Heart Failure Medical Therapy

Mitchell Psotka, MD PhD
Section Chief, Heart Failure and Transplant
Inova Health System

Problem to be Addressed: Heart Failure

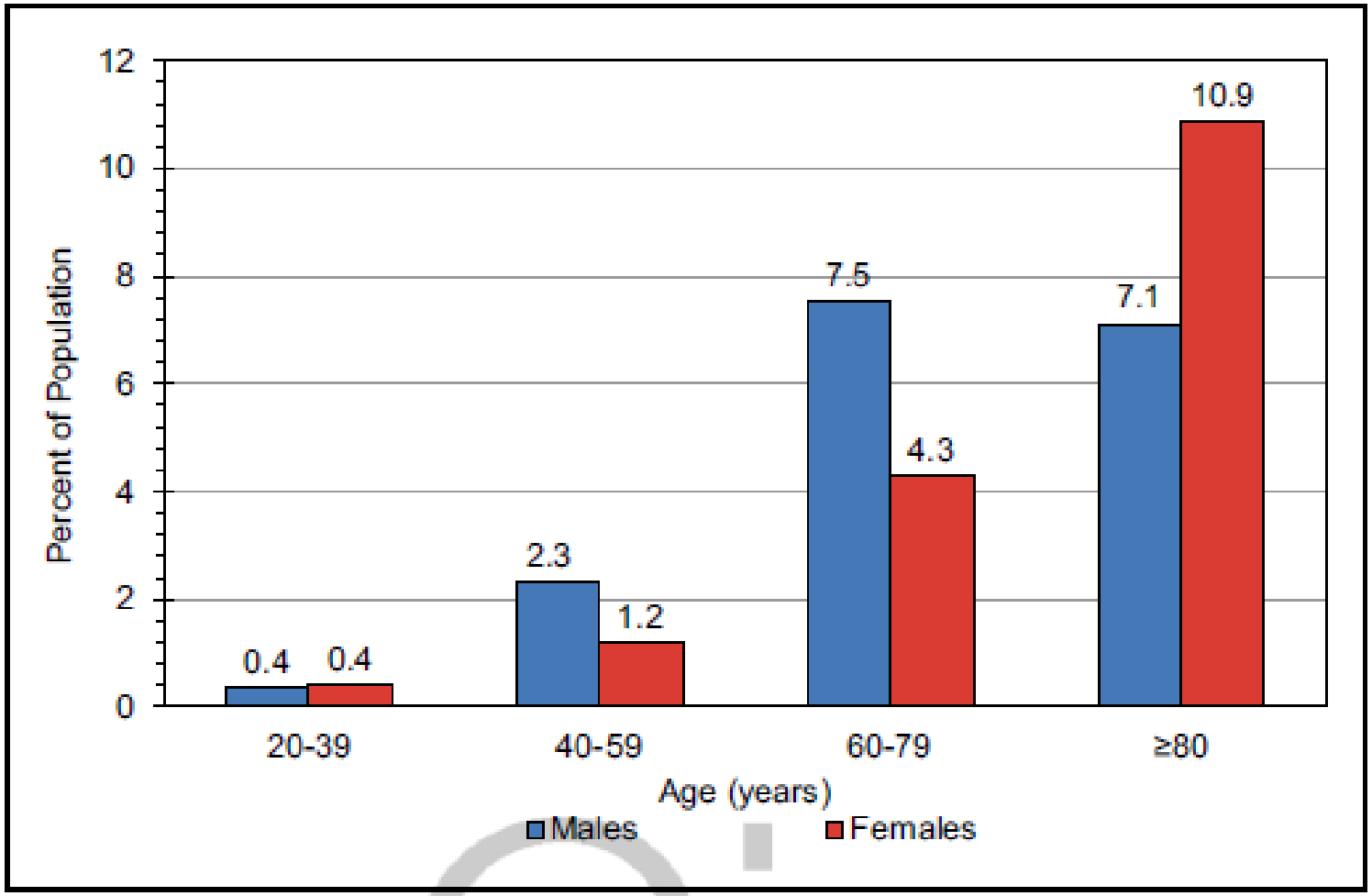


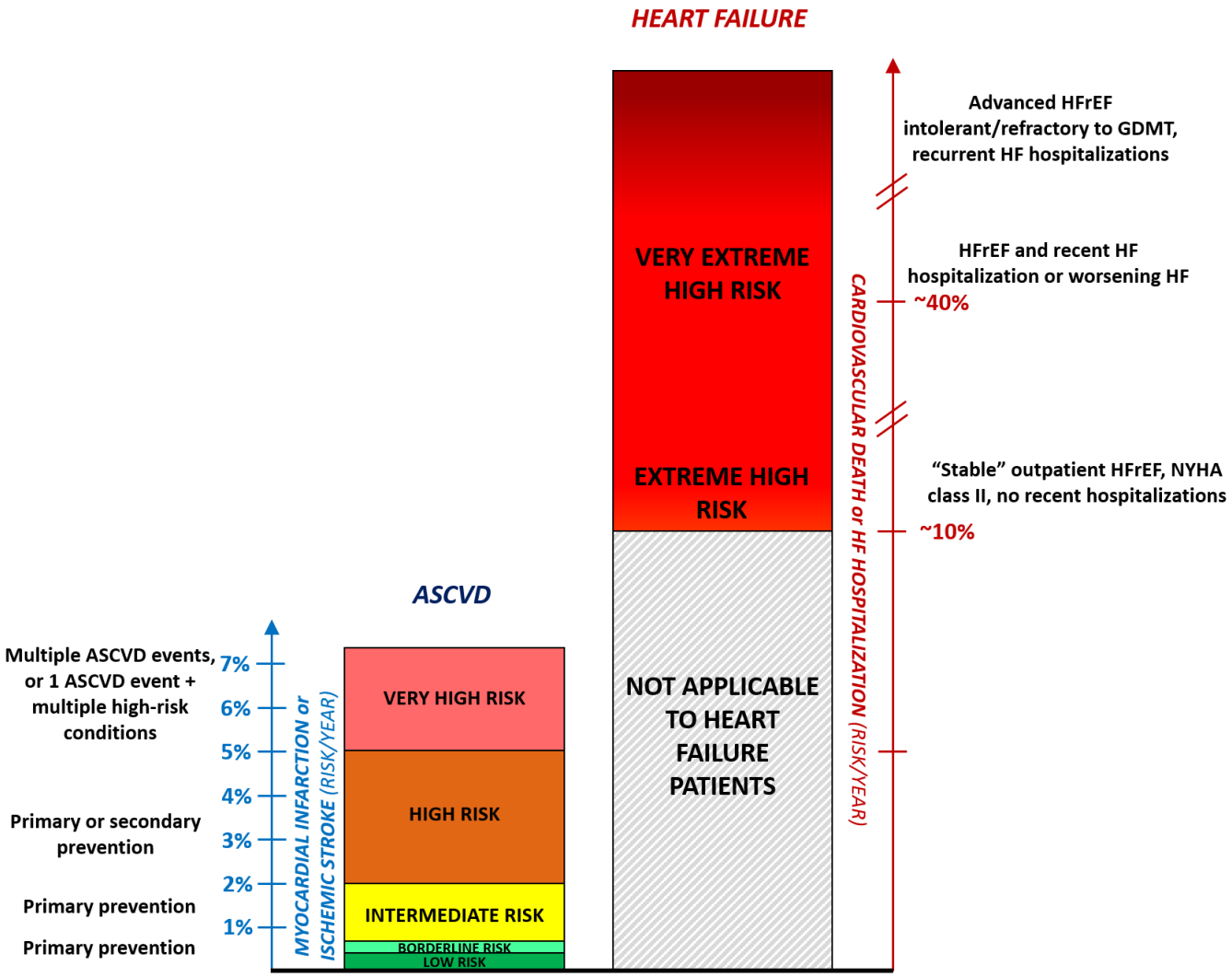
Chart 22-3. Prevalence of HF among US adults ≥20 years of age by sex and age (NHANES, 2017–2020).

Circulation. 2023;147:e00–e00. DOI: 10.1161/CIR.0000000000001123

Problem to be Addressed: HF Risk

INOVA

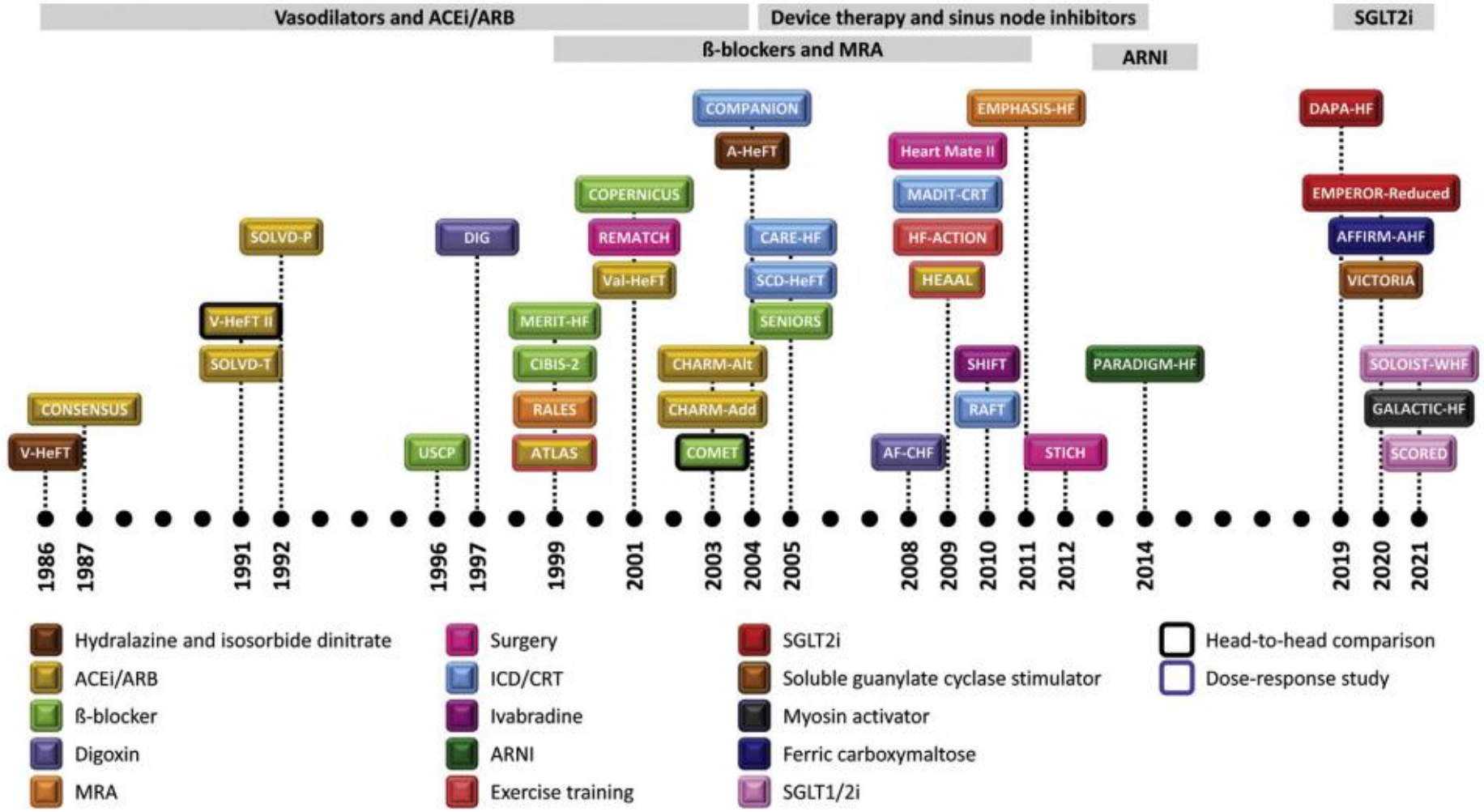
Contextualizing Risk Among Patients with Heart Failure



Heart Failure Clinical Trials

INOVA

FIGURE 1 Summary of Advances in Medical Therapies in Patients With HF and Reduced Ejection Fraction



(J Am Coll Cardiol Basic Trans Science 2022;7:504–517)

Heart Failure Guidelines

INOVA

AHA/ACC/HFSA CLINICAL PRACTICE GUIDELINE

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.

