

*Back to the Future*  
A New Paradigm in Heart  
Failure Management

Isaac Tea, MD, MSc, FACC, FSCAI

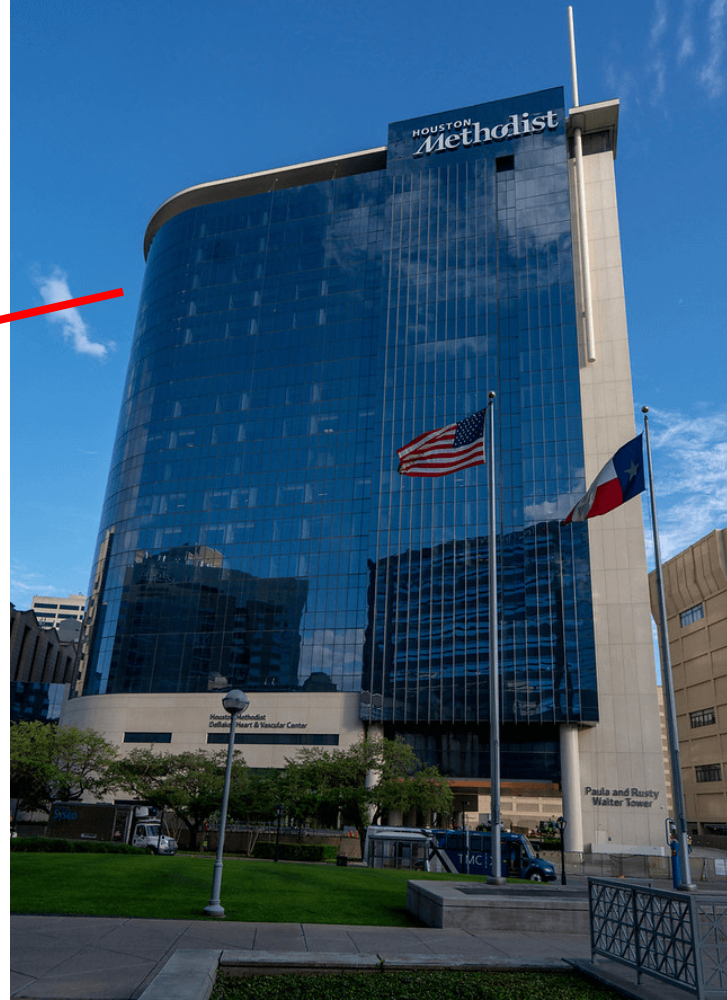
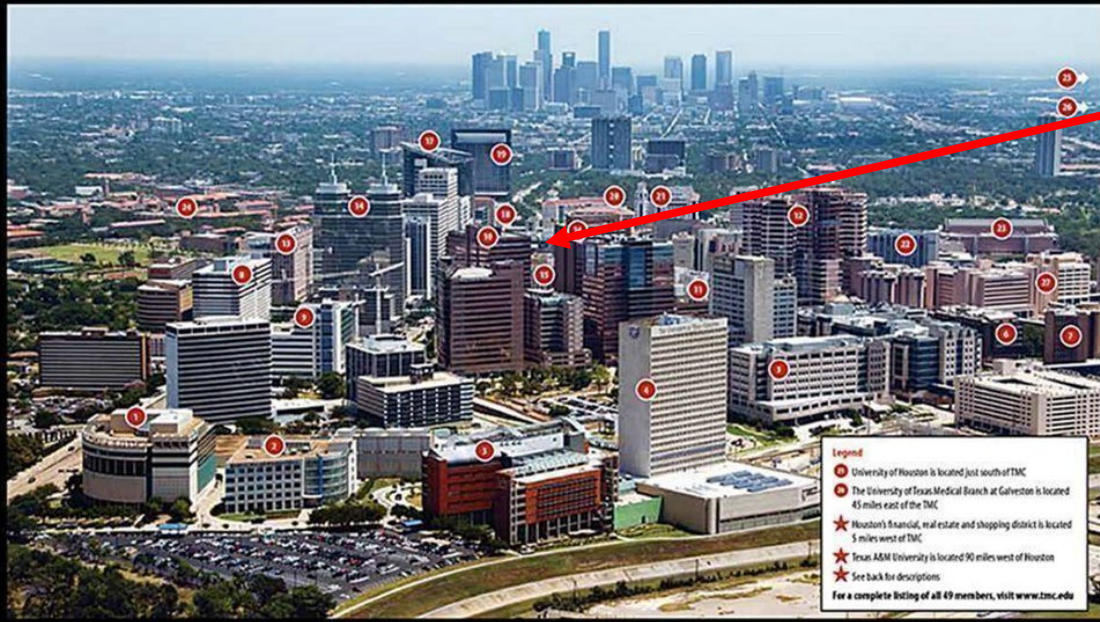


# Disclosures

- None

# Houston's Texas Medical Center Map

LARGEST MEDICAL COMPLEX IN THE WORLD

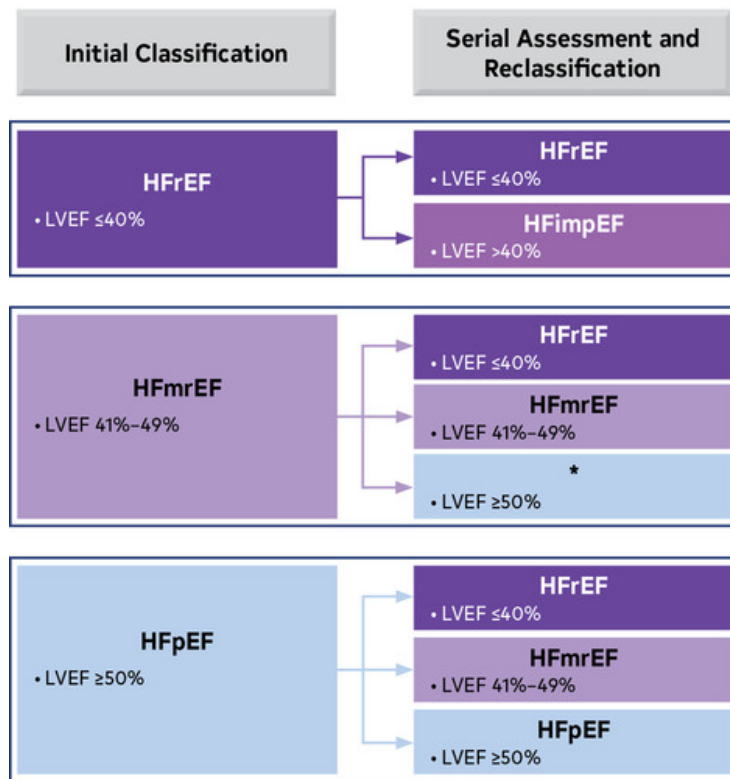


# Definitions

- Heart Failure:
  - A complex clinical syndrome characterized by impaired myocardial performance
  - Leading to **circulatory insufficiency** and **volume overload**
- (Result of) Cardiomyopathy:
  - Structural and functional impairment of the heart muscle
- HFrEF, but don't forget HFpEF
- *Like cancer – you are in remission, but never “cured”*



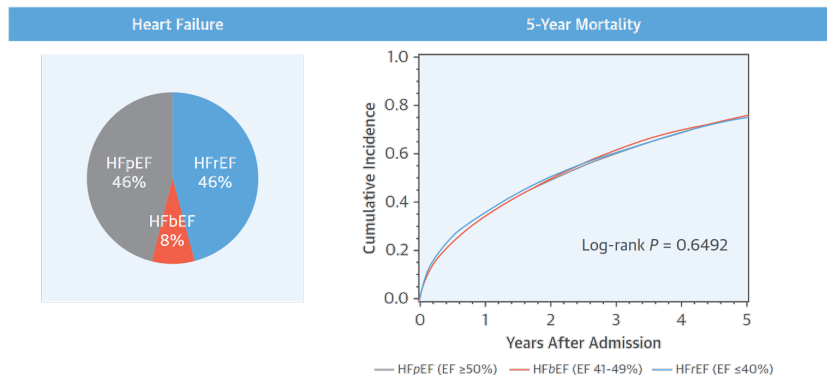
# Classifications of Heart Failure



# 5-Year Outcomes in HF

Among patients hospitalized with HF, patients *across the EF spectrum* have similarly poor 5-year survival with an elevated risk for cardiovascular and HF admission.

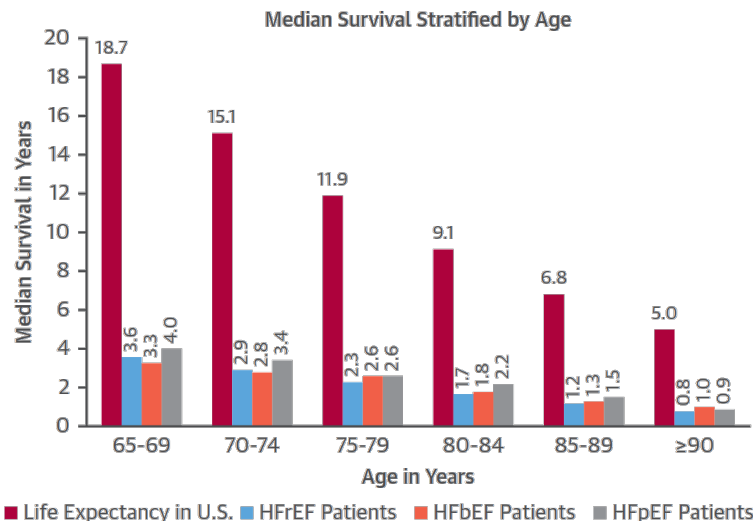
**CENTRAL ILLUSTRATION** 5-Year Outcomes in Patients Hospitalized With HF With Preserved, Borderline, and Reduced EF



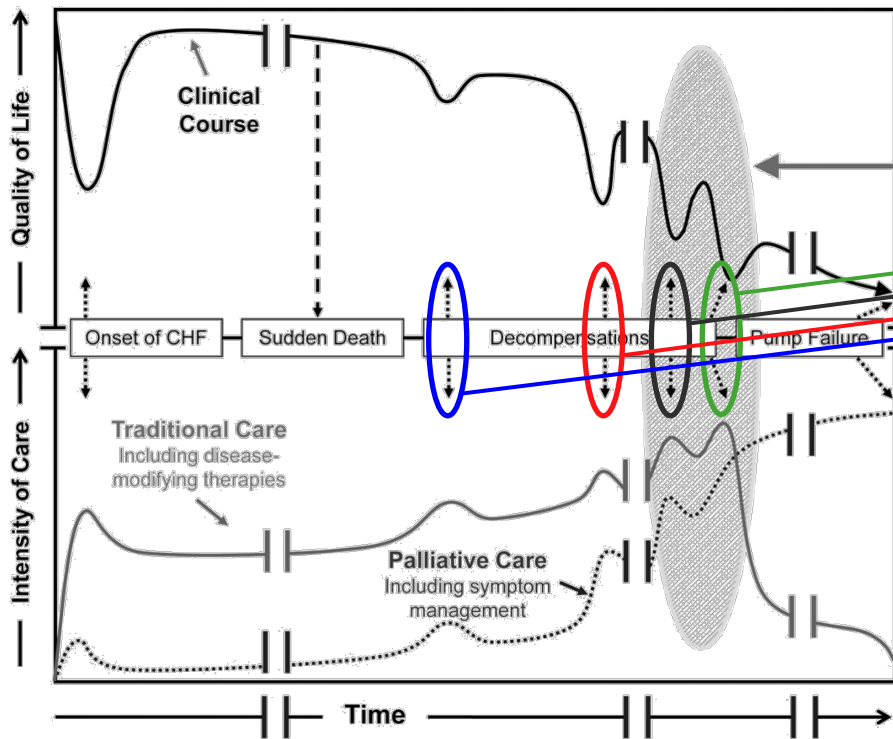
Outcomes - 5-Year Event Rates (%)					
	Mortality	Readmission	CV Readmission	HF Readmission	Mortality/Readmission
HFrEF	75.3	82.2	63.9	48.5	96.4
HFbEF	75.7	85.7	63.3	45.2	97.2
HFpEF	75.7	84.0	58.9	40.5	97.3

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

**FIGURE 2** Median Survival in Years by Age Group in HF Patients Compared With the Life Expectancy in the United States

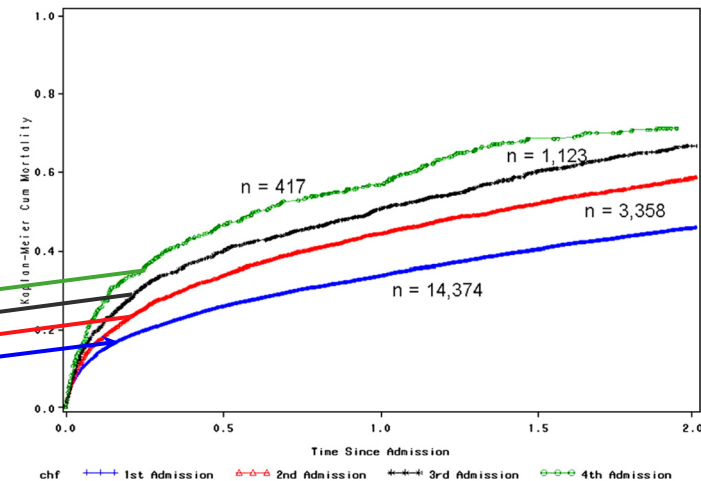


# Every Decompensation is BAD NEWS



## Transition to Advanced Heart Failure:

- Oral therapies failing
- A time for many major decisions
- Consider MCS and/or transplantation, if eligible
- Consider inversion of care plan to one dominated by a palliative approach, which may involve formal hospice



Kaplan-Meier cumulative mortality curve for all-cause mortality after each subsequent hospitalization for HF.



MORTALITY RISK  
**INCREASES**  
AFTER EACH  
HEART FAILURE  
HOSPITALIZATION

# Setting the Stage

- Ms. S, a 54 year-old female
- PMHx: Hypertension
- Presents for 5 days of worsening dyspnea
  - “Can’t Breathe”
  - PND, Orthopnea
  - Bilateral lower extremity edema
- Viral symptoms 2 weeks ago, was COVID-19 +ve

# Setting the Stage

- Admission Vitals: **HR 102**; BP 138/80; **RR 26**, **SpO<sub>2</sub> 86%** on 2L NC; **Temp 101F**.
- Physical exam: **JVP 12cm H<sub>2</sub>O**, S1 + S2 w/ S3 but no murmurs, **diffuse crackles** and **1+ bilateral lower extremity pitting edema**. Warm extremities.



HF Evaluation		Perfusion	
		WARM	COLD
Volume Status	WET	<p>Most common hospital presentation of CHF</p> <ul style="list-style-type: none"> <li>• Relieve symptoms</li> <li>• IV Diuretics</li> <li>• Afterload reduction (ACEI/ARB, Nitrates)</li> <li>• <math>\beta</math>-Blockers <math>\pm</math> Aldosterone antagonists when optimized</li> </ul>	<p>Likely requires ICU care</p> <ul style="list-style-type: none"> <li>• IV Diuretics</li> <li>• Inotropes</li> <li>• Afterload reduction</li> <li>• PA catheter-guided therapy</li> <li>• Advanced Therapies (e.g. LVAD etc.)</li> </ul>
	DRY	<p>Compensated HF</p> <ul style="list-style-type: none"> <li>• Can consider treatment as outpatient</li> <li>• Goals: <ul style="list-style-type: none"> <li>▪ Maintain volume status</li> <li>▪ Prevent disease progression</li> </ul> </li> </ul>	<p>Represents 10% of cases; challenging to treat.</p> <ul style="list-style-type: none"> <li>• Often associated with cardio-renal syndrome.</li> <li>• Inotropes</li> <li>• Afterload reduction</li> <li>• Advanced Therapies</li> </ul>

# Etiology / Triggers of ADHF

- Dietary indiscretion or medication non-adherence (~40%)
- Myocardial ischemia or infarction (~10-15%)
- Myocarditis
- Renal Failure (acute, progression of CKD, insufficient dialysis) → ↑ Preload
- Hypertensive crisis → ↑ Afterload
- Valvular dysfunction (Acute or worsening) – Mitral Regurgitation, Aortic Stenosis etc.
- Arrhythmias – Atrial Fibrillation/Flutter, Ventricular Tachycardia
- Drugs (CCB, NSAIDs, TZDs, etc.), Chemo (Anthracyclines, Trastuzumab, etc.)
- Toxins (Alcohol, Cocaine etc.)
- Others: COPD or PE (↑ R-sided Afterload), Anemia, Systemic infection, Thyroid disease

1. **Coronaries** – ACS/Ischemia
2. **Valve** – Valvular Dysfunction
3. **Electricity** - Arrhythmia
4. **Muscle** - Myocarditis

# Diagnostic Testing

- EKG => ACS/Ischemia, Arrhythmia (Atrial Fibrillation/Flutter), Cardiac Amyloid
- Chest X-Ray => Extent of pulmonary congestion
- Labs:
  - CBC => Anemia
  - CMP => Renal Function, **LFTs (hepatic congestion, shock liver)!!**
  - BNP => Risk stratification, “Severity” compared to prior
    - Pitfalls: Obesity , CKD, Age
    - NT-proBNP for patients on Entresto
  - **Troponin** => ACS vs Type 2 MI
  - **Lactic Acid** => End organ malperfusion, Cardiogenic shock!!
- Echo
  - Urgency depends on acuity of presentation
  - Assess EF, Wall motion abnormalities
  - Valvular disease (Severe AS, Flail MV)
  - Mechanical complications of MI
  - Non-invasive cardiac output/index estimation (LVOT VTI)
  - Diastology for filling pressures

# Causes for Elevated Natriuretic Peptide Levels

<b>Cardiac</b>	<b>Noncardiac</b>
<ul style="list-style-type: none"><li>• Heart failure, including RV syndromes</li><li>• Acute coronary syndrome</li><li>• Heart muscle disease, including LVH</li><li>• Valvular heart disease</li><li>• Pericardial disease</li><li>• Atrial fibrillation</li><li>• Myocarditis</li><li>• Cardiac surgery</li><li>• Cardioversion</li></ul>	<ul style="list-style-type: none"><li>• Advancing age</li><li>• Anemia</li><li>• Renal failure</li><li>• Pulmonary causes: obstructive sleep apnea, severe pneumonia, pulmonary hypertension</li><li>• Critical illness</li><li>• Bacterial sepsis</li><li>• Severe burns</li><li>• Toxic-metabolic insults, including cancer chemotherapy and envenomation</li></ul>

