The Heart (Failure) of the Matter: Updates in Heart Failure

Dawn Battise, PharmD, BCACP

Angie Pegram, PharmD, BCPS, CDCES

Objectives

- Identify new medication approvals related to heart failure management
- Recall key updates to pharmacologic heart failure management
- Apply updated heart failure information to patient scenarios
- Identify potential solutions to challenges in heart failure management

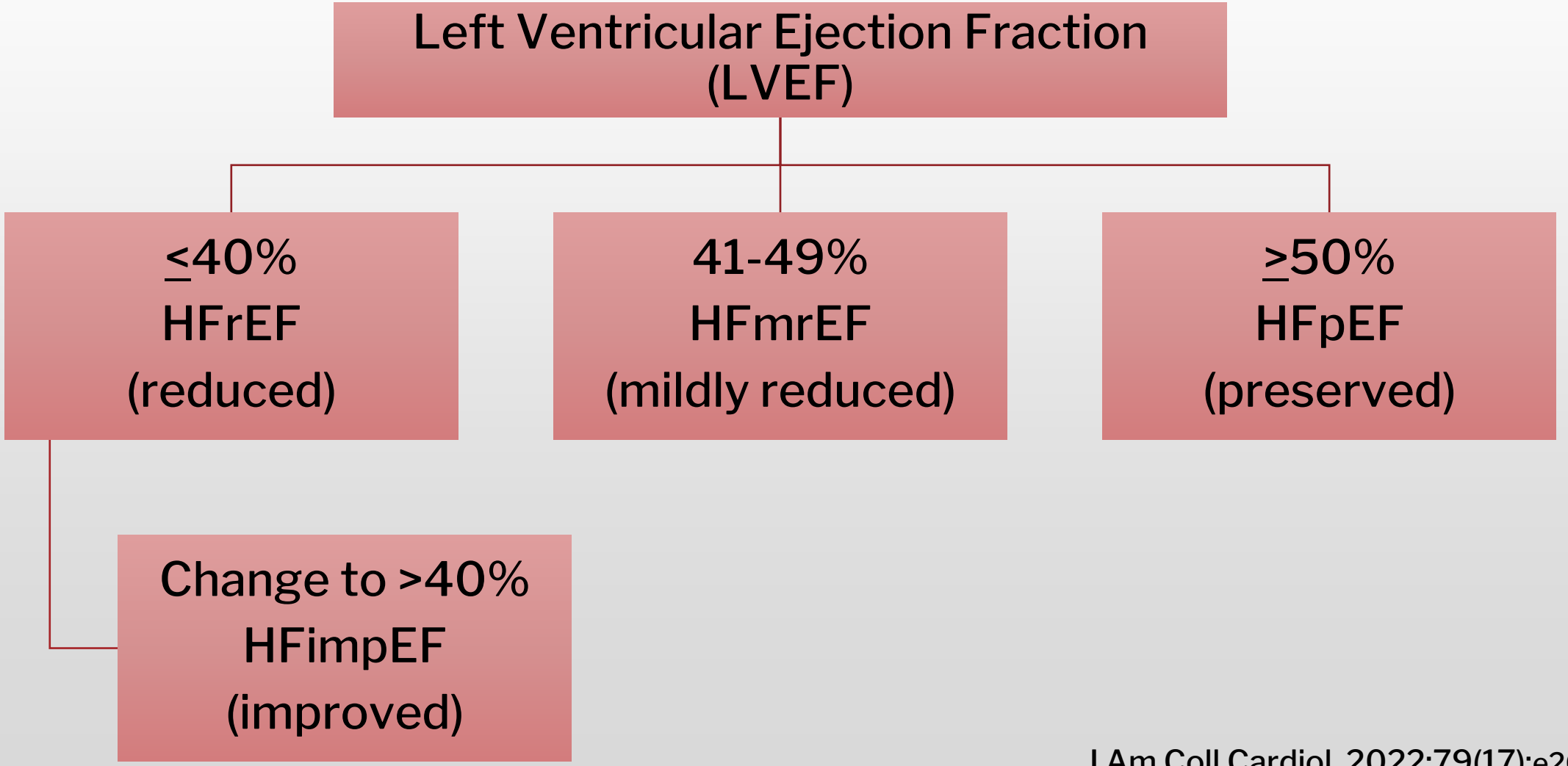
Terminology

- ARNI: angiotensin receptor neprilysin inhibitor
- BB: beta-blocker
- CKD: chronic kidney disease
- CV: cardiovascular
- GDMT: guideline directed medical therapy
- HFrEF: heart failure with reduced ejection fraction
- HFimpEF: heart failure with improved ejection fraction
- HFmrEF: heart failure with mildly reduced ejection fraction
- HFpEF: heart failure with preserved ejection fraction
- ISDN: isosorbide dinitrate
- LVEF: left ventricular ejection fraction
- MACE: major adverse cardiovascular events
- MRA: mineralocorticoid receptor antagonist
- PAD: peripheral artery disease
- SGLT2i: sodium glucose cotransporter-2 inhibitor
- T2DM: type 2 diabetes mellitus

The Heart of the Matter

INTRODUCTION

Heart Failure (HF) Classification



J Am Coll Cardiol. 2022;79(17):e263-421.

Pharmacologic Management Options

- Diuretics
- Beta-blockers
  - Evidence-based: metoprolol succinate, bisoprolol, carvedilol
- ACEi/ARB
- Mineralocorticoid receptor antagonist (MRA)
  - Spironolactone, eplerenone

Approved in Past Ten Years

Hyperpolarization-activated cyclic nucleotide-gated (HCN) channel blocker	Ivabradine (Corlanor®)
Angiotensin receptor/neprilysin inhibitor (ARNI)	Sacubitril/valsartan (Entresto®)
Soluble guanylate cyclase stimulator	Vericiguat (Verquvo®)
SGLT2 inhibitors (SGLT2i)	Empagliflozin (Jardiance®) Dapagliflozin (Farxiga®)
Dual SGLT1 and SGLT2 inhibitor (SGLT1/2i)	Sotagliflozin (Inpefa®)

New(er) Treatments

Select SGLT2i

Dual SGLT1/2i

Sodium Glucose Cotransporter-2 Inhibitors (SGLT2i)

Medication	FDA Approval Date			
	T2DM	HFrEF	HF*	CKD
Empagliflozin (Jardiance)	2014	2020	2021	2023
Dapagliflozin (Farxiga)	2014	2020	2023	2021

*independent of LVEF

New drug application 202293. Drugs@FDA:FDA Approved Drugs.
New drug application 204629. Drugs@FDA:FDA Approved Drugs.

SGLT2i MOA

Inhibit SGLT2 in the proximal renal tubules which results in…

↑ urinary glucose excretion

- ↑ renal threshold for glucose
- ↓ reabsorption of glucose

↓ sodium reabsorption

- ↑ Na delivery to distal tubule
- ↓ pre-load and after-load?
- ↓ sympathetic activity?

