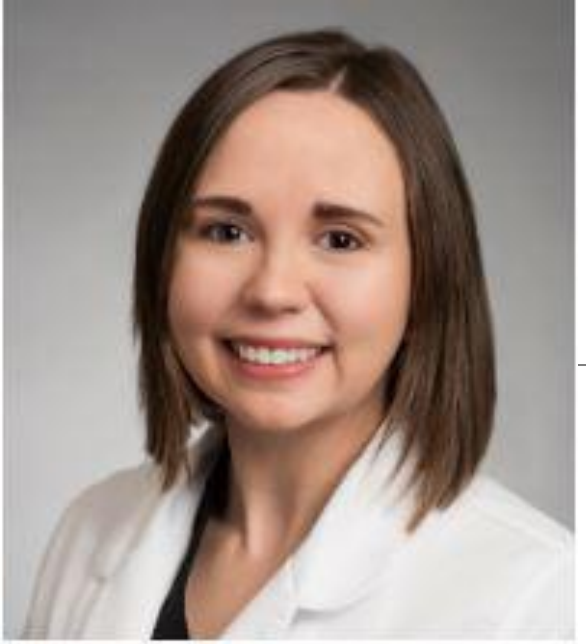
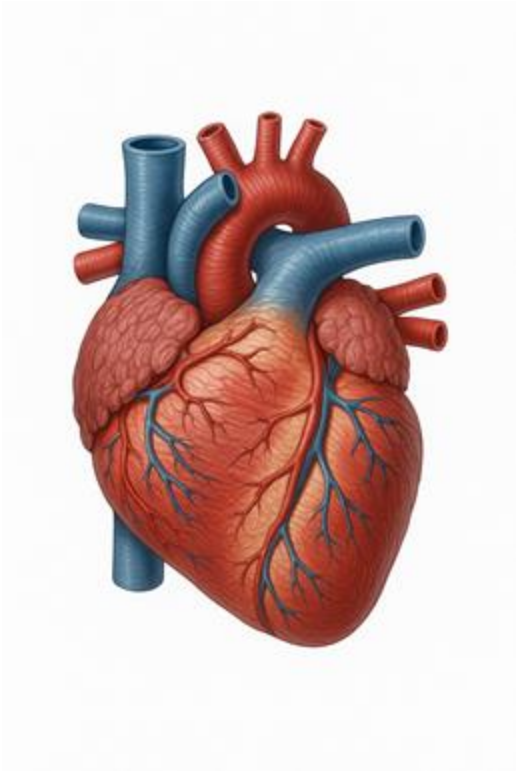


Laurie graduated with a Bachelor of Science in Nursing from The University of Alabama. She earned her Master of Science in Nursing as a Family Nurse Practitioner from the University of South Alabama and later completed a Post-Master's Certificate for her Adult-Gerontology Acute Care Nurse Practitioner at Texas Woman's University. She has practiced as a cardiology nurse practitioner at Memorial Hermann the Woodlands for the past eight years, providing comprehensive care to patients with a wide range of cardiovascular conditions including heart failure and collaborating closely with multidisciplinary teams to optimize patient outcomes. Her role includes managing both acute and chronic cardiac illnesses, guiding patients through treatment plans, and supporting cardiovascular health through education and preventive care.



# Guideline-Directed… or Misguided? Pearls and Pitfalls in GDMT for Systolic Heart Failure

LAURIE WEEKS, MSN, APRN, AGACNP-BC, FNP-C

# Disclosures

I have no financial relationships or conflicts of interest to disclose in relation to this presentation.

