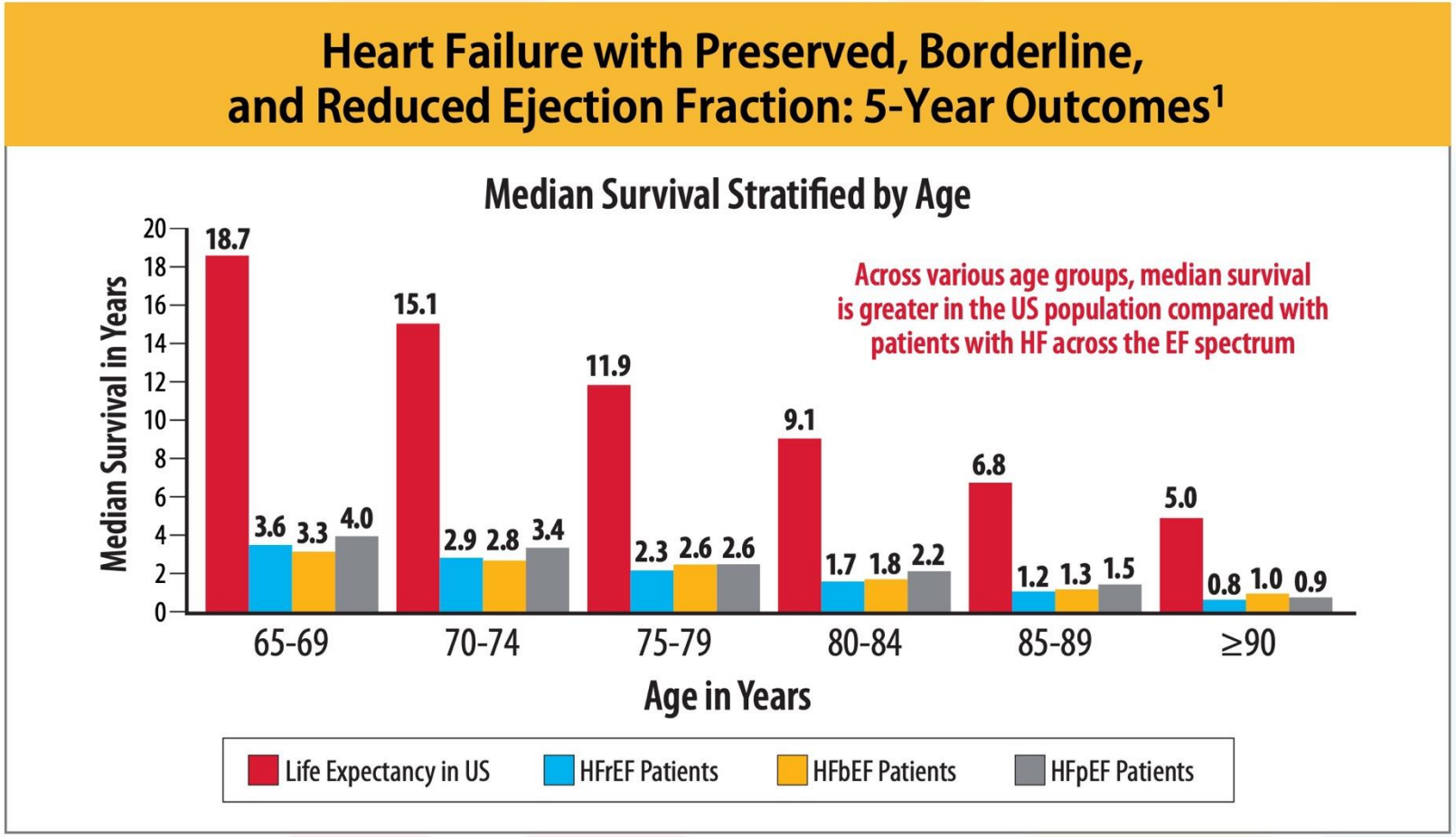
Classifications of Heart Failure

Type of HF According to LVEF	Criteria
HFrEF (HF with reduced EF)	LVEF ≤40%
HFimpEF (HF with improved EF)	Previous LVEF ≤40% and a follow-up measurement of LVEF >40%
HFmrEF (HF with mildly reduced EF)	LVEF 41%–49% Evidence of spontaneous or provokable increased LV filling pressures (eg, elevated natriuretic peptide, noninvasive and invasive hemodynamic measurement)
HFpEF (HF with preserved EF)	LVEF ≥50% Evidence of spontaneous or provokable increased LV filling pressures (eg, elevated natriuretic peptide, noninvasive and invasive hemodynamic measurement)

2022 ACC/AHA/HFSA Guidelines

HFSTATS℠
EPIDEMIOLOGY AND OUTCOMES

Heart Failure with Preserved, Borderline, and Reduced Ejection Fraction: 5-Year Outcomes[1]



EF = ejection fraction; HF = heart failure; HfbEF = heart failure with borderline ejection fraction; HfpEF = heart failure with preserved ejection fraction; HFrEF = heart failure with reduced ejection fraction; US = United States

1. Shah KS, Xu H, Matsouaka RA, Bhatt DL, Heidenreich PA, Hernandez AF, et al. Heart Failure with Preserved, Borderline, and Reduced Ejection Fraction: 5-Year Outcomes. *J Am Coll Cardiol*. 2017 Nov 14;70(20):2476–86.

JCF Bozkurt et al DOI:10.1016/j.cardfail.2023.07.006

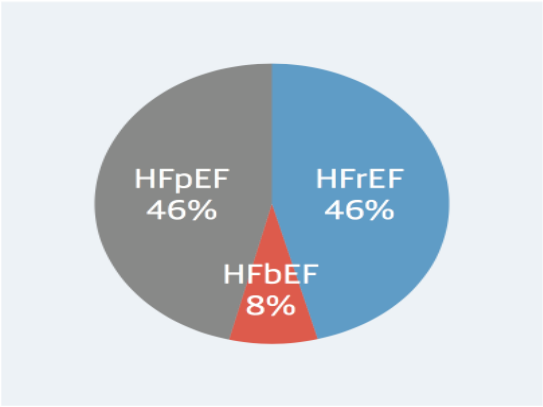
hfsa.org/hf-stats

HFSA
HEART FAILURE SOCIETY OF AMERICA

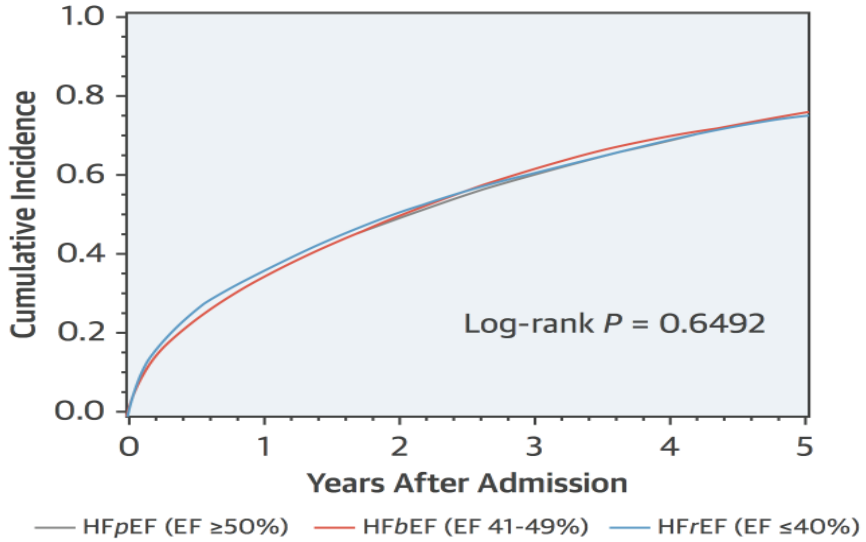
Survival after HF Hospitalization

CENTRAL ILLUSTRATION **5-Year Outcomes in Patients Hospitalized With HF With Preserved, Borderline, and Reduced EF**