Product package inserts

SGLT2i Data in HFrEF

Feature	EMPEROR REDUCED (n = 3730)	DAPA-HF (n = 4744)
Participants	NYHA Class II - IV LVEF ≤40%	
Primary Outcome, Risk Reduction	CV death or HF hospitalization, ↓25%	CV death or worsening HF, ↓27%
Key Secondary Outcomes, Risk Reduction	HF hospitalization, ↓31% CV death, 8%	HF hospitalization, ↓30% CV death, ↓18%

SGLT2i Data in HFpEF

Feature	EMPEROR Preserved (n = 5988)	DELIVER (n = 6263)
Participants	NYHA Class II - IV LVEF >40% Elevated NT-pro BNP	
Primary Outcome, Risk Reduction	CV death or HF hospitalization, ↓21%	CV death or worsening HF, ↓18%
Key Secondary Outcomes, Risk Reduction	HF hospitalization, ↓29% CV death, 9%	HF hospitalization, ↓27% CV death, ↓12%

Sotagliflozin (Inpefa®): Dual SGLT2/SGLT1 Inhibitor

- Approved: May 2023
- Indication: reduce risk of CV death, HF hospitalization, or urgent HF visit in individuals with…
  - 1) HF *or*
  - 2) T2DM, CKD and other CV risk factors
- 200 and 400 mg tab
- Counseling: similar to other SGLT2i *plus*
  - Take no more than 1 hour before 1st meal of day
  - Do not cut, crush, chew
  - AE: increased risk diarrhea

Product package insert

SGLT2/SGLT1i MOA

SGLT2i in proximal renal tubules

- ↑ urinary glucose excretion
- ↓ sodium reabsorption ★

SGLT1i in intestines

- ↓ glucose and Na reabsorption

Product package insert

Sotagliflozin Data

Feature	SCORED (n = 10584)	SOLOIST-WHF (n = 1222)
Participants	T2DM, CV risk factors, GFR 25-60	T2DM, admitted for worsening HF
Primary Outcome, Risk Reduction	CV death, urgent HF visit, HF hospitalization, ↓25%	CV death, urgent HF visit, HF hospitalization, ↓33%
Key Secondary Outcomes, Risk Reduction	Urgent HF visit, hospitalization, ↓33% CV death, ↓10%	Urgent HF visit, hospitalization, ↓36% CV death, ↓16%

Treatment Updates

2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure

J Am Coll Cardiol. 2022;79(17):e263-421.

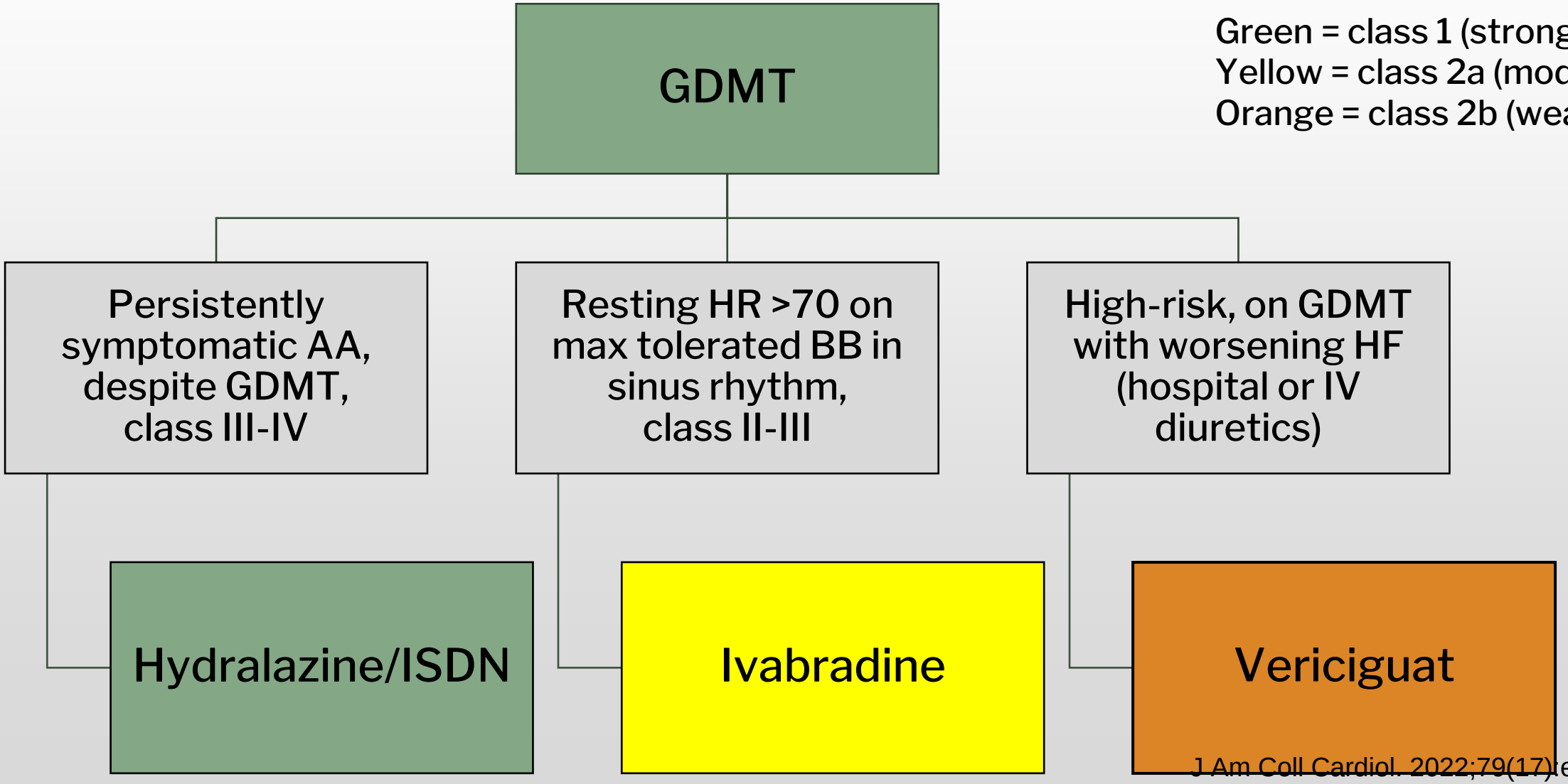
HFrEF by Stage

Stage A	Stage B	Stage C/D
• SGLT2i in T2DM • Manage BP/CVD	• SGLT2i in T2DM • ACEi/ARB • Beta-blocker • Manage BP/CVD	• Diuretics prn • SGLT2i • ARNI/ACEi/ARB • MRA • Evidence-based beta-blocker

Green = class 1 (strong)

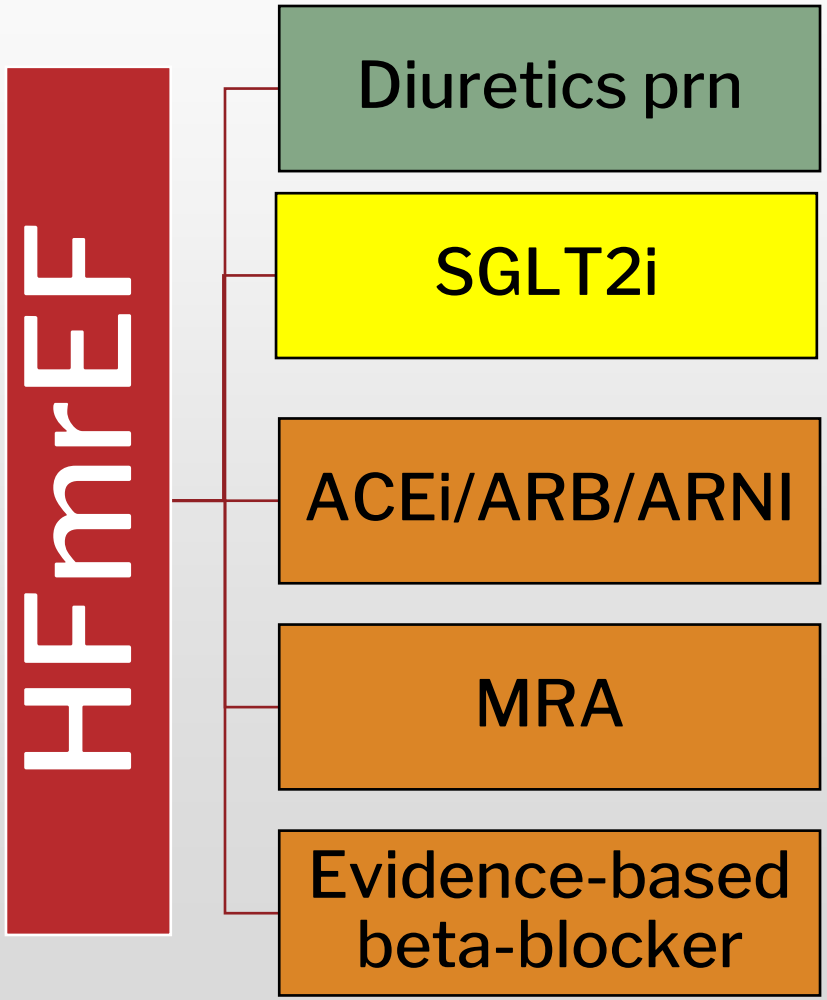
J Am Coll Cardiol. 2022;79(17):e263-421.