# BNP When to Check?

1. Suspicion

2. Admission

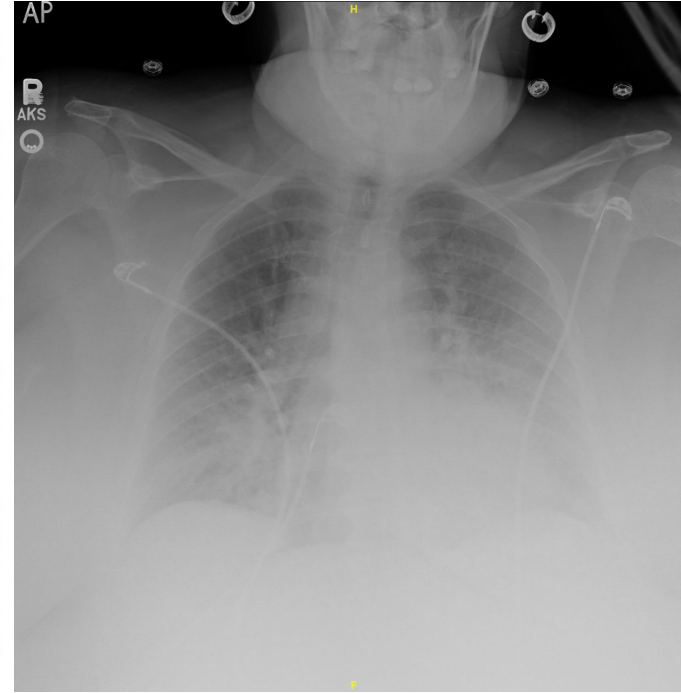
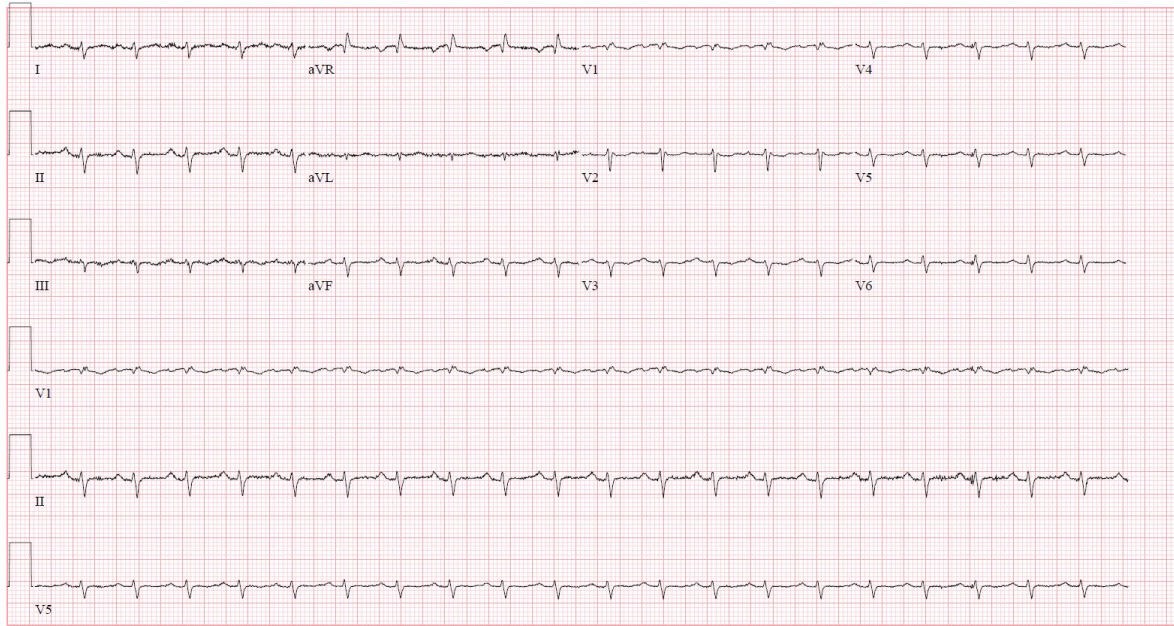
3. NO TRENDING

4. Discharge

X Entresto\*\*\*



# Admission EKG & CXR



# Setting The Stage Again

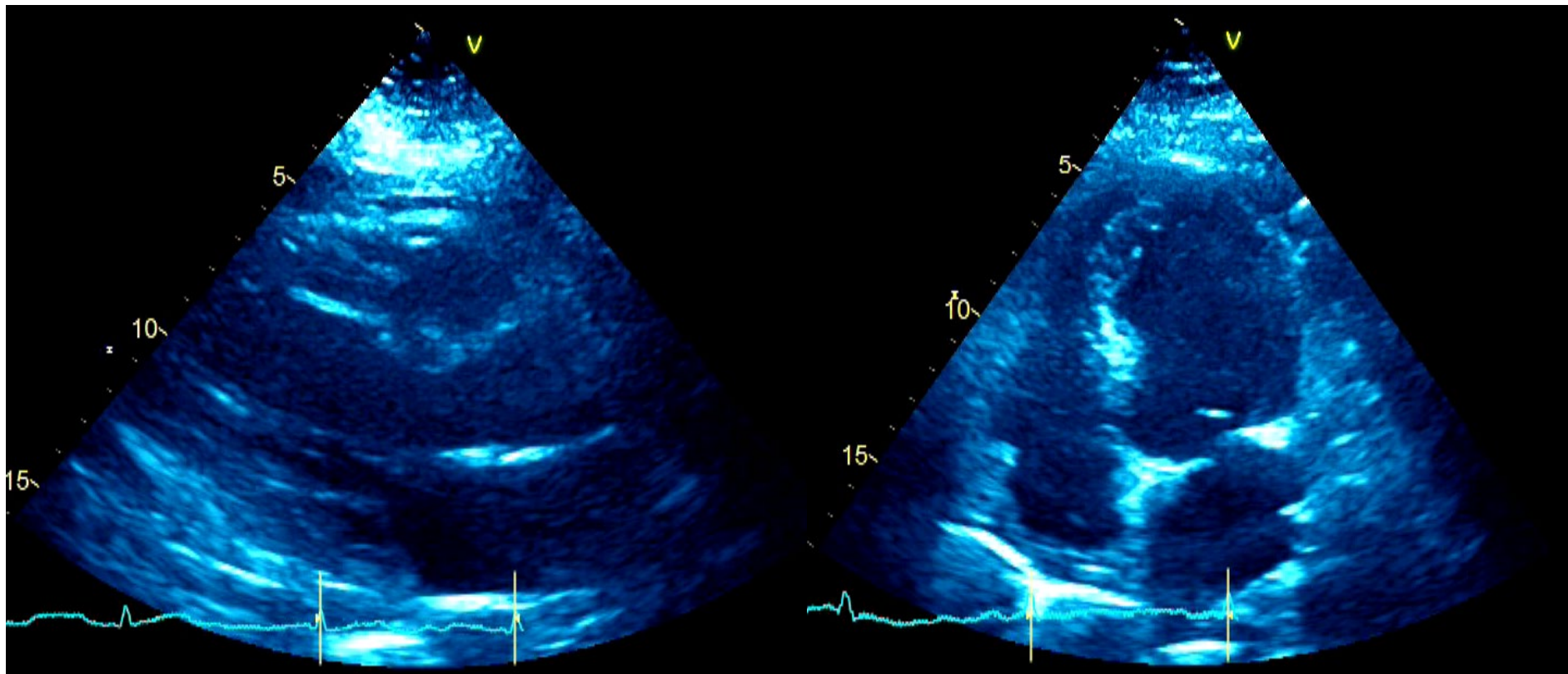
Mrs. S in ED 16

- **Admission Vitals: HR 142; BP 118/70; RR 24, SpO<sub>2</sub> 92% on 4L NC; Temp 100.8F.**
- **Physical exam: JVP 12cm H<sub>2</sub>O, S1 + S2 w/ S3 but no murmurs, bibasilar crackles and 1+ bilateral lower extremity edema.**

- **Labs:**

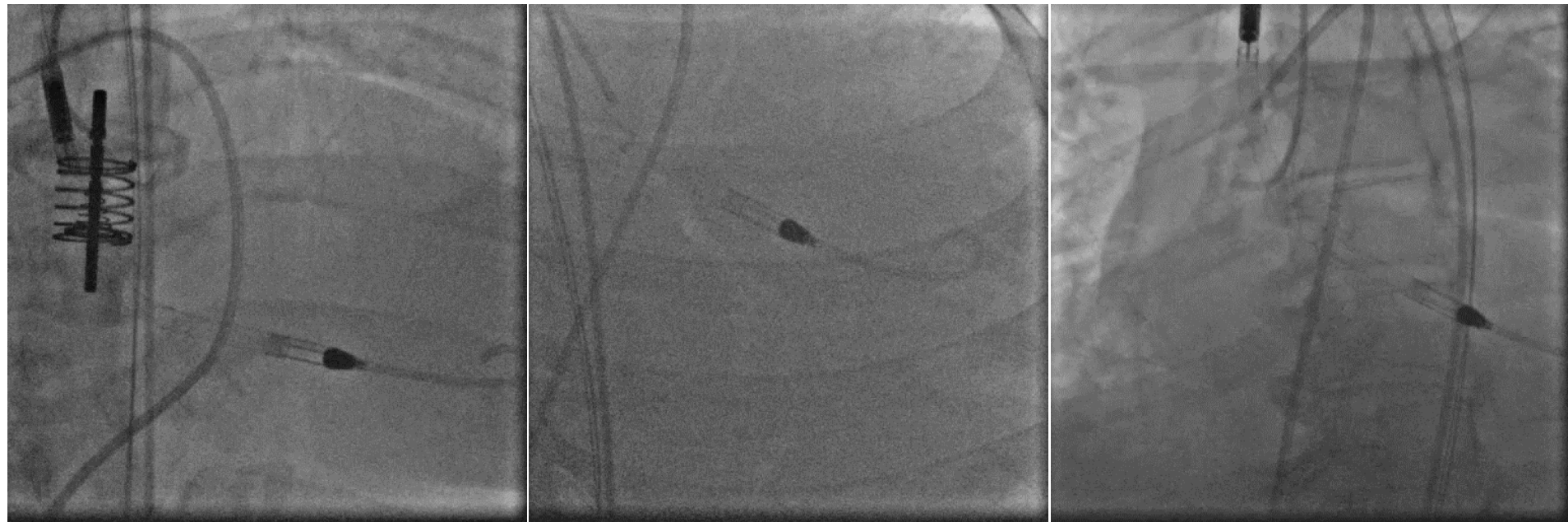
Troponin	68	Creatinine	0.9
BNP	780	Alk Phos	72
		ALT	66
Lactic Acid	6.0	AST	131

# Echocardiogram



# Non-Obstructive CAD => MINOCA

Taken to Cath Lab





# Respiratory Support

REVIEW

Annals of Internal Medicine

## Meta-analysis: Noninvasive Ventilation in Acute Cardiogenic Pulmonary Edema

Cui-Lian Weng, MD; Yun-Tao Zhao, PhD; Qing-Hua Liu, MM; Chang-Jun Fu, PhD; Feng Sun, PhD; Yan-Liang Ma, MD; Yan-Wen Chen, MD; and Quan-Ying He, MD

- CPAP **reduces mortality and intubation rates** in patients with ACPE, especially those with myocardial ischemia or MI at presentation.
- BiPAP ventilation **reduces the need for intubation** compared with standard therapy.
  - **NNT to avoid intubation:**
    - ✓ CPAP = 6
    - ✓ BiPAP = 7
- CPAP vs BiPAP = **NO Difference.**

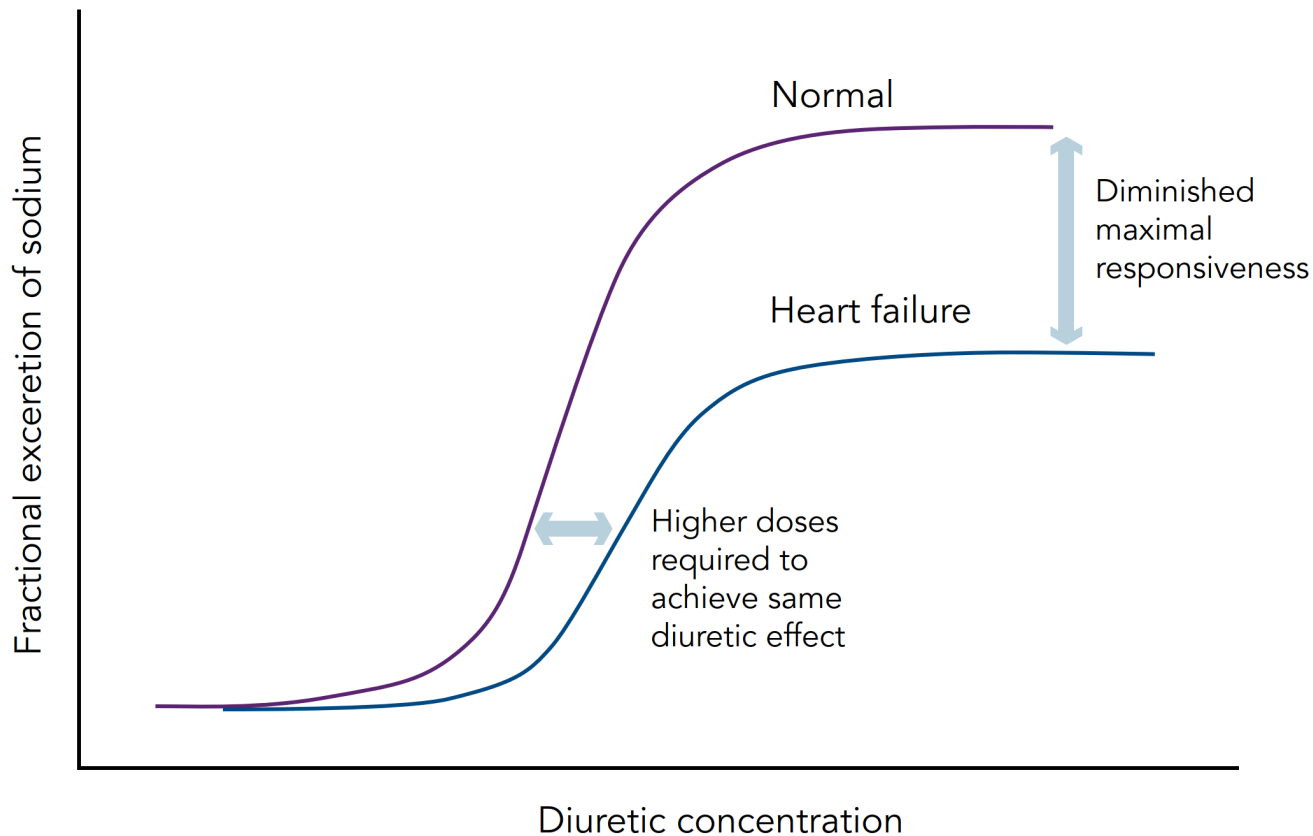
Effect of non-invasive positive pressure ventilation (NIPPV) on mortality in patients with acute cardiogenic pulmonary oedema: a meta-analysis

*John Victor Peter, John L Moran, Jennie Phillips-Hughes, Petra Graham, Andrew D Bersten*

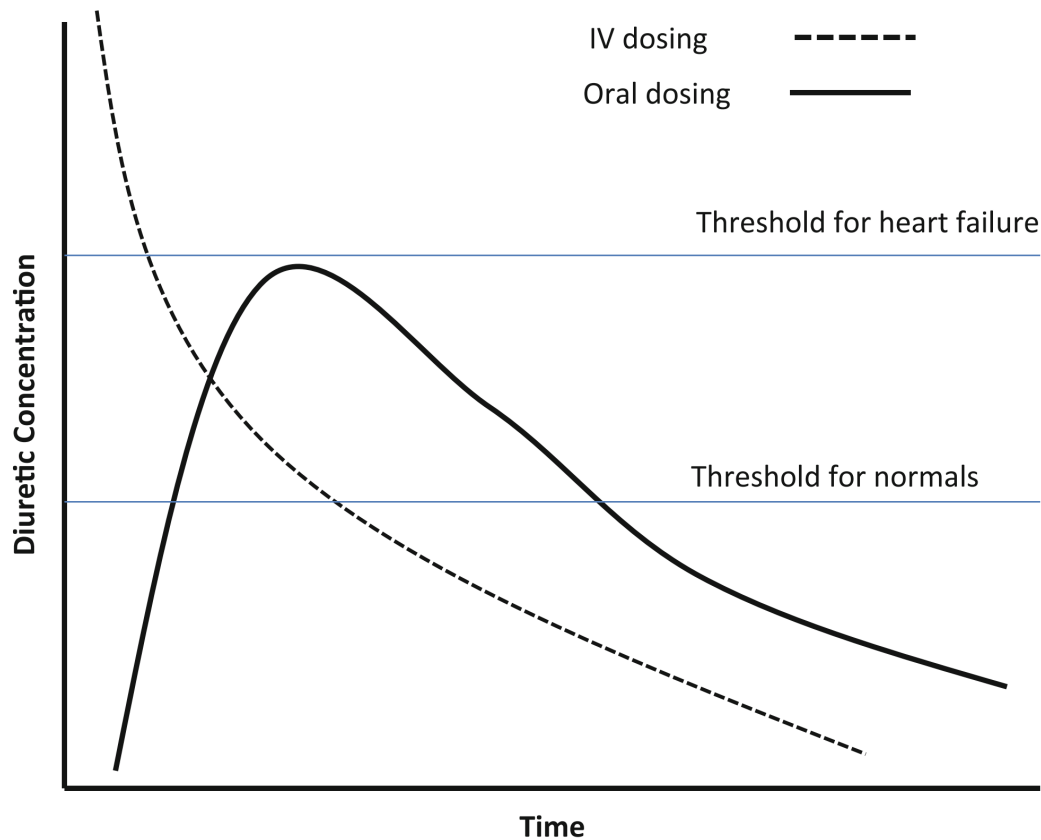




# Understanding Loop Diuretics



# IV vs Oral Loop Diuretics



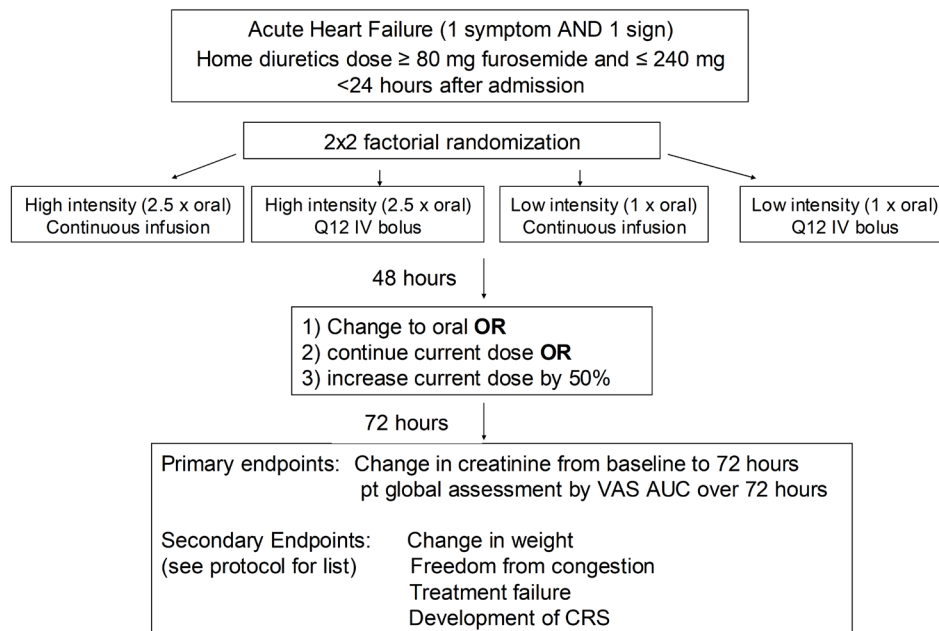
# Pharmacokinetics of Loop Diuretics

	Furosemide		Torsemide	Bumetanide
Route	PO	IV	PO/IV	PO/IV
Dose (mg)	40	20	20	1
Bioavailability	~50%	100%	~80%/100%	~80%/100%
Half-life (hrs)	0.5-2		3-4	1
Time to Peak (mins)	108	108	52	72
Onset of Action (mins)	30-60	5	60/10	30-60/15-30
Duration of Action (hrs)	6-8	2	6-8	4-6/2-3