Heart Failure



5-Year Mortality

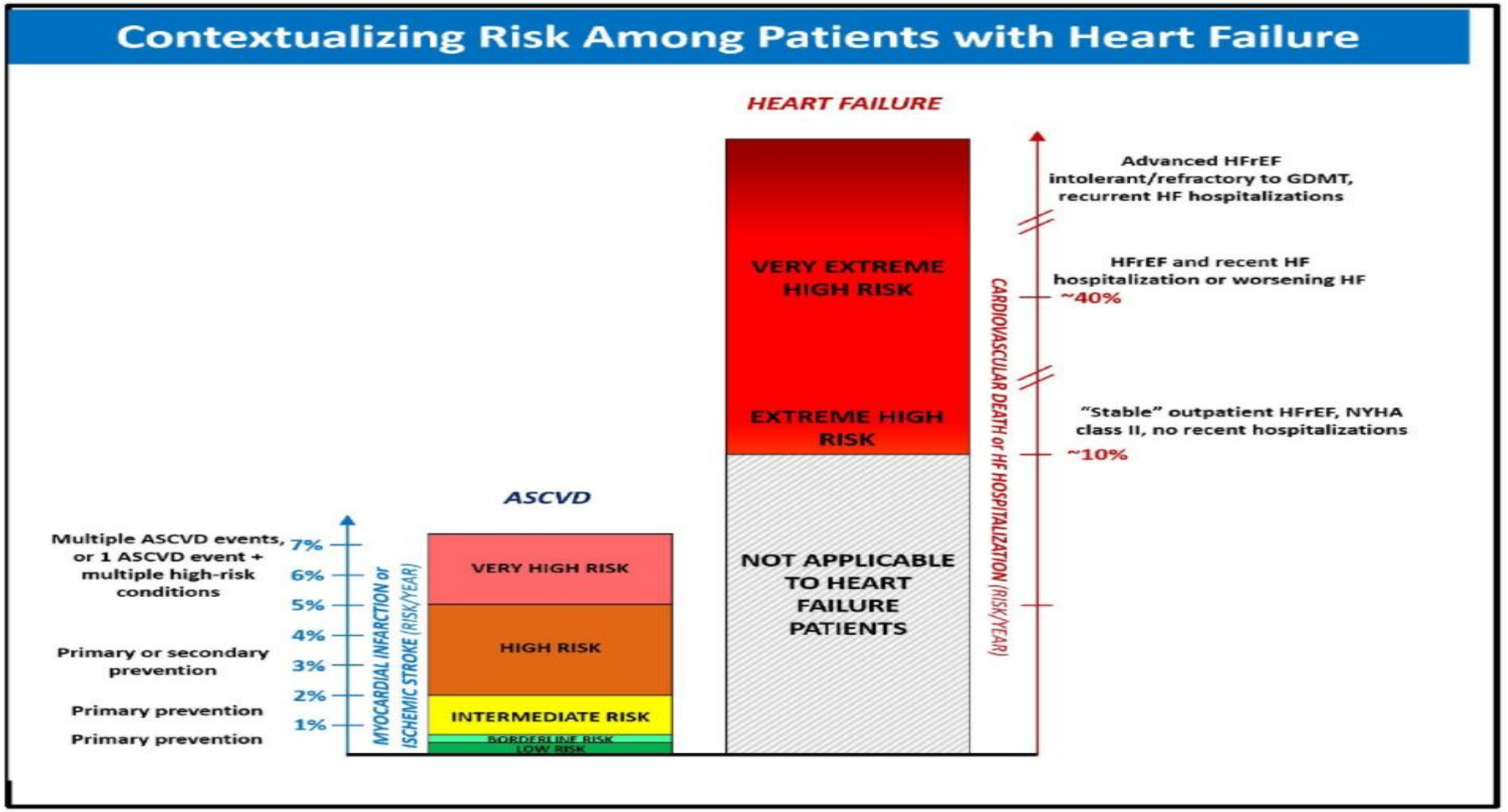


Outcomes – 5-Year Event Rates (%)					
	Mortality	Readmission	CV Readmission	HF Readmission	Mortality/Readmission
HFrEF	75.3	82.2	63.9	48.5	96.4
HFbEF	75.7	85.7	63.3	45.2	97.2
HFpEF	75.7	84.0	58.9	40.5	97.3

Shah, K.S. et al. J Am Coll Cardiol. 2017;70(20):2476–86.

- 40,000 patients from 254 hospitals
- Admitted for HF between 2005-2009
- Overall median survival 2.1 years