HFrEF Stage C – Additional Agents

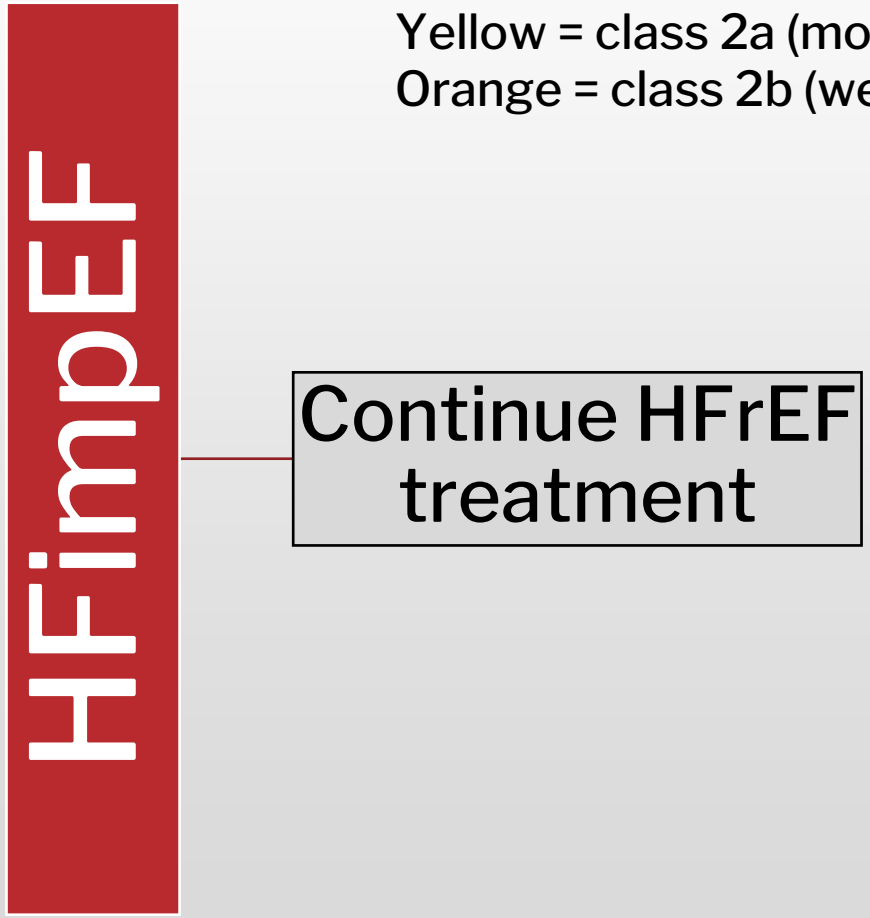


J Am Coll Cardiol. 2022;79(17):e263-421.

Mildly Reduced and Improved EF



Green = class 1 (strong)
Yellow = class 2a (moderate)
Orange = class 2b (weak)



J Am Coll Cardiol. 2022;79(17):e263-421.

Patient Case: Joseph James

- 72 year old African American male
- PMH: HTN, HFrEF, CAD (MI at age 68), stage 3 CKD, obesity
- Medications: furosemide 10 mg daily, metoprolol succinate 50 mg twice daily, lisinopril 20 mg daily, spironolactone 25 mg daily, aspirin 81 mg daily
- Objective Data:
  - BP 142/83
  - HR 80
  - BMP WNL except SCr 1.5 (GFR 40)
  - LVEF: 30%

- He is symptomatic. → How will you optimize treatment?

Patient Case: Joseph James

- Assess safety/adherence
- Add SGLT2i
- Change ACEi to ARNI
  - 36 hour washout period!
- Assess target doses
- Future hydralazine/ISDN?

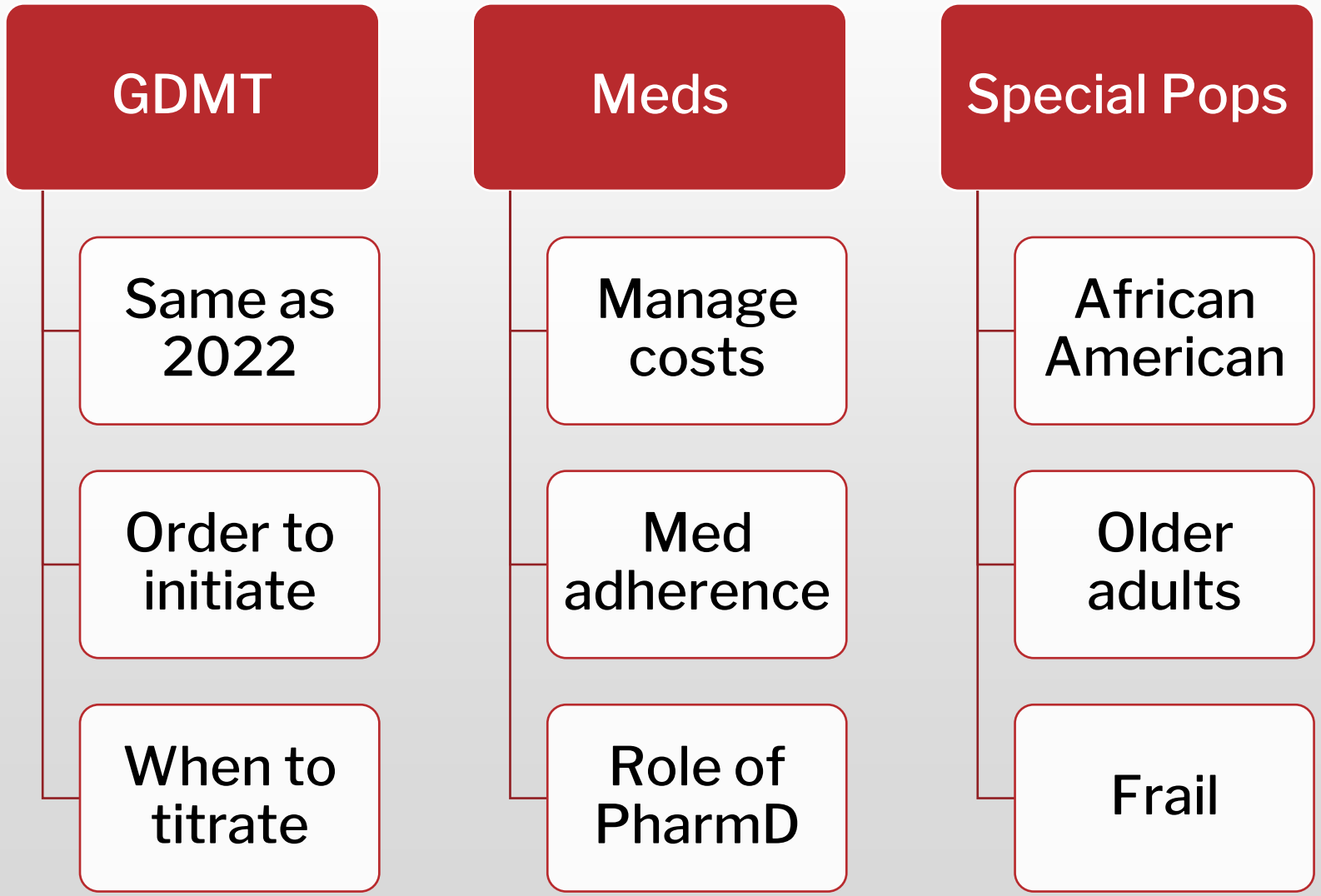
- 72 yoAAM
- PMH: HTN, HFrEF, CAD (MI at age 68), stage 3 CKD, obesity
- Medications: furosemide 10 mg daily, metoprolol succinate 50 mg twice daily, lisinopril 20 mg daily, spironolactone 25 mg daily, aspirin 81 mg daily

- BP 142/83
- HR 80
- BMP WNL except SCr 1.5 (GFR 40)
- LVEF: 30%

2024 ACC Expert Consensus Decision Pathway for Treatment of HFrEF

J Am Coll Cardiol.
2024;83(15):1444–1488.