# DOSE TRIAL

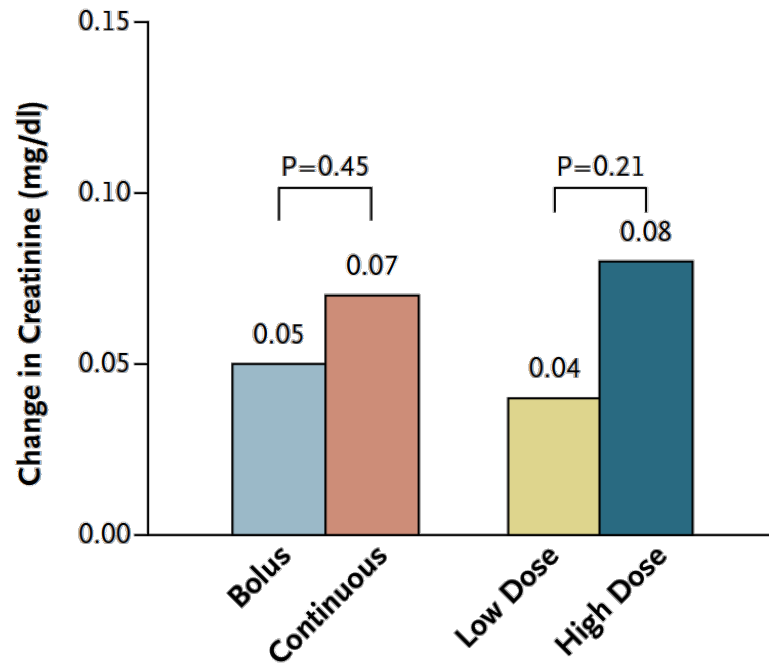
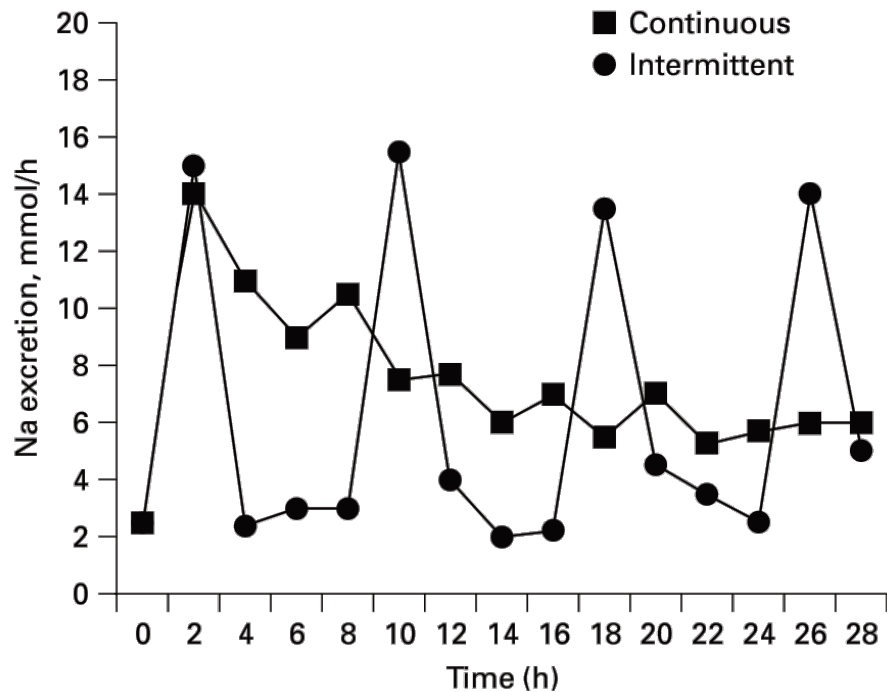
## Diuretic Strategies in Patients with Acute Decompensated Heart Failure

G. Michael Felker, M.D., M.H.S., Kerry L. Lee, Ph.D., David A. Bull, M.D., Margaret M. Redfield, M.D., Lynne W. Stevenson, M.D., Steven R. Goldsmith, M.D., Martin M. LeWinter, M.D., Anita Deswal, M.D., M.P.H., Jean L. Rouleau, M.D., Elizabeth O. Ofili, M.D., M.P.H., Kevin J. Anstrom, Ph.D., Adrian F. Hernandez, M.D., [et al.](#), for the NHLBI Heart Failure Clinical Research Network\*



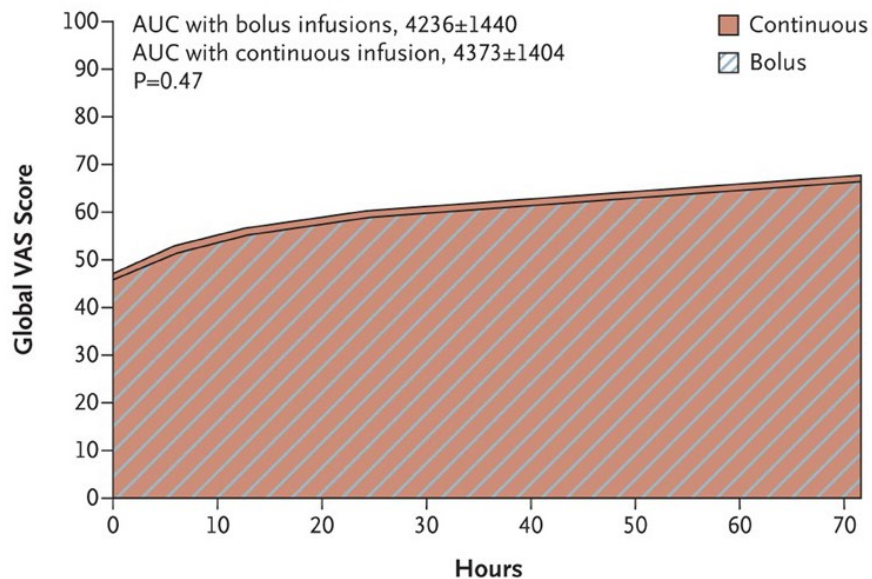


# Continuous Infusion vs Intermittent Bolus

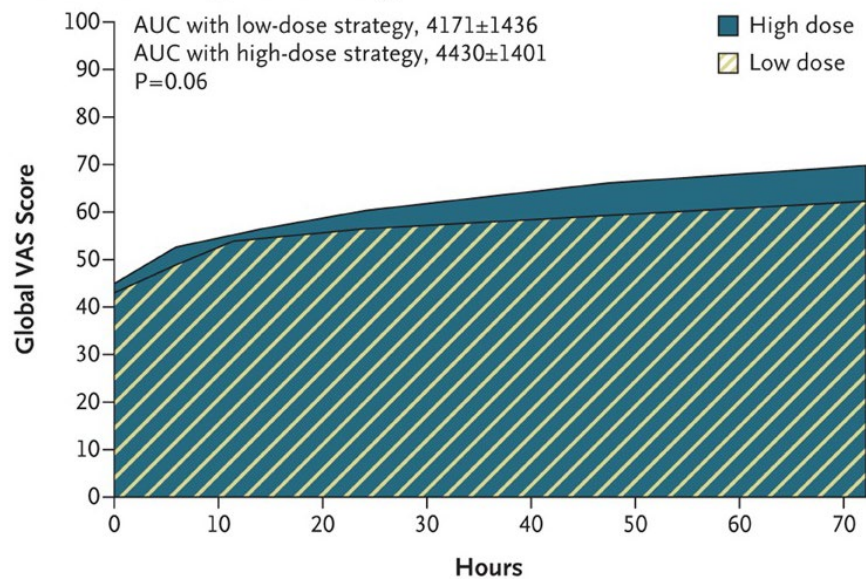


# Symptom Improvement Within 72 Hours

**A Bolus vs. Continuous Infusion**

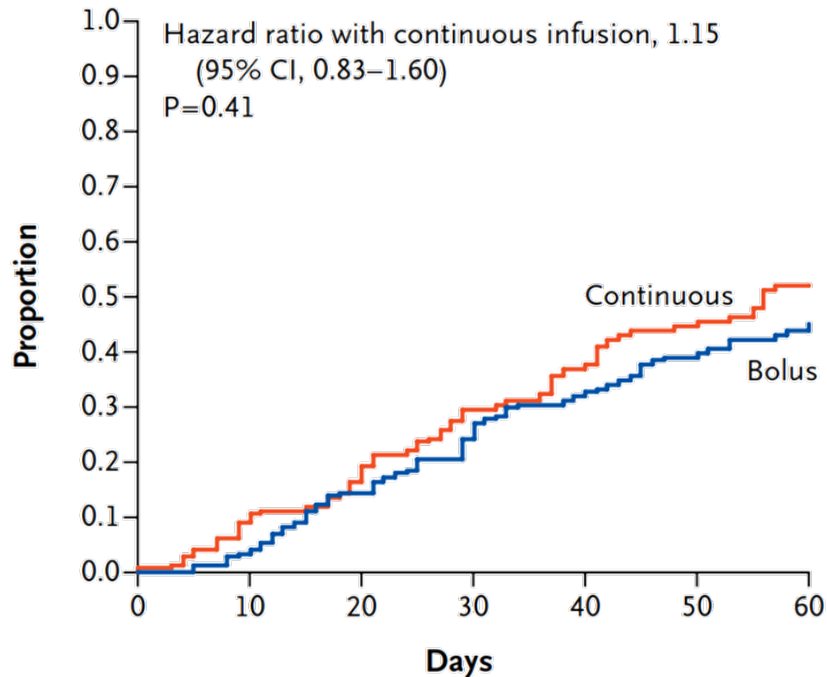


**B Low-Dose vs. High-Dose Strategy**

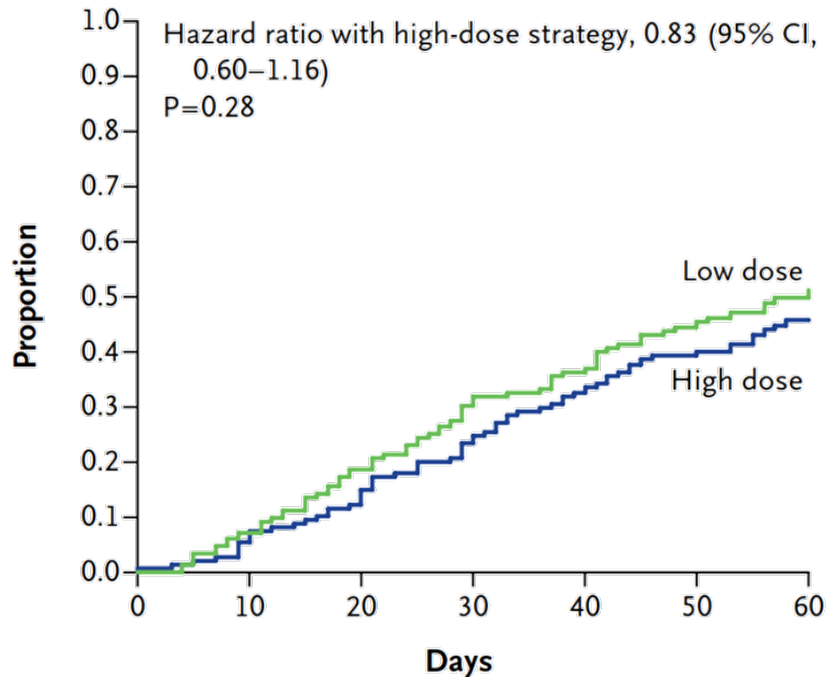


# Endpoints (No Difference!)

**A Bolus vs. Continuous Infusion**



**B Low-Dose vs. High-Dose Strategy**



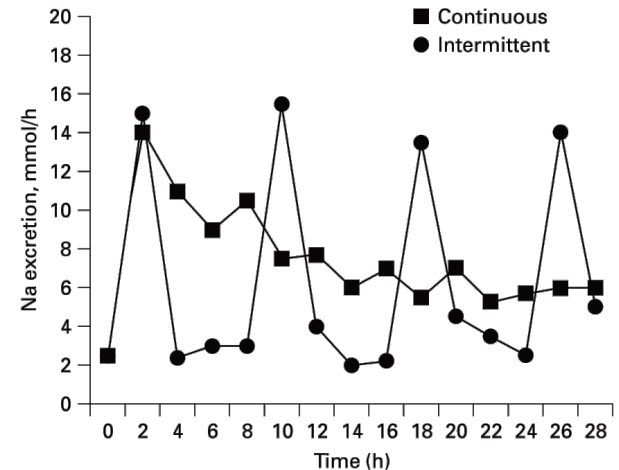
# Symptom Improvement Within 72 Hours

**Table 2. Secondary End Points for Each Treatment Comparison.\***

End Point	Bolus Every 12 Hr (N=156)	Continuous Infusion (N=152)	P Value	Low Dose (N=151)	High Dose (N=157)	P Value
AUC for dyspnea at 72 hr	4456±1468	4699±1573	0.36	4478±1550	4668±1496	0.04
Freedom from congestion at 72 hr — no./total no. (%)	22/153 (14)	22/144 (15)	0.78	16/143 (11)	28/154 (18)	0.09
Change in weight at 72 hr — lb	-6.8±7.8	-8.1±10.3	0.20	-6.1±9.5	-8.7±8.5	0.01
Net fluid loss at 72 hr — ml	4237±3208	4249±3104	0.89	3575±2635	4899±3479	0.001
Change in NT-proBNP at 72 hr — pg/ml	-1316±4364	-1773±3828	0.44	-1194±4094	-1882±4105	0.06
Worsening or persistent heart failure — no./total no. (%)	38/154 (25)	34/145 (23)	0.78	38/145 (26)	34/154 (22)	0.40
Treatment failure — no./total no. (%)†	59/155 (38)	57/147 (39)	0.88	54/147 (37)	62/155 (40)	0.56
Increase in creatinine of >0.3 mg/dl within 72 hr — no./total no. (%)	27/155 (17)	28/146 (19)	0.64	20/147 (14)	35/154 (23)	0.04
Length of stay in hospital — days			0.97			0.55
Median	5	5		6	5	
Interquartile range	3–9	3–8		4–9	3–8	
Alive and out of hospital — days			0.36			0.42
Median	51	51		50	52	
Interquartile range	42–55	38–55		39–54	42–56	

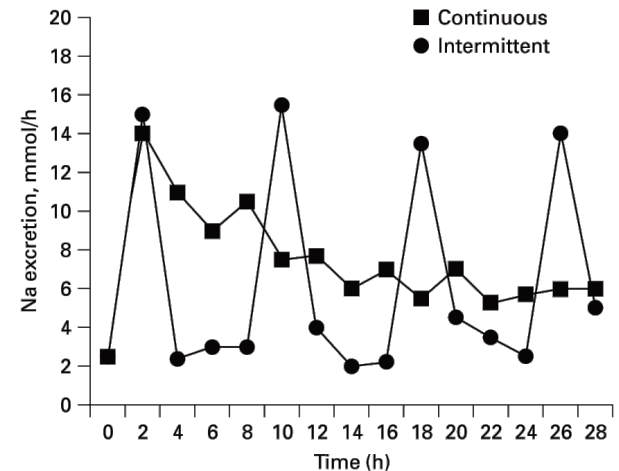
# The Diuretic Dosing Algorithm

1. Right diuretic **DOSE** (2.5x Oral Dose), use **IV**, increase PRN (*Class I, Level B*)
2. Right diuretic **FREQUENCY**, at least **BID**, increase PRN (*Class I, Level B*)



# The Diuretic Dosing Algorithm

1. Right diuretic **DOSE** (2.5x Oral Dose), use **IV**, increase PRN (*Class I, Level B*)
2. Right diuretic **FREQUENCY**, at least **BID**, increase PRN (*Class I, Level B*)
3. Continuous vs. Bolus
  - DOSE Trial: No difference in symptoms or renal function between either.
  - IV infusion may however be helpful in patients who are borderline hypotensive and are sensitive to bolus diuretics that may drop their BP.
  - IV infusion will deliver same total dose without hypotension.



# The Diuretic Dosing Algorithm

1. Right diuretic **DOSE (2.5x Oral Dose)**, use IV, increase PRN

2. Right diuretic **FREQUENCY**, e.g. **BID**, increase PRN

3. Continuous vs. Bolus

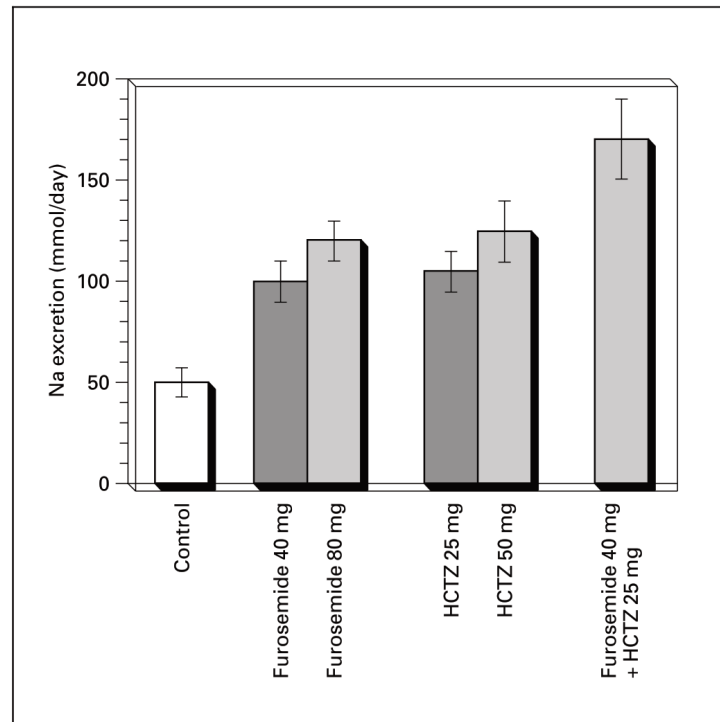
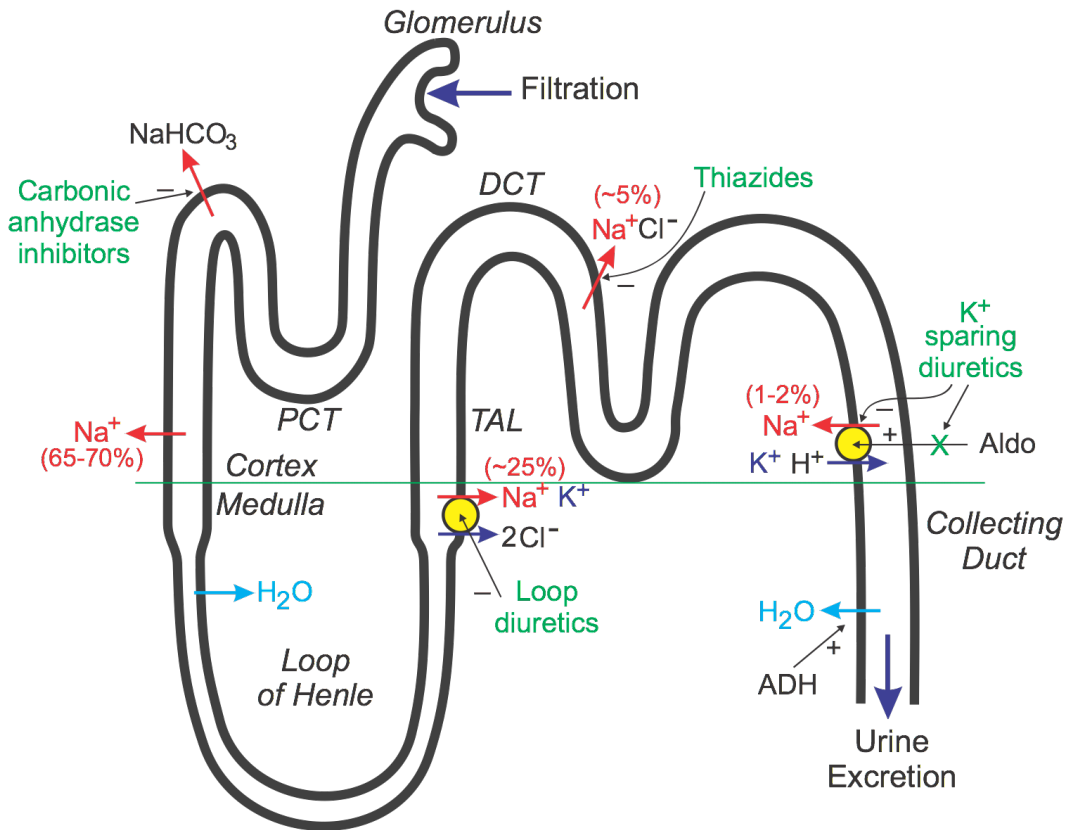
- DOSE Trial: No difference in symptoms or renal function between either.
- IV infusion may be more or better tolerated in patients who are hypotensive and are sensitive to bolus diuretics that may drop their BP.
- IV infusion will deliver same total dose without hypotension.