LVEF Classification

INOVA

Table 4. Classification of HF by LVEF

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)

LVEF Classification

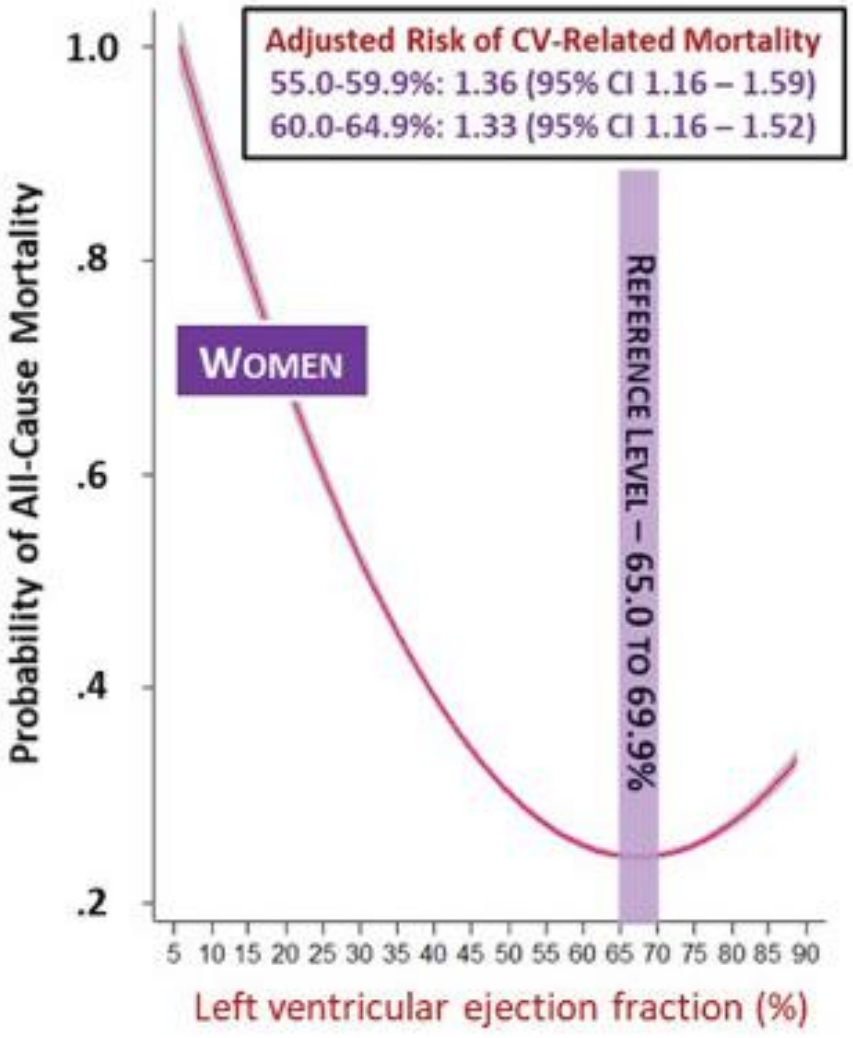
INOVA

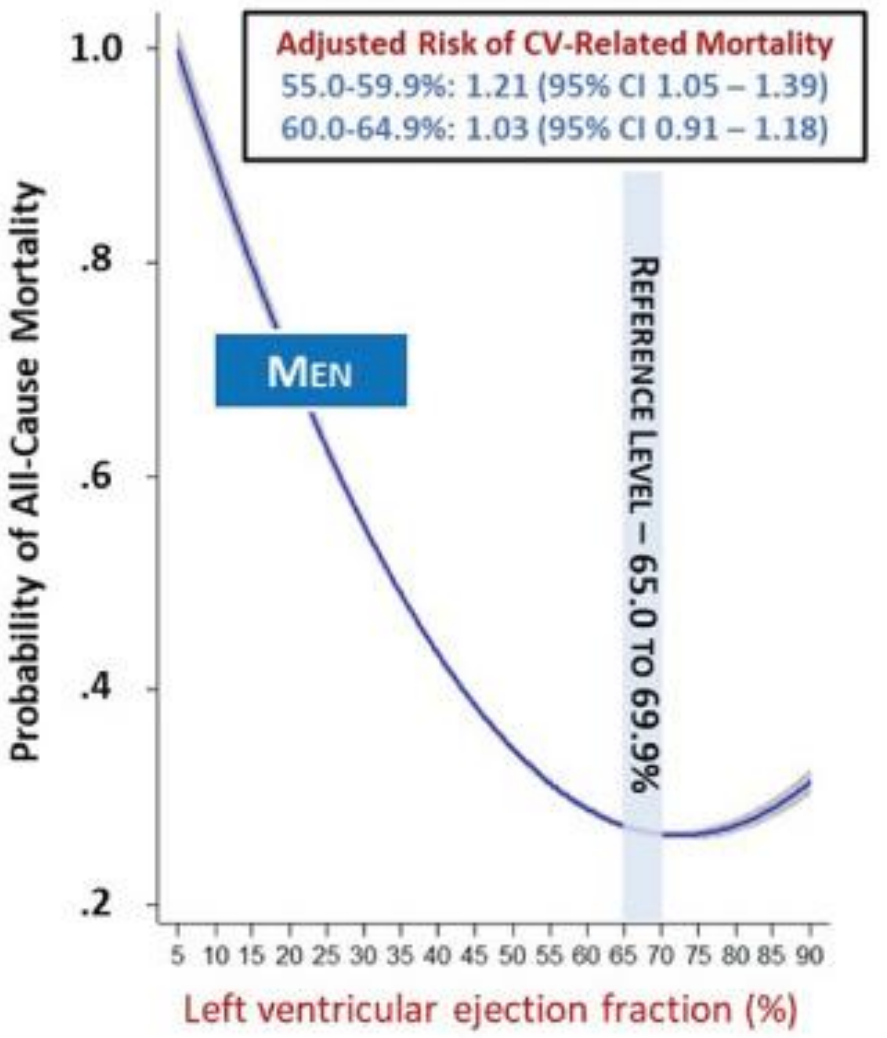
Table 4. Classification of HF by LVEF

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)

HFrEF

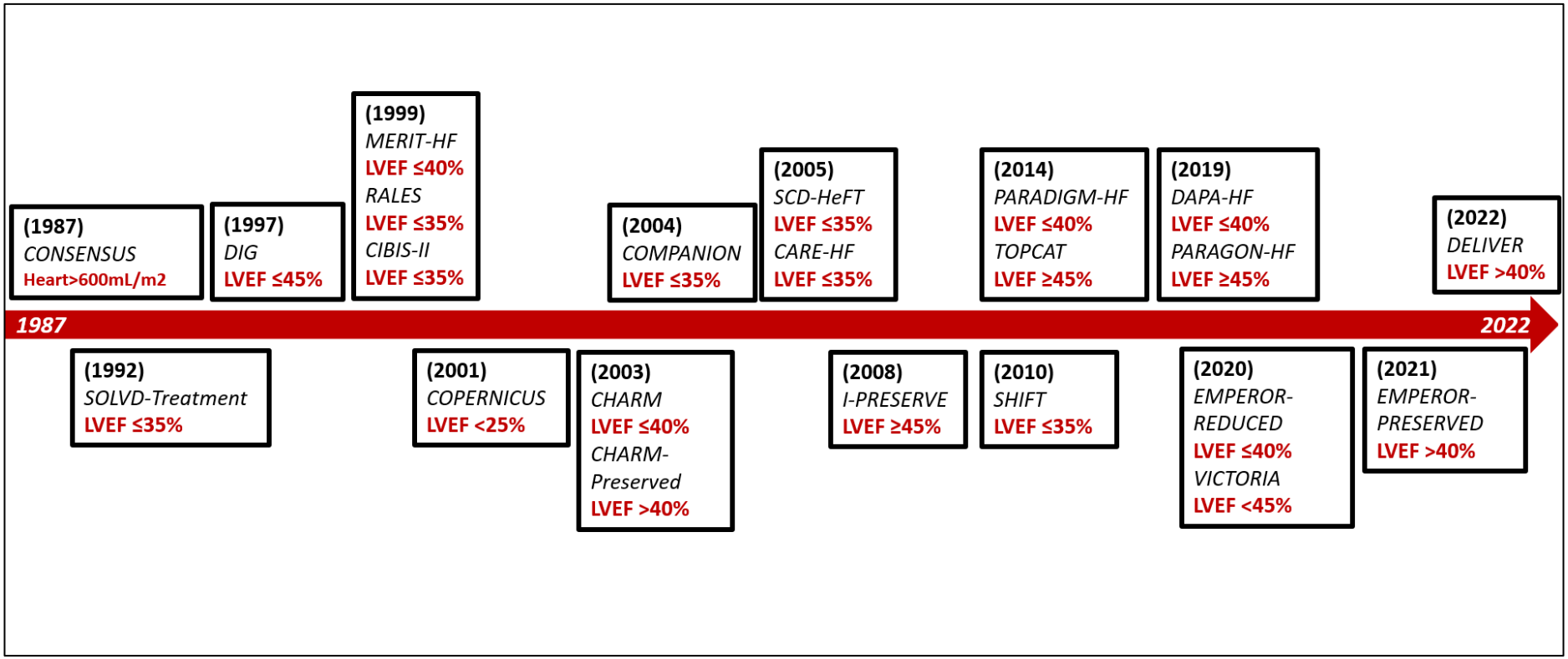
Heart Failure Across LVEF





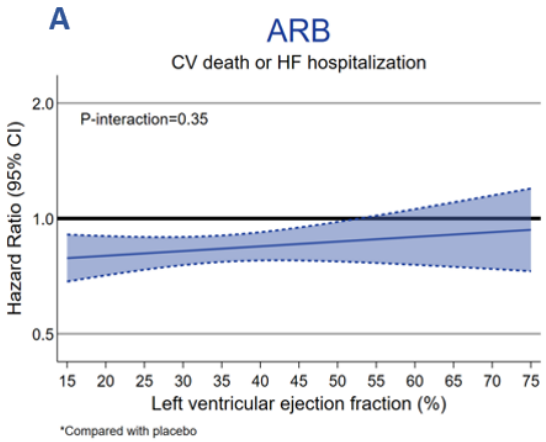
Stewart S et al. *European Journal of Heart Failure.* 2021;23(3):406-416.