Beyond the Four Pillars

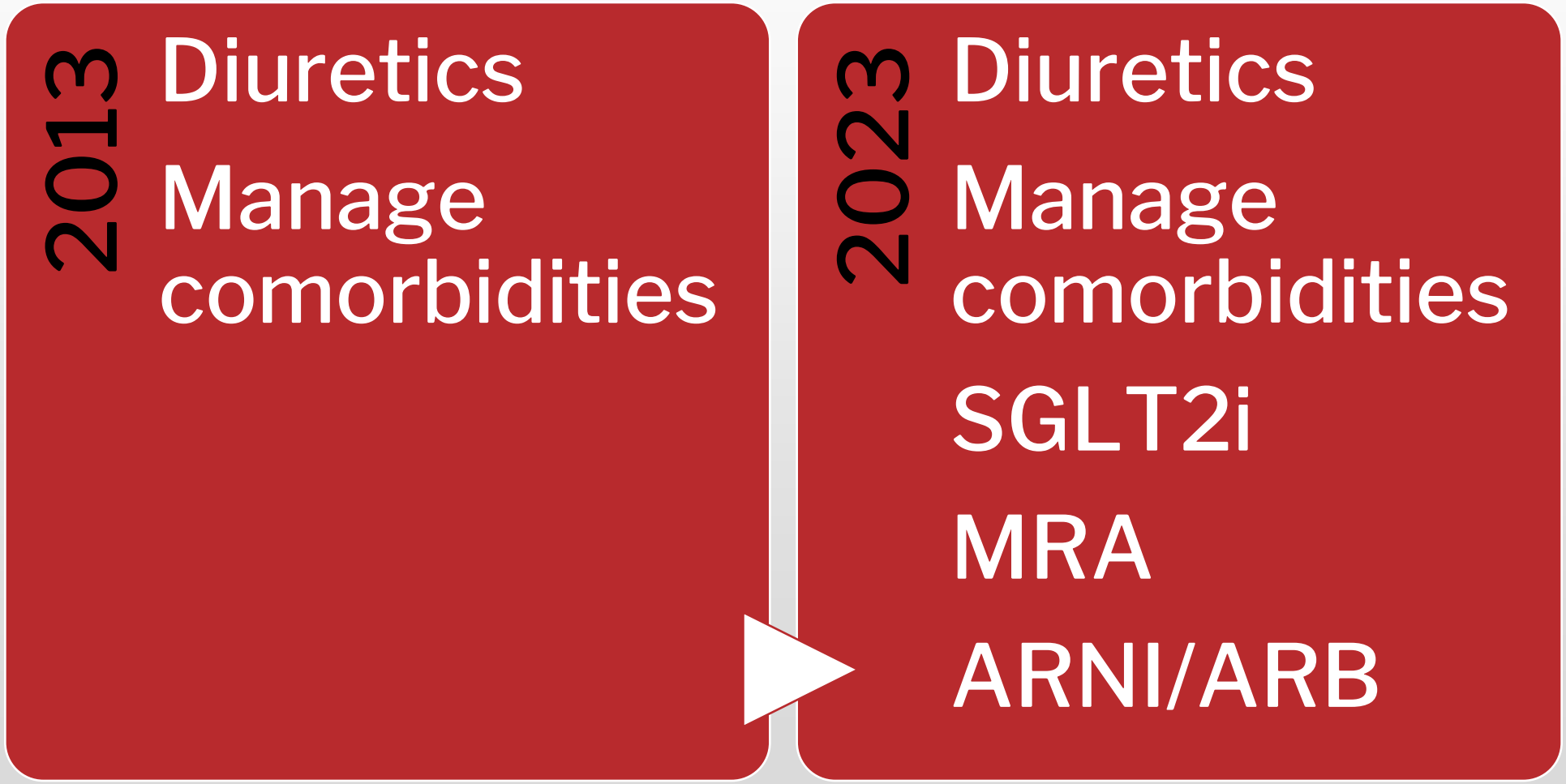


J Am Coll Cardiol. 2024; 83(15):1444–1488.

2023 ACC Expert Consensus Decision Pathway on Management of HFpEF

JACC. 2023;81(18):1836-1878.

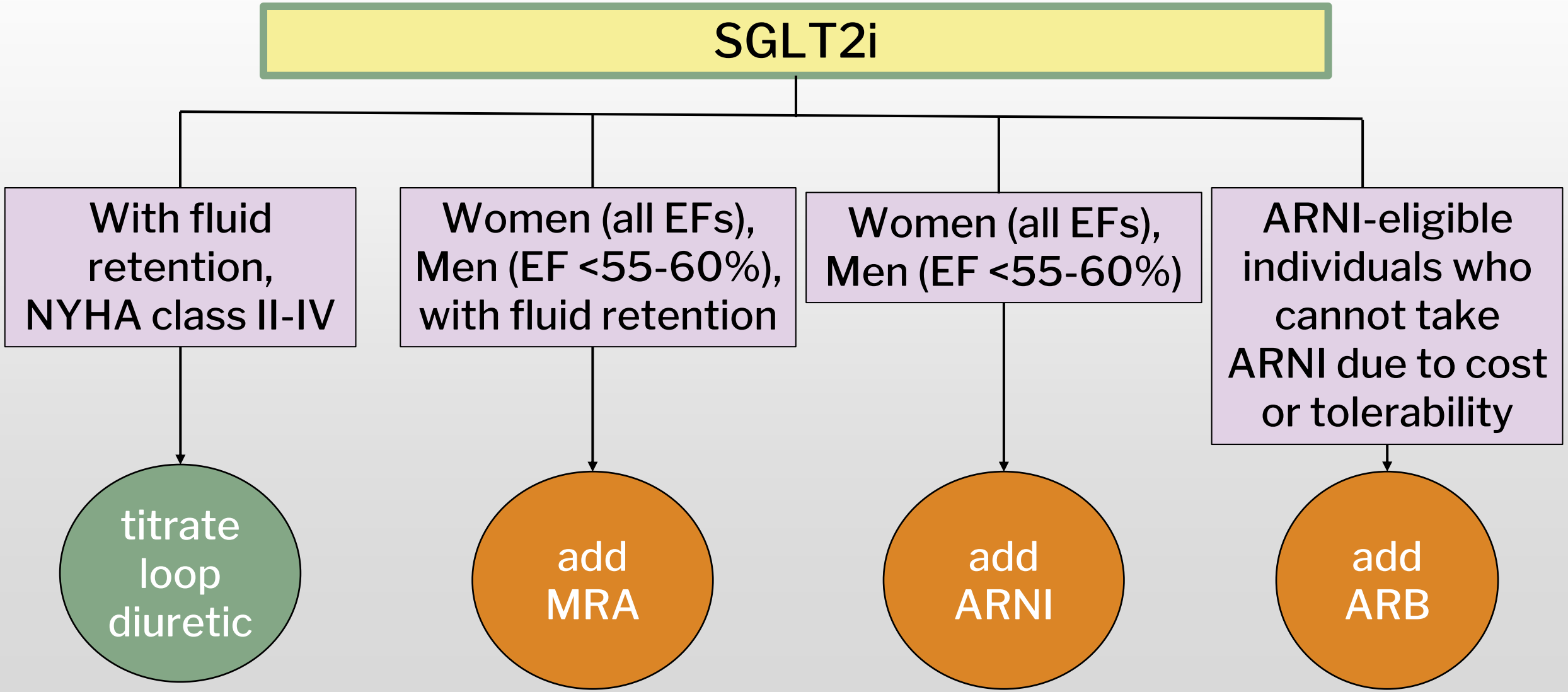
A Decade of Progress



Circulation. 2013;128:e1–e114., JACC. 2023;81(18):1836-1878.