4. Combination Rx => **Sequential Nephron Blockade (Class IIa, Level B)**  
e.g. Furosemide + Metolazone

## DIURETIC

## RESISTANCE

# Sequential Nephron Blockade





## To a Ceiling Dose of Loop Diuretic Add:

<i>Distal Convoluted Tubule (DCT)</i>	<b>Metolazone</b>	2.5-10mg daily
	<b>Hydrochlorothiazide</b>	25-100mg daily
	<b>Chlorothiazide</b>	500-1,000mg
<i>Proximal Tubule</i>	<b>Acetazolamide</b>	250-375mg daily or up to 500mg
<i>Collecting Duct</i>	<b>Spironolactone</b>	100-200mg daily
	<b>Amiloride</b>	5-10mg daily

# The Diuretic Dosing Algorithm

1. Right diuretic **DOSE** (2.5x Oral Dose) use IV, increase PRN (Class I, Level B)
2. Right diuretic **FREQUENCY** (at least 50% increase PRN (Class I, Level B)
3. Continuous vs. Bolus
  - DOSE Titration: No difference in symptoms or renal function between either
  - IV infusion may not be the best in patients with underlying hypotensive and are sensitive to bolus diuretics that may drop their BP.
  - IV infusion will deliver same total dose without hypotension.
4. Combination **Blockade** (Class I, Level B)  
e.g. Furosemide + Metolazone
5. V<sub>2</sub> vasopressin receptor antagonist => Vaptans (Class IIb, Level B)
6. Inotropes
7. Ultrafiltration (Class IIb, Level C)

CONSULT

CARDIOLOGY +/-

NEPHROLOGY

# The Diuretic Dosing Algorithm

1. Right diuretic **DOSE** (2.5x Oral Dose), use IV, increase PRN (*Class I, Level B*)
2. Right diuretic **FREQUENCY**, at least **BID**, increase PRN (*Class I, Level B*)
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  - DOSE Trial: No difference in symptoms or renal function between either.
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e.g. Furosemide + Metolazone
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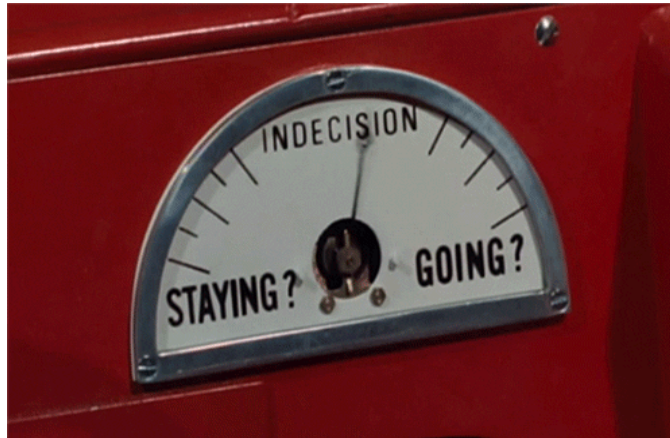
# What About OUTPATIENT ?

1. Right diuretic **DOSE** (2.5x Oral Dose)
2. Right diuretic **FREQUENCY**, at least **BID**
3. If already on Furosemide, consider switch to Torsemide or Bumetanide
  - Especially if Chronic Kidney Disease
  - If not responding to Furosemide
4. Combination Rx => **Sequential Nephron Blockade** (*Class IIa, Level B*)  
e.g. Furosemide + Metolazone
5. *Diuretic infusion clinic or admission?*

# What to do with GDMT?

- Maintenance of GDMT during ADHF in the absence of hemodynamic instability  
*(Class I, Level B)*

## $\beta$ -Blockers

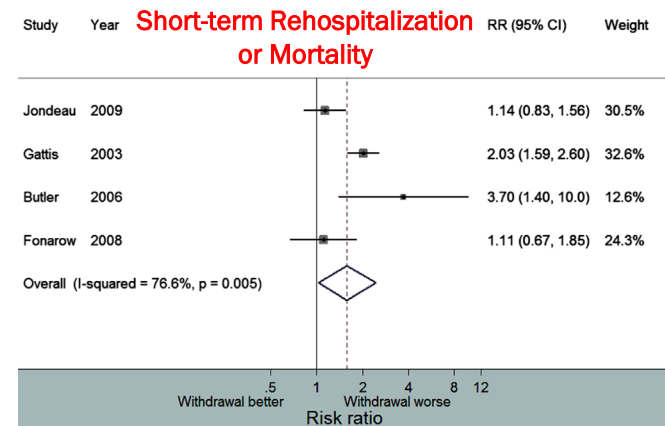
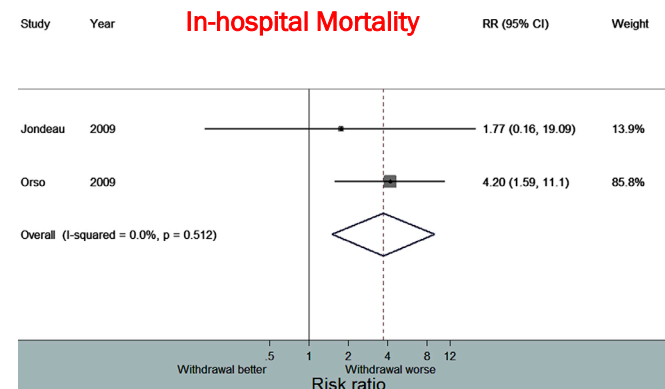


# What to do with GDMT?

- Maintenance of GDMT during ADHF in the absence of hemodynamic instability  
*(Class I, Level B)*

## $\beta$ -Blockers

- Do **NOT** withdraw in exacerbation unless patient is hypotensive or in cardiogenic shock
- Do **NOT** initiate in acute setting
  - Wait for adequate diuresis and euvolemia
  - Extra caution in patients who required inotropes on admission



# Questionable Interventions

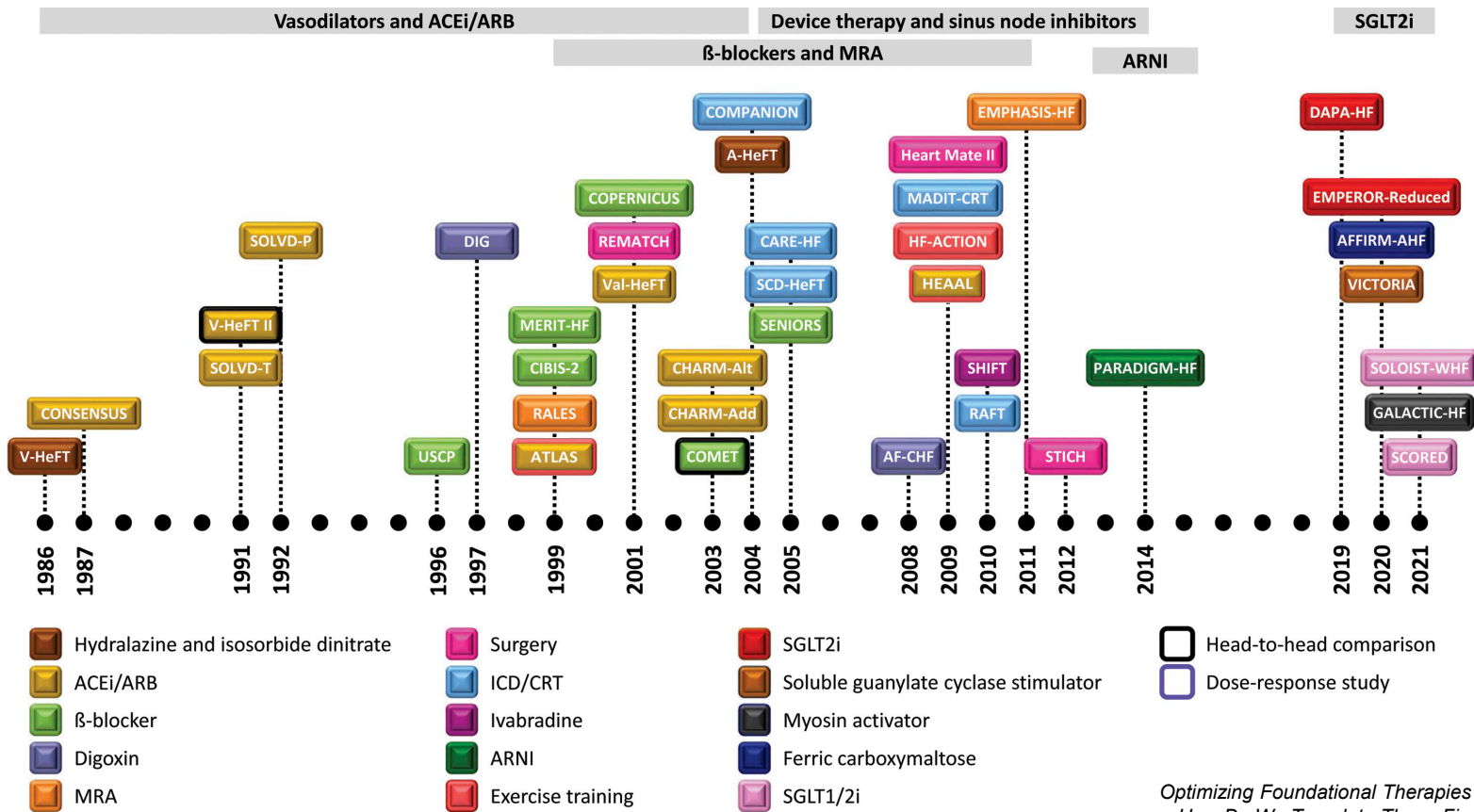
- Routine Inotropes: **DON'T do it.**
  - Hypotension, Arrhythmia risks
  - Harmful in **OPTIME-CHF**
- Routine Nesiritide: **DON'T do it.**
  - **ASCEND-HF**: Borderline significant trend in reducing dyspnea, but increased hypotension
  - No change in death or rehospitalization at 30 days
- Routine Serelaxin: **DON'T do it.**
  - **RELAX-AHF-2**: Did not result in a lower incidence of death from cardiovascular causes at 180 days or worsening heart failure at 5 days than placebo
- Routine Dopamine: **DON'T do it.**
  - **ROSE**: Both Dopamine and Nesiritide do not enhance decongestion or improve renal function when added to diuretic therapy



# Clinical Course

- Does well with IV diuretics => 8L over 48 hours
- Day 4 – Impella Explant
- Day 6 – Started Metoprolol Succinate 25mg Qday
- Day 8 – Discharged for outpatient Heart Failure Clinic follow up

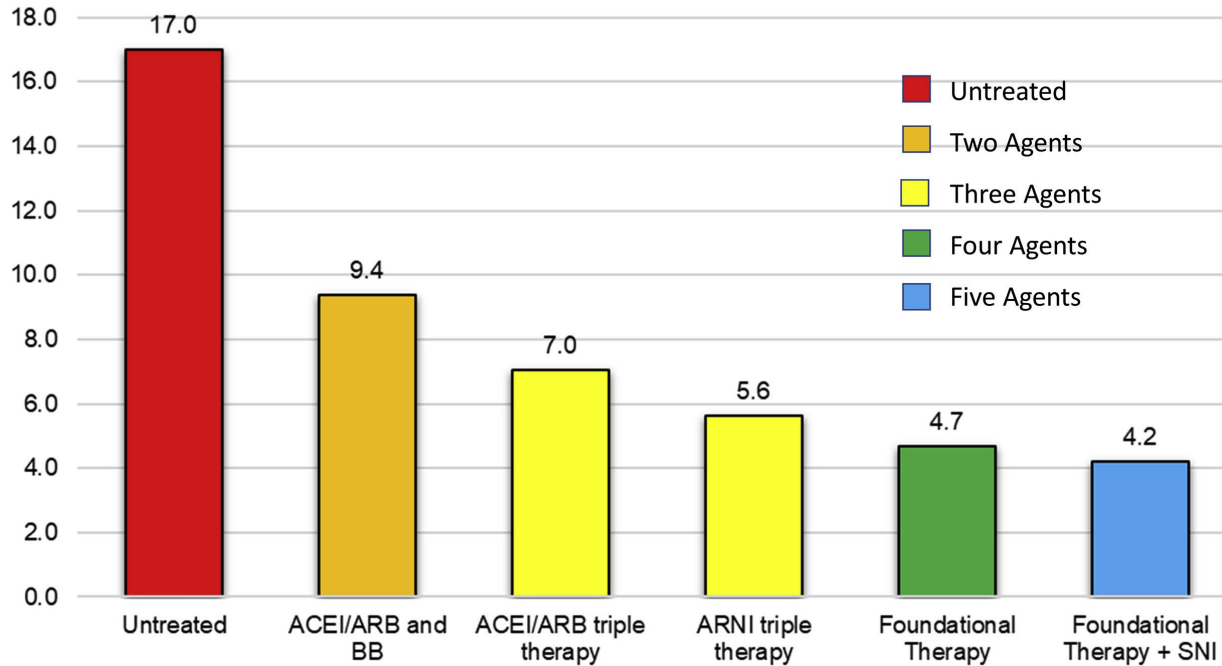
# Evolution of GDMT



Optimizing Foundational Therapies in Patients With HFrEF: How Do We Translate These Findings Into Clinical Care?

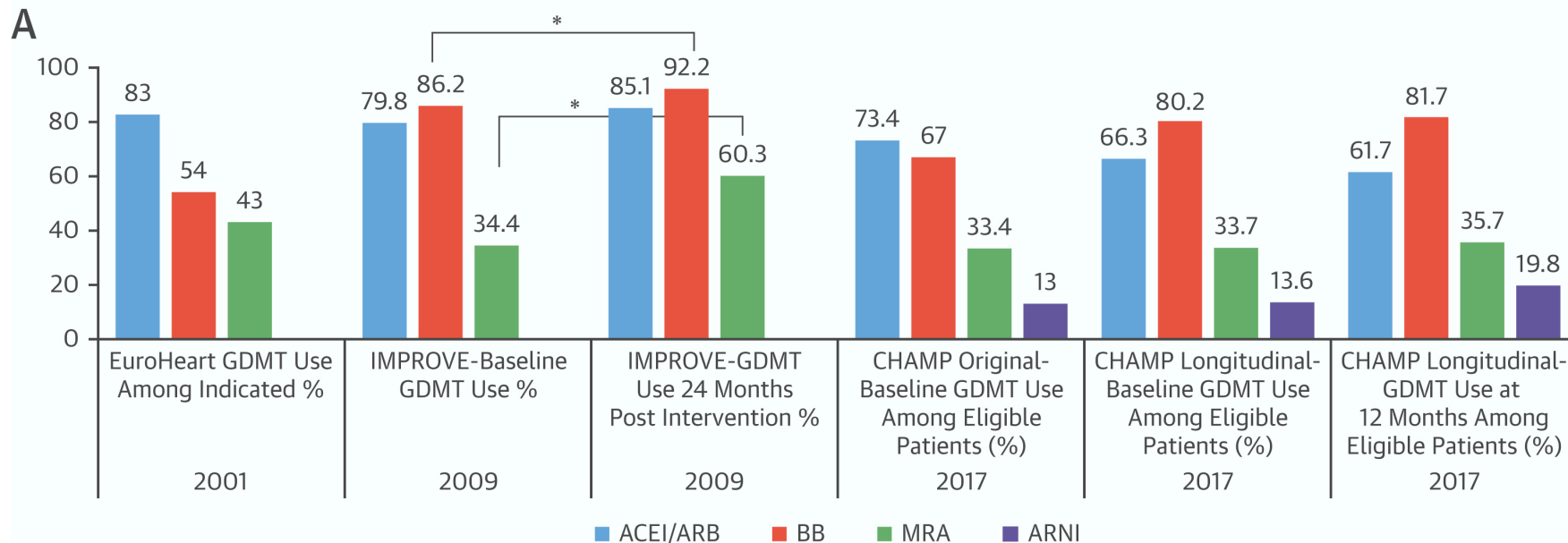
# Significant Mortality Benefit !!!

One-year Mortality with Combinations of Medical Therapy



# Do We Achieve GDMT ?

Prescription Rates for HF Medications in Heart Failure Registries



# Therapy Initiation - Historical

- Historical paradigm followed clinical trial timeline
  - Initiation of ‘foundational quadruple therapy
  - ACE/ARB, BB, MRA, followed by possible ARNI, SGLT2i
- Titrate first two classes to target dose, then add and titrate next class
- Every two weeks
  - Now as fast as tolerated
- Goal of **TRIPLE** therapy
  - Now QUADRUPLE therapy

# Therapy Initiation - Historical

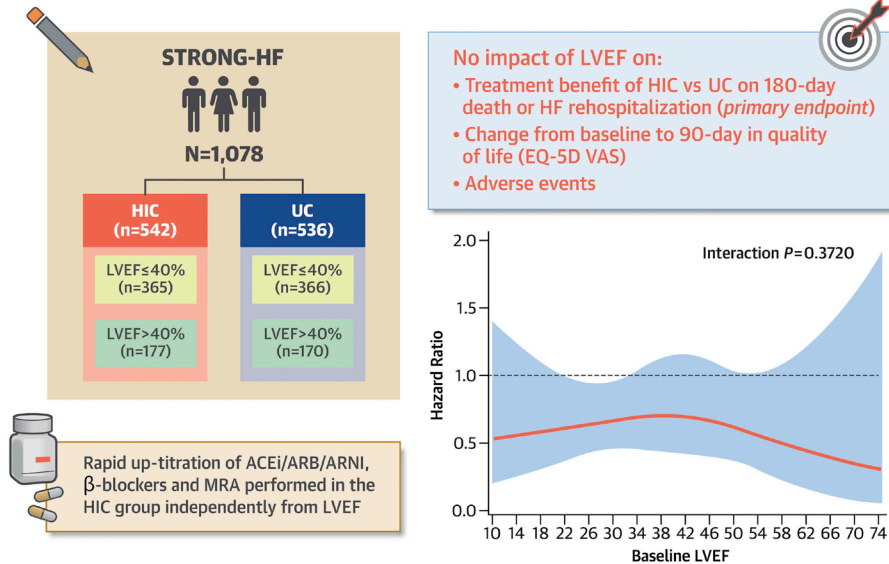
- Significant delays in GDMT optimization
  - Up to 6 months to follow this sequential dosing
  - Fails to consider early achievement of statistically significant benefit
- Optimal GDMT is historical, not biological
  - Significant difference in background therapy across trials
  - Phase 3 trials of quadruple therapy show similar magnitude of benefit regardless of background
  - Suggests therapeutic efficiencies are functionally independent
- Benefits seen without optimal GDMT in recent trials
  - 52% MRA use in PARADIGM-HF, 10% ARNI use in DAPA-HF

# Therapy Initiation - Historical

- Low dose GDMT has therapeutic efficiency
  - 64% of MERIT patients, 60% EMPHASIS patients met target dose
  - ATLAS/HEALL showed no mortality difference with lisinopril/losartan low vs high dose
- Initiation of multiple up-front therapies facilitates GDMT optimization later
  - Inpatient to Outpatient
  - ARB (instead of ACE-I) directly to ARNI

# STRONG HF – Godspeed...

## CENTRAL ILLUSTRATION: Left Ventricular Ejection Fraction and Medical Therapy Uptitration in STRONG-HF



Pagnesi M, et al. J Am Coll Cardiol. 2023;81(22):2131-2144.