Contextualizing Risk Among Patients With Heart Failure

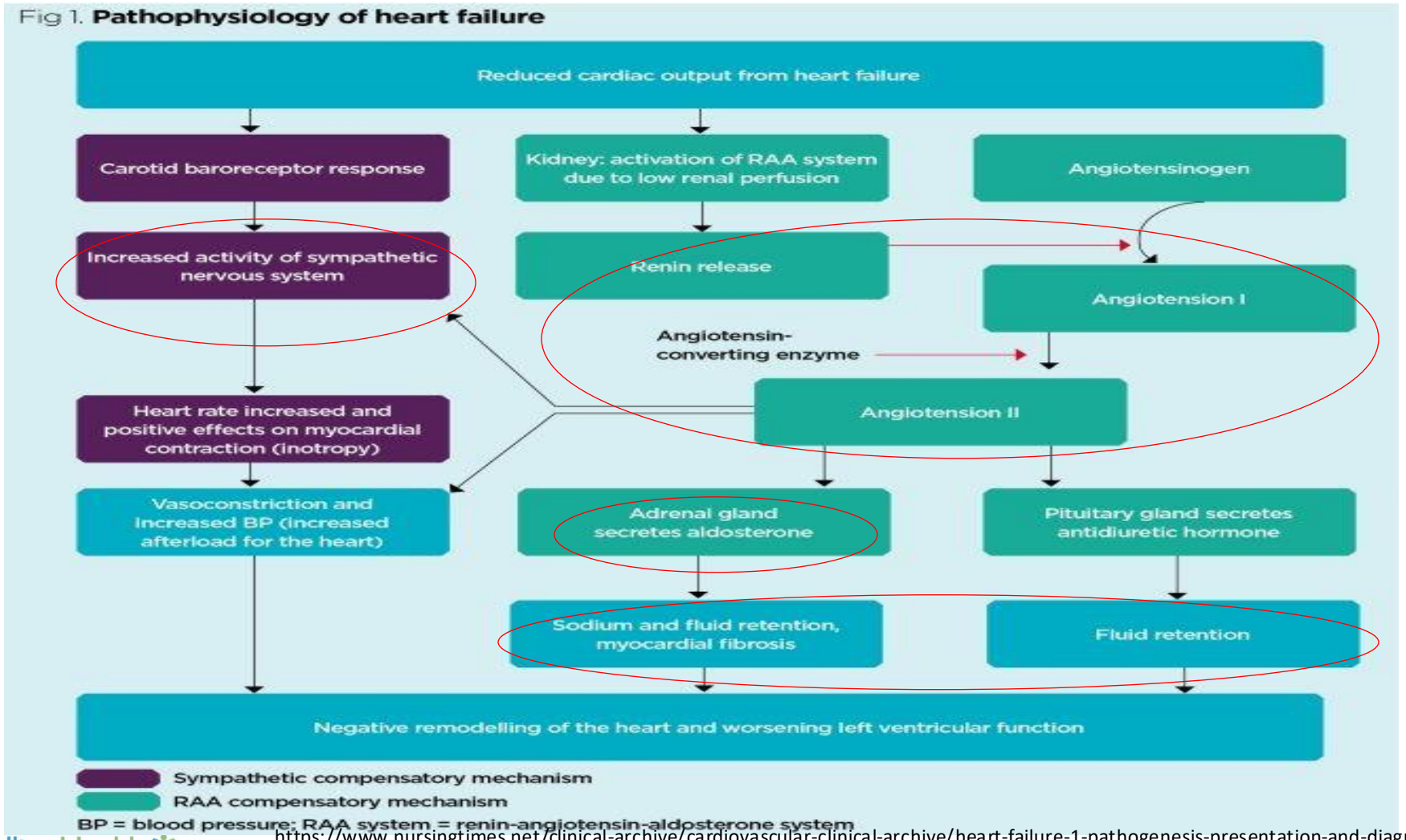


From Fonarow G based on https://ja.ma/3IRItEY

Goals of Guideline Directed Medical Therapy (GDMT) for HFrEF

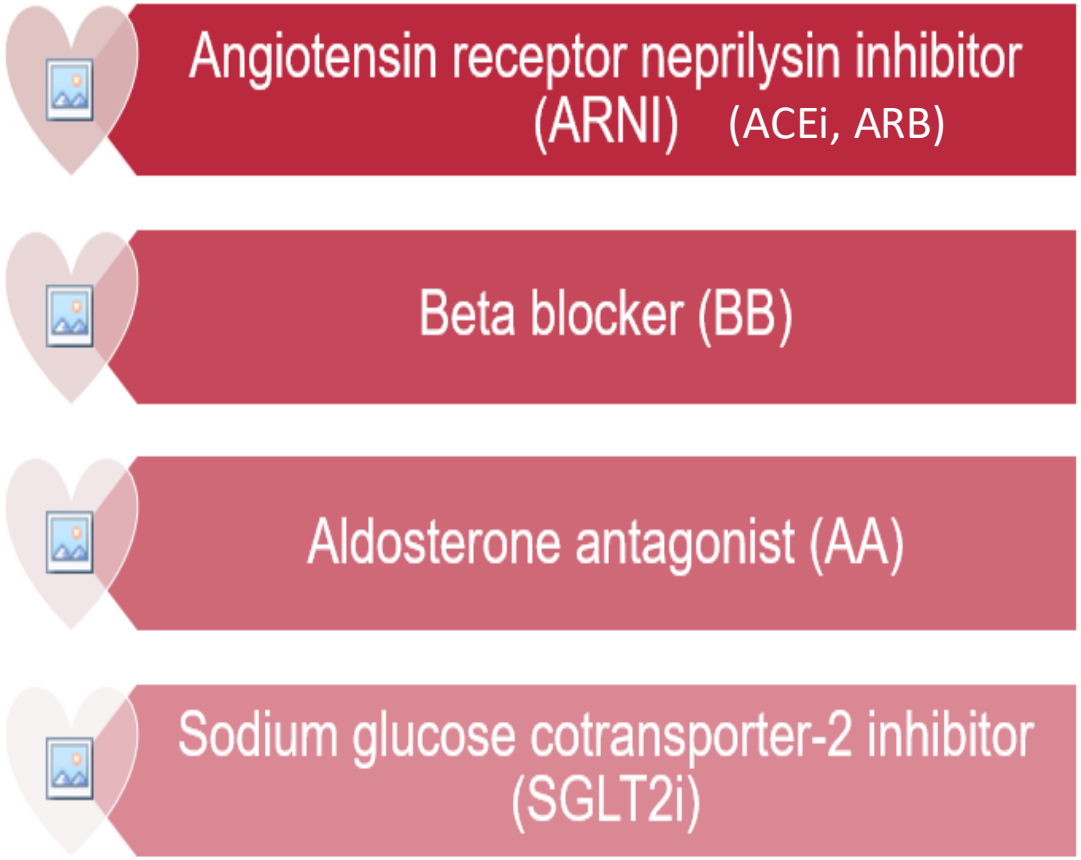
- Slow/reverse disease process/progression
- Improve symptoms
- Improve/maintain QOL
- Prevent hospital admissions
- Improve survival
- HF should be approached like a cancer diagnosis
  - The minute a malignancy is suspected, a seek and destroy mission is launched
  - Mainstay of therapy is GDMT – BUT adherence is as low as 20-30%

Neurohormonal Cascade in HFrEF



https://www.nursingtimes.net/clinical-archive/cardiovascular-clinical-archive/heart-failure-1-pathogenesis-presentation-and-diagnosis-21-08-2017/

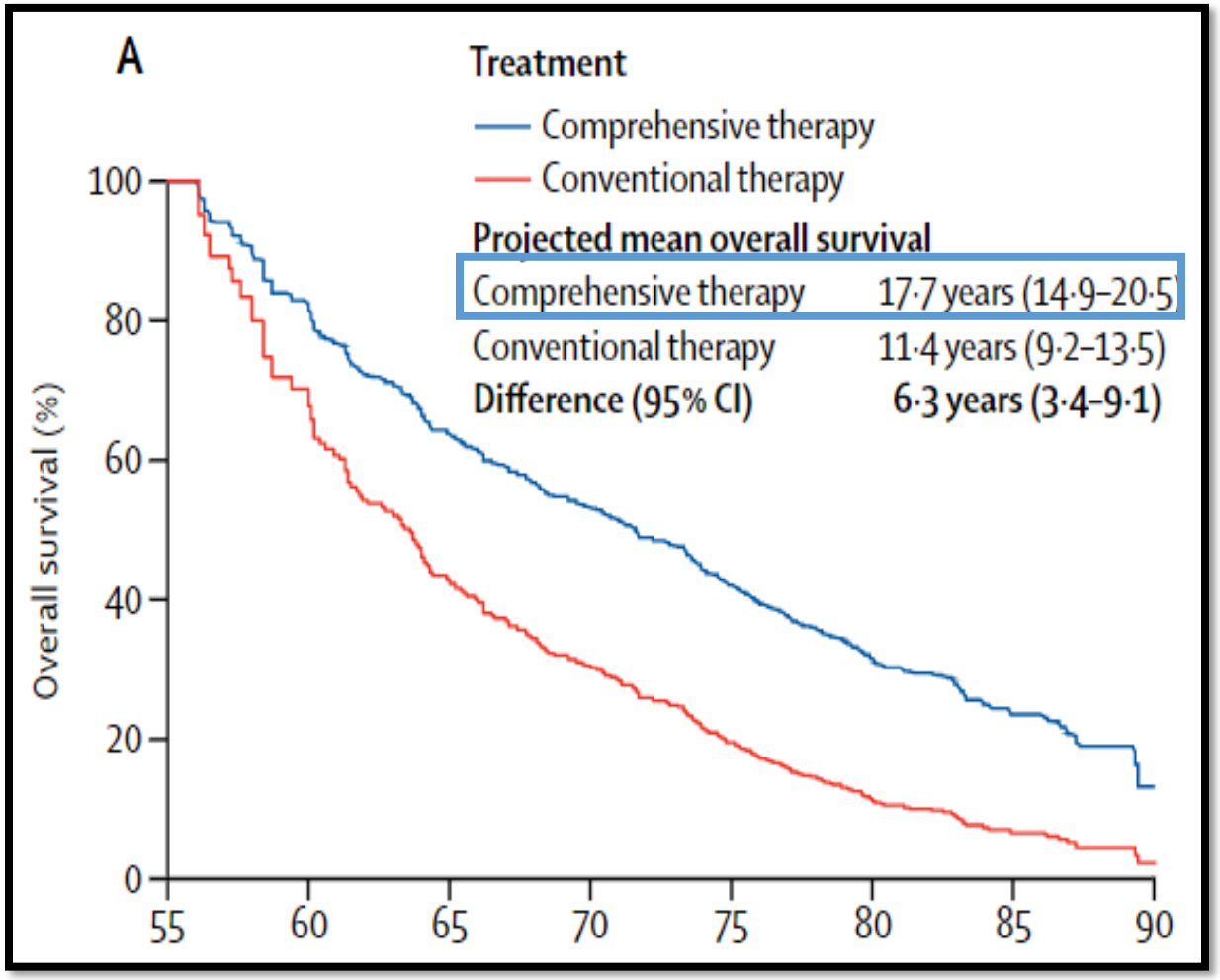
The Four Pillars of GDMT for HFrEF



- Cumulative reduction in all-cause mortality if ALL FOUR evidence-based medical therapies are used:
  - Relative risk reduction: 72.9%
  - Absolute risk reduction: 25.5%
  - Number needed to treat (NNT) = 3.9, over 24 months

Quadruple therapy saves lives

- **Comprehensive therapy = ARNI + BB + AA + SGLT2i**
- **Conventional therapy = ACEI + BB**



Vaduganathan et al. Lancet 2020; 396:121-28.