# Objectives

1. Review the foundational pharmacologic components of GDMT for HFrEF
2. Apply evidence-based strategies to to optimize therapy across diverse patient populations
3. Identify common pitfalls and clinical missteps in prescribing or titrating GDMT
4. Interpret case-based examples highlighting real-world complexities

# What Is HFrEF and Why Does It Progress?

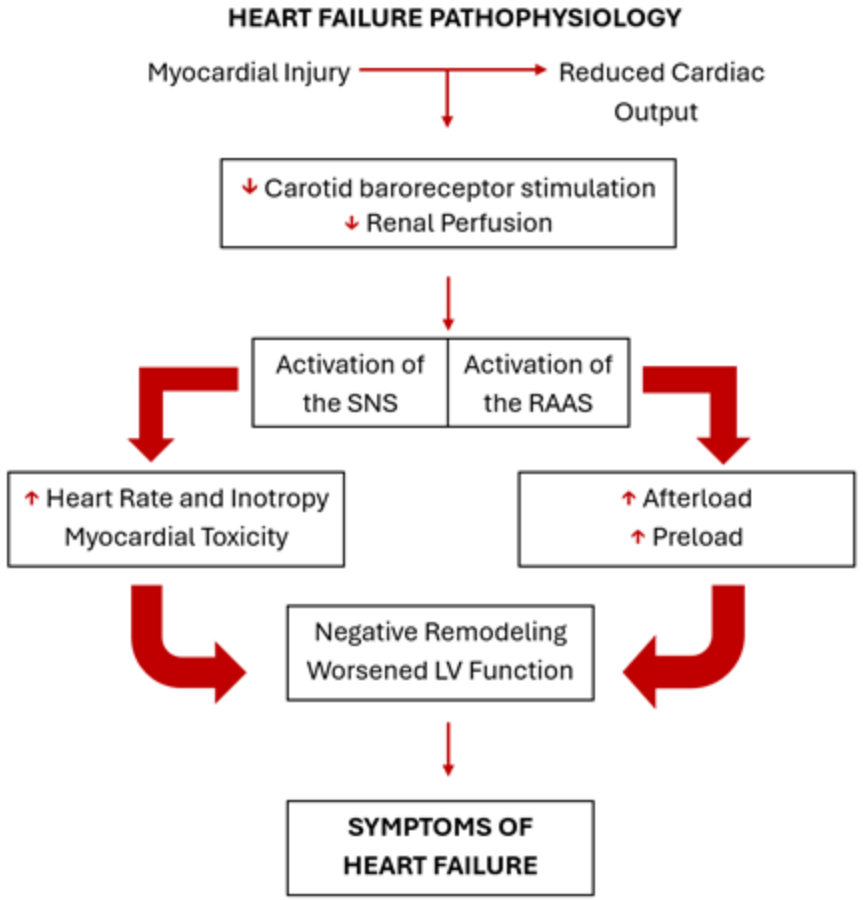
HFrEF = Heart failure with reduced ejection fraction (EF ≤ 40%)

Caused by structural or functional damage to the myocardium

Neurohormonal activation (RAAS, SNS) leads to:

- Vasoconstriction, sodium retention, and remodeling
- Worsening systolic dysfunction over time

Targeting these pathways = the foundation of GDMT



| Drug Class | Examples | Target | Key Benefit |
|---|---|---|---|
| **ARNI** (preferred over ACEi/ARB) | Sacubitril/valsartan | RAAS inhibition + natriuretic peptide | ↓ Mortality, ↓ Hosp. (PARADIGM-HF) |
| **Beta-blockers** | Metoprolol succinate, Carvedilol, Bisoprolol | Sympathetic overactivation | ↓ Mortality, improves EF (MERIT-HF) |
| **MRA** | Spironolactone, Eplerenone | Aldosterone blockade | ↓ Mortality (RALES, EMPHASIS-HF) |
| **SGLT2i** | Dapagliflozin, Empagliflozin | Osmotic diuresis, metabolic modulation | ↓ HF hospitalization, mortality (DAPA-HF, EMPEROR-Reduced) |

# The 4 Pillars of Guideline-Directed Medical Therapy

# Inhibiting the RAAS: ARNI Preferred, ACEi/ARB Alternatives

**ARNI (sacubitril/valsartan):**

First-line unless contraindicated

Superior to enalapril in PARADIGM-HF: ↓ CV death & HF hospitalization by 20%

Requires 36-hour washout if switching from ACEi

Starting dose depends on prior ACEI/ARB use:

- ≤10 mg enalapril or ≤160 mg valsartan: 24/26 mg BID
- 10 mg enalapril or >160 mg valsartan: 49/51 mg BID

Titration: 1–2 weeks

- If tolerated, increase toward target: 97/103 mg BID
- Monitor BP, electrolytes, kidney function

**ACEi/ARB (if ARNI not tolerated):**

Still reduce mortality/morbidity (SOLVD, CHARM)

Caution with renal function, hyperkalemia, hypotension

**Pitfalls:**

- Not switching from ACEi to ARNI due to inertia
- Avoiding ARNI for stable patients “doing well enough”
- Withholding due to mild creatinine bump or low-normal BP

# Beta-Blockers: Improving EF and Survival by Countering SNS Overdrive

**Mechanism:**

Block sympathetic nervous system (SNS) overactivation

↓ HR, ↓ myocardial oxygen demand, ↑ LV filling time

Allow reverse remodeling of LV

**MERIT-HF (metoprolol succinate)**, **COPERNICUS (carvedilol)**, **CIBIS-II (bisoprolol)**

↓ Mortality ~35%, ↑ EF by 5–10%

**Use:**

Metoprolol succinate: 12.5–25 mg daily → target 200 mg daily

Carvedilol: 3.125 mg BID → target 25 mg BID for weight <85 kg and 50 mg BID for weight > 85 kg

Bisoprolol: 1.25 mg daily → target 10 mg daily

**Pitfalls:**

Withholding due to low EF (they work *because* EF is low)

Not titrating beyond starter dose

Avoiding in mild hypotension or well-tolerated bradycardia

# Aldosterone Antagonists: Small Pill, Big Survival Benefit

**Mechanism:**

Block **aldosterone**, reducing sodium retention, fibrosis, and ventricular remodeling

**Evidence:**

**RALES** (spironolactone) and **EMPHASIS-HF** (eplerenone)

↓ Mortality and HF hospitalizations by 30–35%

**Use:**

Indicated for NYHA II–IV HFrEF with **eGFR >30** and **K+ <5.0**

Spironolactone: starting 12.5-25 mg daily→ target 25- 50 mg daily

Eplerenone: 25 mg daily → 50 mg daily

**Pitfalls:**

Avoided due to fear of **hyperkalemia** or **mild CKD**

Infrequent **lab monitoring** after initiation

Confusion with its role—often seen as optional, but it's **Class I** recommendation

# SGLT2 Inhibitors: From Diabetes Drugs to Heart Failure Game-Changers

**Mechanism:**

Inhibit sodium-glucose cotransporter-2 in proximal tubule

Promote **natriuresis**, **osmotic diuresis**, reduce preload/afterload

Improve **cardiac energy metabolism**, ↓ inflammation

**Evidence:**

**DAPA-HF** (dapagliflozin), **EMPEROR-Reduced** (empagliflozin)

↓ CV death or HF hospitalization by ~25–30%

Benefits seen **regardless of diabetes status**

**Use:**

Dapagliflozin 10 mg daily

Empagliflozin 10 mg daily

No need to titrate

**Pitfalls:**

Misperceived as only for diabetes

Not started inpatient during stabilization

Concerns about **eGFR**, though benefits persist even in CKD

# Additional Therapies in HFrEF: When, Why, and For Whom?

**Ivabradine**

For patients with HR ≥70 bpm in sinus rhythm despite max BB

SHIFT trial: ↓ HF hospitalizations

Use if unable to tolerate BB titration or HR remains elevated

Dose: starting 2.5-5 mg BID → Titrate to heart rate 50-60 beats/min. Maximum dose 7.5 mg BID

**Hydralazine + Isosorbide Dinitrate**

For persistently symptomatic African-American patients despite ARNI/BB/MRA/SGLT inhibitors with NYHA III–IV HFrEF