Treatment Algorithm for GDMT in HFpEF

JACC 2023;81(18):1836-1878. Modified Fig. 9



Patient Case: Ruth Rosales

- 68 year old Caucasian female
- PMH: T2DM, HTN, obesity, sleep apnea
- Medications: metformin 1000 mg twice daily, Trulicity (dulaglutide) 4.5 mg once weekly, lisinopril 10 mg daily
- Objective Data:
  - BP 135/78
  - BMP WNL, GFR 85
  - A1c 7.8%
  - LVEF: 55%
- Now dx with HFpEF. → How will you optimize treatment?

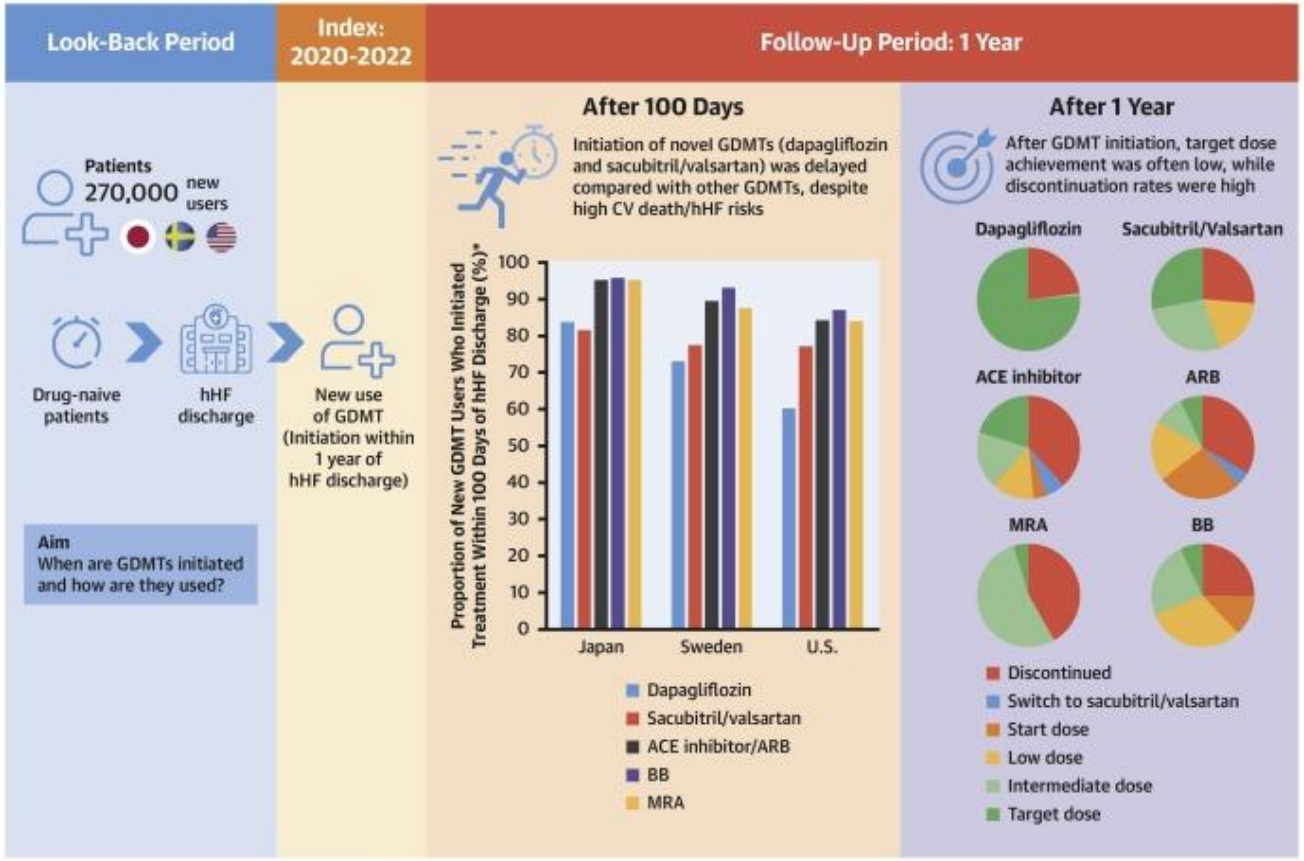
Patient Case: Ruth Rosales

- *Add SGLT2i*
- Consider loop diuretic
- Change ACEi to ARNI
- Optimize comorbidity management

- 68 yo CF
- PMH: T2DM, HTN, obesity, sleep apnea
- Meds: metformin 1000 mg daily, Trulicity 4.5 mg once weekly, lisinopril 10 mg daily
- BP 135/78 BMP WNL, GFR 85
- A1c 7.8% LVEF: 55%

Challenges in Care

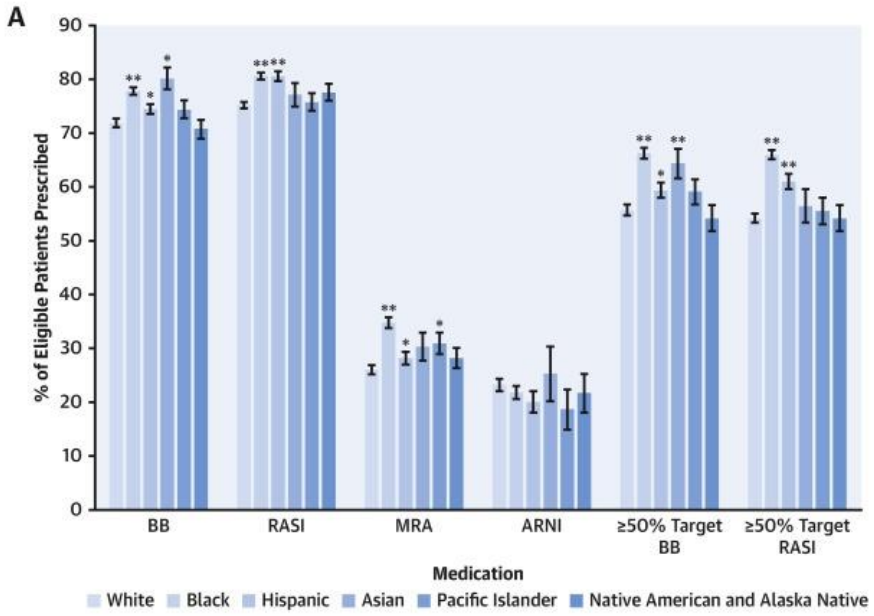
CENTRAL ILLUSTRATION: Initiation, Titration to Target Dose, and Discontinuation of GDMTs Among New Users of GDMTs After hHF, in Japan, Sweden, and the United States

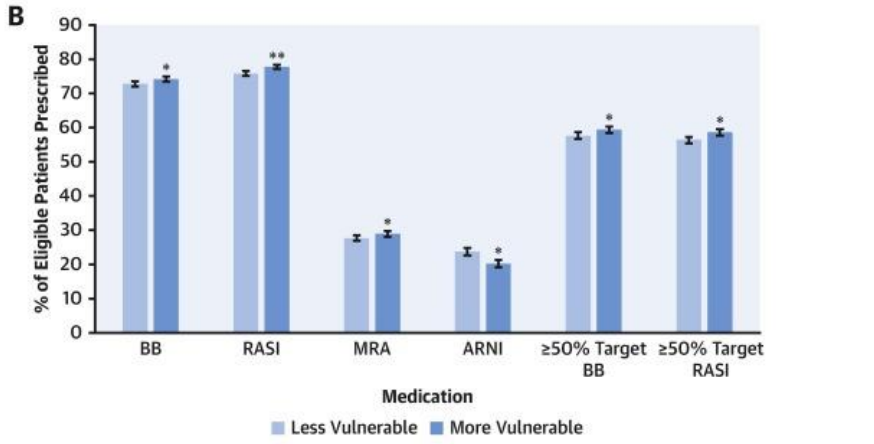


Savarese G, et al. J Am Coll Cardiol HF. 2023;11(1):1-14.