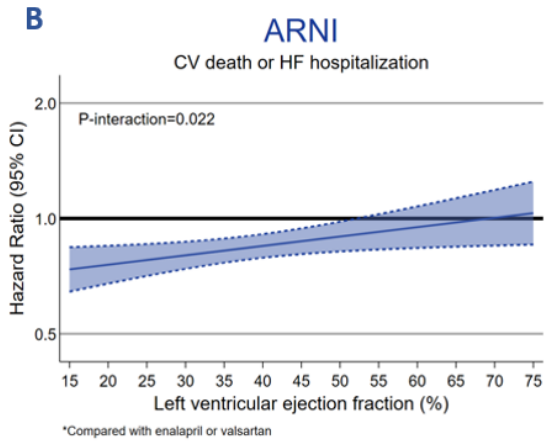
Clinical Trials Across LVEF

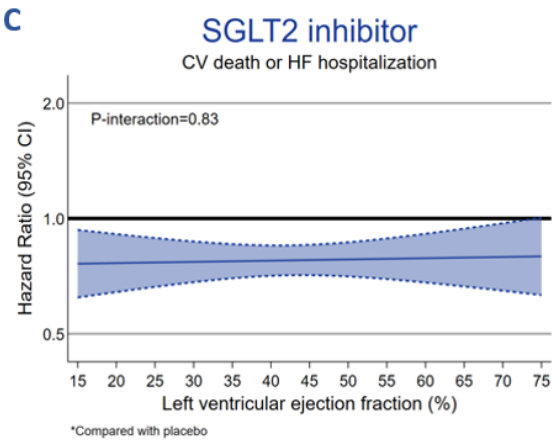


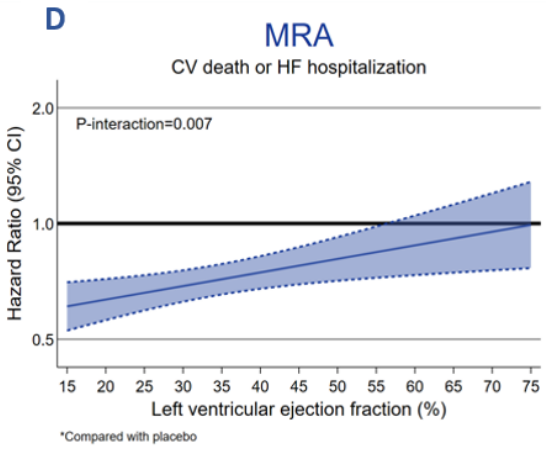
Dimond et al. (2023) *Unpublished.*

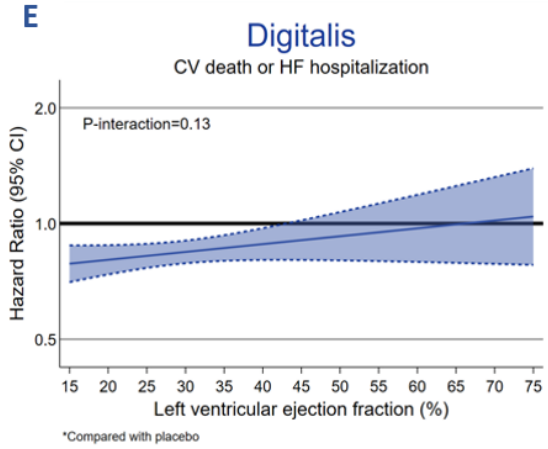
Medication Effects Across LVEF







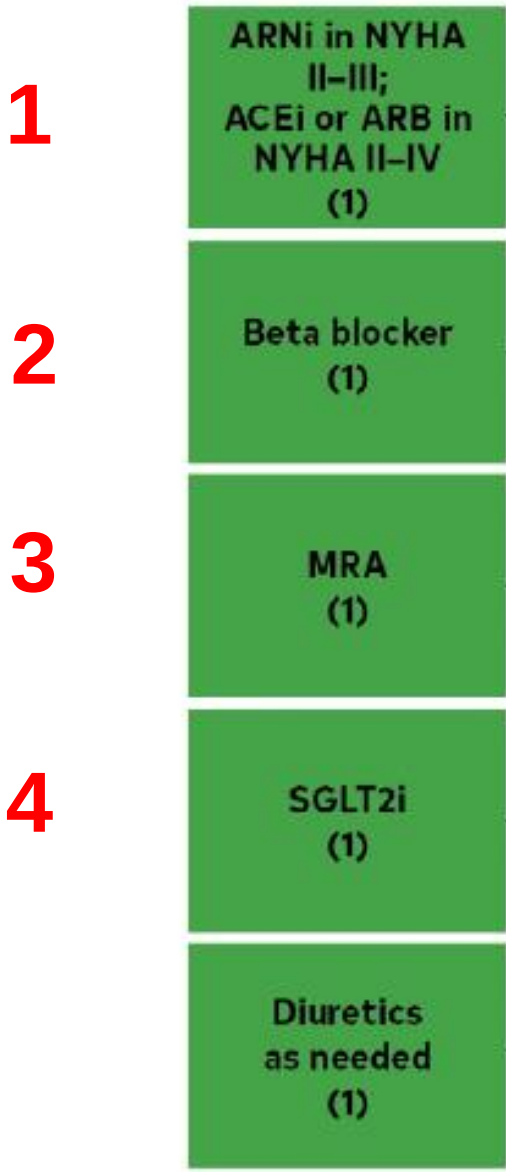




Dimond et al. (2023) *Unpublished.*

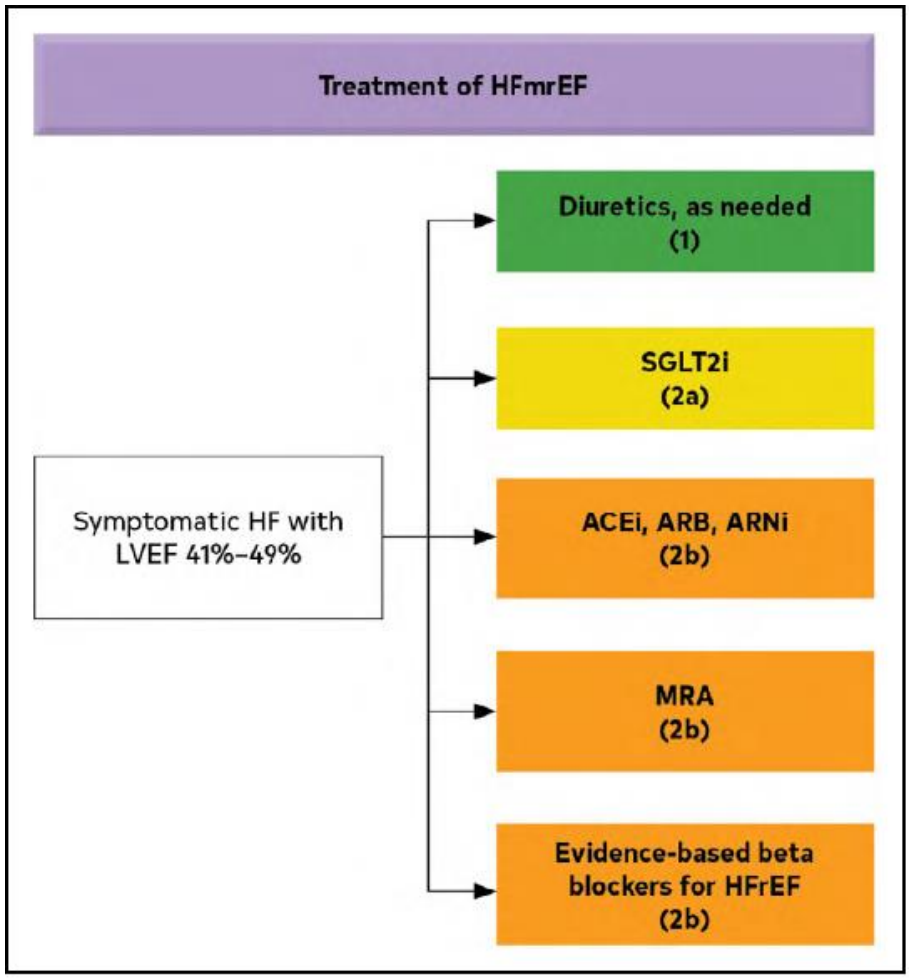
“Reduced” LVEF

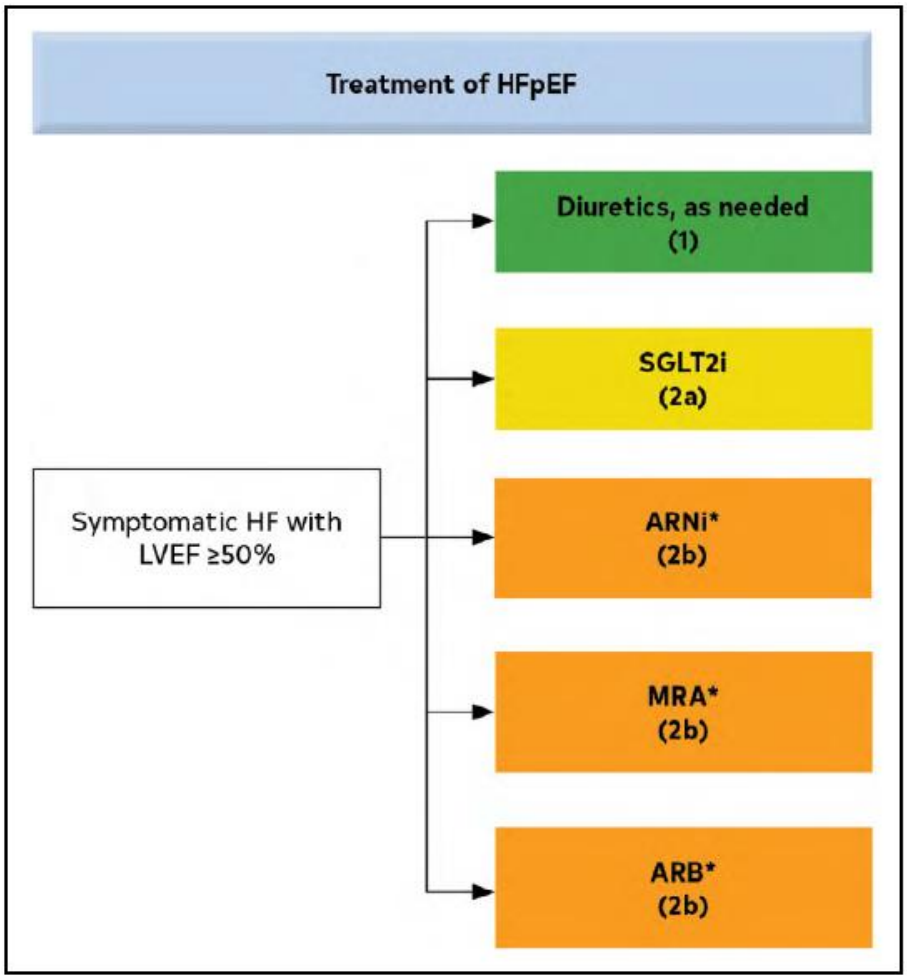
INOVA



Circulation. 2022;145:e895–e1032.

Higher LVEF





Circulation. 2022;145:e895–e1032.

LVEF Classification

INOVA

Table 4. Classification of HF by LVEF

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)

HFrEF

Medications for LVEF<50%

INOVA

Table 2: Relative Risk Reduction in Mortality and Heart Failure Hospitalisation

CDMMT	Relative Risk Reduction in Mortality	Absolute 2-year Mortality Rate	Relative Risk Reduction in HF Hospitalisations	Absolute 2-year HF Hospitalisation Rate
None	NA	35%	NA	39%
ACEI or ARB	17%	29%	31%	27%
ARNI*	16%	24%	21%	21%
β-blocker	35%	16%	41%	13%
MRA	30%	11%	35%	8%
SGLT2i	17%	9%	30%	6%
Cumulative	**74% RRR**	**26% ARR**	**85% RRR**	**33% ARR**

**Replacing ACEI/ARB. ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; ARR = absolute risk reduction; ARNI = angiotensin receptor-neprilysin inhibitor; CDMMT = comprehensive disease-modifying medical therapy; HF = heart failure; MRA = mineralocorticoid receptor antagonist; RRR = relative risk reduction; SGLT2 = sodium glucose cotransporter 2 inhibitor. Source: Fonarow et al. 2021.*[37,39]

Cardiac Failure Review 2021;7:e18.

Medications for LVEF<50%

INOVA

Table 15. Benefits of Evidence-Based Therapies for Patients With HFrEF[3–6,8,10–14,23,31–42]

Evidence-Based Therapy	Relative Risk Reduction in All-Cause Mortality in Pivotal RCTs, %	NNT to Prevent All-Cause Mortality Over Time*	NNT for All-Cause Mortality (Standardized to 12 mo)	NNT for All- Cause Mortality (Standardized to 36 mo)
ACEi or ARB	17	22 over 42 mo	77	26
ARNi†	16	36 over 27 mo	80	27
Beta blocker	34	28 over 12 mo	28	9
Mineralocorticoid receptor antagonist	30	9 over 24 mo	18	6
SGLT2i	17	43 over 18 mo	63	22

Circulation. 2022;145:e895–e1032.

Medications for LVEF<50%

INOVA

Table 15. Benefits of Evidence-Based Therapies for Patients With HFrEF[3–6,8,10–14,23,31–42]

Evidence-Based Therapy	Relative Risk Reduction in All-Cause Mortality in Pivotal RCTs, %	NNT to Prevent All-Cause Mortality Over Time*	NNT for All-Cause Mortality (Standardized to 12 mo)	NNT for All- Cause Mortality (Standardized to 36 mo)
ACEi or ARB	17	22 over 42 mo	77	26
ARNi†	16	36 over 27 mo	80	27
Beta blocker	34	28 over 12 mo	28	9
Mineralocorticoid receptor antagonist	30	9 over 24 mo	18	6
SGLT2i	17	43 over 18 mo	63	22

Circulation. 2022;145:e895–e1032.

