Timing of In-Hospital GDMT Initiation

When to Initiate Each Component

SGLT2 Inhibitors
- Start within 24-48 hours of admission
- Safe even during active diuresis
- No titration needed - fixed dose

ARNI/ACEi/ARB
- Start once hemodynamically stable
- SBP ≥100 mmHg recommended
- 36-hr ACEi washout for ARNI switch

Beta-Blockers
- Wait until euvolemic, off IV inotropes
- Can continue home dose if stable
- Do NOT uptitrate during acute phase

MRAs
- Start when K+ <5.0 and eGFR >30
- Safe early with lab monitoring

Key Principle: Don't Wait

STRONG-HF: Rapid initiation at 50% target dose before discharge with close follow-up reduced 180-day HF readmission/death by 34%

Hold/Delay GDMT If:

- Cardiogenic shock or IV inotropes
- SBP <90 mmHg (except SGLT2i: <90)
- Acute kidney injury with Cr >2× baseline
- K+ >5.5 mEq/L (for MRA/ACEi/ARB)
- Symptomatic bradycardia (for BB)
- Active decompensation (for BB titration)

Mebazaa A, et al. Lancet 2019;393:61-73. Velazquez EJ, et al. N Engl J Med 2019;380:539-548.

Timing of In-Hospital GDMT Initiation

When to Initiate Each Component

1. SGLT2 Inhibitors

- Start within 24–48 hours of admission — safe during active diuresis
- Fixed dose, no titration: Dapagliflozin 10 mg or Empagliflozin 10 mg daily
- Continue regardless of diabetes status; hold only if eGFR <20 or DKA
- DAPA-HF: 26% ↓ CV death/HF hosp; NNT=21 (HR 0.74, p<0.001)

2. ARNI / ACEi / ARB

- Initiate once hemodynamically stable — SBP ≥100 mmHg
- Sacubitril/valsartan preferred: start 24/26 mg BID, target 97/103 mg BID
- Require 36-hr ACEi washout before ARNI (no washout from ARB)
- PIONEER-HF: safe in-hospital initiation, greater NT-proBNP reduction

3. Beta-Blockers

- Wait until euvolemic state confirmed — no resting dyspnea or IV inotropes
- Continue existing home dose; do NOT uptitrate during acute decompensation
- Carvedilol, Metoprolol succinate, or Bisoprolol — target HR 50–70 bpm
- Double dose every 2 weeks as tolerated; verify hemodynamic stability first

4. MRAs (Spironolactone / Eplerenone)

- Start when K+ <5.0 mEq/L and eGFR >30 mL/min/1.73m²
- Spironolactone 25 mg daily; switch to Eplerenone for gynecomastia
- Recheck K+ and creatinine within 1 week of initiation
- RALES: 30% mortality reduction; EMPHASIS-HF: 37% ↓ HF hospitalization

Hold / Delay GDMT If:

- Cardiogenic shock or requiring IV inotropes for perfusion
- SBP <90 mmHg (all agents); SGLT2i if SBP <80 mmHg
- Acute kidney injury: Cr >2× baseline or rising rapidly
- K+ >5.5 mEq/L (for MRA, ACEi, ARB, ARNI — hold and recheck)
- Symptomatic bradycardia or AV block (for beta-blocker)
- Active decompensation ongoing (defer BB uptitration)
- eGFR <20 mL/min (SGLT2i only absolute contraindication)
- History of DKA or Type 1 diabetes (SGLT2i contraindicated)

STRONG-HF KEY PRINCIPLE

Hospitalization = Opportunity

STRONG-HF: Rapid initiation to 50% target dose in-hospital with 7-day follow-up reduced 180-day HF readmission/death by **34%** (HR 0.66, 95% CI 0.50–0.86; p=0.003). Pharmacist-led optimization achieved target doses in 2 weeks vs <5% in usual care. No increase in adverse events.

References: 1. Mebazaa A, et al. Lancet 2019;393:61-73. | 2. Velazquez EJ, et al. N Engl J Med 2019;380:539-548 (PIONEER-HF). | 3. Mebazaa A, et al. Eur Heart J 2022;43:4362-4373 (STRONG-HF). | 4. Greene SJ, et al. JACC Heart Fail 2021;9:476-487.

In-Hospital GDMT Optimization Pathway

DAY 1–2 STABILIZATION

- IV diuretics: 1–2× home oral dose IV; bolus or continuous
- Target 3–5 L net negative over first 24–48 hours
- Hemodynamic profiling: warm/cold, wet/dry phenotype
- Baseline: BMP, BNP, CBC, LFTs, TSH, iron studies
- Initiate SGLT2i within 24 hrs — safe during diuresis
- Echo to classify HFrEF vs. HFpEF; establish dry weight

DAY 2–3 INITIATION

- SGLT2i at fixed dose — no titration required
- Beta-blocker low dose when hemodynamically stable
- ACEi / ARB or ARNI — PIONEER-HF confirms safety
- MRA when K+ <5.0 mEq/L and eGFR >30 mL/min
- Pharmacist medication optimization + reconciliation
- Begin teach-back: daily weights, warning signs

DAY 3–5 UPTITRATION

- Double GDMT doses every 24–48 hrs as tolerated
- Monitor BP, HR, BMP (Cr, K+, Mg^{2+}) daily
- Target 50% of guideline dose before discharge
- IMPLEMENT-HF pharmacist uptitration model
- Document titration plan in discharge summary
- EP referral if EF ≤35% — ICD/CRT candidacy

DISCHARGE + F/U

- 7-day clinic visit — core STRONG-HF protocol
- Labs: BMP + BNP/NT-proBNP at 1–2 weeks
- Continue GDMT uptitration toward target dose
- Goal: reach 100% target dose by 6 weeks
- Remote weight monitoring if high-risk
- PCP communication and handoff within 24 hrs

DOSE Trial (NEJM 2011)

High-dose IV furosemide (2.5× oral dose) produced greater diuresis and symptom relief vs. low-dose without significantly different renal outcomes. Bolus vs. continuous infusion showed no significant difference in primary endpoints.