ACEI/ARB/ARNI

Medication (initial vs goal dose)	
ACEI	
I: lisinopril 2.5 – 5 mg daily	G: lisinopril 40 mg daily
I: captopril 6.25 mg TID	G: captopril 50 mg TID
I: enalapril 2.5 mg BID	G: enalapril 10 mg BID
I: ramipril 1.25 – 2.5 mg BID	G: ramipril 10 mg BID
ARB	
I: losartan 12.5 – 25 mg daily or BID	G: losartan 150 mg daily or spilt dose BID
I: valsartan 40 mg BID	G: valsartan 160 mg BID
I: candesartan 4 – 8 mg daily	G: candesartan 32 mg daily
ARNI	
I: sacubitril-valsartan 24-26 or 49-51 mg BID	G: sacubitril-valsartan 97-103 mg BID

Objective data

❖ **Factors limiting up-titration:**

✓ MAP < 70 mmHg
✓ K > 5 mEq/L
✓ SCr > 2 mg/dL
✓ eGFR < 30 mL/min

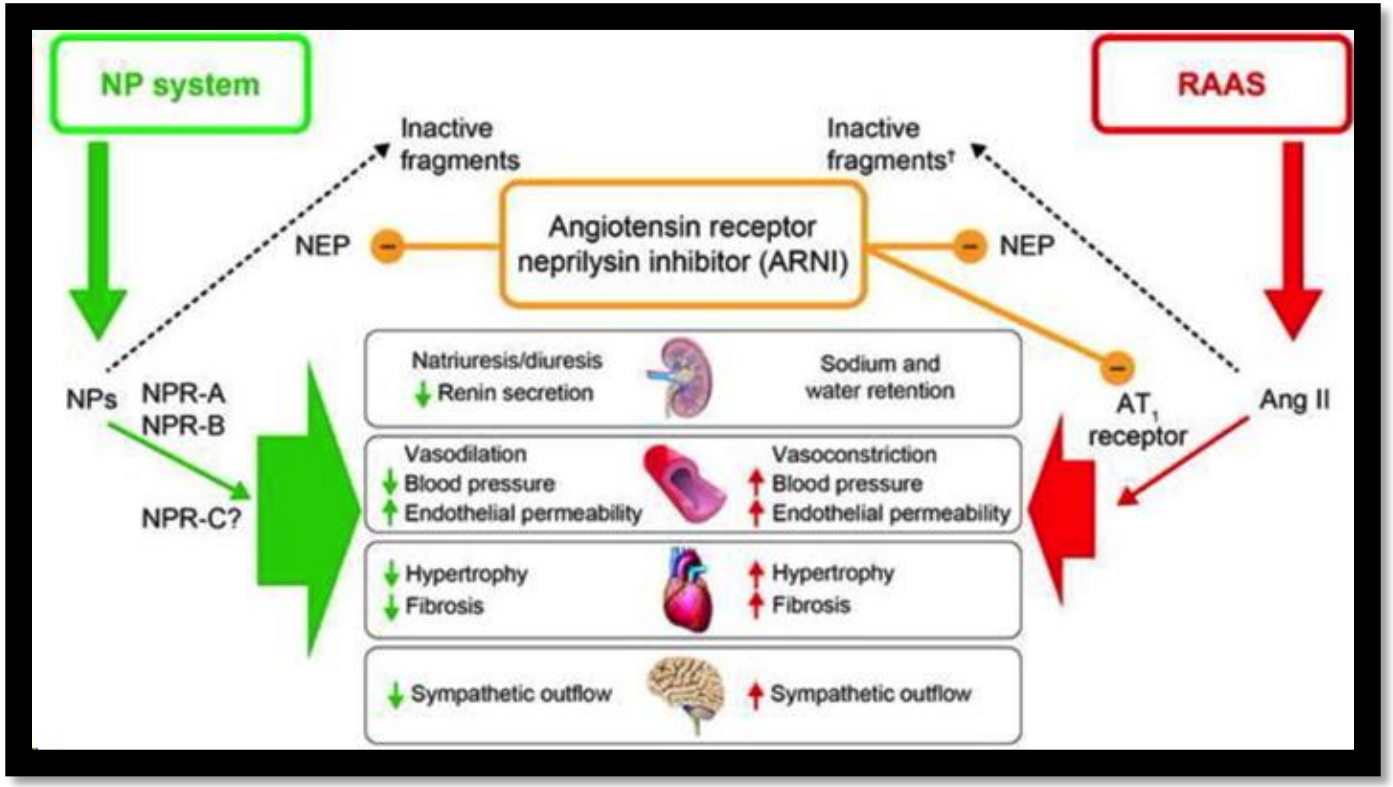
❖ **Contraindications:**

✓ Pregnancy
✓ Bilateral renal artery stenosis
✓ Angioedema
✓ Active prescription for aliskiren

2022 AHA/ACC/HFSA Heart Failure Guidelines; Circulation

ARNI Background

- **Mechanism:**
  - Sacubitril – neprilysin inhibitor
  - Valsartan – angiotensin receptor blocker (ARB)
- **Drug class:**
  - Angiotensin-receptor neprilysin inhibitor (ARNI)
- **FDA approved indication:**
  - Chronic heart failure, class II-IV
  - HFrEF (EF ≤40%)



Entresto ® [prescribing information]. Novartis. October 2021.

RAAS Inhibition Dosing

Equivalent Doses		
ACEIs	**ARNI**	**ARBs**
Enalapril 10 mg daily	Sacubitril/valsartan 49/51 mg BID	Candesartan 16 mg daily
Captopril 25 mg TID		Losartan 50 mg daily
Lisinopril 10 mg daily		Valsartan 80 mg BID
Ramipril 5 mg daily		

Valsartan Equivalents		
Sacubitril/valsartan 24/26 mg BID	Sacubitril-valsartan 49/51 mg BID	Sacubitril-valsartan 97/103 mg BID
Valsartan 40 mg BID	Valsartan 80 mg BID	Valsartan 160 mg BID

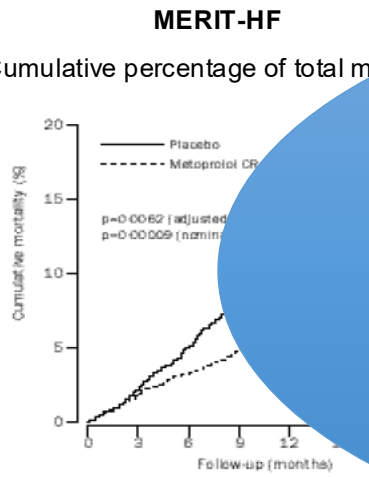
Eur Heart J. 2013;15:1062-1073.
Entresto ® [prescribing information]. Novartis. October 2021.

Beta-blockers

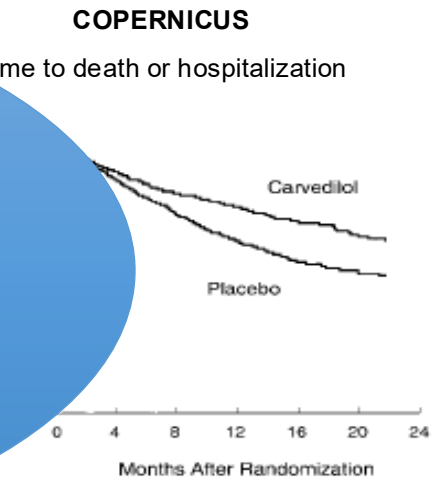
Guideline directed BB:

- Metoprolol succinate
- Carvedilol
- Bisoprolol

All stable HF patients with LVEF ≤40% (use clinically proven beta-blocker) (Class I, Level A)



Up to 44% reduction in mortality



MERIT-HF Study Group. *Lancet* 1999;353:2001-7. CIB[illegible];353:9-13.