Problem to be Addressed: Survival

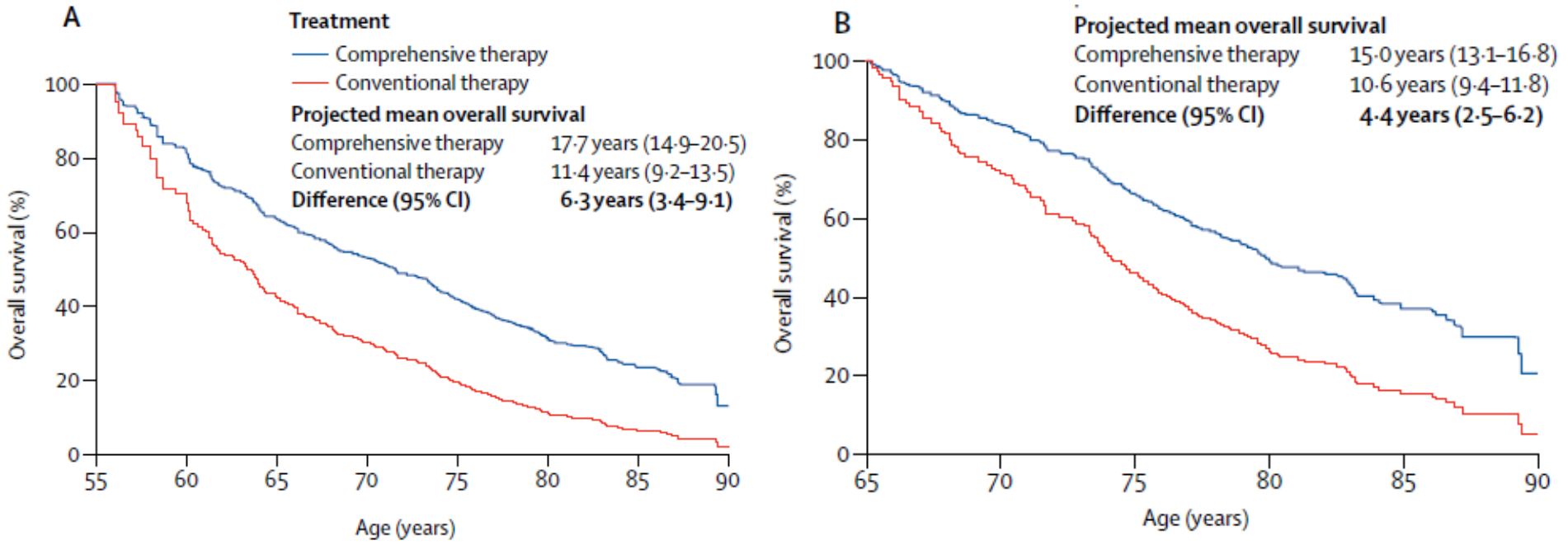


***Figure 3*: Long-term overall survival with comprehensive disease-modifying therapy *vs* conventional therapy**

Kaplan-Meier estimated curves for patients starting at age 55 years (A) and 65 years (B) for overall survival. Residual lifespan was estimated using the area under the survival curve up to a maximum of 90 years. Comprehensive therapy (simulated) consisted of an ARNI, β blocker, MRA, and SGLT2 inhibitor; conventional therapy (EMPHASIS-HF[6] control group) consisted of an ACE inhibitor or ARB and β blocker. ACE inhibitor=angiotensin-converting enzyme inhibitor. ARB=angiotensin receptor blocker. ARNI=angiotensin receptor–neprilysin inhibitor. MRA=mineralocorticoid receptor antagonist. SGLT2 inhibitor=sodium/glucose cotransporter 2 inhibitor.

Lancet 2020; 396: 121–28

Problem to be Addressed: Good Life

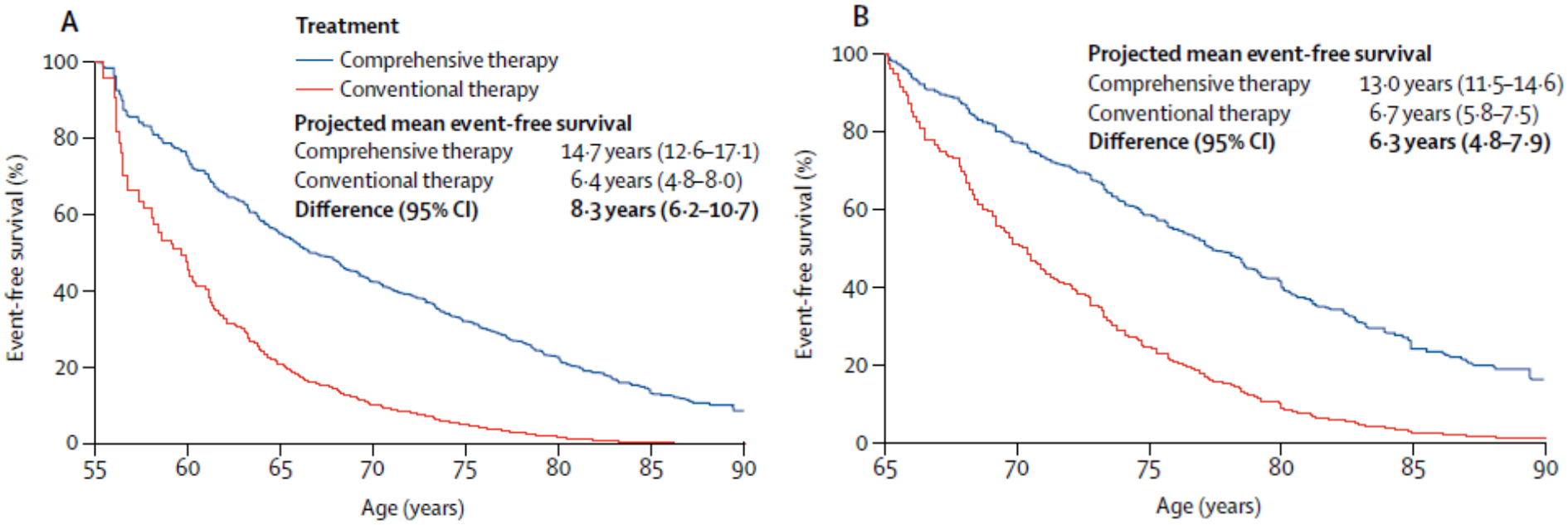


Figure 2: **Event-free survival with comprehensive disease-modifying therapy *vs* conventional therapy**

Kaplan-Meier estimated curves for patients starting at age 55 years (A) and 65 years (B) for primary endpoint event-free survival. Comprehensive therapy (simulated) consisted of an ARNI, β blocker, MRA, and SGLT2 inhibitor; conventional therapy (EMPHASIS-HF[6] control group) consisted of an ACE inhibitor or ARB and β blocker. ACE inhibitor=angiotensin-converting enzyme inhibitor. ARB=angiotensin receptor blocker. ARNI=angiotensin receptor–neprilysin inhibitor. MRA=mineralocorticoid receptor antagonist. SGLT2 inhibitor=sodium/glucose cotransporter 2 inhibitor.

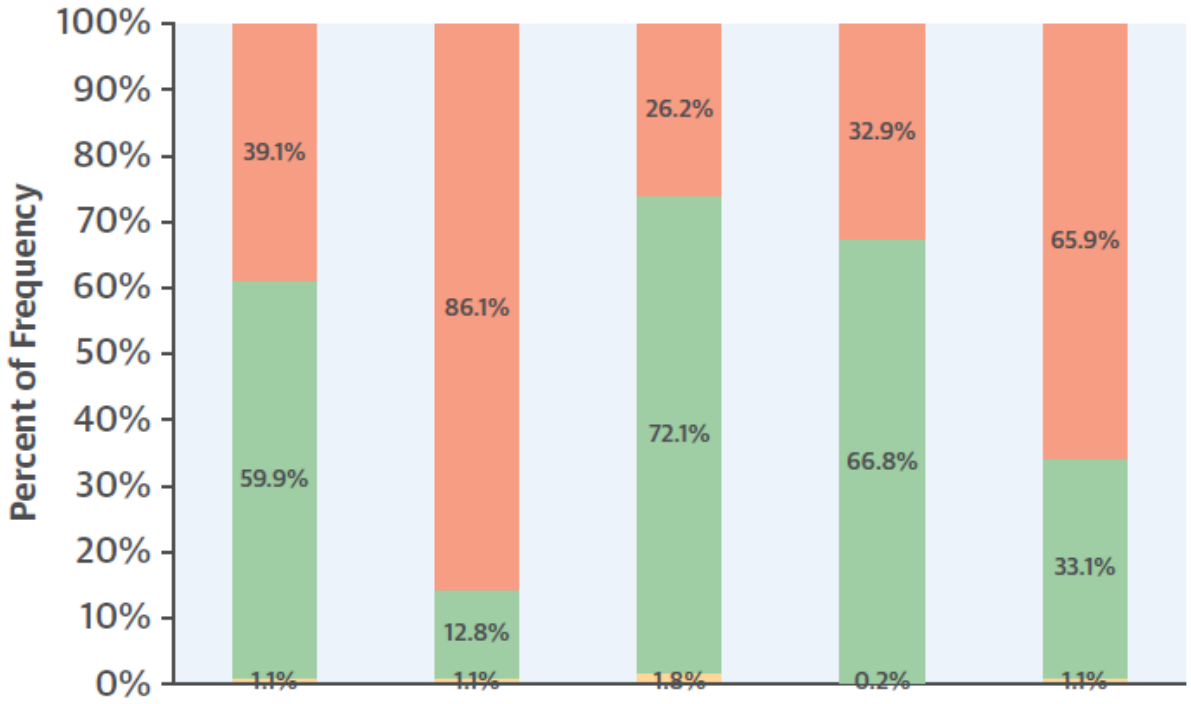
Lancet 2020; 396: 121–28

Problem to be Addressed: Good Life

INOVA

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)

Consensus Management Strategies

INOVA

EXPERT CONSENSUS DECISION PATHWAY

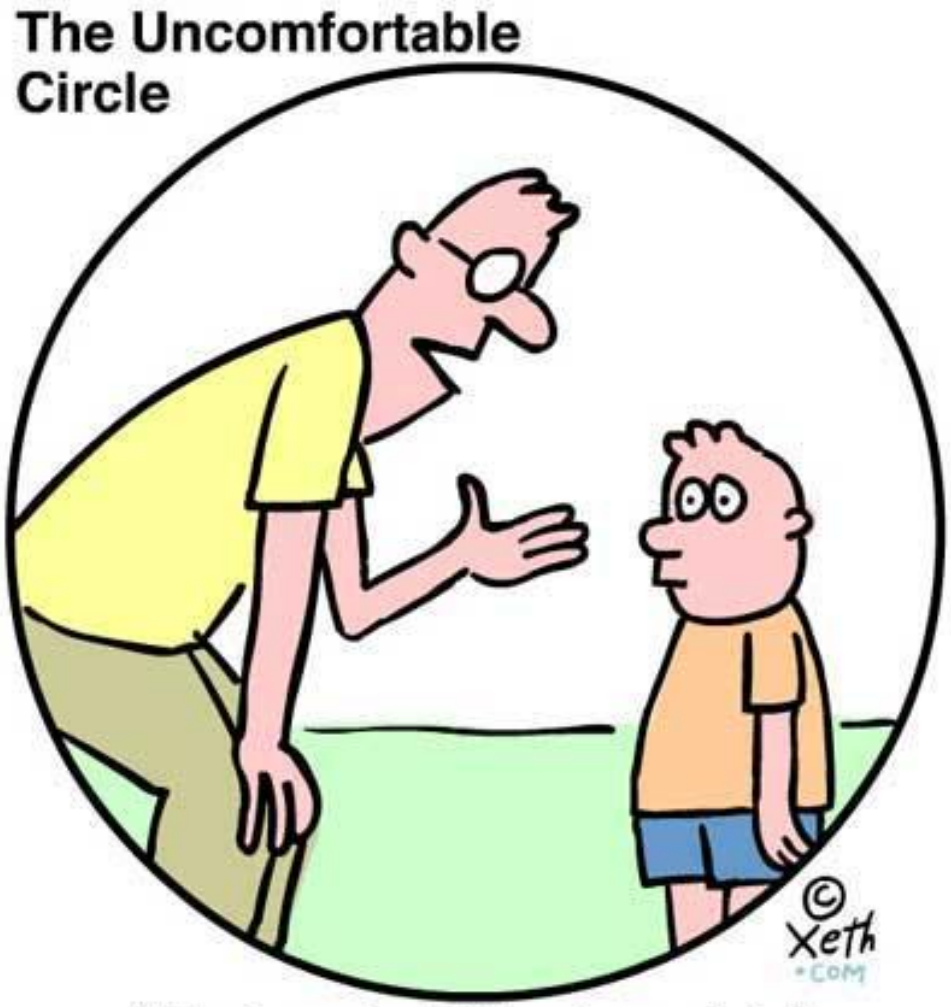
2021 Update to the 2017 ACC Expert Consensus Decision Pathway for Optimization of Heart Failure Treatment: Answers to 10 Pivotal Issues About Heart Failure With Reduced Ejection Fraction

A Report of the American College of Cardiology Solution Set Oversight Committee

J Am Coll Cardiol 2021;77:772-810.