Guideline Directed Medication Therapy—How are we doing?

CENTRAL ILLUSTRATION: Variation in Therapy Rates Across Sociodemographic Characteristics

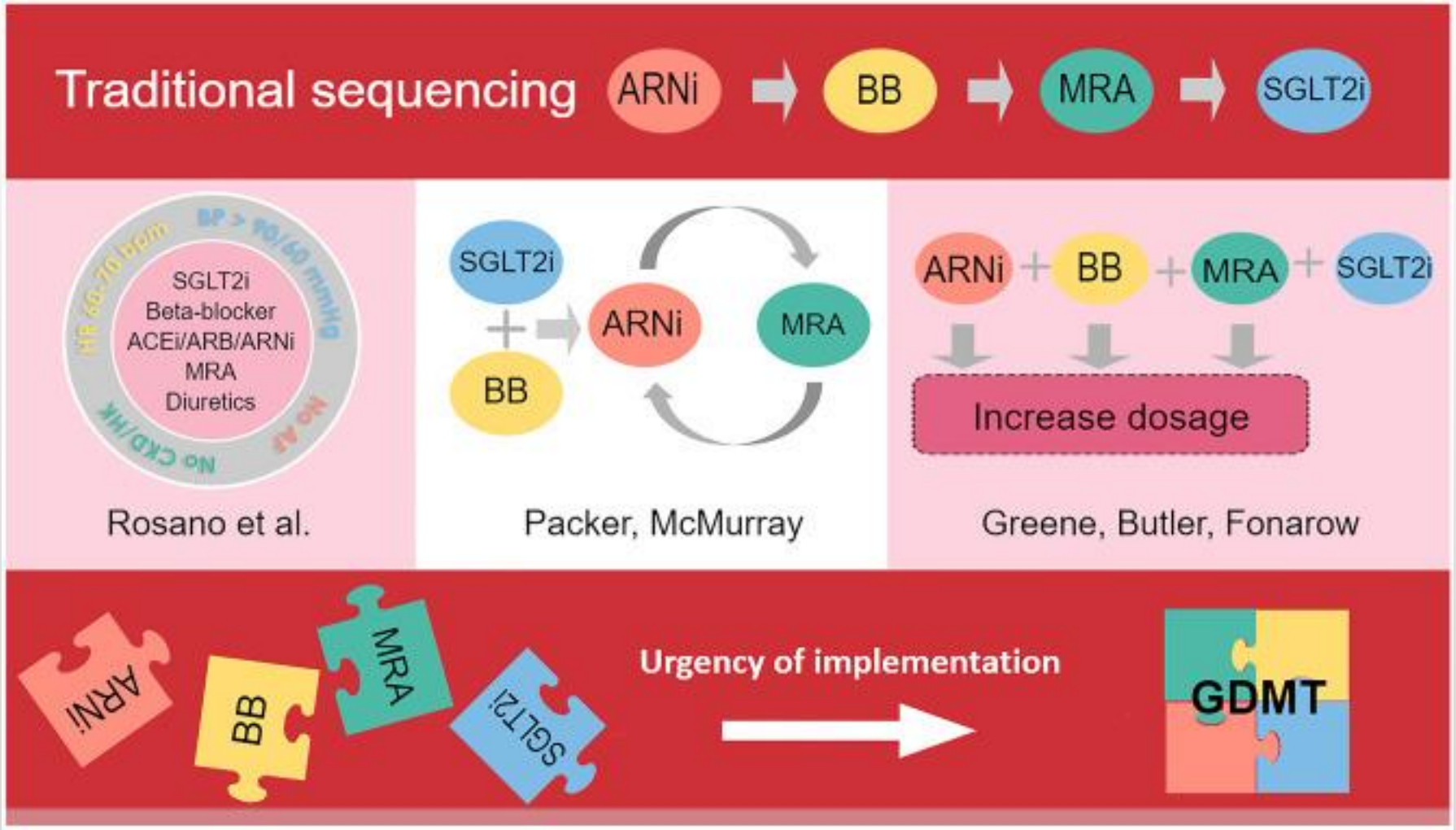




Witting C, et al. J Am Coll Cardiol HF. 2023;11(2):161-172.

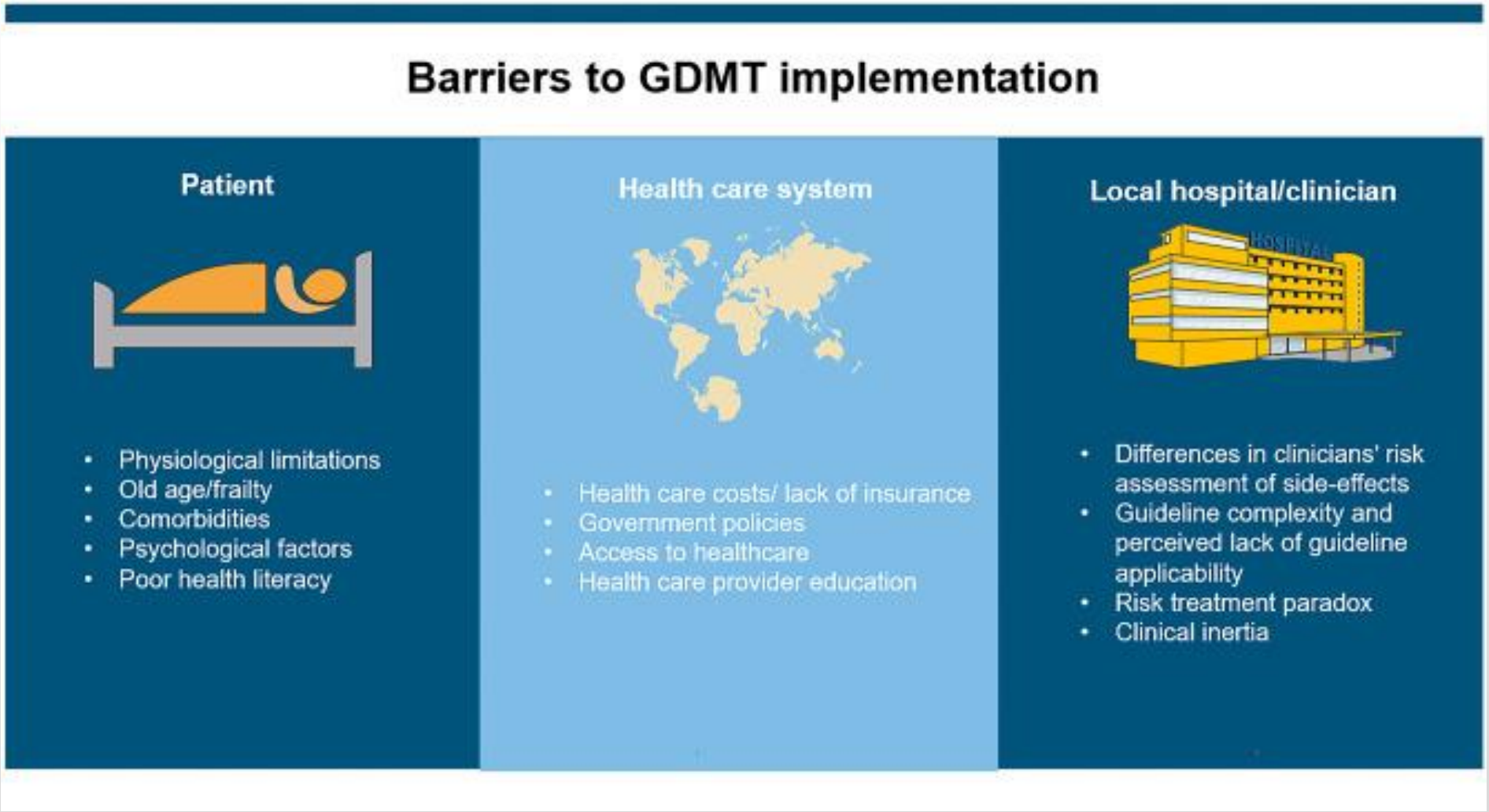
GDMT — Differences in Race and Vulnerable Populations

GDMT Sequencing for HF treatment



Heart Fail Rev. 2023; 28(5): 1221–1234.