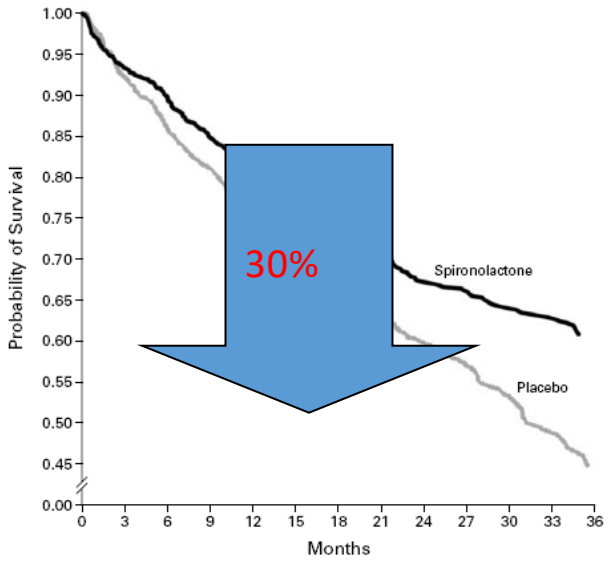
Packer M et al. *Circulation* 2002;106:2194-9.

Mineralocorticoid receptor Antagonists (MRA)

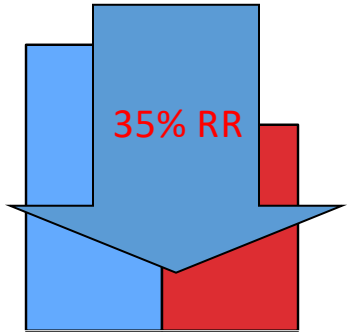
Patients with LVEF ≤35% and moderate to severe symptoms despite optimized other therapies (Class I, Level A)

MRAs
- Spironolactone
- Eplerenone
- Finerenone

RALES - Probability of survival



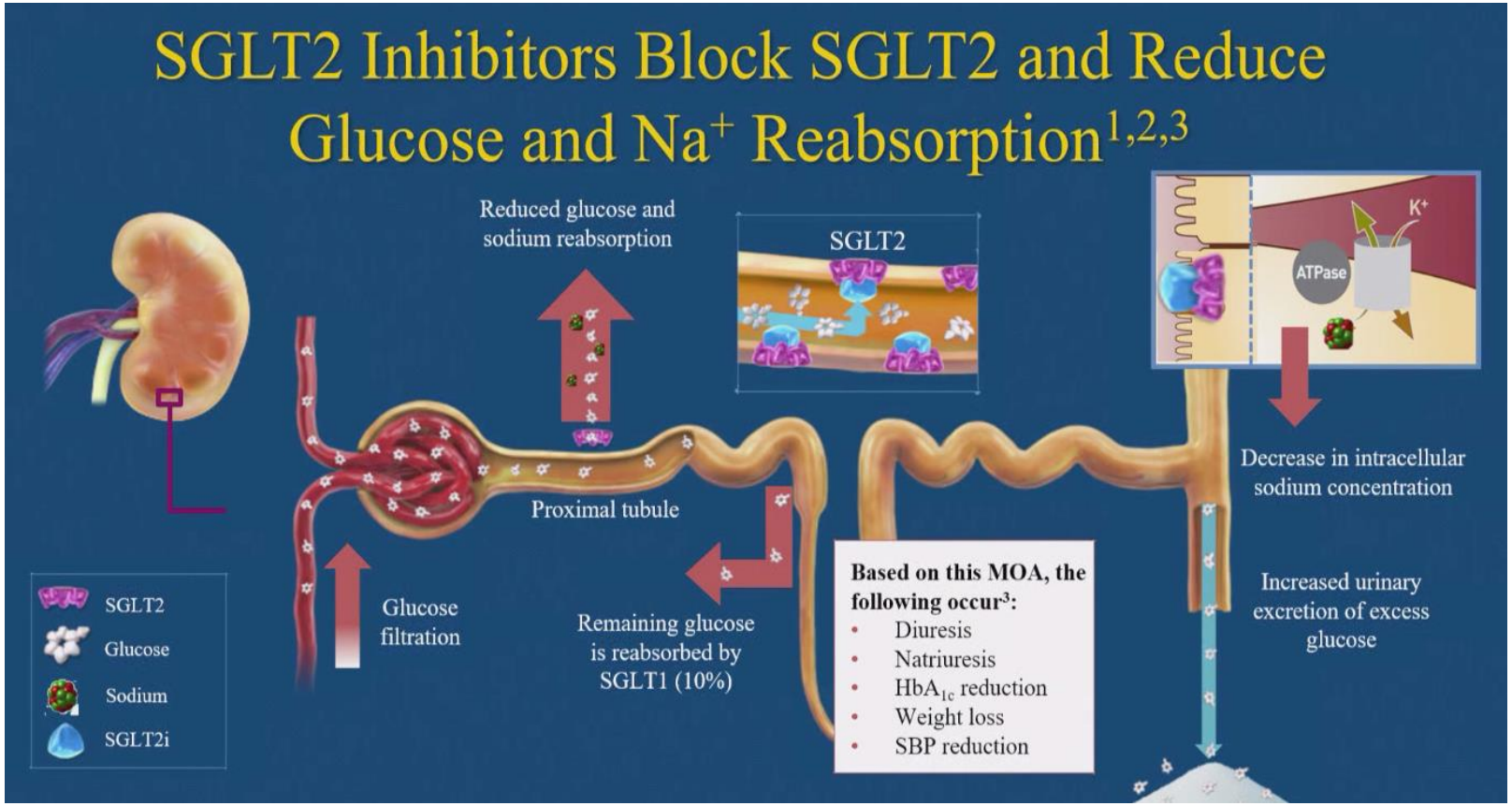
RALES - Hospitalizations for worsening HF



Pitt B et al. *N Engl J Med* 1999;341:709-17.

SGLT2i Background

- **Mechanism:**
  - Inhibits SGLT2 protein, which reduces reabsorption of filtered glucose and promotes urinary glucose excretion
- **Drugs in class:**
  - Dapagliflozin (Farxiga)
  - Empagliflozin (Jardiance)
  - Sotagliflozin (Inpefa)
  - Canagliflozin (Invokana)
- **FDA approved indication:**
  - Type II Diabetes
  - Chronic kidney disease
  - Heart failure with or without diabetes
  - CV risk reduction

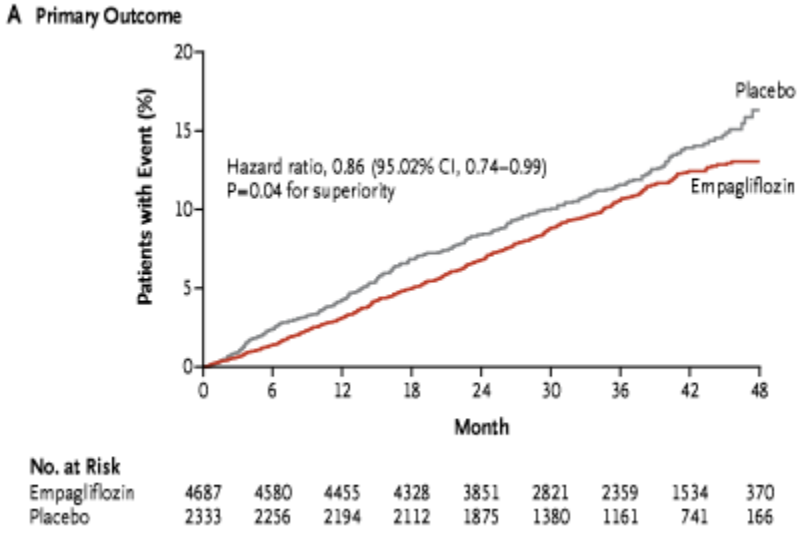


Farxiga ® [prescribing information]. AstraZeneca. October 2021.
Jardiance ® [prescribing information]. Boehringer-Ingelheim. October 2021.
2022 AHA/ACC/HFSA Guidelines for the Management of Heart Failure