Consensus Management Strategies

INOVA



"The important thing is you tried.
You tried and you failed. And you failed BIG.
That's what's important. You're a big failure
who tried and failed. Big time."

Consensus Management Strategies

INOVA

TABLE 1 Starting and Target Doses of Select GDMT and Novel Therapies for HF (choice and timing of each therapy and in whom they should be added discussed in the text)*

	Starting Dose	Target Dose
Beta-Blockers		
Bisoprolol	1.25 mg once daily	10 mg once daily
Carvedilol	3.125 mg twice daily	25 mg twice daily for weight <85 kg and 50 mg twice daily for weight ≥85 kg
Metoprolol succinate	12.5-25 mg daily	200 mg daily
ARNIs		
Sacubitril/valsartan	24/26 mg-49/51 mg twice daily	97/103 mg twice daily
ACEIs		
Captopril	6.25 mg 3× daily	50 mg 3× daily
Enalapril	2.5 mg twice daily	10-20 mg twice daily
Lisinopril	2.5-5 mg daily	20-40 mg daily
Ramipril	1.25 mg daily	10 mg daily
ARBs		
Candesartan	4-8 mg daily	32 mg daily
Losartan	25-50 mg daily	150 mg daily
Valsartan	40 mg twice daily	160 mg twice daily
Aldosterone antagonists		
Eplerenone	25 mg daily	50 mg daily
Spironolactone	12.5-25 mg daily	25-50 mg daily
SGLT2 inhibitors		
Dapagliflozin	10 mg daily	10 mg daily
Empagliflozin	10 mg daily	10 mg daily

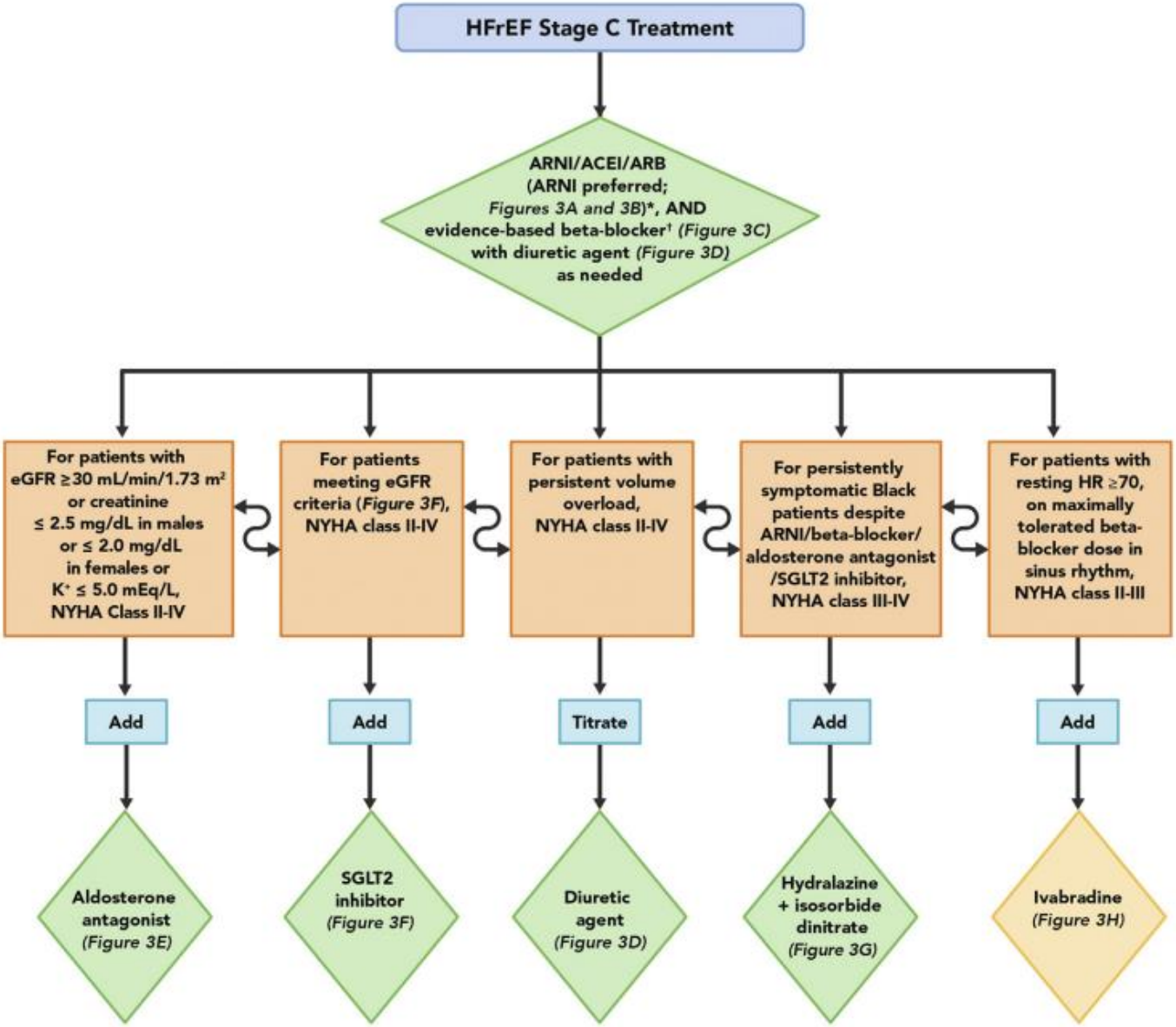
J Am Coll Cardiol 2021;77:772-810.

Niche Medications

Vasodilators		
Hydralazine	25 mg 3× daily	75 mg 3× daily
Isosorbide dinitrate[†]	20 mg 3× daily	40 mg 3× daily
Fixed-dose combination isosorbide dinitrate/hydralazine[‡]	20 mg/37.5 mg (1 tab) 3× daily	2 tabs 3× daily
Ivabradine		
Ivabradine	2.5-5 mg twice daily	Titrate to heart rate 50-60 beats/min. Maximum dose 7.5 mg twice daily

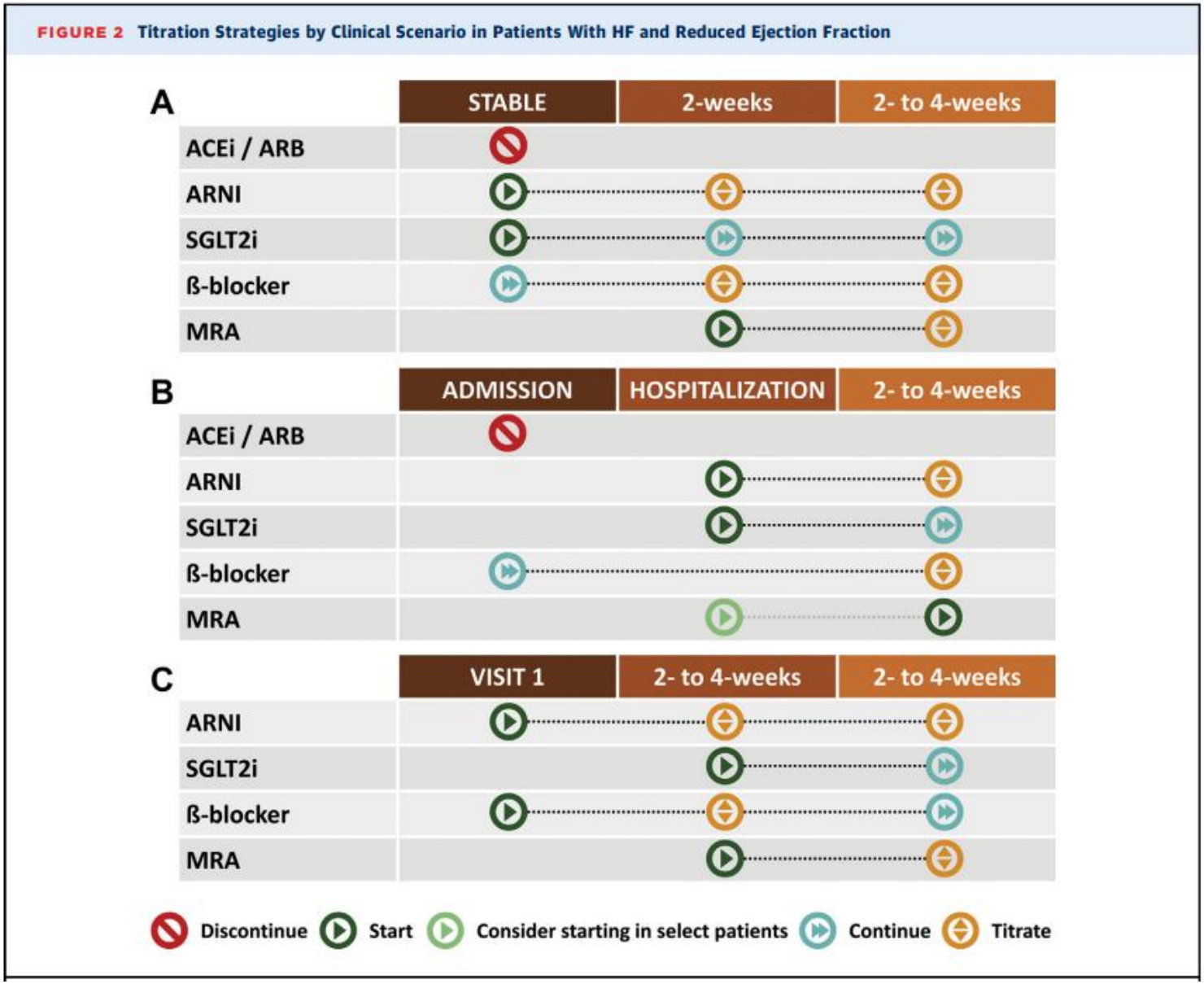
J Am Coll Cardiol 2021;77:772-810.

Niche Medications



J Am Coll Cardiol 2021;77:772-810.