- Safety, Tolerability and Efficacy of Rapid Optimization, Helped by NT-ProBNP Testing, of Heart Failure Therapies
- Among patients with hospitalization for acute decompensated HF, rapid up-titration of HF treatments in a high-intensity care model was safe and associated with a **reduced risk of death or being readmitted for HF at 180 days, irrespective of baseline EF or baseline NT-proBNP**
- Improvements in quality of life, blood pressure, and body weight were also noted.
- Serious adverse events were similar.
- The reductions in readmission and improvements in quality of life are of value in the HF population given the substantial burden of disease and the morbidity associated with hospital stays.



# β-Blockers

- Reduce morbidity and mortality, Slow disease progression (beneficial LV remodeling), Decreases PVCs/NSVT
- For: **All** patients with current or prior symptomatic HFrEF
- 1 of 3 β-Blockers:
  - Metoprolol Succinate (*MERIT-HF*) ~~Metoprolol Tartrate~~
  - Carvedilol (*COMET, COPERNICUS, PRECISE*)
  - Bisoprolol (*CIBIS II*)

# β-Blockers

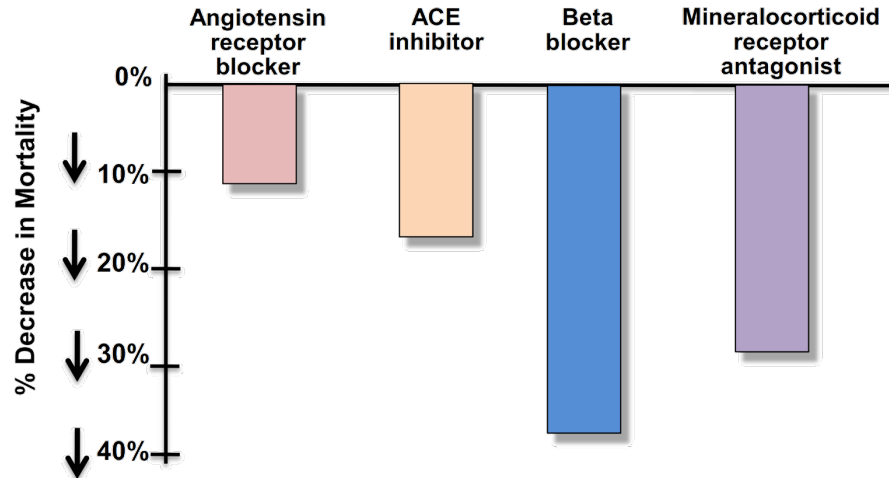
- Do NOT withdraw in exacerbation unless patient is hypotensive or in cardiogenic shock
  - *COMET, OPTIME-CHF, ESCAPE*
- Do NOT initiate in acute setting
  - *OPTIMIZE-HF, IMPACT-HF*
  - Adequate diuresis/Near Euvolemia

- Dosing:

	Initial	TARGET
<b>Metoprolol Succinate</b>	12.5-25mg Daily	200mg Daily
<b>Carvedilol</b>	3.125mg BID	50mg BID
<b>Bisoprolol</b>	1.25mg Daily	10mg Daily

# ACE Inhibitors

- Symptom improvement, Mortality benefit, Reduce hospitalization, Stops adverse LV remodeling;
- Independent of Anti-Hypertensive effect

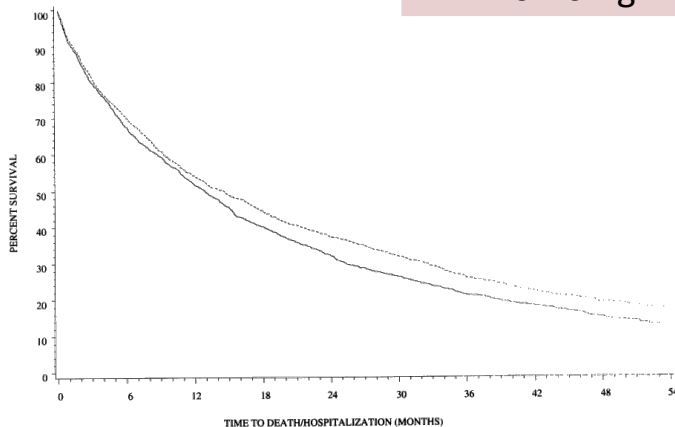


# ACE Inhibitors

For: **All** patients with current or prior symptomatic HFrEF

- Enalapril: **CONSENSUS, SOLVD**
- Captopril: **SAVE**
- Lisinopril: **ATLAS**
- Ramipril: **AIRE**
- TARGET Dosing (**ATLAS**):

Lisinopril	Captopril	Enalapril
20-40mg	50mg q8h	10-20mg q12h



Solid line: low-dose group (2.5-5.0mg)  
Dotted line: high-dose group (32.5-35mg)

Compared with the **low-dose** group, patients in the **high-dose** group had a **12% lower risk of death or hospitalization**,  $p=0.002$ .

# Angiotensin Receptor Blockers

- Similar benefits as ACE-I
  - Candesartan: *CHARM -Alternative, -Added, -Overall*
  - Valsartan: *Val-HeFT*
  - Valsartan vs Captopril: *VALIANT*
  - Losartan: *HEAAL*
  - Losartan vs Captopril: *ELITE II*
- ACE-I Cough => ARB substitution
- ACE-I + ARB? = NO
  - *RESOLVD, Val-HeFT, CHARM*

# Angiotensin Receptor Blockers

- Take home:
  - Routine use ACE-I + ARB = Potentially Harmful
- TARGET Dosing (*HEAAL*):

	Initial	TARGET
<b>Losartan</b>	25-50mg Daily	150mg Daily
<b>Candesartan</b>	4-8mg Daily	32mg Daily
<b>Valsartan</b>	20-40mg BID	160mg BID

# $\beta$ -Blockers or ACE-I/ARB First?

- **CARMEN**

- Carvedilol 25mg BID, Enalapril 10mg BID, or combination
- **Combination therapy** led to a greater improvement in end systolic volume *followed by carvedilol and enalapril monotherapy.*
- No difference in mortality or rehospitalization

- **CIBIS III**

- Bisoprolol 10mg QD vs Enalapril 10mg BID
- **As safe and efficacious** to initiate treatment for CHF with bisoprolol as with enalapril.

- In patients taking low dose ACE-I, addition of a  $\beta$ -blocker produces greater improvement in symptoms and reduction in risk of death than dose an increase in dose of ACE-I.
- $\beta$ -Blockers **do not provide a hemodynamic rescue** for the acutely decompensated patient with volume overload and/or low output.
  - In fact, in such settings,  $\beta$ -blockers should either be cut back or withheld.
  - But still reasonable to begin ACE-I even in patients with moderately severe to advanced symptoms and/or a decompensated state => **afterload reduction increases stroke volume.**

# $\beta$ -Blockers or ACE-I/ARB First?

- **NO RIGHT ANSWER** => feel reassured that we can **tailor our approach to our patients** without harm.
- Where **blood pressure is limiting**, ACE-I should be cut back to maximize  $\beta$ -blocker doses, as has been done in all  $\beta$ -blocker trials to date.
- In **tachycardic** patients who are clinically well perfused, euvolemic,  $\beta$ -blockers can be initiated first and titrated to goal doses.
- Other considerations:
  - CKD
  - Atrial Fibrillation => Rate Control
  - Symptomatic Bradycardia
  - Pregnant



# Nitrates + Hydralazine

- Combination confers Mortality benefit, Reduces hospitalizations, Improves quality of life in **self identified African American** patients.
- Trials:
  - *V-HeFT I* => *A-HeFT*
  - Enalapril vs ISDN/Hydralazine: *V-HeFT II*
    - ACE-I confers mortality benefit vs ISDN/hydralazine
    - 18% vs 25% at 2 years and overall

# Nitrates + Hydralazine

- Indications:
  - Self Identified African American Population
  - NYHA Class III-IV HF & LVEF <40%
  - ACE-I/ARB Intolerant (*V-HeFT II*)
- Dosing:

	Initial	TARGET
<b>Isosorbide Mononitrate</b>	30mg Daily	120mg Daily
<b>Isosorbide Dinitrate</b>	20-30mg q8h	40mg q8h (120mg daily)
<b>Hydralazine</b>	25-50mg q8h	100mg q8h (300mg Daily)

# Mineralocorticoid Receptor Antagonists

- Survival benefit:
  - Blocking mineralocorticoid activity and preventing cardiac remodeling;
  - K<sup>+</sup> sparing action lowers risk of hypokalemia-associated arrhythmia
- Trials
  - Spironolactone: **RALES** (NYHA class III-IV HF, LVEF <35%)
  - Eplerenone:
    - **EPHESUS**
    - **EMPHASIS-HF** (NYHA class II HF + LVEF ≤30%)

# Mineralocorticoid Receptor Antagonists

- Indications:
  - NYHA class II-IV & LVEF  $\leq 35\%$ 
    - If NYHA class II, should have prior CV hospitalization or elevated BNP
  - After MI if LVEF  $\leq 40\%$  with HF symptoms or Diabetes
- Contraindication to initiation:
  - Creatinine  $>2.5$  mg/dL (Men) or  $>2.0$  mg/dL (Women)
  - GFR  $<30$  mL/min/ $1.73$  m<sup>2</sup>
  - Potassium  $\geq 5.0$  mEq/L
- Dosing:

	Initial	TARGET
Spirolactone	12.5-25mg Daily	25mg Daily or BID
Eplerenone	25mg Daily	50mg Daily

# Mineralocorticoid Receptor Antagonists, Blood Pressure, and Outcomes in Heart Failure With Reduced Ejection Fraction

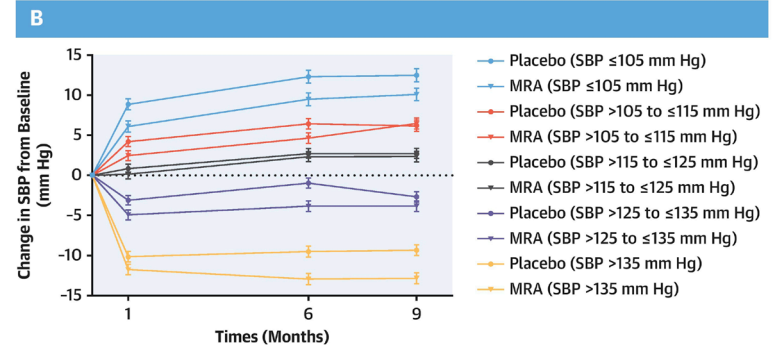
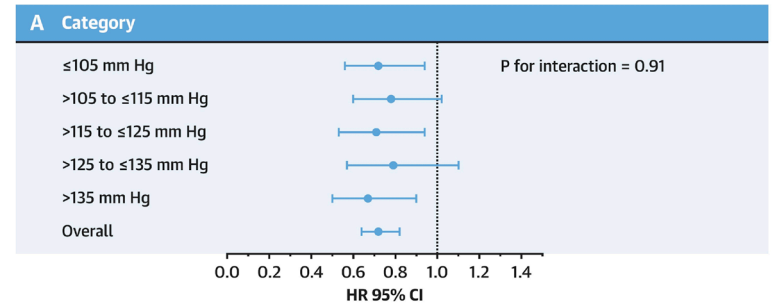
## Clinical Research

Matteo Serenelli, Alice Jackson, Pooja Dewan, Pardeep S. Jhund, Mark C. Petrie, Patrick Rossignol, Gianluca Campo, Bertram Pitt, Faiez Zannad, João Pedro Ferreira, and John J.V. McMurray

J Am Coll Cardiol Heart Fail. 2020 Jan, 8 (3) 188–198

- MRAs underused in HFrEF because of fear of adverse events  
=> Hyperkalemia, Hypotension
- 4,396 patients with HFrEF from RALES & EMPHASIS-HF trials
- MRA treatment had:
  - Little effect on SBP in patients with HFrEF
  - Infrequently caused hypotension, even when the baseline SBP was low
- **Low SBP is not a reason to withhold MRA therapy in patients with HFrEF.**

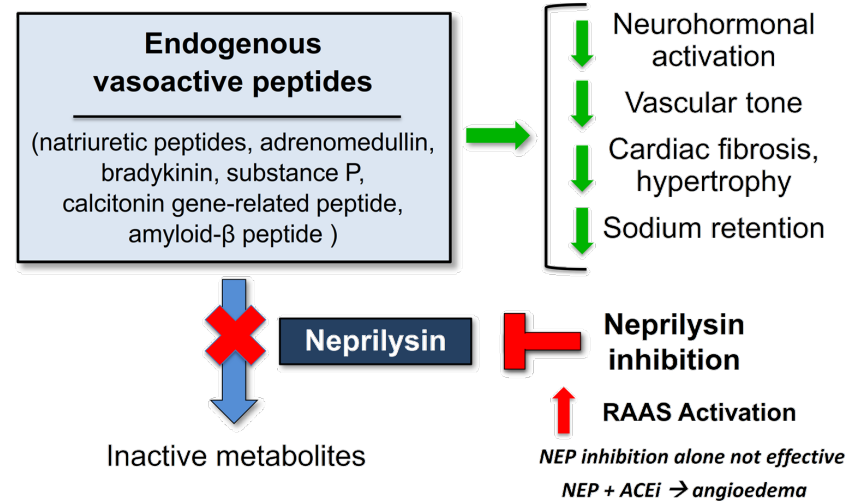
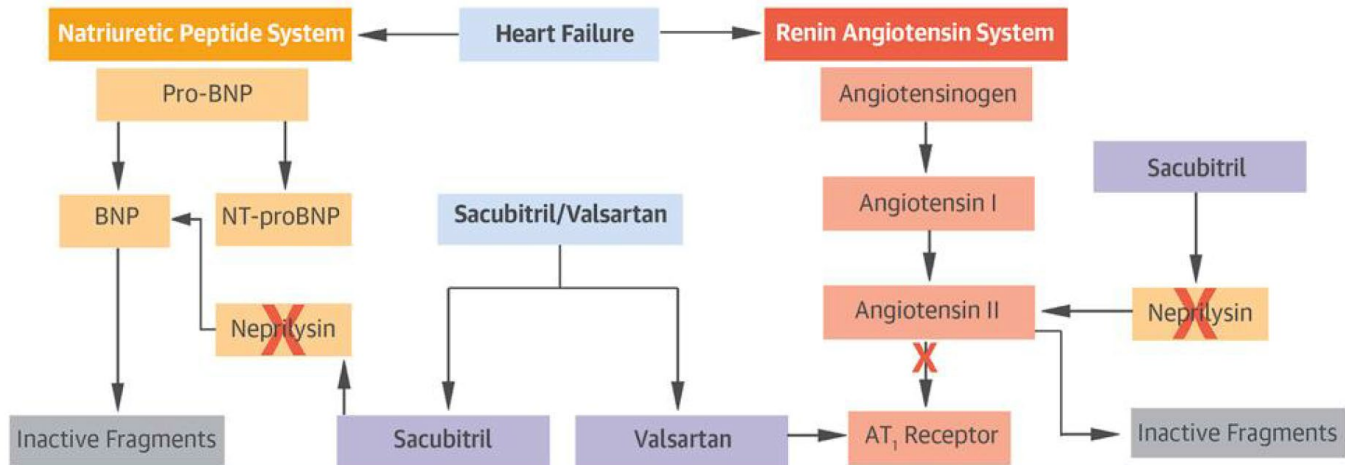
### CENTRAL ILLUSTRATION: Adjusted Hazard Ratios for All-Cause Death and Changes in SBP From Baseline



Serenelli, M. et al. J Am Coll Cardiol HF. 2020;8(3):188-98.

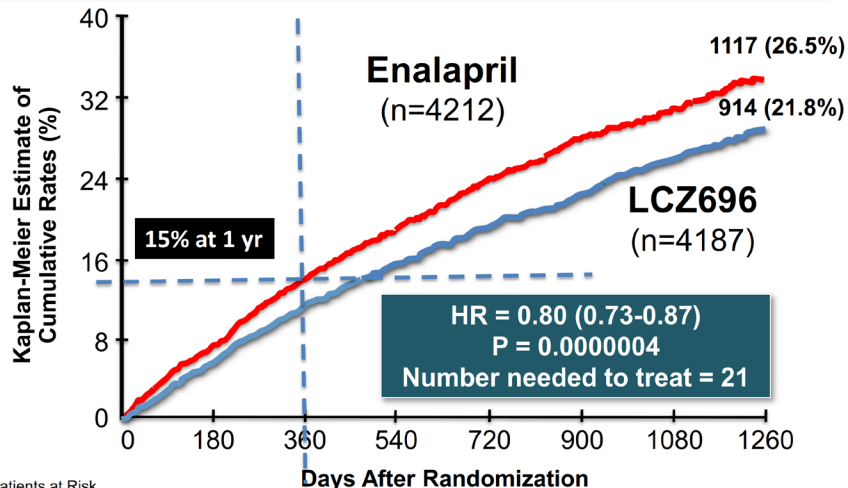
# Angiotensin Receptor-Neprilysin Inhibitor

- Angiotensin receptor-Neprilysin inhibitor (ARNI)
- *PARADIGM-HF* (Outpatients); *PIONEER-HF* (Inpatients)
  - Valsartan/Sacubitril 97/103mg BID vs Enalapril 10mg BID
- **Superior** to Enalapril:
  - Reduction in all-cause mortality (17.0% vs. 19.8%; NNT 36)
  - Reduced CV mortality or HF hospitalizations (21.8% vs. 26.5%; NNT 21)



# Angiotensin Receptor-Nepriylsin Inhibitor

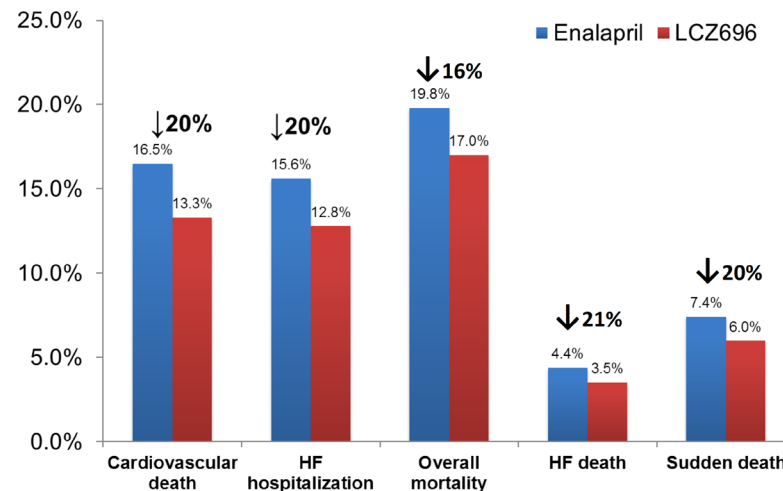
## PARADIGM-HF: CV Death or HF Hospitalization (Primary Endpoint)



Patients at Risk	0	180	360	540	720	900	1080	1260
LCZ696	4187	3922	3663	3018	2257	1544	896	249
Enalapril	4212	3883	3579	2922	2123	1488	853	236

McMurray et al. NEJM 2014

## Other Key Endpoints



McMurray, NEJM 2014; Desai et al. European Heart Journal 2015



# Angiotensin Receptor-Nepriylsin Inhibitor

- Patients studied:
  - Clinically Stable with Regular follow-up
  - **Mild HF; 70% NYHA Class II**
  - **Already on Optimal Medical Therapy ( $\beta$ -Blockers + ACE-I/ARB)**
  - Replacing their ACE-I/ARB with a better drug

- Adverse events:

	LCZ696 (n=4187)	Enalapril (n=4212)	P Value
<b>Prospectively identified adverse events</b>			
Symptomatic hypotension	588 (14%)	388 (9.2%)	< 0.001
Serum potassium > 6.0 mmol/l	181 (4.3%)	236 (5.6%)	0.007
Serum creatinine $\geq$ 2.5 mg/dl	139 (3.3%)	188 (4.5%)	0.007
Cough	474 (11.3%)	601 (14.3%)	< 0.001
<b>Angioedema (adjudicated)</b>	<b>19</b>	<b>10</b>	
Medications, no hospitalization	16	9	
Hospitalized; no airway compromise	3	1	
Black Subjects	2.4%	0.5%	
Nonblack Subjects	0.4%	0.2%	