Class IIa for others who can't tolerate ACEi/ARB/ARNI

A-HeFT trial: ↓ mortality in Black patients

Often underprescribed

**Digoxin**

lacks contemporary data

Considered for rate control in AF with low blood pressure

Watch for toxicity in renal dysfunction or drug interactions

**Loop Diuretics (furosemide, torsemide)**

Symptom relief only—no mortality benefit

Still essential for volume management

Adjust based on daily weights, symptoms, and renal function

# Systolic HF: Still Under-Treated Despite Strong Evidence

HFrEF = EF ≤ 40%; progressive neurohormonal dysregulation

GDMT improves mortality, morbidity, and quality of life

Real-world uptake remains poor—especially full regimen and dosing

Under-treatment contributes to high readmission and mortality rates

# GDMT Use in Practice: A Stark Reality Check

| Drug Class | Any Use (%) | Target Dose (%) |
|---|---|---|
| ACEi/ARB/ARNI | 65–83% | ~45% |
| Beta-blocker | 64–81% | ~21% |
| MRA | 24–41% | ~78% (if prescribed) |
| SGLT2i | 3–44% | High if started |
| All 4 Classes | <10% | <2% |

# Case-Based Learning: Putting GDMT Into Practice

- Realistic patient cases that highlight key GDMT challenges
- What would you do? Applying clinical reasoning to uncover hidden pitfalls
- Each case reveals a common pitfall—and a better approach

# Case 1: Low Blood Pressure, Lower Expectations?

**Patient Snapshot:**

68-year-old male with HFrEF (EF 30%) admitted for volume overload

Currently on furosemide and metoprolol succinate 25 mg daily

BP: 98/58 mmHg, HR: 74 bpm, asymptomatic, euvolemic on exam

Creatinine: 1.3, K+: 4.3, Na+: 136

Discharge plan includes furosemide and continuing low-dose BB only

**Pearls**

**Low blood pressure is not a contraindication in asymptomatic, euvolemic, stable patients**

It's about perfusion, not just the number

Discontinue non-GDMT BP meds contributing to low BP

SGLT2i and MRA often well tolerated even at lower pressures

ANRI use is not prohibitive but cautioned

**Pitfalls**

"He's too hypotensive to tolerate any more meds."

No MRA, ARNI/ACEi/ARB or SGLT2i added

Missed opportunity to optimize foundational therapy

# Case 2: Started... But Never Finished

**Patient Snapshot:**

74-year-old female with chronic HFrEF (EF 35%)

On carvedilol 3.125 mg BID for sacubitril/valsartan 24/26 mg BID, and spironolactone 12.5 mg daily 6 months

On empagliflozin 10 mg , furosemide 40 mg daily

No hospitalizations in past year, NYHA Class II symptoms

BP: 115/64 mmHg, HR: 68 bpm, stable labs

No changes made at follow-up visit due to “stable status”

🟢 **Pearl:**

**Initiation is not optimization**

Target doses all GDMT

Evidence of improved mortality and reverse remodeling with higher doses

Vital signs stable—room to titrate cautiously

Monitor HR, BP, symptoms—don’t stall on clinical inertia

🔴 **Pitfall:**

“She’s already on the 4 pillars—she’s doing well.”

But still on starter dose, never titrated

No effort made to reach target or maximally tolerated dose

# Case 3: Overcorrecting the Labs, Undermining the Patient

**Patient Snapshot:**

65-year-old male with HFrEF (EF 28%)

On bisprolol 10 mg daily, Recently started on sacubitril/valsartan 24/26 mg BID and spironolactone 25 mg daily

Baseline creatinine: 1.1 → now 1.4

Potassium increased from 4.2 to 5.0

BP: 109/60 mmHg, euvolemic

PCP discontinues both agents after lab review

**Pearls**

**Mild increases in creatinine or potassium are expected, not a reason to panic**

ANRI and MRA may cause a transient bump—often stabilizes

Guidelines accept creatinine rise up to 30% from baseline

Monitor potassium and renal function; adjust diuretics and remove NSAIDs first.