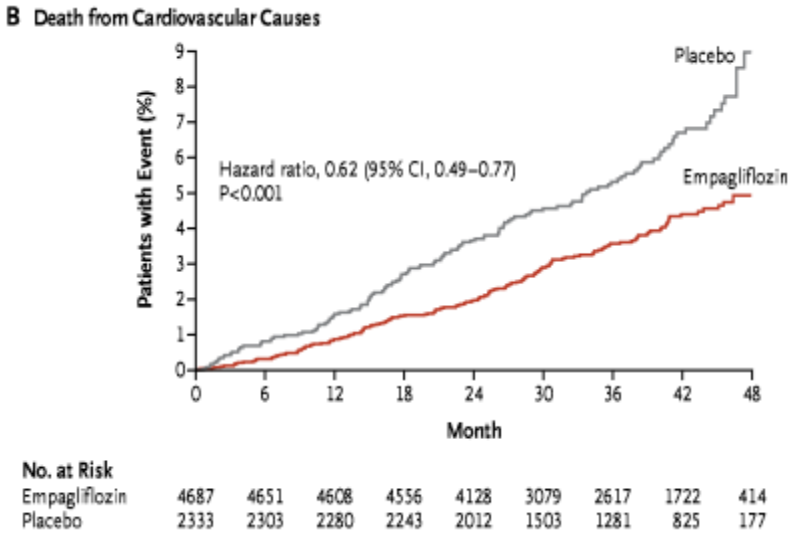
SGLT2i Mechanisms of Action

Mechanism	Effect in Heart Failure
Natriuresis & osmotic diuresis	↓ Congestion and preload
BP reduction	↓ Afterload
Improved myocardial energetics	↑ Cardiac efficiency
Anti-inflammatory & anti-fibrotic effects	↓ LV remodeling and progression of CM
Renal: reduced pressure on the glomeruli; kidneys don't work as hard to reabsorb glucose	Preserves kidney function
Reduced sympathetic tone	Improved hemodynamics and less arrhythmia risk

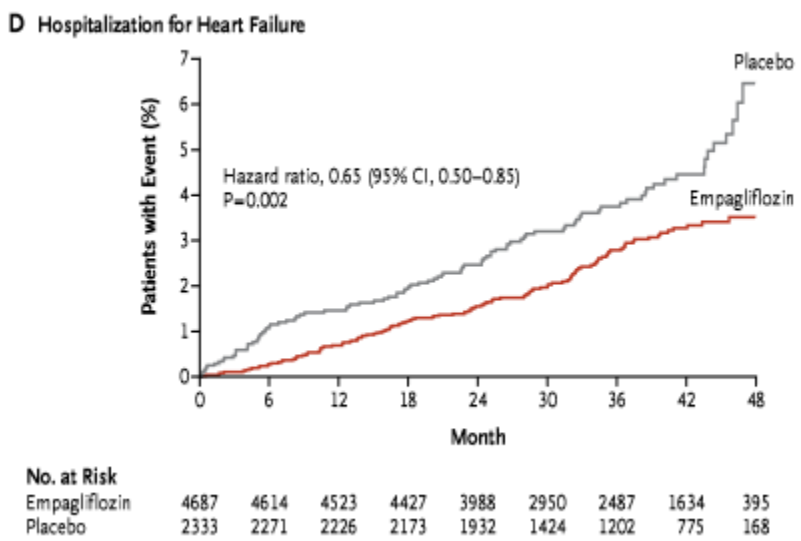
EMPA-REG OUTCOME 2015



HR 0.86 (0.74 – 0.99)



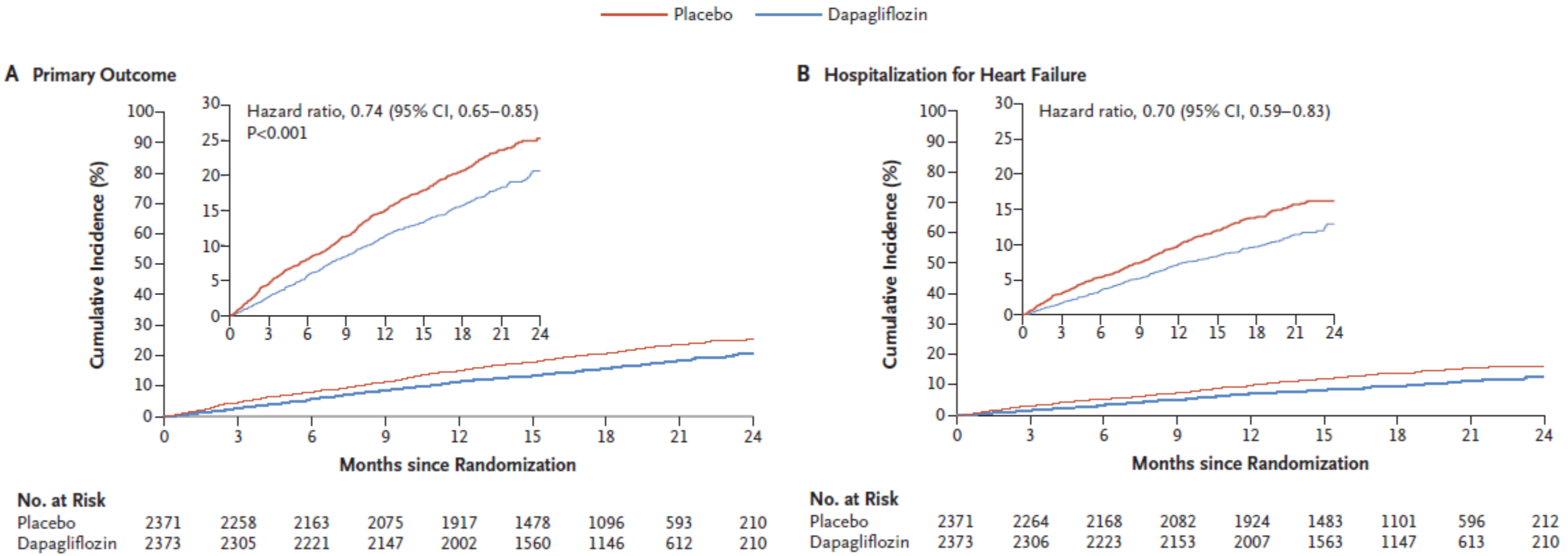
HR 0.62 (0.49 – 0.77)



HR 0.65 (0.50 – 0.85)

Zinman B et al. N Eng J Med. 2015.

DAPA-HF 2019



HR 0.74 (0.65 – 0.85)

HR 0.70 (0.59 - 0.83)

McMurray et al. N Eng J Med. 2019.

Additional HFrEF medications

- Loop and thiazide diuretics
- Digoxin
- Hydralazine and isosorbide dinitrate
- Arginine Vasopressin Antagonists: Tolvaptan, Conavaptan
- Ivabradine
- Soluble guanylate cyclase stimulator: Vericiguat

What about HFpEF?