PIONEER-HF (NEJM 2019)

In-hospital sacubitril/valsartan initiation was safe within 24 hrs of hemodynamic stabilization. Greater NT-proBNP reduction vs. enalapril (HR 0.71). No excess hypotension, hyperkalemia, or AKI at 8 weeks.

IMPLEMENT-HF (JAMA Cardiol 2021)

Virtual physician-pharmacist team achieved near-complete GDMT initiation before discharge. No increase in LOS, AKI, hyperkalemia, or hypotension vs. usual care. Model validated as scalable across settings.

STRONG-HF (Eur Heart J 2022)

34% reduction in 180-day HF readmission/death (HR 0.66, p=0.003). Intensive arm reached full target doses in 2 weeks vs. <5% usual care. KCCQ QoL improved +5.5 pts at 90 days. No safety concerns identified.

STRONG-HF Key Outcomes: 34%↓ Death/HF Rehospitalization (HR 0.66) | 2 Weeks to Full Dose | +5.5 pts KCCQ at 90 Days | <5% Usual Care Optimized

References: 1. Mebazaa A, et al. Eur Heart J 2022;43:4362-4373 (STRONG-HF). | 2. Greene SJ, et al. JAMA Cardiol 2021;6:645-654 (IMPLEMENT-HF). | 3. Velazquez EJ, et al. N Engl J Med 2019;380:539-548 (PIONEER-HF). | 4. Felker GM, et al. N Engl J Med 2011;364:797-805 (DOSE Trial).

American College of Physicians

Comprehensive GDMT Pathway in HFrEF: Hospital to Home

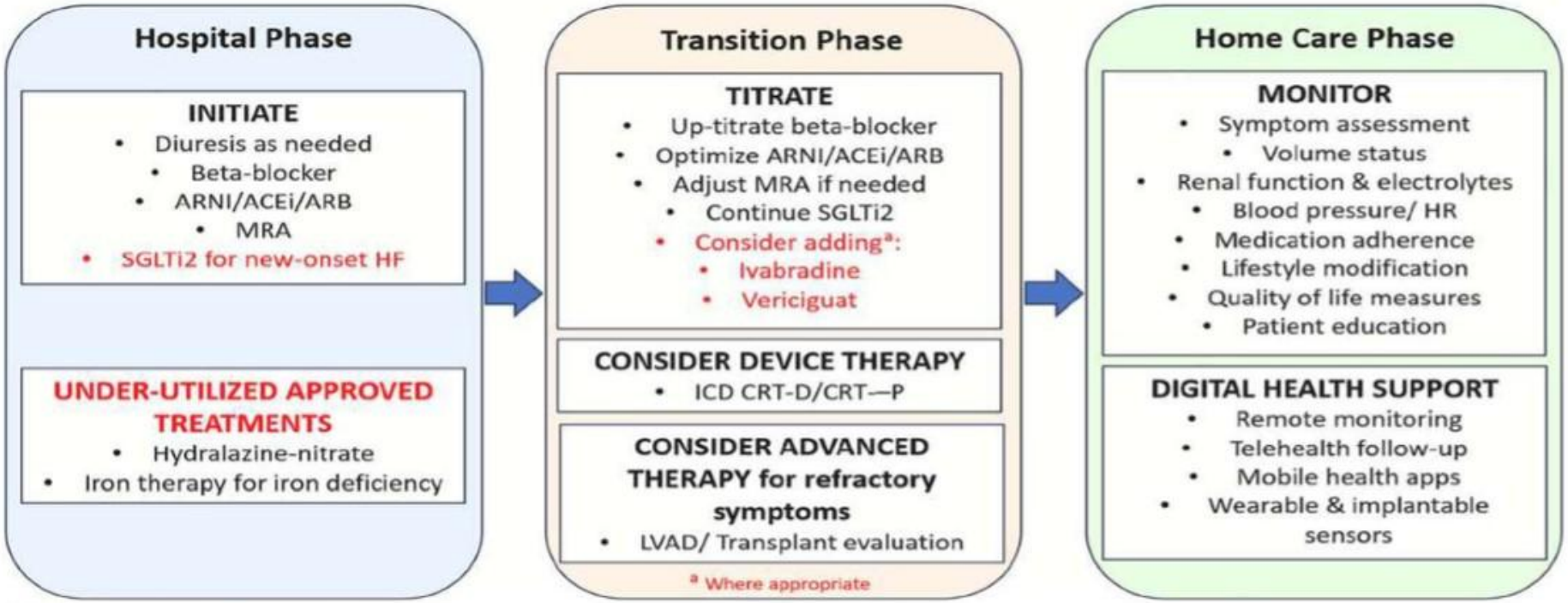

FIG. 1

Recommendations for initiation and titration of GDMT in HFrEF from the hospital phase of care to home: initiate/titrate/monitor. ARNI, angiotensin receptor-neprilysin inhibitor; GDMT, guidelines-directed medical therapy; SGLT2i, sodium-glucose cotransporter-2 inhibitors.

Barkoudah and Yancy. Heart Failure with Reduced Ejection Fraction. Med Clin North Am. 2025 Nov;109(6):1157-1173.