Barriers to GDMT Implementation



Heart Fail Rev. 2023; 28(5): 1221–1234

Polypharmacy or Hyperpolypharmacy????

- “…patients with HF are prescribed an average of 6 different medications totaling more than 10 daily doses.” From 2024 ACC expert consensus on HFrEF

- 2007–2014 Medicare claims data (Part A, Part B, and Part D) linked to electronic health records from 2 large networks in Boston, 2258 patients with HFrEF had 11.3 ± 5.7 of total filled prescriptions for distinct medications.

Hyperpolypharmacy in Heart Failure (NHANES)

Medication Profile According to Hyperpolypharmacy

Variable	All	No HPP	HPP	*P*-value
Prevalence of Hyperpolypharmacy	26%	–	–	–
Total Medication Count, mean (SD)	7.2 (3.7)	5.5 (2.5)	11.9 (2.0)	<0.001
Heart Failure Medications, mean (SD)	2.1 (1.3)	1.9 (1.3)	2.8 (1.2)	<0.001
Beta blockers, %	61	56	77	<0.001
ACEI or ARB, %	58	55	66	0.02
Aldosterone antagonist, %	11	9	16	0.01
Vasodilators, %	10	7	18	0.001
Diuretics, %	60	53	78	<0.001
Digoxin, %	13	12	17	0.08
Other Cardiovascular Agents, mean (SD)	1.6 (1.3)	1.3 (1.1)	2.5 (1.3)	<0.001
Lipid Lowering, %	60	53	80	<0.001
Anti-platelet agents, %	21	14	40	<0.001
Anti-coagulation agents, %	21	19	26	0.06
Anti-arrhythmic agents, %	26	23	32	0.02
Calcium-channel blockers, %	22	19	31	0.001
Anti-anginal agents, %	12	7	27	<0.001

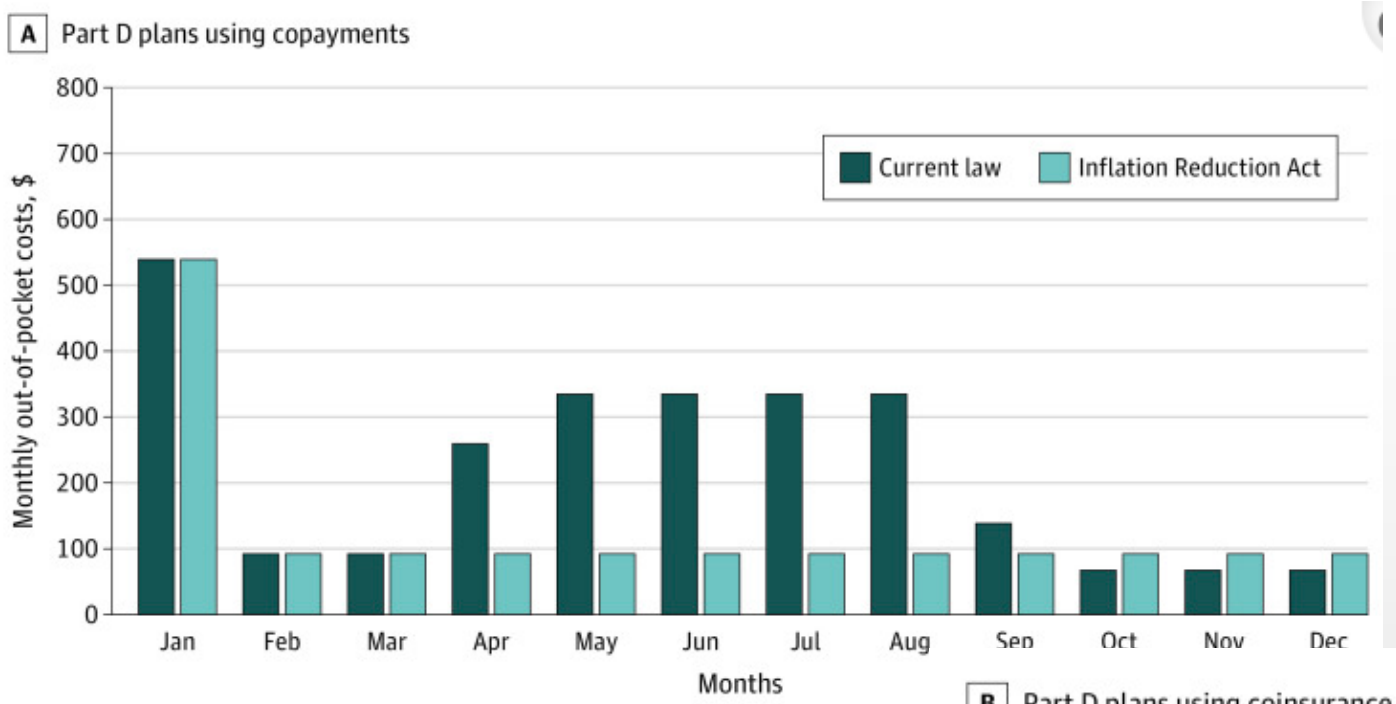
BMC Cardiovasc Disord. 2019: 19:76.