# ARNI Dosing



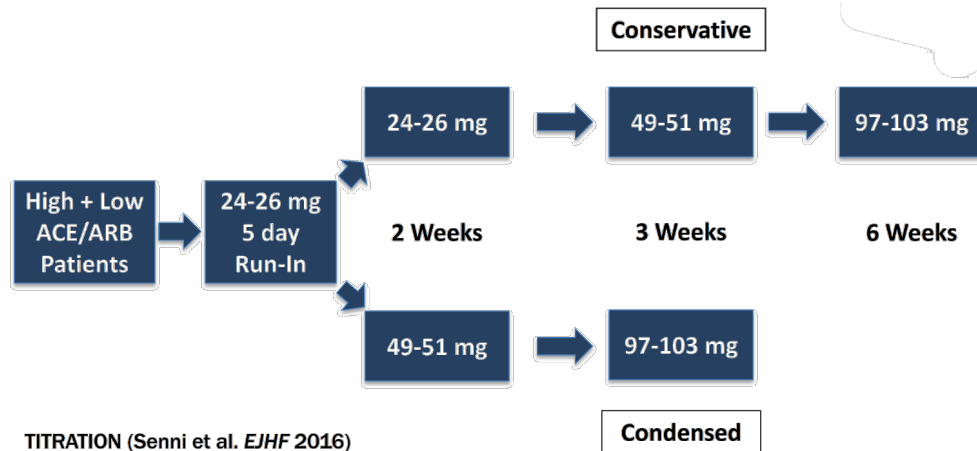
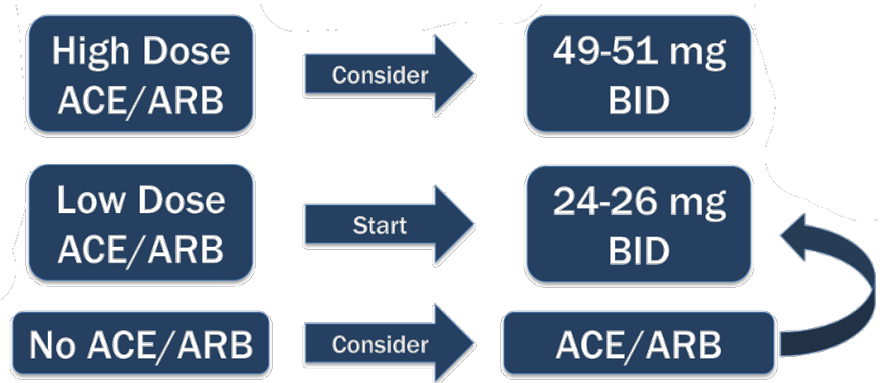
Stop taking your  
**ACE**  
inhibitor\*



Wait for  
**36**  
hours



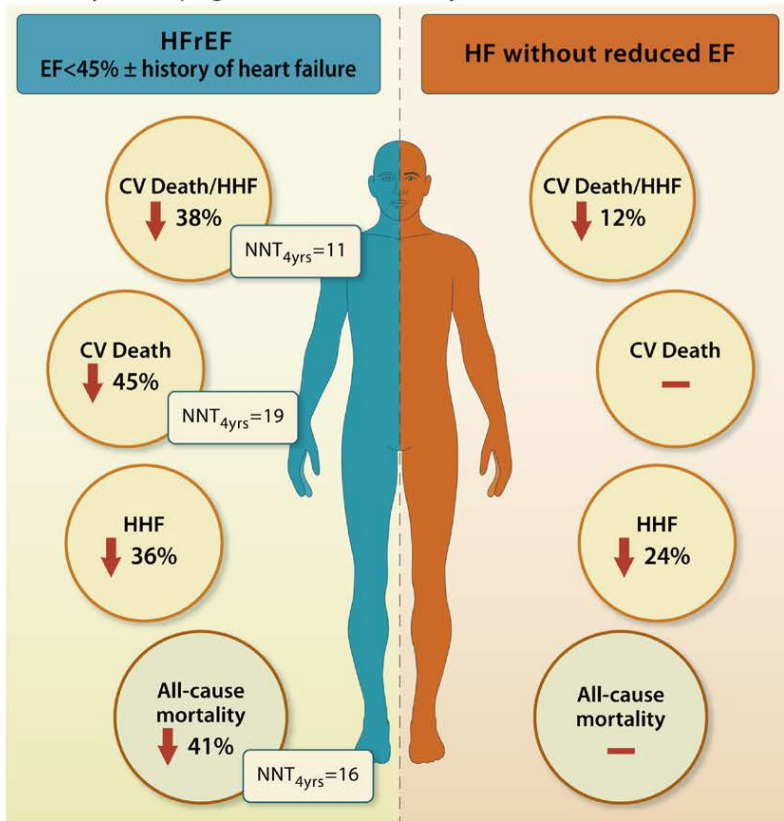
Start taking  
**ENTRESTO**,  
as prescribed



TITRATION (Senni et al. *EJHF* 2016)

# SGLT2 Inhibitors

## Efficacy of Dapagliflozin Based on Ejection Fraction



## • Trials

- *DAPA-HF, DECLARE-TIMI 58*: Dapagliflozin
- *EMPEROR-Reduced*: Empagliflozin
- *SOLOIST-WHF*: Sotagliflozin

- SGLT2 inhibition with or on top of GDMT reduced all-cause and cardiovascular death, HF hospitalizations, and serious adverse renal outcomes in HFrEF.

### Drug Type

Canagliflozin, dapagliflozin, & empagliflozin with similar efficacy profile in reducing HF events

### Starting Dose (once daily in AM)

- Canagliflozin (100mg)
- Dapagliflozin (5mg)
- Empagliflozin (10mg)
- Ertugliflozin (5mg)

### Metformin+SGLT2i

#### Combination Therapies

Consider to limit non-adherence and pill burden

### Stable Hemodynamic and Clinical Status

#### Pre-Initiation eGFR must be above:

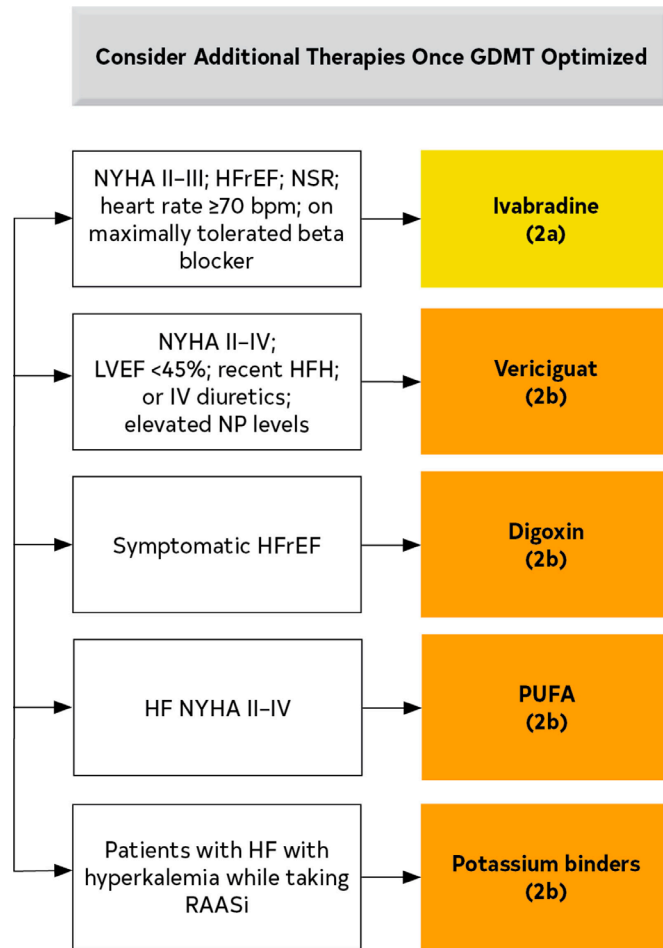
- 60 mL/min/1.73 m<sup>2</sup> (dapagliflozin, ertugliflozin)
- 45 mL/min/1.73 m<sup>2</sup> (canagliflozin, empagliflozin)

# SGLT2 Inhibitors

## Multi-system effects of SGLT-2 inhibitors

	Heart failure	Type 2 diabetes	Chronic kidney disease
Efficacy	Reduces heart failure hospitalizations and cardiovascular mortality across the complete ejection fraction spectrum	Improves glycemic control, and decreases risk of cardiovascular death in patients at high cardiovascular risk	Reduces decline of glomerular filtration rate and risk of renal and cardiovascular death
Drugs currently approved	Dapagliflozin, empagliflozin	Canagliflozin, dapagliflozin, empagliflozin, ertugliflozin	Canagliflozin, dapagliflozin, empagliflozin
Key guideline recommendations	<p><b>Class 1 Recommendation:</b> Chronic stable heart failure with reduced ejection fraction</p> <p><b>Class 2A Recommendation:</b> Chronic stable heart failure with mildly reduced and preserved ejection fraction</p>	Designated first-line therapy in addition to metformin in patients with type 2 diabetes at high cardiovascular risk, including patients with chronic kidney disease and heart failure	<p><b>Class 1 Recommendation:</b> Type 2 diabetes and chronic kidney disease in patients with estimated glomerular filtration rate &gt;20 mL/min/1.73 m<sup>2</sup></p>

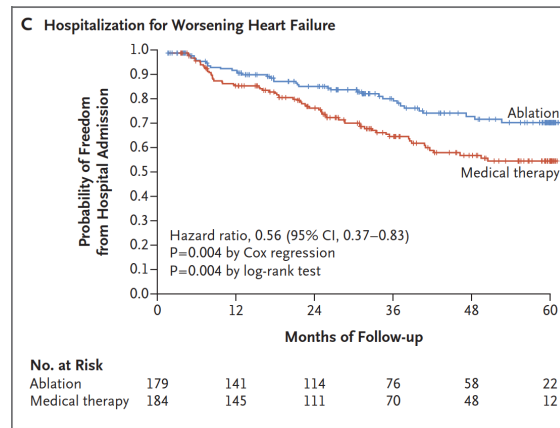
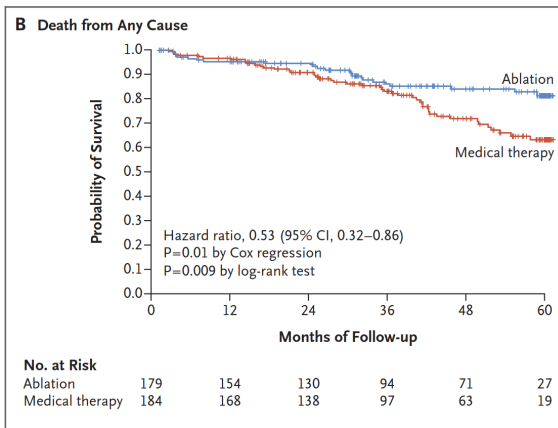
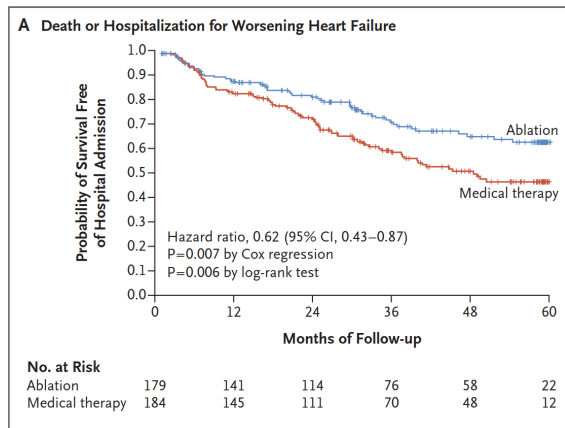
# Additional Therapies



# Therapy NOT to use

COR	LOE	Recommendations
3: No Benefit	A	1. In patients with HFrEF, dihydropyridine calcium channel-blocking drugs are not recommended for HF. <sup>1,2</sup>
3: No Benefit	B-R	2. In patients with HFrEF, vitamins, nutritional supplements, and hormonal therapy are not recommended other than to correct specific deficiencies. <sup>3-9</sup>
3: Harm	A	3. In patients with HFrEF, nondihydropyridine calcium channel-blocking drugs are not recommended. <sup>10-13</sup>
3: Harm	A	4. In patients with HFrEF, class IC antiarrhythmic medications and dronedarone may increase the risk of mortality. <sup>14-16</sup>
3: Harm	A	5. In patients with HFrEF, thiazolidinediones increase the risk of worsening HF symptoms and hospitalizations. <sup>17-21</sup>
3: Harm	B-R	6. In patients with type 2 diabetes and high cardiovascular risk, the dipeptidyl peptidase-4 (DPP-4) inhibitors saxagliptin and alogliptin increase the risk of HF hospitalization and should be avoided in patients with HF. <sup>22-24</sup>
3: Harm	B-NR	7. In patients with HFrEF, NSAIDs worsen HF symptoms and should be avoided or withdrawn whenever possible. <sup>25-28</sup>
3: No Benefit	B-R	3. In patients with chronic HFrEF without a specific indication (eg, venous thromboembolism [VTE], AF, a previous thromboembolic event, or a cardioembolic source), anticoagulation is not recommended. <sup>7-9</sup>

# Atrial Fibrillation & Heart Failure

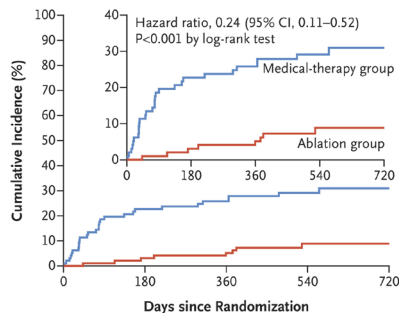


## **CASTLE-AF** Trial (2018)

- In patients AFib and symptomatic (NYHA II-IV) HFrEF (EF ≤ 35%)
- Catheter ablation is associated with a 16.1% absolute reduction in death or hospitalization for heart failure *when compared to medical therapy (rate or rhythm control)*.
- Driven both by a **11.6% absolute reduction in death** and a **15.2% absolute reduction in hospitalization** for heart failure.
- Catheter ablation was also associated with greater improvement in LVEF and long-term maintenance of sinus rhythm.

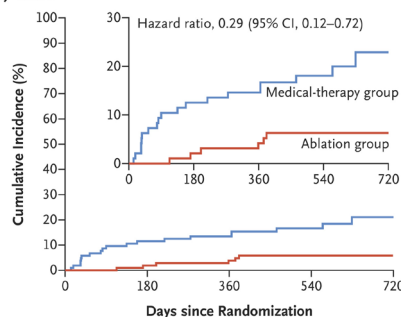
# Atrial Fibrillation & Heart Failure

**A Primary End Point**



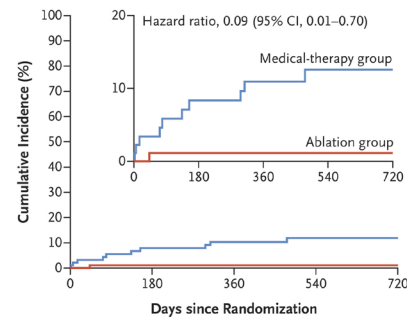
No. at Risk	0	180	360	540	720
Medical-therapy group	97	75	72	41	12
Ablation group	97	94	88	50	20

**B Death from Any Cause**



No. at Risk	0	180	360	540	720
Medical-therapy group	97	85	83	45	13
Ablation group	97	95	93	51	20

**C Implantation of a Left Ventricular Assist Device**



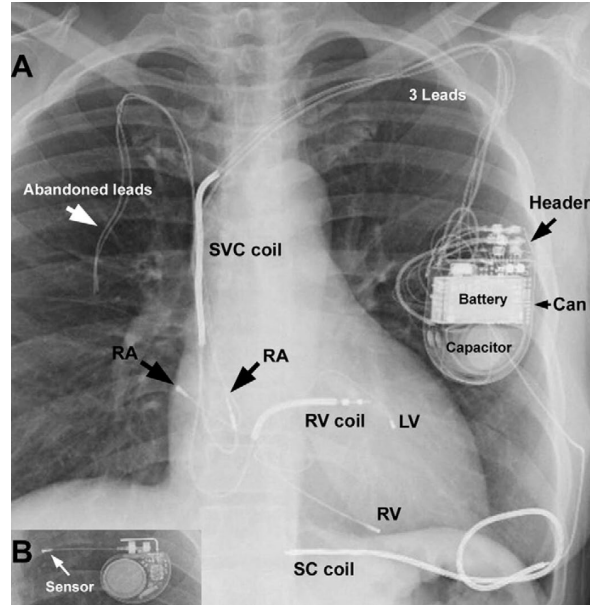
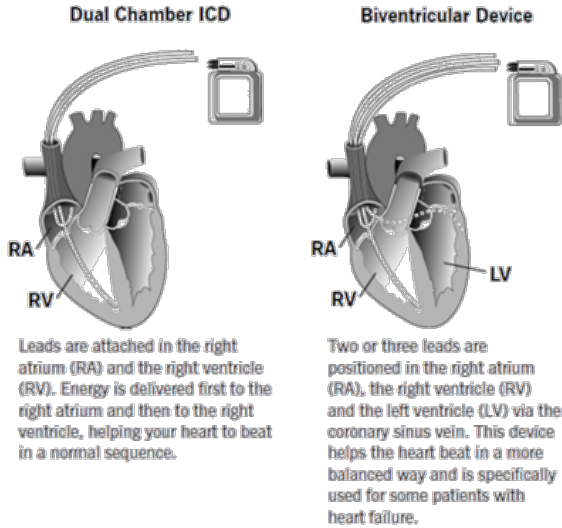
No. at Risk	0	180	360	540	720
Medical-therapy group	97	79	76	42	12
Ablation group	97	94	92	51	20

## **CASTLE-HTx** Trial (2023)

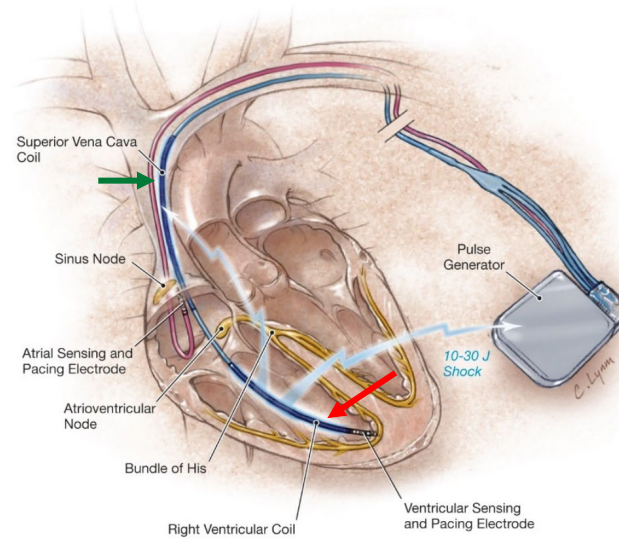
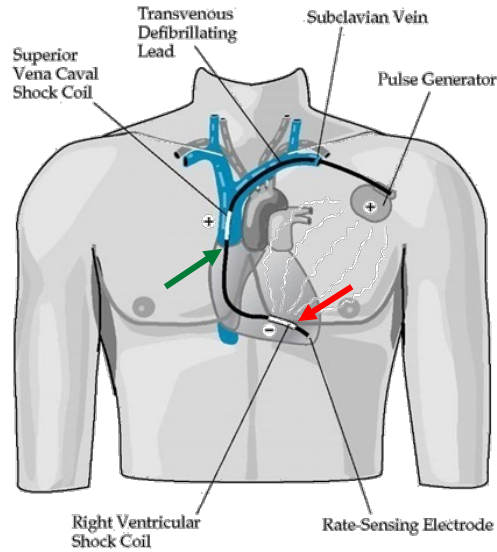
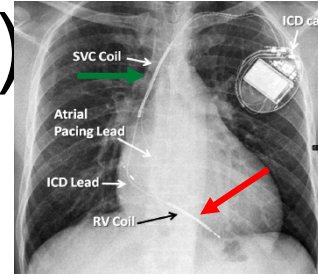
- Reduction in all-cause mortality, LVAD implantation, and urgent HT with catheter ablation compared with medical therapy alone in end-stage HFrEF with symptomatic AF.
- Driven primarily by reduction in all-cause death and LVAD implantation and was observed despite significant crossover between treatment arms within weeks of randomization, prompting early termination of the trial for efficacy.
- Mean LVEF: 29% vs. 25% (catheter ablation vs. medical therapy, respectively)
- Mean AF duration: 4 vs. 3 years (catheter ablation vs. medical therapy, respectively)