Titration Strategies



(J Am Coll Cardiol Basic Trans Science 2022;7:504–517)

Problem to be Addressed: Survival

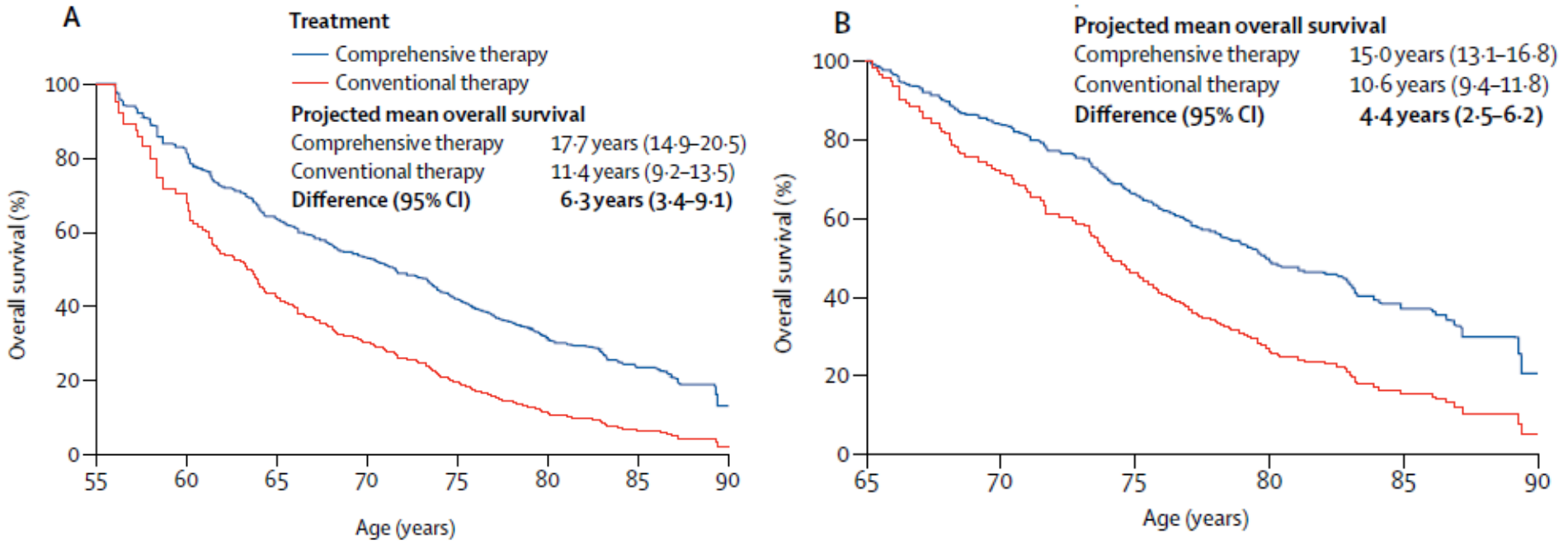


***Figure 3*: Long-term overall survival with comprehensive disease-modifying therapy *vs* conventional therapy**

Kaplan-Meier estimated curves for patients starting at age 55 years (A) and 65 years (B) for overall survival. Residual lifespan was estimated using the area under the survival curve up to a maximum of 90 years. Comprehensive therapy (simulated) consisted of an ARNI, β blocker, MRA, and SGLT2 inhibitor; conventional therapy (EMPHASIS-HF[6] control group) consisted of an ACE inhibitor or ARB and β blocker. ACE inhibitor=angiotensin-converting enzyme inhibitor. ARB=angiotensin receptor blocker. ARNI=angiotensin receptor–neprilysin inhibitor. MRA=mineralocorticoid receptor antagonist. SGLT2 inhibitor=sodium/glucose cotransporter 2 inhibitor.

Lancet 2020; 396: 121–28

EXPERT CONSENSUS DECISION PATHWAY

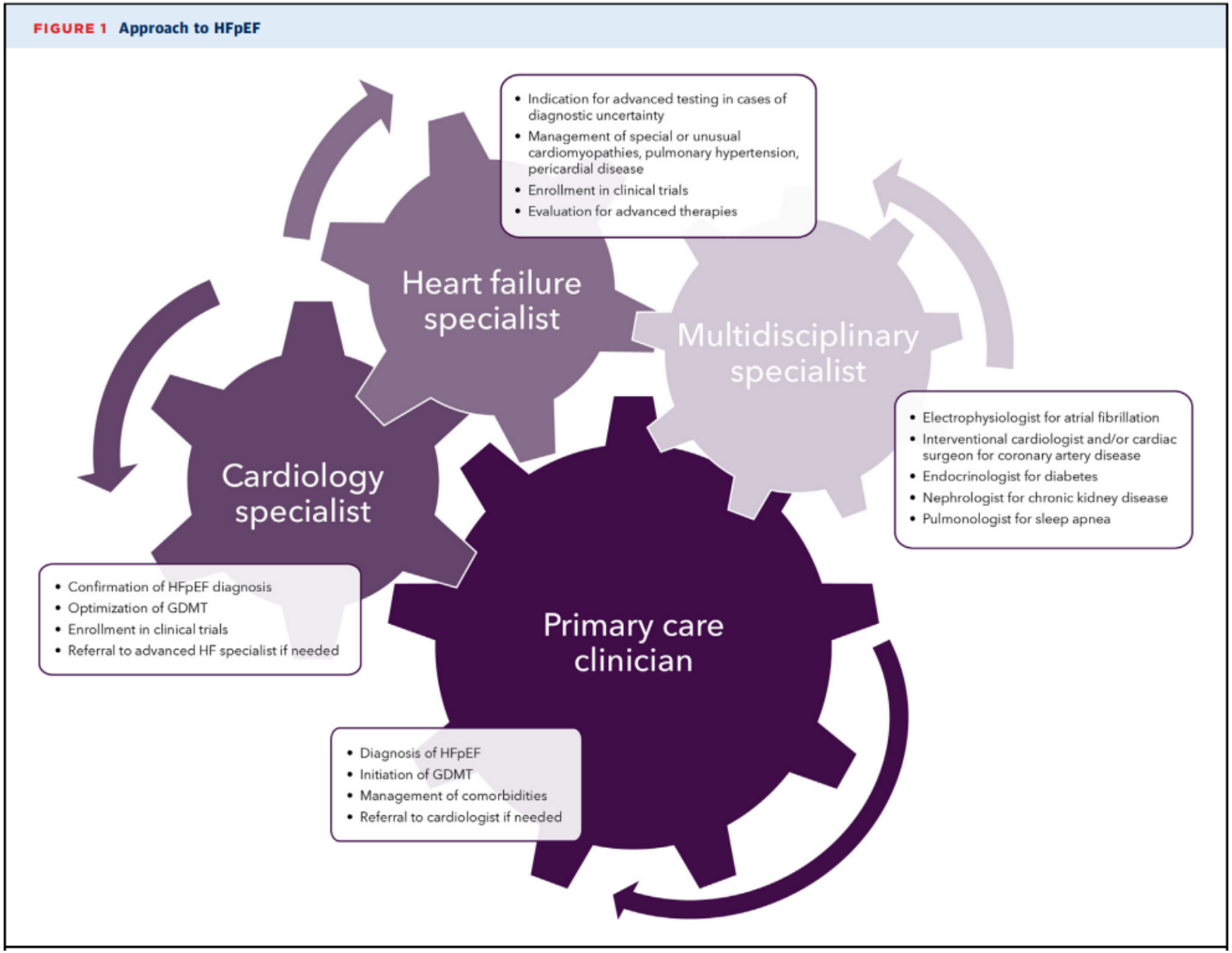
2023 ACC Expert Consensus Decision Pathway on Management of Heart Failure With Preserved Ejection Fraction

A Report of the American College of Cardiology Solution Set Oversight Committee

J Am Coll Cardiol. Published online April 19, 2023.

Consensus Management Strategies

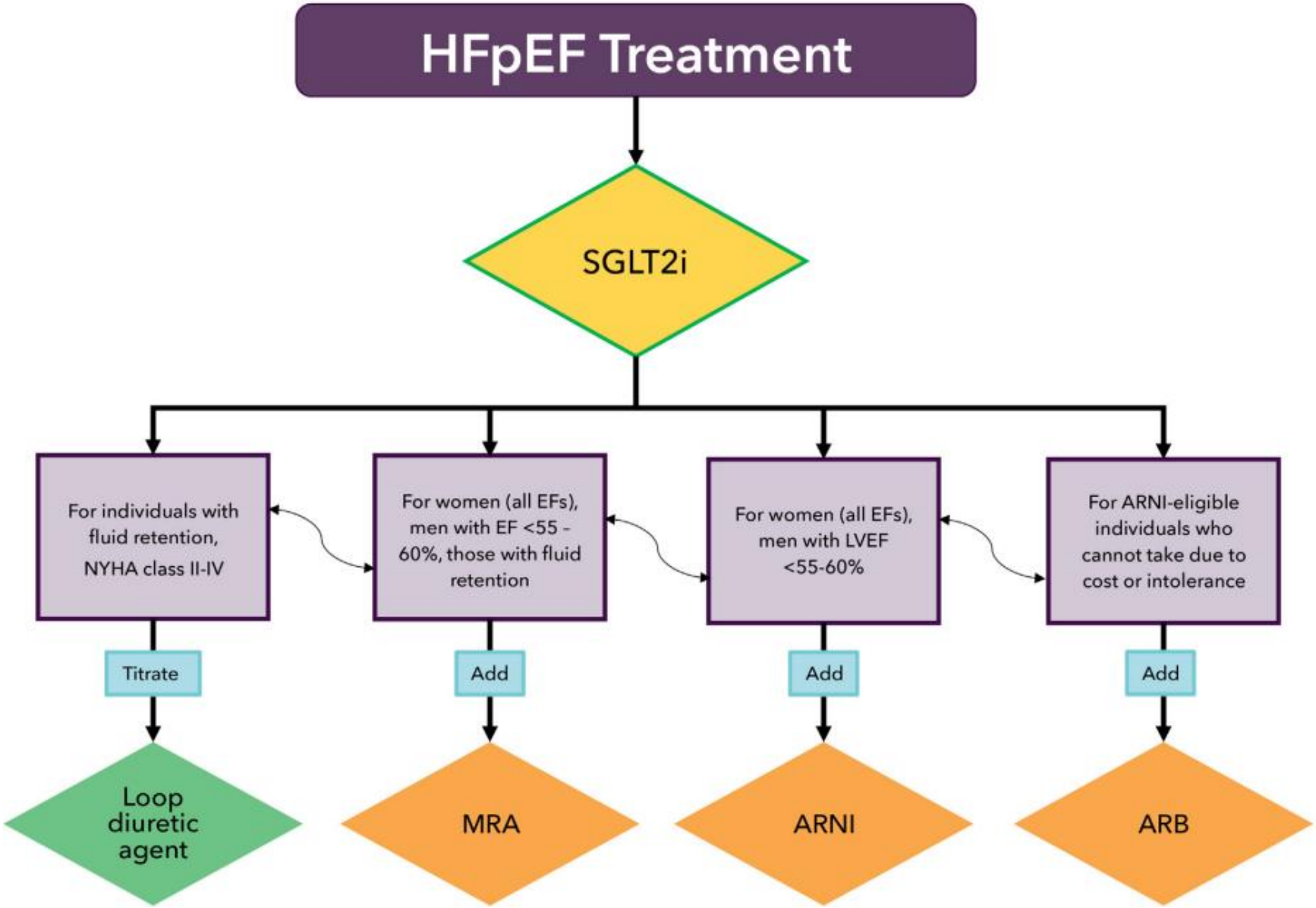
INOVA



J Am Coll Cardiol. Published online April 19, 2023.

Consensus Management Strategies

INOVA



J Am Coll Cardiol. Published online April 19, 2023.

Indications for Heart Failure Referral

INOVA

TABLE 6 Triggers for HF Patient Referral to a Specialist/Program

Clinical Scenario	
	1. New-onset HF (regardless of EF): Refer for evaluation of etiology, guideline-directed evaluation and management of recommended therapies, and assistance in disease management, including consideration of advanced imaging, endomyocardial biopsy, or genetic testing for primary evaluation of new-onset HF
	2. Chronic HF with high-risk features, such as development or persistence of one or more of the following risk factors: ■ Need for chronic intravenous inotropes ■ Persistent NYHA functional class III-IV symptoms of congestion or profound fatigue ■ Systolic blood pressure ≤90 mm Hg or symptomatic hypotension ■ Creatinine ≥1.8 mg/dL or BUN ≥43 mg/dL ■ Onset of atrial fibrillation, ventricular arrhythmias, or repetitive ICD shocks ■ Two or more emergency department visits or hospitalizations for worsening HF in the prior 12 months ■ Inability to tolerate optimally dosed beta-blockers and/or ACEI/ARB/ARNI and/or aldosterone antagonists ■ Clinical deterioration, as indicated by worsening edema, rising biomarkers (BNP, NT-proBNP, others), worsened exercise testing, decompensated hemodynamics, or evidence of progressive remodeling on imaging ■ High mortality risk using a validated risk model for further assessment and consideration of advanced therapies, such as the Seattle Heart Failure Model
	3. Persistently reduced LVEF ≤35% despite GDMT for ≥3 months: refer for consideration of device therapy in those patients without prior placement of ICD or CRT, unless device therapy is contraindicated or inconsistent with overall goals of care
	4. Second opinion needed regarding etiology of HF; for example: ■ Coronary ischemia and the possible value of revascularization ■ Valvular heart disease and the possible value of valve repair ■ Suspected myocarditis ■ Established or suspected specific cardiomyopathies (e.g., hypertrophic cardiomyopathy, arrhythmogenic right ventricular dysplasia, Chagas disease, restrictive cardiomyopathy, cardiac sarcoidosis, amyloid, aortic stenosis)
	5. Annual review needed for patients with established advanced HF in which patients/caregivers and clinicians discuss current and potential therapies for both anticipated and unanticipated events, possible HF disease trajectory and prognosis, patient preferences, and advanced care planning
	6. Assessment of patient for possible participation in a clinical trial

J Am Coll Cardiol 2021;77:772-810.