**Pitfalls**

**Panic and discontinue**

“His kidney numbers are rising—better stop those meds.”

Both GDMT agents discontinued despite expected mild lab changes

Lost mortality and remodeling benefit

# Case 4: Overlooking the New Kid on the Block

**Patient Snapshot:**

72-year-old female with HFrEF (EF 32%), NYHA Class II

No history of diabetes

Meds: carvedilol 25 mg BID, sacubitril/valsartan 49/51 mg daily, spironolactone 25 mg daily

Volume status stable; creatinine: 1.1; eGFR: 48, K+ 4.4

Seen in follow-up, but no SGLT2i discussed or prescribed

Provider comment: “She doesn’t have diabetes.”

**Pearls**

**DAPA-HF and EMPEROR-Reduced showed strong benefit in patients with or without diabetes**

↓ HF hospitalization and CV death by ~25–30%

Well-tolerated, no titration needed

Can be started if eGFR ≥20–25 (check product-specific cutoffs)

Adds renal protection and modest BP reduction

**Pitfalls**

“SGLT2 inhibitors are only for diabetics.”

Missed opportunity to initiate proven therapy with CV and renal benefit

Reinforces old paradigm, delays uptake of new evidence

# Case 5: Stable... but Stalled

**Patient Snapshot:**

60-year-old male with longstanding HFrEF (EF 35%)

On metoprolol succinate 50 mg, lisinopril 20 mg, furosemide 40 mg

No MRA, no ARNI, no SGLT2i

Vitals: BP 118/66, HR 72, euvolemic

Symptoms: mild exertional fatigue, NYHA Class II

Provider notes: “Doing well—no changes today follow up 3 months”

🟢 **Pearls**

**Stable is not optimized**

In HFrEF, symptom control isn’t enough — prioritize full GDMT: target-dose beta-blocker, MRA, ARNI over ACEi, and SGLT2i.

Every visit should include GDMT reassessment and titration plan

🔴 **Pitfalls**

**Treating symptoms but not disease**

“He’s stable—let’s not rock the boat.”

No titration or medication optimization

No plan for up-titration or GDMT addition

Inertia leads to chronic under-treatment

# Titration Strategy:

All 4 pillars can be initiated in euvolemic, stable patients

Prioritize ARNI, beta-blocker, MRA, SGLT2i early—even inpatient

Titrate every 1–2 weeks if tolerated

Monitor BP, HR, Cr, $K^+$, volume status

De-escalate non-GDMT agents if needed to tolerate core meds

# *Tailoring GDMT: One Size Doesn't Fit All*

- **Older adults**: Tolerate lower BP—monitor perfusion, not just numbers
- **CKD**: ACEi/ARNI, MRA often safe with Cr ≤2.5–3.0 and $K^+$ <5.0
- **Black patients**: Consider hydralazine/ISDN combo
- **Low BP**: May need to de-prescribe non-essential antihypertensives
- **Women**: Under-prescribed GDMT despite equal or greater benefit

# Clinical Pearls: What We Do Right

Initiate GDMT early—even inpatient

Titrate every 1–2 weeks if tolerated

Don’t undertreat due to low BP or mild kidney dysfunction

SGLT2i = heart failure drugs, not just diabetes drugs

Always reassess and re-optimize

# Common Pitfalls: What Holds Us Back

Clinical inertia: “He’s stable” ≠ optimized

Fear of hypotension or renal bump

Failure to titrate

Mislabeling meds (SGLT2i = DM only)

Delaying for “next visit”

# Final Thoughts:

# What I Hope You'll Remember

- GDMT saves lives—but only if implemented fully
- Every visit is a chance to optimize therapy
- Use labs and vitals to guide, not to avoid
- Stay current—evidence evolves, but principles remain
- Small decisions = big impact

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