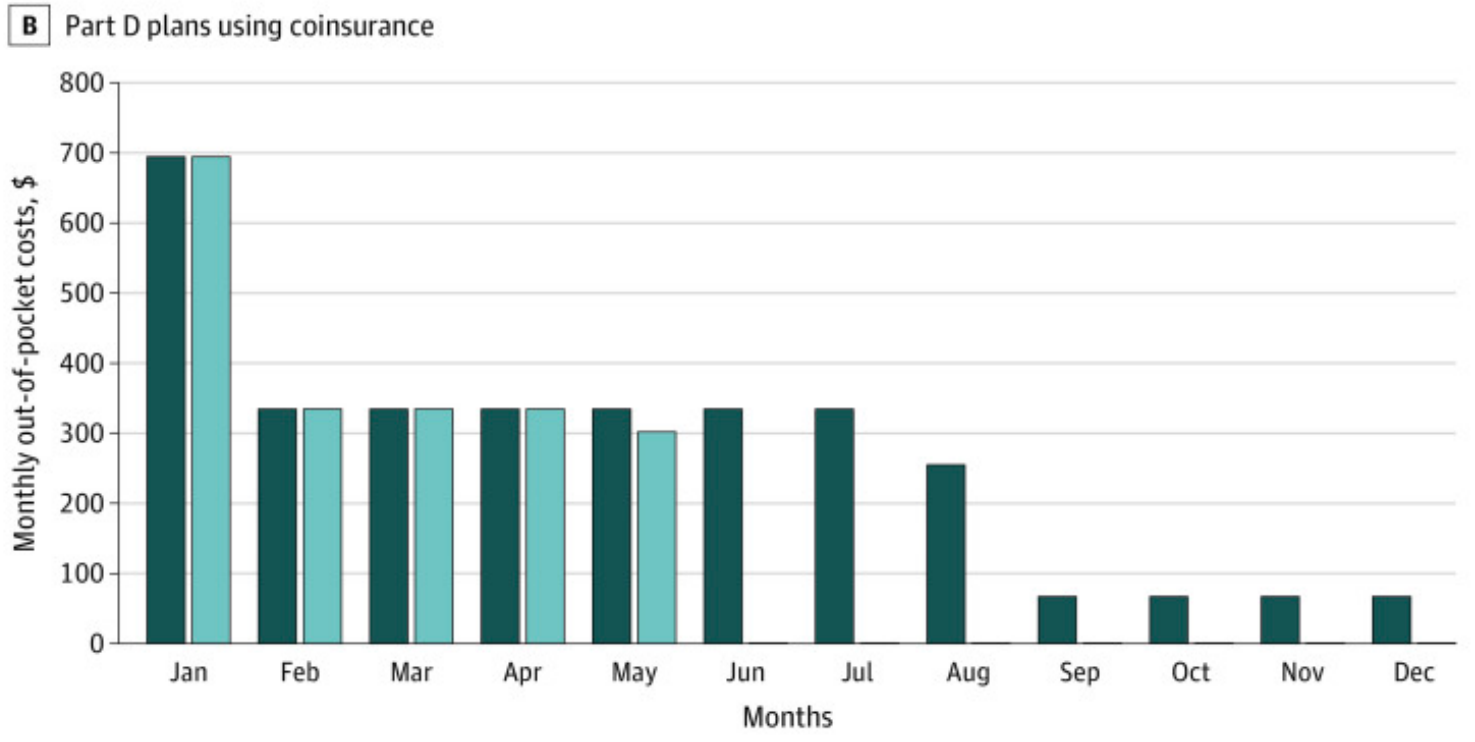
Cost of GDMT therapy

Medication regimen	Description	Cost, $				
		List price, monthly	Expected annual OOP spending			
			Plans with copayments		Plans with coinsurance	
			Current law	IRA	Current law	IRA
Metoprolol succinate, lisinopril, spironolactone	Generics only	44	482	482	492	492
Metoprolol succinate, lisinopril, spironolactone, empagliflozin	Generics + SGLT2i	614	1518	1007	2203	2000
Metoprolol succinate, sacubitril/valsartan, spironolactone	Generics + ARNI	768	1917	1015	2663	2000
Metoprolol succinate, sacubitril/valsartan, spironolactone, empagliflozin	Comprehensive therapy	1338	2659	1551	3224	2000
Carvedilol, sacubitril/valsartan, spironolactone, empagliflozin	Comprehensive therapy, lowest cost	1314	2644	1527	3210	2000
Metoprolol succinate, sacubitril/valsartan, eplerenone, dapagliflozin	Comprehensive therapy, highest cost	1546	2849	2000	3349	2000

JAMA Cardiol. 2023 Mar; 8(3): 299–301.

Medicare Patient OOP costs—Copay vs. Coinsurance

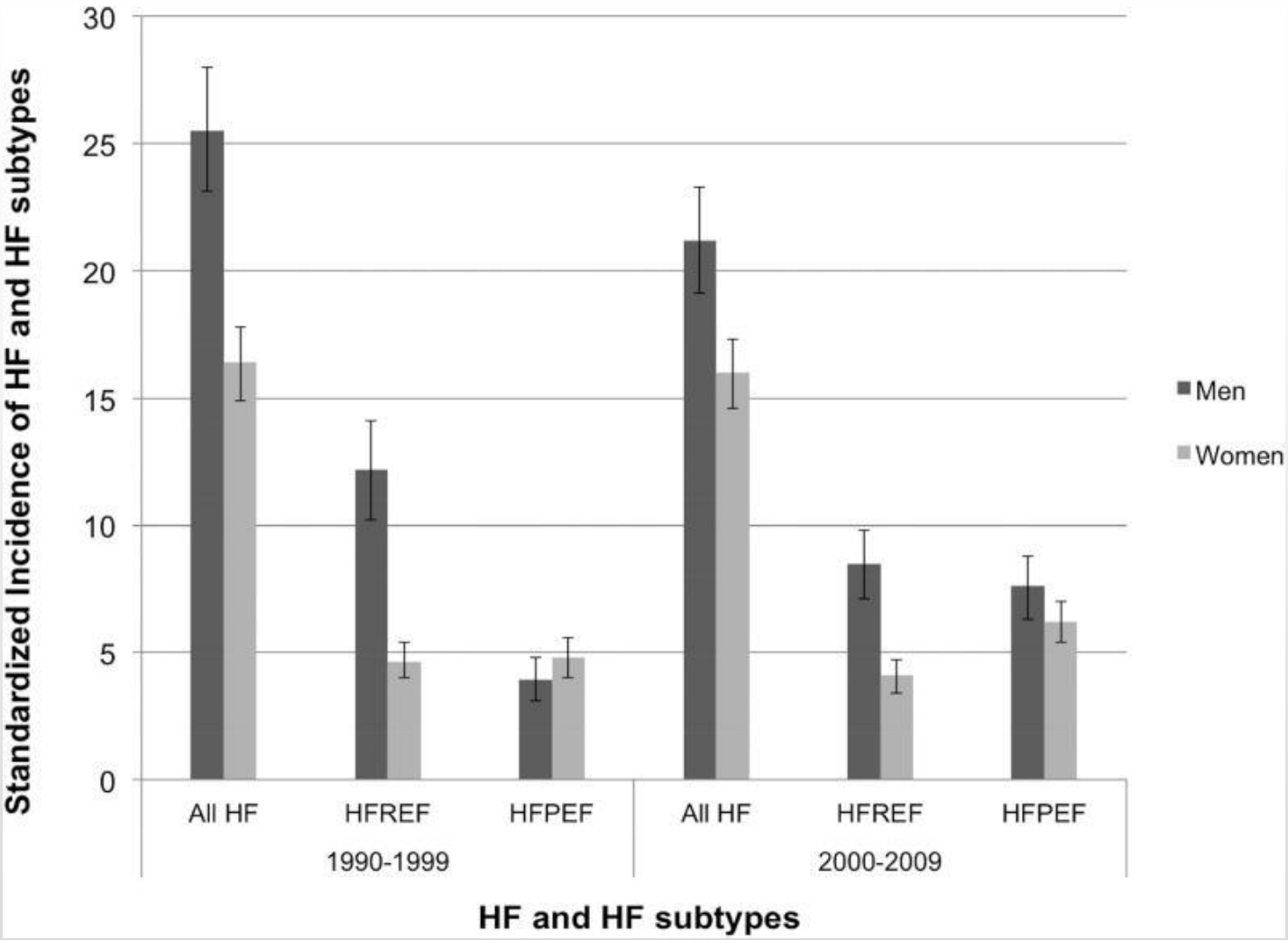




Using metoprolol succinate, sacubitril/valsartan, spironolactone and empagliflozin

JAMA Cardiol. 2023 Mar; 8(3): 299–301

Shifting Tides of Heart Failure



JACC Heart Fail. 2018 Aug; 6(8): 678–685.

Putting it Together

Final Case—Return to Joseph James

- 72 year old African American male
- PMH: HTN, HFrEF, CAD (MI at age 68), stage 3 CKD, obesity
- Medications: furosemide 10 mg daily, metoprolol succinate 50 mg twice daily, lisinopril 20 mg daily, spironolactone 25 mg daily, aspirin 81 mg daily
- Select Vitals/Labs: BP 142/83, HR=80, eGFR=40, LVEF=30%

- Patient has Medicare Part D with coinsurance coverage. He can only afford to spend $125 monthly for his medications.
- How do you handle GDMT for his HFrEF???

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