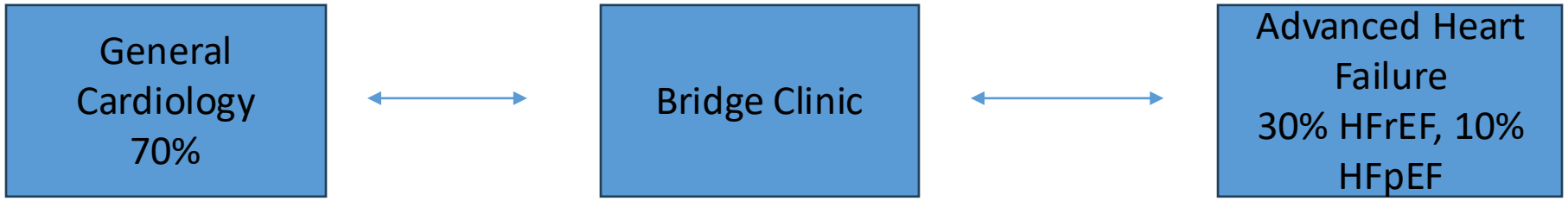
7.7.1. HF With Preserved Ejection Fraction

Recommendations for HF With Preserved Ejection Fraction* Referenced studies that support the recommendations are summarized in the Online Data Supplements.		
COR	**LOE**	**Recommendations**
1	C-LD	1. Patients with HFpEF and hypertension should have medication titrated to attain blood pressure targets in accordance with published clinical practice guidelines to prevent morbidity.[1–3]
2a	B-R	2. In patients with HFpEF, SGLT2i can be beneficial in decreasing HF hospitalizations and cardiovascular mortality.[4]
2a	C-EO	3. In patients with HFpEF, management of AF can be useful to improve symptoms.
2b	B-R	4. In selected patients with HFpEF, MRAs may be considered to decrease hospitalizations, particularly among patients with LVEF on the lower end of this spectrum.[5–7]
2b	B-R	5. In selected patients with HFpEF, the use of ARB may be considered to decrease hospitalizations, particularly among patients with LVEF on the lower end of this spectrum.[8,9]
2b	B-R	6. In selected patients with HFpEF, ARNi may be considered to decrease hospitalizations, particularly among patients with LVEF on the lower end of this spectrum.[10,11]
3: No-Benefit	B-R	7. In patients with HFpEF, routine use of nitrates or phosphodiesterase-5 inhibitors to increase activity or QOL is ineffective.[12,13]

- Control BP
- Manage volume
- Manage comorbidities
  - Atrial fibrillation
  - SDB
  - DM
  - Anemia, iron deficiency
- SGLT2i
- MRA
- No benefit
  - Long-acting nitrates
  - PDE-5 inhibitors: sildenafil, tadalafil
- Caution with Beta blockers

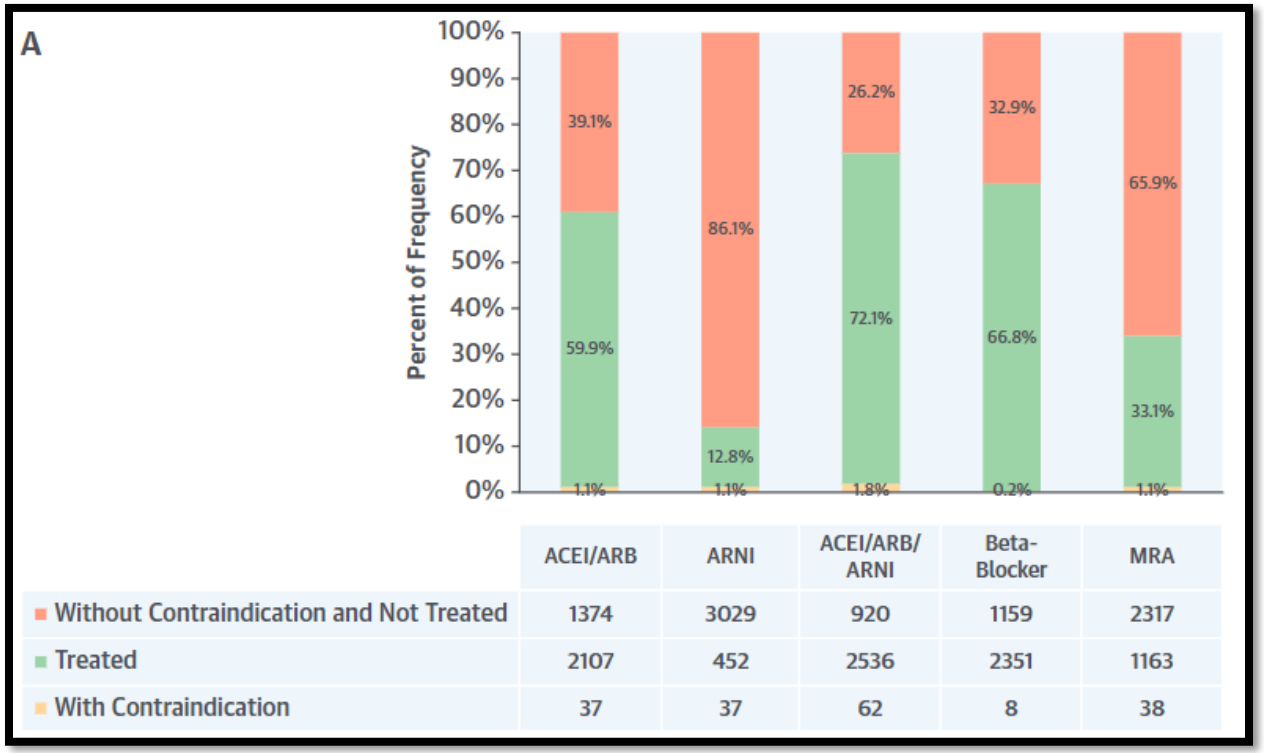
Gaps in Heart Failure Care at MHI

- Prior to 2020, MHI did not have a program for chronic HF disease management

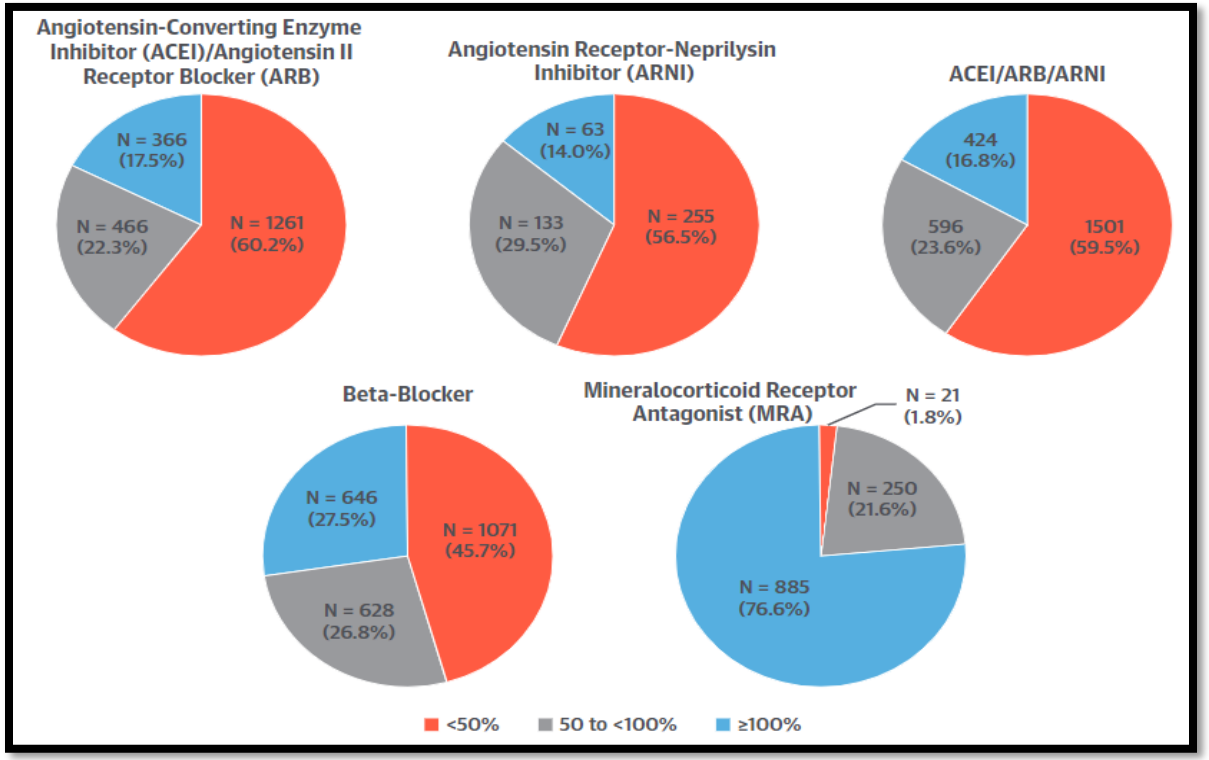


- MHI model was MD heavy, relatively infrequent visits
  - GDMT for HFrEF was not optimized
  - No effective mechanism for telephone support and management
  - No standard patient education

What really happens in clinical practice…



	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



GDMT is not implemented

MHI	MHI HF
• 83%	• 91%
• 73%	• 78%
• 34%	• 56%

GDMT is not titrated

CHAMP HF; Greene SJ et al. JACC 2018; 72(4):351-66.
Jefferies JL et al. JACC 2018;72:367-369.