Indications for Heart Failure Referral

INOVA

TABLE 6 Triggers for HF Patient Referral to a Specialist/Program

Clinical Scenario	
	1. New-onset HF (regardless of EF): Refer for evaluation of etiology, guideline-directed evaluation and management of recommended therapies, and assistance in disease management, including consideration of advanced imaging, endomyocardial biopsy, or genetic testing for primary evaluation of new-onset HF
	2. Chronic HF with high-risk features, such as development or persistence of one or more of the following risk factors: ■ Need for chronic intravenous inotropes ■ Persistent NYHA functional class III-IV symptoms of congestion or profound fatigue ■ Systolic blood pressure ≤90 mm Hg or symptomatic hypotension ■ Creatinine ≥1.8 mg/dL or BUN ≥43 mg/dL ■ Onset of atrial fibrillation, ventricular arrhythmias, or repetitive ICD shocks ■ Two or more emergency department visits or hospitalizations for worsening HF in the prior 12 months ■ Inability to tolerate optimally dosed beta-blockers and/or ACEI/ARB/ARNI and/or aldosterone antagonists ■ Clinical deterioration, as indicated by worsening edema, rising biomarkers (BNP, NT-proBNP, others), worsened exercise testing, decompensated hemodynamics, or evidence of progressive remodeling on imaging ■ High mortality risk using a validated risk model for further assessment and consideration of advanced therapies, such as the Seattle Heart Failure Model
	3. Persistently reduced LVEF ≤35% despite GDMT for ≥3 months: refer for consideration of device therapy in those patients without prior placement of ICD or CRT, unless device therapy is contraindicated or inconsistent with overall goals of care
	4. Second opinion needed regarding etiology of HF; for example: ■ Coronary ischemia and the possible value of revascularization ■ Valvular heart disease and the possible value of valve repair ■ Suspected myocarditis ■ Established or suspected specific cardiomyopathies (e.g., hypertrophic cardiomyopathy, arrhythmogenic right ventricular dysplasia, Chagas disease, restrictive cardiomyopathy, cardiac sarcoidosis, amyloid, aortic stenosis)
	5. Annual review needed for patients with established advanced HF in which patients/caregivers and clinicians discuss current and potential therapies for both anticipated and unanticipated events, possible HF disease trajectory and prognosis, patient preferences, and advanced care planning
	6. Assessment of patient for possible participation in a clinical trial

J Am Coll Cardiol 2021;77:772-810.

Conclusions

- Patients with Heart Failure are at high risk of adverse events including death.
- Heart Failure medical therapy is a cocktail of typically 4 medications that improve **survival**, reduce **hospitalizations**, and improve **quality of life** for patients.
- LVEF is a *continuous* measure. As LVEF increases to 'normal' and above, only the SGLT2i clearly retain effectiveness, but the cutoff to where others have effectiveness is not clear.
- The best initiation and titration strategies for these medications are currently under study.

Thank you!

"Right now I take a blue pill, a purple pill, an orange pill, a white pill, and a yellow pill. I need you to prescribe a green pill to complete my collection."

PROMPT-HF Collaboration

INOVA

PROMPT-HF

PRagmatic Trial Of Messaging to Providers about Treatment of Heart Failure (PROMPT-HF)

HEART FAILURE COLLABORATORY

Digital Health | Regulatory Policy & Implementation
Representative Populations | Research Networks

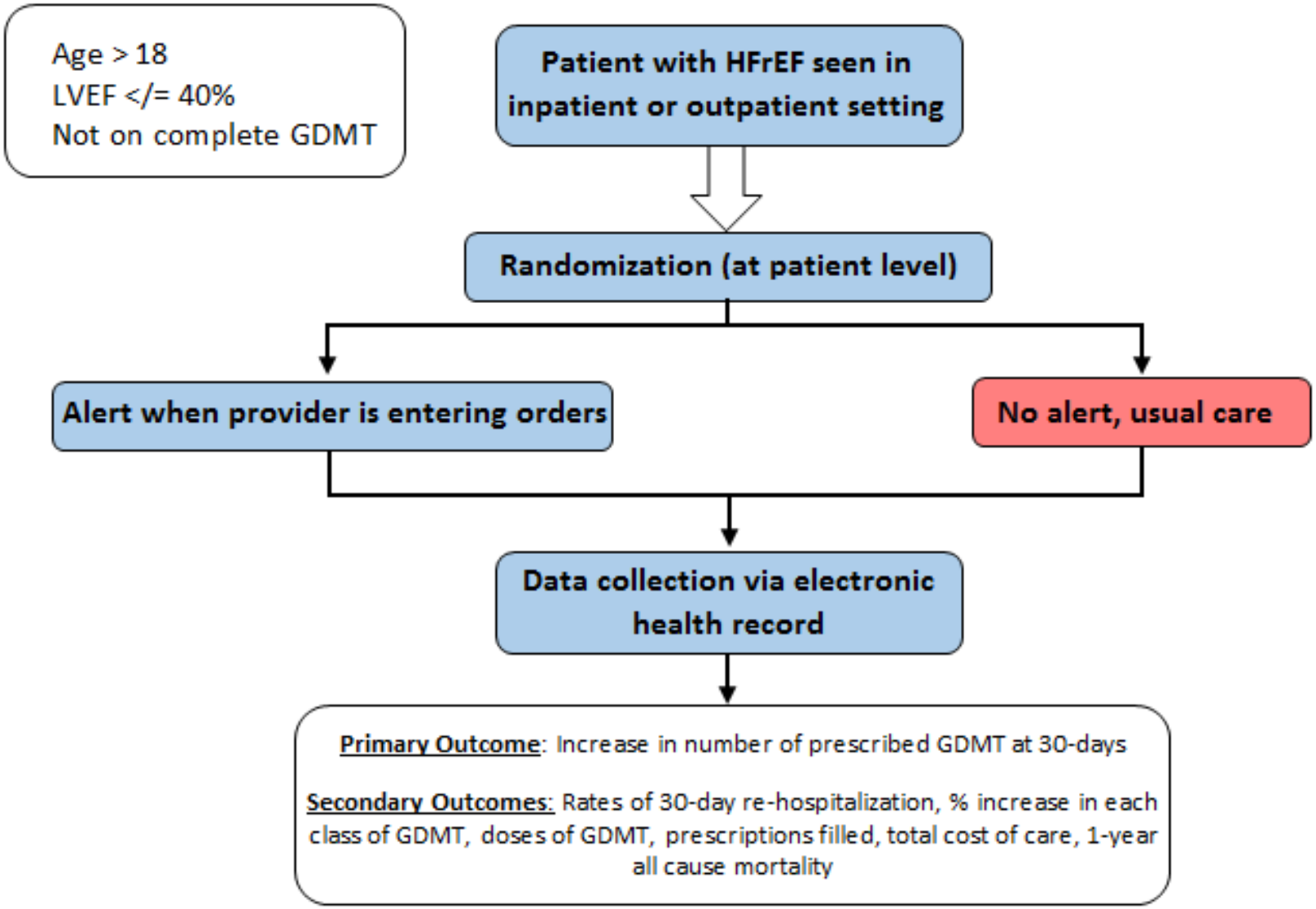
Collaboration: Clinical & Research Personnel

INOVA

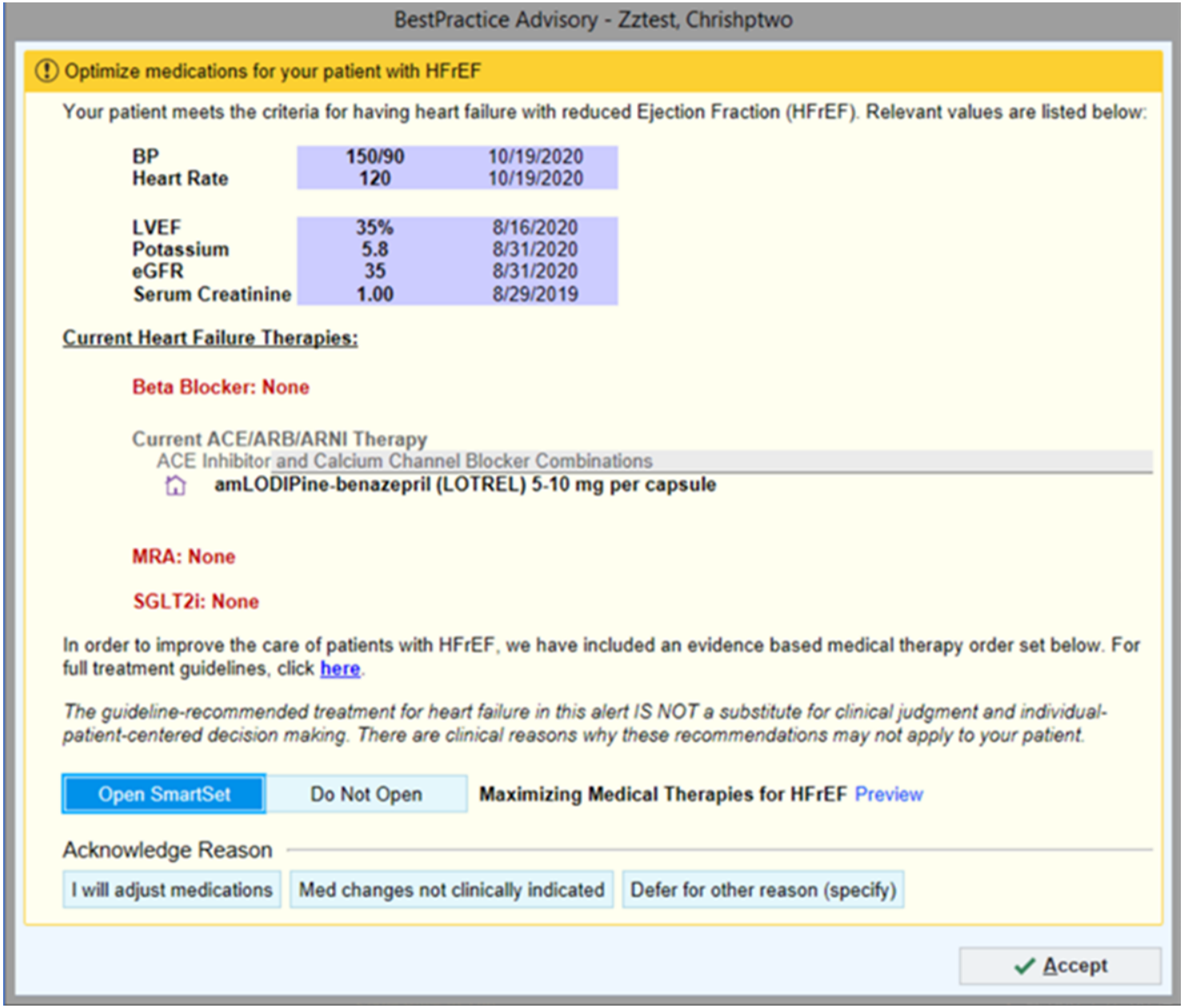
- **Mitchell Psotka, MD, PhD** (HF Section Chief)
- **Matt Dimond** (IHVI Research, HF Collaboratory)

- **Tina Slottow, MD** (Medical Director, Cardiovascular Information Systems)
- **Stu Sheifer, MD** (VA Heart cardiologist)
- **Christine Czajkowski** (Epic Applications Manager)
- **Christa Callahan** (Epic Sr. Analyst)
- **Phil Stiff** (VP, Information Technology)