# ICD / CRT-(P/D)



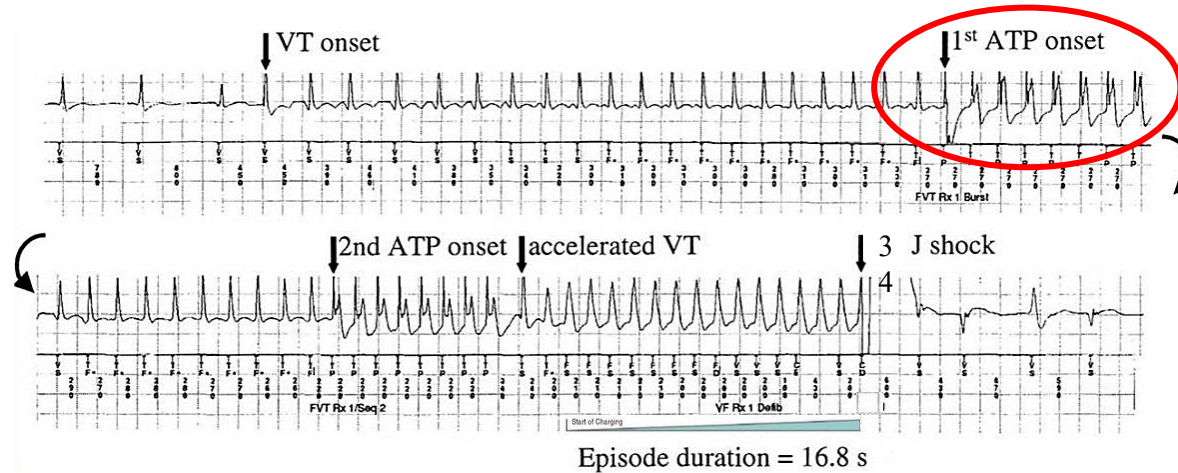
# ICD / CRT-(P/D)



# ICD Functions

1. Sensing
2. Pacing *(all modern ICDs function as pacemakers)*
  - Anti-tachycardia pacing
  - Bradycardia pacing
3. Cardioversion: low energy shock
4. Defibrillation: high energy shock

# ICD / CRT-(P/D)

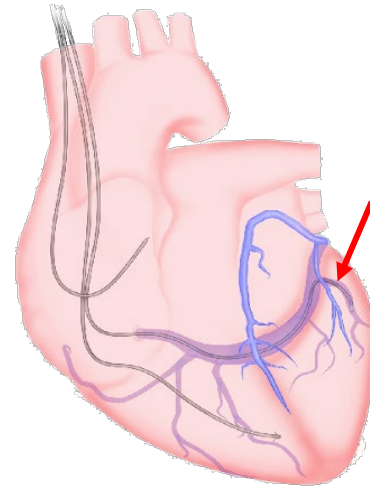
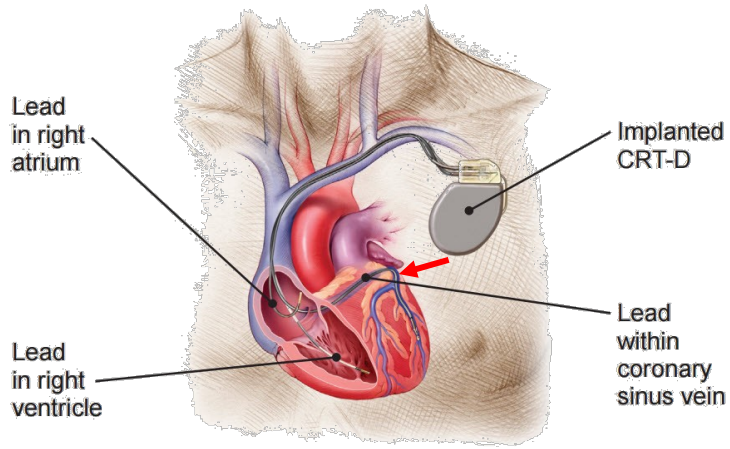
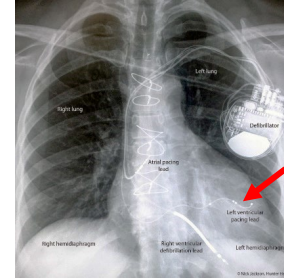


# ICD / CRT-(P/D)

## ICD:

- Primary & Secondary prevention of Sudden Cardiac Death
- *MADIT I & II, MUSTT*
- *SCD-HeFT*: ICD vs Amiodarone
- Mortality benefit for:
  - **Non-ischemic dilated cardiomyopathy** or **ICM  $\geq 40$  days post MI**
    - *DINAMIT*: Prophylactic implantation of an ICD 6-40 days after acute MI reduces arrhythmic deaths but does not improve all-cause mortality.
  - With **LVEF  $\leq 35\%$**  and NYHA class II or III symptoms
  - On **GDMT (at least 3 months)** with expected survival  $>1$  year

# ICD / CRT-(P/D)



# ICD / CRT-P

## **CRT indicated if:**

- LVEF  $\leq 35\%$  on *optimal medical therapy* with:
  - **Sinus rhythm, LBBB, QRS  $\geq 150$ msec, and NYHA class II, III, ambulatory class IV**
  - Sinus rhythm, NO LBBB, QRS  $\geq 150$ msec, with NYHA class III, ambulatory class IV
  - Sinus rhythm, LBBB, QRS 120-149msec, with NYHA class II, III, ambulatory class IV
  - Atrial Fibrillation if requiring V-pacing or meeting other CRT criteria and rate will allow near 100% V-pacing with CRT either by AV-nodal ablation or rate-controlling medications

# Who needs a Right Heart Catheterization?

- Early identification of the **STAGE D HF** patient

**Supplementary Table 14** 'I Need Help' markers of advanced heart failure

<b>I</b>	Inotropes	Previous or ongoing requirement for dobutamine, milrinone, dopamine, or levosimendan
<b>N</b>	NYHA class/NP	Persisting NYHA class III or IV and/or persistently high BNP or NT-proBNP
<b>E</b>	End-Organ Dysfunction	Worsening renal or liver dysfunction in the setting of HF
<b>E</b>	Ejection Fraction	Very low EF <20%
<b>D</b>	Defibrillator shocks	Recurrent appropriate defibrillator shocks
<b>H</b>	Hospitalizations	More than 1 hospitalization with HF in the last 12 months
<b>E</b>	Edema/Escalating diuretics	Persisting fluid overload and/or increasing diuretic requirement
<b>L</b>	Low blood pressure	Consistently low blood pressure with SBP <90 to 100 mmHg
<b>P</b>	Prognostic medication	Inability to uptitrate (or need to decrease/cease) ACE-Is, beta-blockers, ARNIs, or MRAs

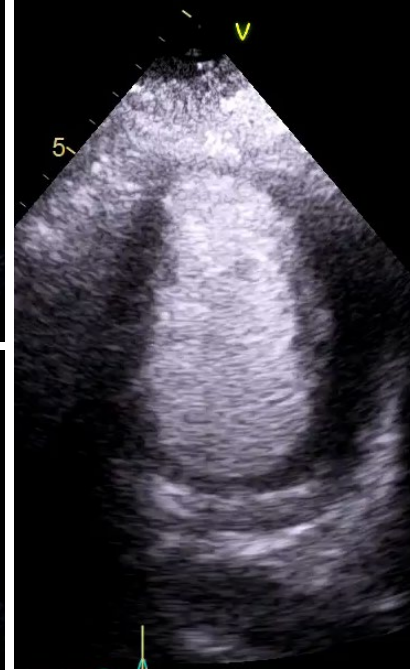
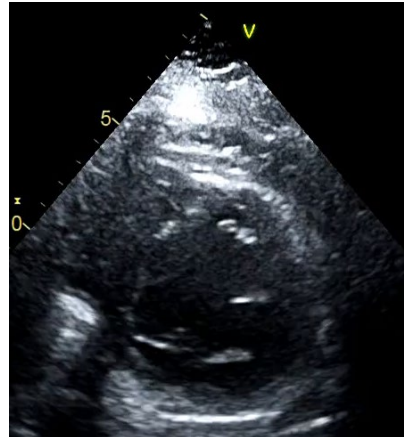
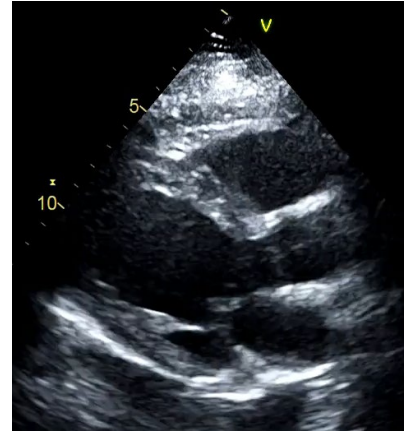
©ESC 2021

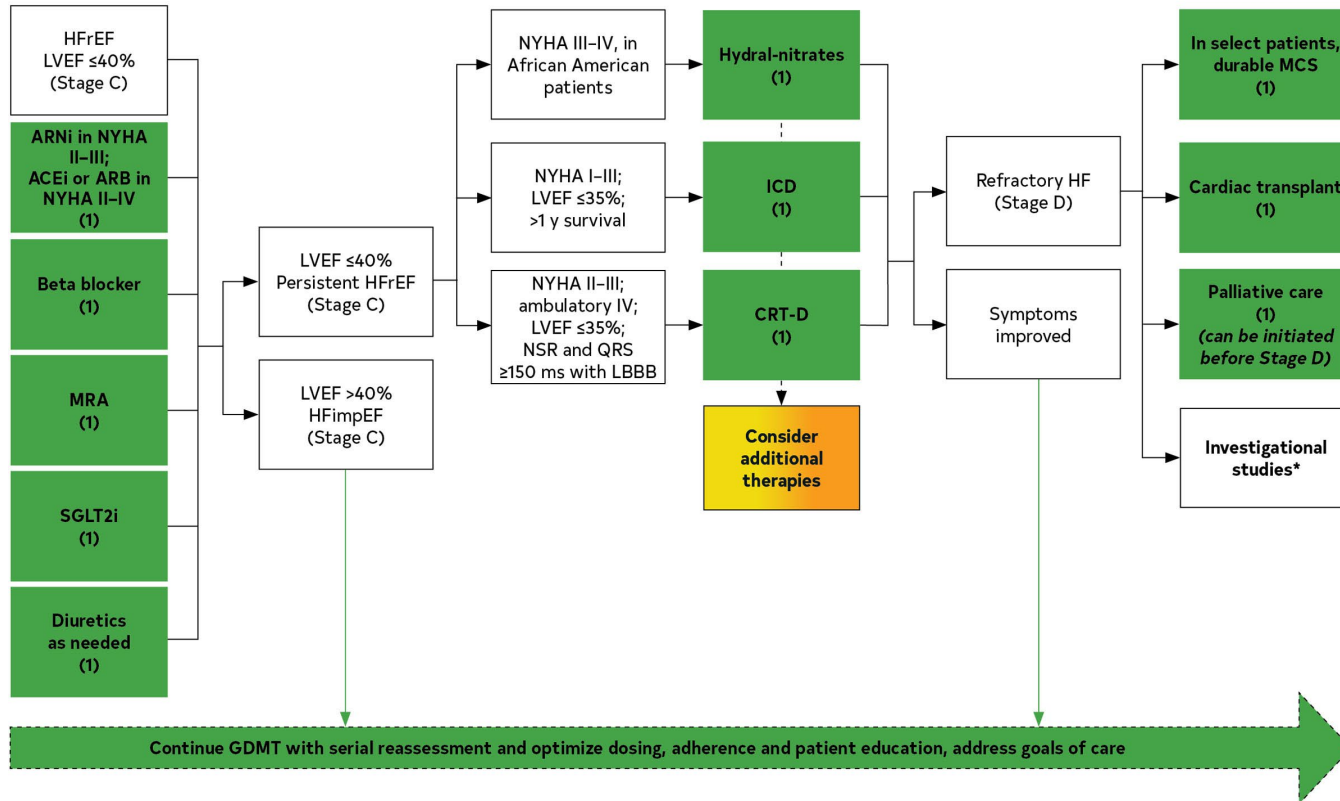
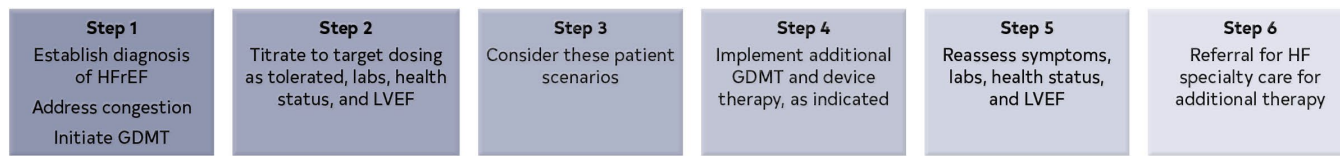
- Early identification of the AT RISK CARDIOGENIC SHOCK patient
  - SCAI Stage B Cardiogenic Shock
  - Early escalation of care
  - Inotropes

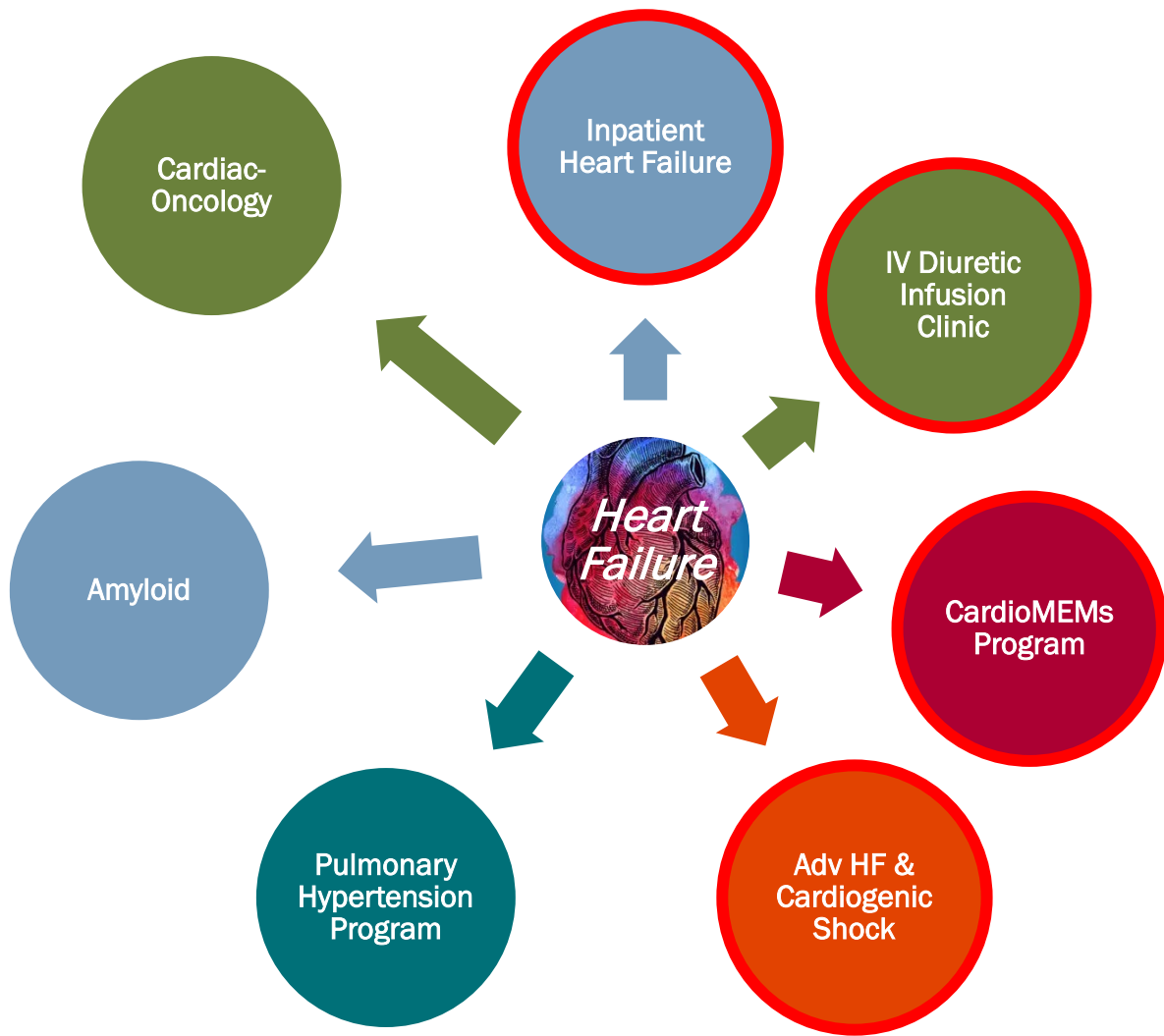


# Recovered EF & Discharged!

- EMBx: active lymphocytic myocarditis.  
Negative EBV, adenovirus, CMV
- Solumedrol 1gm x3 => Prednisone
- IVIG x3
- Repeat TTE: EF 55-59%
- Total 18 day hospital stay
  - 8 days on IABP
- Walked out of hospital, discharged home
  - Biggest issue now is chronic back pain







# Inpatient Heart Failure

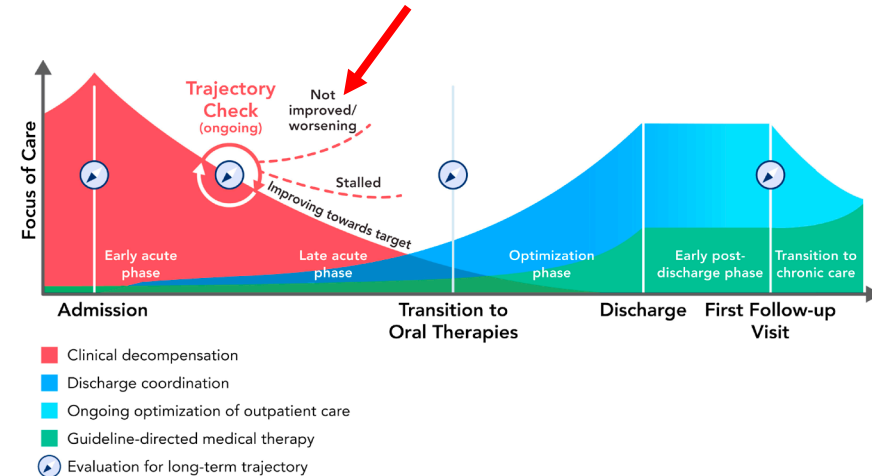
- Who:

- APP – Kayla Olson
- Cardiologist – Rotating (Point Person Dr. Tea)

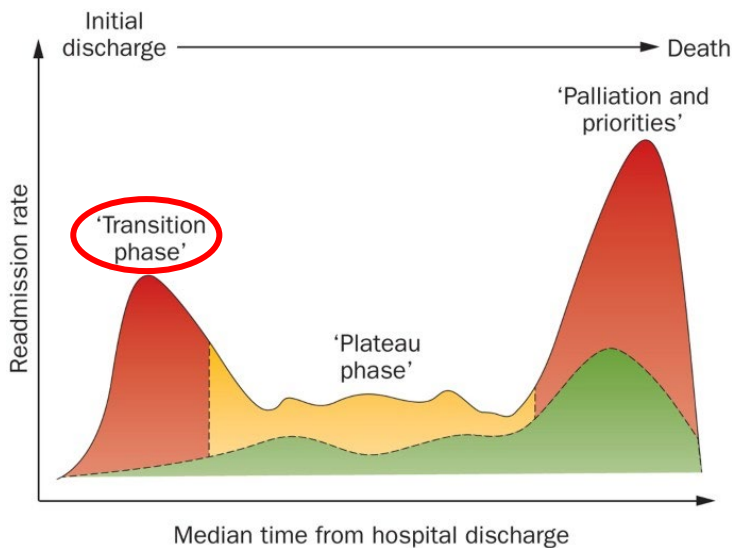
- What it is (Assistance with):

- ✓ Formalization of HF consult to improve outcomes
- ✓ Aggressive upfront diuresis
- ✓ Comprehensive evaluation if new diagnosis
- ✓ Patient education
- ✓ Assess Trajectory
- ✓ Initiation & Titration of GDMT
- ✓ Device candidacy – ICD, CRT-P, CRT-D
- ✓ CardioMEMs candidacy (to reduce exacerbations/readmissions)
- ✓ Early (but safe) discharge with care coordination!!!