MHI | Allina Health HEART INSTITUTE

What is CHAMP?

- Comprehensive heart failure management program for any MHI patient with heart failure
  - Short or longterm
- Patients will be followed by HF APP and HF nurse **in conjunction with** the patient's primary cardiologist
- Locations: Minneapolis, Edina, Chaska, Shakopee, West Health, Eden Prairie, Lakeville, Baxter, New Ulm, Sleepy Eye, Cambridge
- Patient sees primary cardiologist at least once per year and as recommended by the APP

Components of CHAMP

- APP directed outpatient care
- Access to CHAMP nurses
  - HF trained nurses to help with phone management/triage of symptoms, education, and support
- Pharmacist support as needed
- Patient continues to follow with primary general cardiologist

Goals of CHAMP

- Provide collaborative, guideline directed management of patients with HF throughout MHI
- Decrease heart failure related ED visits and hospital admissions
- Optimize GDMT for patients with HFrEF
- Early intervention for Heart Failure symptoms with HF nursing support
- Increased utilization of heart failure remote monitoring
- Refer patients for HF-specific research trials
- Refer patients for Advanced Heart Failure therapies when appropriate

MHI West CHAMP Clinic Volumes

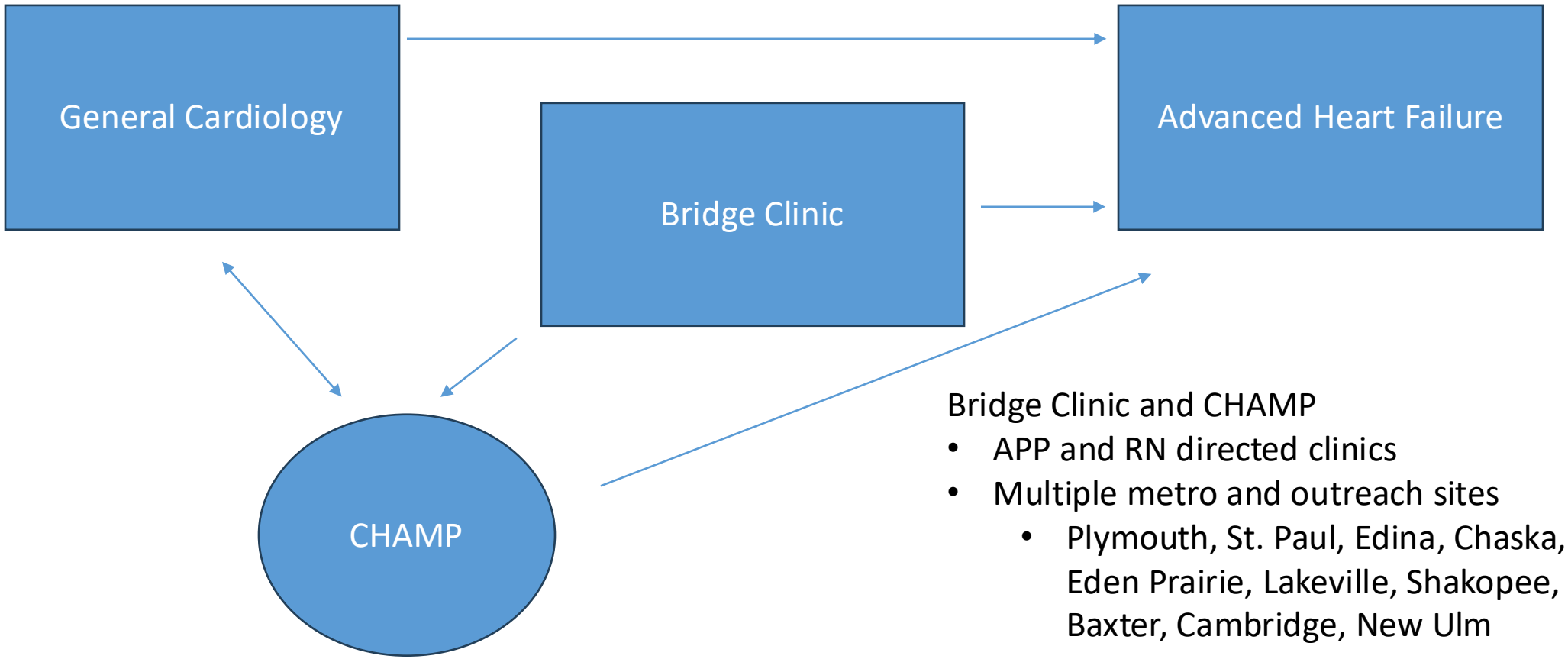
	2020	2021	2022	2023	2024	2025
# Attended (AHF)	65	228	303	305	368	382
# No Show (AHF)	5	14	37	25	36	29
# Attended (Gen)	0	0	7	137	82	94
# No Show (Gen)	0	0	0	20	13	5
Total Attended	**65**	**228**	**310**	**442**	**450**	**476**
Total No Show	**0**	**14**	**37**	**45**	**49**	**34**

GDMT Optimization

Heart Failure	MHI Group AVG - Allina PCP	Champ Allina PCP (n = 275)		MHI Group AVG	Champ AVG (n = 426)
Ace Arb Arni	82.6%	94.7%		82.5%	93.2%
Composite GDMT	78.9%	87.4%		72.6%	86.8%
Composite GDMT with SGLT2i	69.9%	80.7%		65.4%	80.9%
CRT	26.1%	12.5%		28.2%	14.3%
ICD	26.0%	12.5%		24.0%	20.0%
Long-acting Beta Blocker	88.1%	92.6%		86.5%	92.7%
MRA	51.9%	62.5%		52.0%	63.5%
Potassium Creatinine	79.2%	82.0%		64.4%	77.1%
SGLT2i	54.2%	74.3%		56.0%	74.5%
Spironolactone	40.3%	52.9%		44.2%	63.4%

CHAMP data 7/2025

AHMHI Heart Failure



Bridge Clinic and CHAMP

- APP and RN directed clinics
- Multiple metro and outreach sites
  - Plymouth, St. Paul, Edina, Chaska, Eden Prairie, Lakeville, Shakopee, Baxter, Cambridge, New Ulm


Questions?
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References

- Heidenreich PA, Bozkurt B, Aguilar D, Allen LA, Byun JJ, Colvin MM, Deswal A, Drazner MH, Dunlay SM, Evers LR, Fang JC, Fedson SE, Fonarow GC, Hayek SS, Hernandez AF, Khazanie P, Kittleson MM, Lee CS, Link MS, Milano CA, Nnacheta LC, Sandhu AT, Stevenson LW, Vardeny O, Vest AR, Yancy CW. *2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines*. **Circulation. 2022;145:e895–e1032.** DOI: 10.1161/CIR.0000000000001063
- See individual slides for additional references