PROMPT-HF at Inova



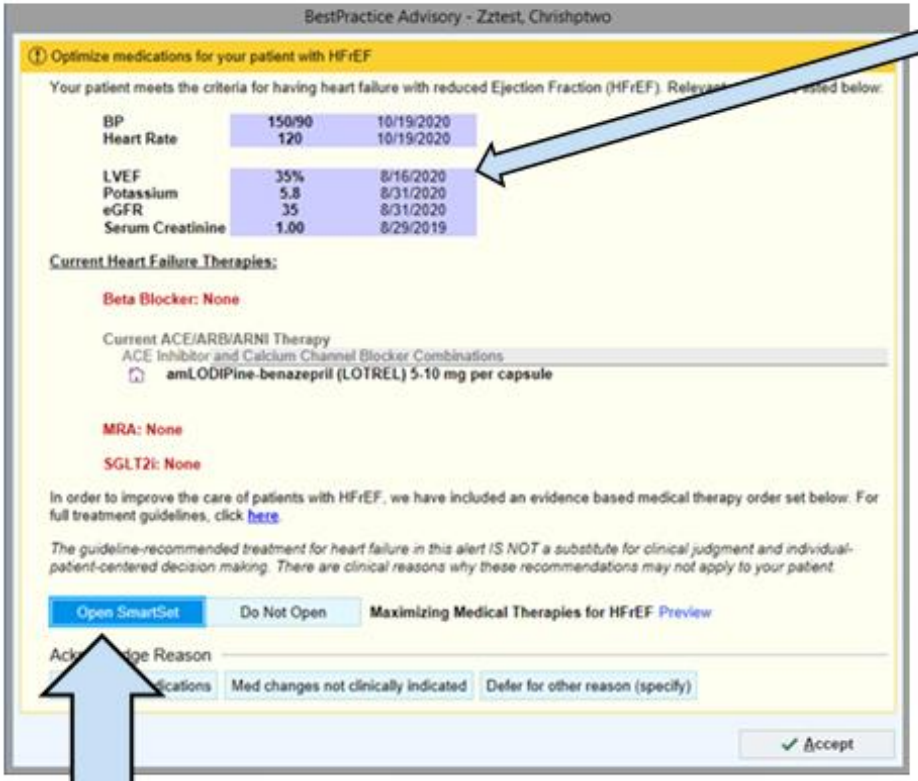
PROMPT-HF Alerts

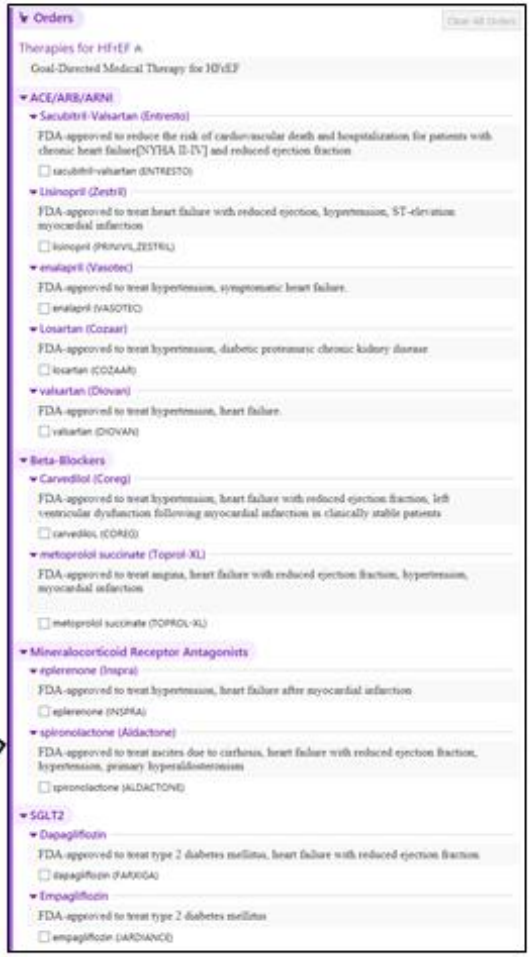


PROMPT-HF Alerts and Orders

INOVA

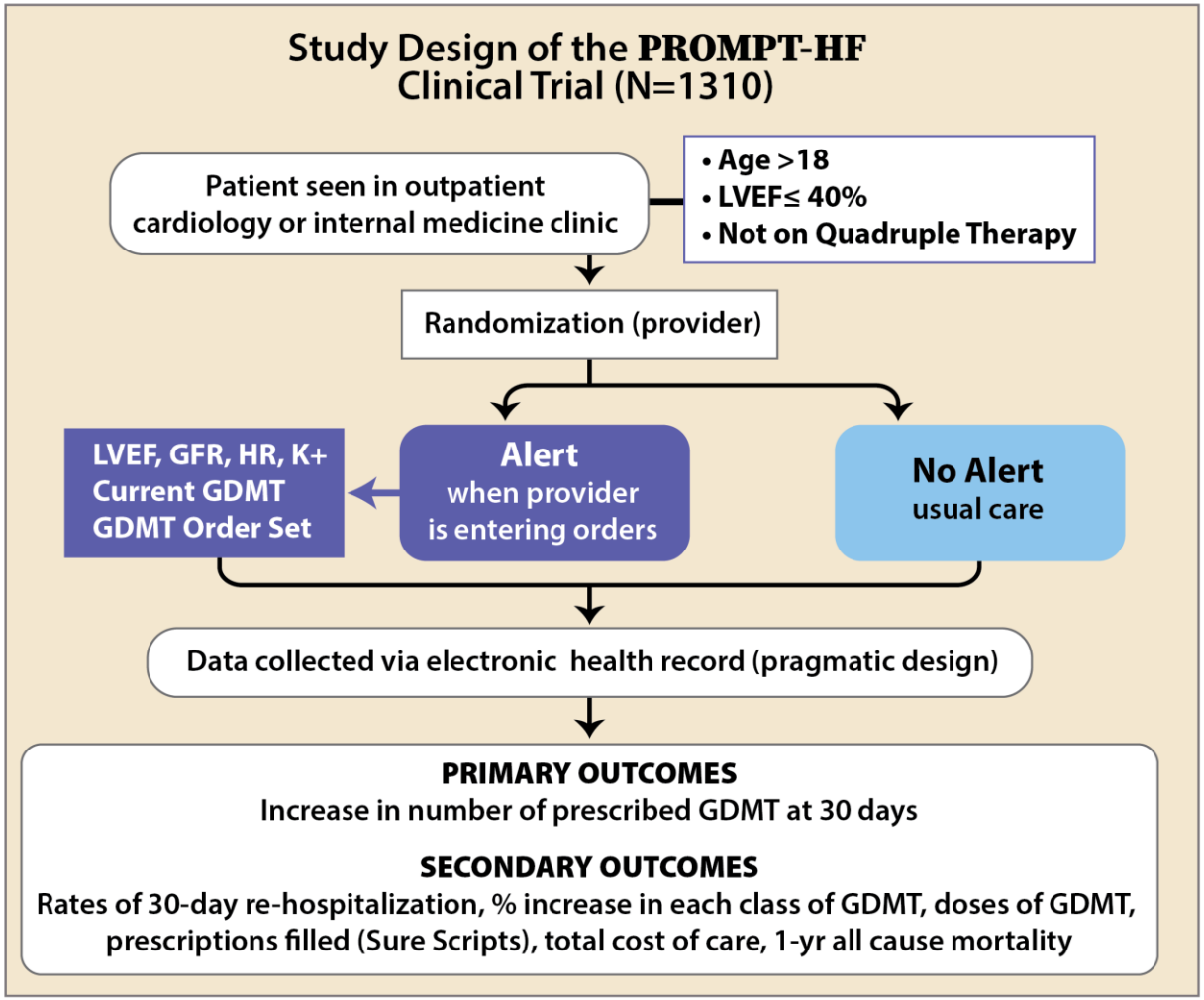
Patient Information





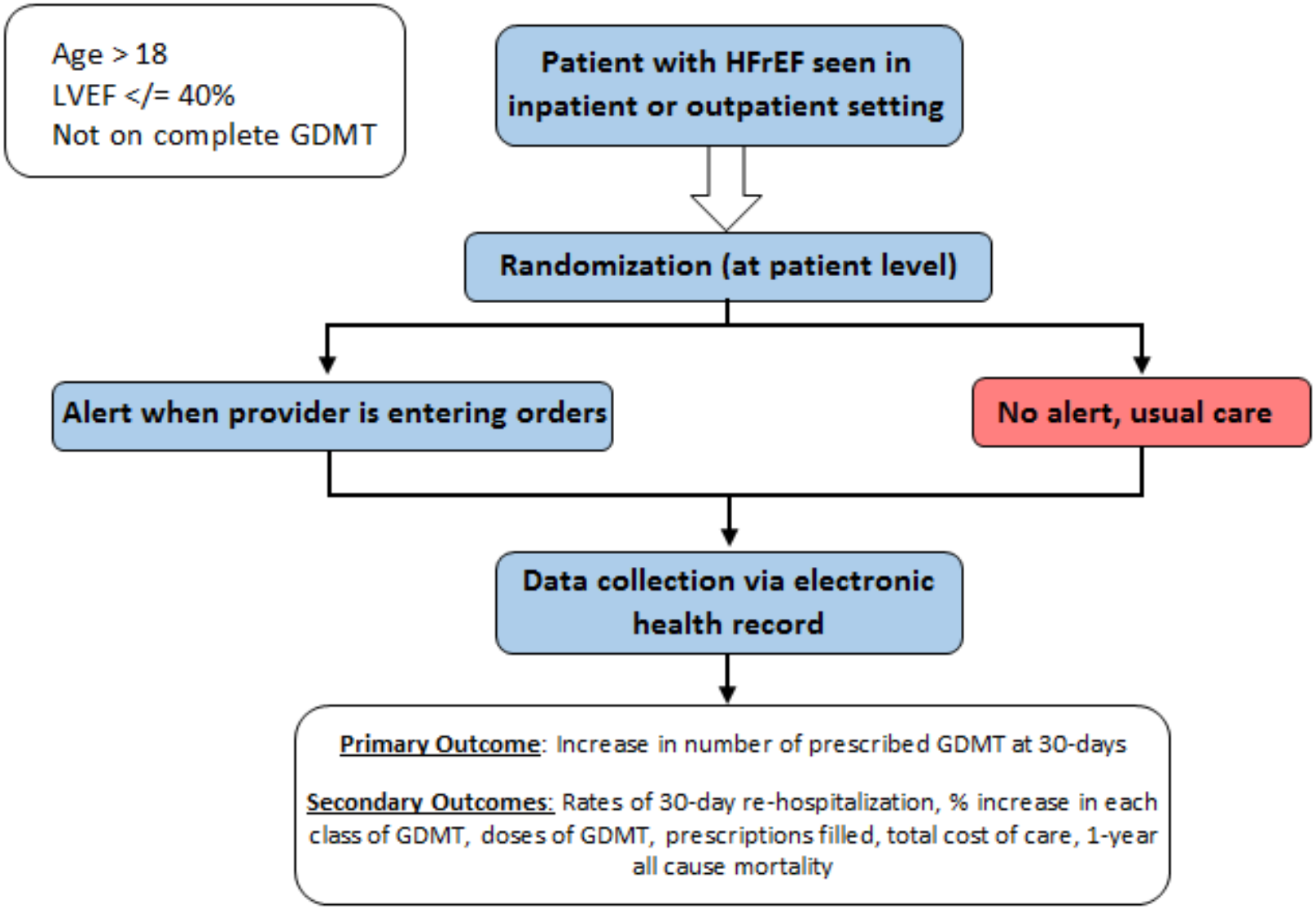
Informational
During Order Entry
Does NOT mandate action

Study Design



Lama Ghazi et al. AHJ 2021; 9:409-419

PROMPT-HF at Inova



Goals of Implementation at Inova

- Provide excellent guideline-based standard of care
- Establish ourselves as leaders in heart failure care by generating evidence to establish this methodology

Merging the *Care Path* framework with PROMPT-HF

- Implementation of heart failure medical therapy (GDMT) through the CarePath can be achieved using the previously tested PROMPT-HF framework
- PROMPT-HF Inova best practice alerts (BPAs) will be the pharmacological therapy component within the more extensive Care Path
- The randomized controlled trial portion of the CarePath implementation will assess the utility of the intervention and facilitate iteration