- Primary Dr. continues to take the lead, we are here to assist as consultants



# Outpatient Heart Failure Follow-Up “Vulnerable Phase”



- Within 1-2 weeks of discharge
- Prevent readmission
- Referral to outpatient IV infusion clinic if necessary
- Ensure oral diuretics are adequate to maintain euvolemia
- Further titration of GDMT
- 1-3 appointments (depending on how patient is doing)
- **Continue to follow with PCP/Cardiologist regularly as before**

# Outpatient IV Diuretic Infusion – Where Losing is Winning

## GOALS:

- Prevent hospitalization or readmission
- Improve quality of life
- Provide an environment for development of HF self-management skills through education
- Identify patients who would benefit from CardioMEMS implant

## • Availability:

- Specials (Infusions)
- Monday to Friday 8am to 3pm
- **Furosemide IV 40 to 180mg infusion, with adjustment of home PO diuretic**

## • Who:

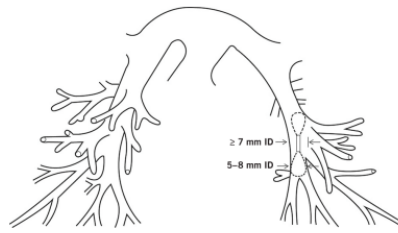
- APP – Kayla Olson
- Cardiologist – Rotating (Point Person Dr. Tea)

## • Launched Thursday September 29<sup>th</sup> 2022

- Avoided readmission of > 40 patients and growing

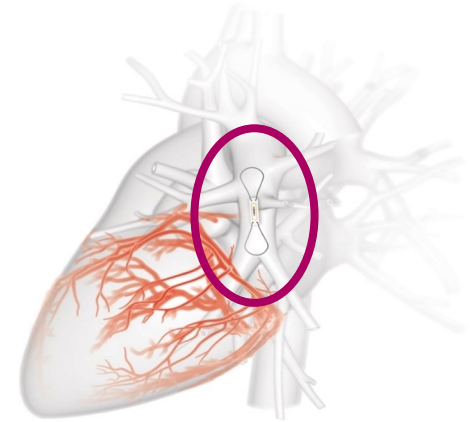
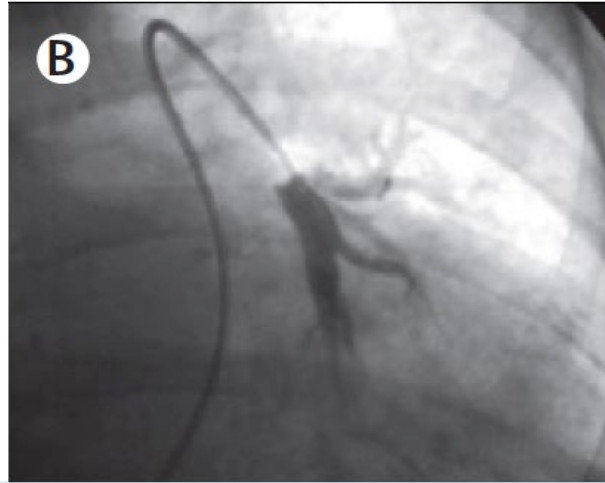
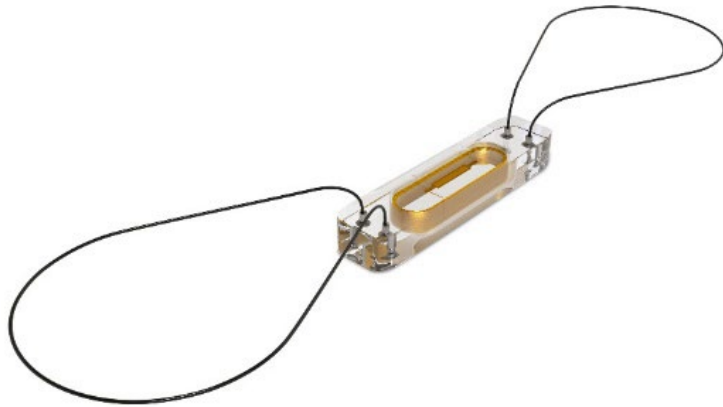
# CardioMEMS<sup>®</sup>

PA PRESSURE MONITORING SYSTEM

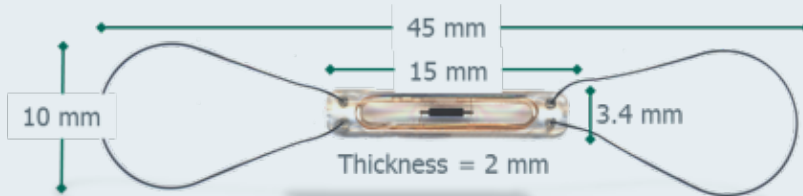


TARGET IMPLANT SITE

TARGET LOCATION  
FOR  
PA PRESSURE SENSOR

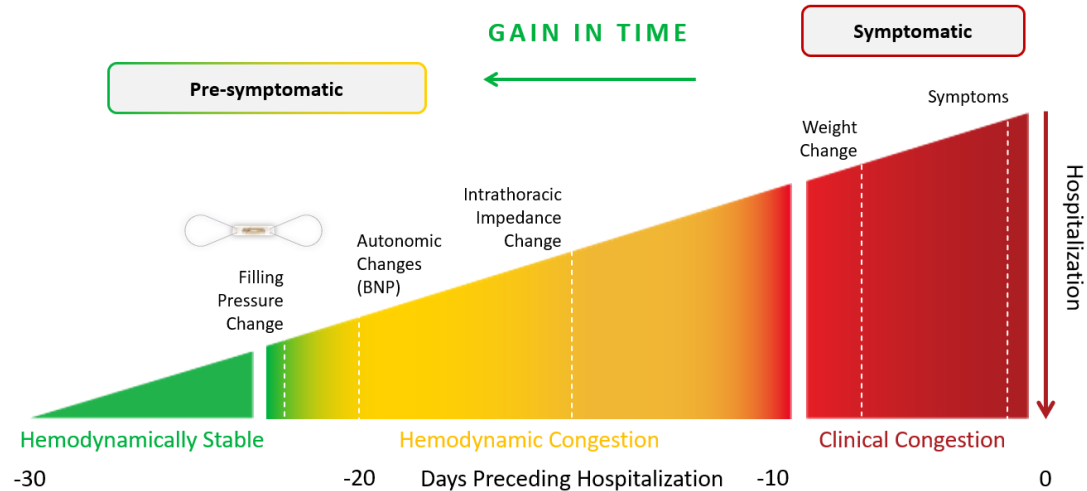


PULMONARY  
ARTERY  
PRESSURE  
SENSOR



# CardioMEMS<sup>®</sup>

- Slow the progression of heart failure with early intervention using pre-symptomatic data
- Both HFrEF and HFpEF
- Early indicator of the onset of worsening heart failure.
- Titrate medications
- Great for remote patients who live far away/don't like to come in
- Decrease readmissions





# Weight Change

*POOR SENSITIVITY FOR RULING OUT HEART FAILURE EXACERBATION*

WEIGHT GAIN	SENSITIVITY	SPECIFICITY
2 kg (4.5 lbs) weight gain over 48-72 hrs <sup>2</sup>	9%	97%
2% weight gain over 48-72 hrs <sup>2</sup>	17%	94%
3 lbs in 1 day or 5 lbs in 3 days	22.5%	-

**NO CORRELATION** – Daily weights *do not* correlate with filling pressures

# Patient Management Workflow

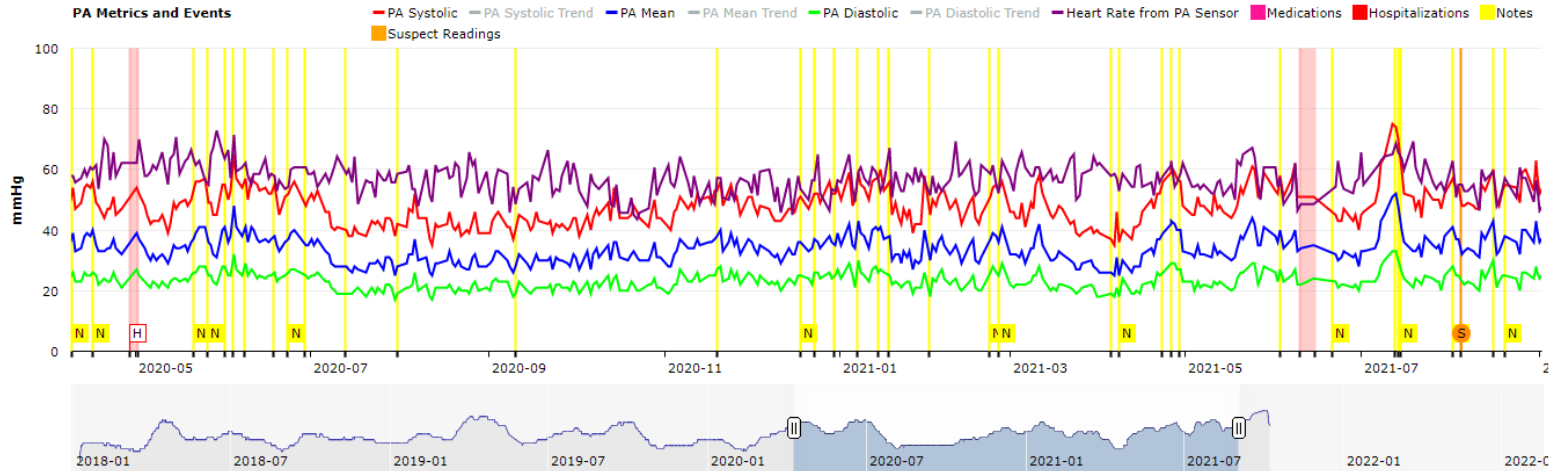
PA Diastolic Pressure Goal: 22 mmHg, Lower 20 mmHg, Upper 24 mmHg  
Right Heart Cath Implant Values

Last Reviewed: 2021-10-08  
Last Billed: 2021-09-20  
Last Export: ---

Fixed Auto

From: 2020-04-08 To: 2021-09-01

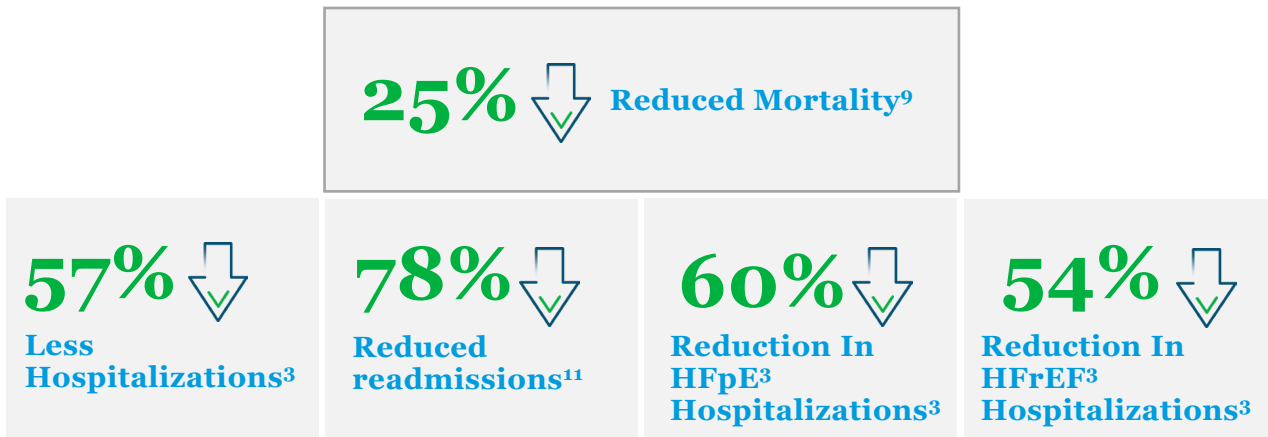
Date Range: 30 days 90 days 180 days All



# Driven By Data

- Proven clinical benefit in a variety of clinical studies including 4 prospective trials totaling over 3,000 patients.
- RCTs: CHAMPION, GUIDE-HF, MONITOR-HF

## PROVEN IN A VARIETY OF CLINICAL STUDIES



1. Lindenfeld J, Zile MR, Desai AS, et al. Hemodynamic-guided management of heart failure (GUIDE-HF): a randomized controlled trial. *The Lancet* 2021;398:991-1001. 2. Abraham WT, Adamson PB, Bourge RC, et al. Wireless pulmonary artery haemodynamic monitoring in chronic heart failure: a randomized controlled trial. *The Lancet*. 2011;377(9766):658-666. 3. Shavelle D, Desai A, Abraham W, et al. Lower rates of heart failure and all-cause hospitalizations during pulmonary artery pressure-guided therapy for ambulatory heart failure. *Circulation: Heart Failure*. Published online 2020. <https://doi.org/10.1161/CIRCHEARTFAILURE.119.006863> 4. Angermann C, A&musB, et al. Pulmonary-Artery-Pressure-Guided Therapy in Ambulatory Patients with Symptomatic Heart Failure: The CardioMEMS™ European Monitoring Study for Heart Failure (MEMS-HF). *European J of Heart Failure*. 2020. 10.1002/ehf.1943. 5. Heywood JT, Jermyn R, Shavelle D, et al. Impact of practice-based management of PA pressures in 2000 patients implanted with the CardioMEMS™ sensor. *Circulation*. 2017; 135: 1509-17. 6. Desai AS, et al. Ambulatory Hemodynamic Monitoring Reduces Heart Failure Hospitalizations in "Real-World" Clinical Practice. *J Am Coll Cardiol*. 2017; 69(19):2357-65. 7. Abraham J, et al. Association of Ambulatory Hemodynamic Monitoring with Clinical Outcomes in a Concurrent Matched Cohort Analysis. *JAMA Cardiology*. 2019;4(6):556-563. 8. Muhammad Shahzeb Khan, Jayakumar Sreenivasan, Norman Lateef, Marwan S. Abougergi, Stephen J. Greene, Tariq Ahmad, Stefan D. Anker, Gregg C. Fonarow, Javed Butler. Trends in 30- and 90-Day Readmission Rates for Heart Failure. *AHA Journals*. 2021; <https://doi.org/10.1161/CIRCHEARTFAILURE.121.008335> 9. Adamson, et al. Pulmonary artery pressure-guided heart failure management reduces 30-day readmissions. *Circulation: Heart Failure*. 2016;115.002600.10. Lindenfeld J; GUIDE-HF, CHAMPION, and LAPTOP-HF investigators. Longer-term Effects of Hemodynamic Monitoring on Outcomes: A Combined Data Analysis of HFpEF Patients in CHAMPION, GUIDE-HF, and LAPTOP-HF. Presented at: THT Conference; March 2023; Boston, MA 10. Brugts, J et al. Remote haemodynamic monitoring of pulmonary artery pressures in patients with chronic heart failure (MONITOR-HF): a randomised clinical trial. *The Lancet*. May 20, 2023. [https://doi.org/10.1016/S0140-6736\(23\)00923-6](https://doi.org/10.1016/S0140-6736(23)00923-6). 11. Adamson, et al. Pulmonary artery pressure-guided heart failure management reduces 30-day readmissions. *Circulation: Heart Failure*. 2016;115.002600.

## INDICATIONS

- NYHA class II-IV
- HF admission within the previous 12 months **AND/OR**
- Elevated BNP or NT-ProBNP

## What about Chronic Kidney Disease?

- Maintaining euvolemia is key to preventing further GFR loss from Cardio-Renal syndrome
- GFR is a moving target, consider their baseline
- Input from Nephrology
- Are they likely to be on HD in the next year?
- Diuretic responsiveness
  - What is their total daily diuretic dose?
- Underlying etiology for the patient's CKD
  - Diabetic or HTN vs. Cardiorenal

• THE CARDIOMEMS™ HF SYSTEM

# Merlin.net™ PCN Scorecard

CardioMEMS™ Merlin.Net™ Scorecard (USA)

## Summary Dashboard

Merlin data updated: 09/16/2023

 Choose Clinic

500246 - Altru Cardiology Clinic (Grand Forks, NORTH DAKOTA)

Overview

Patients

Thresholds

POI

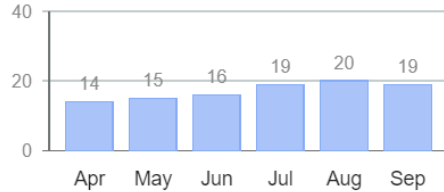
Email

DirectCall™

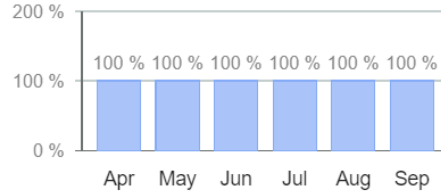
Review Actions

National

Active Patients

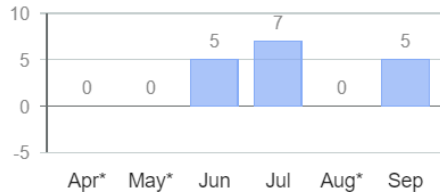


% Patients with Custom Thresholds

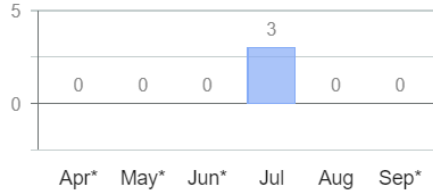


Updated as of:	09/16/2023
Active Patients	19
Associated EP Portal	Y


DirectCalls Sent Last 30 Days



Patients with Hospitalizations



**68%**   
Readmissions  
Prevented  
**NATIONALLY**

**79%**   
Readmissions  
Prevented  
**ALTRU**

# Patient success stories - UPDATE

**Patient 1**



**Patient 2**



**Patient 3**



	John T	Sex: M	Terry	Sex: M	Age: Carol B	Sex:
Pre CardioMEMS	8 hospitalizations		Hospitalized, fluid overload, couldn't volunteer as much he wanted to		4 months of HFH	
Post CardioMEMS	1 hospitalization(not HF related)		"Feels great. Volunteering more" hasn't been hospitalized, sleeping in his bed again		No HFH since MEMS	
Key takeaway						

*We can do better.*

*Contact Info*

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(610) 203-4340

