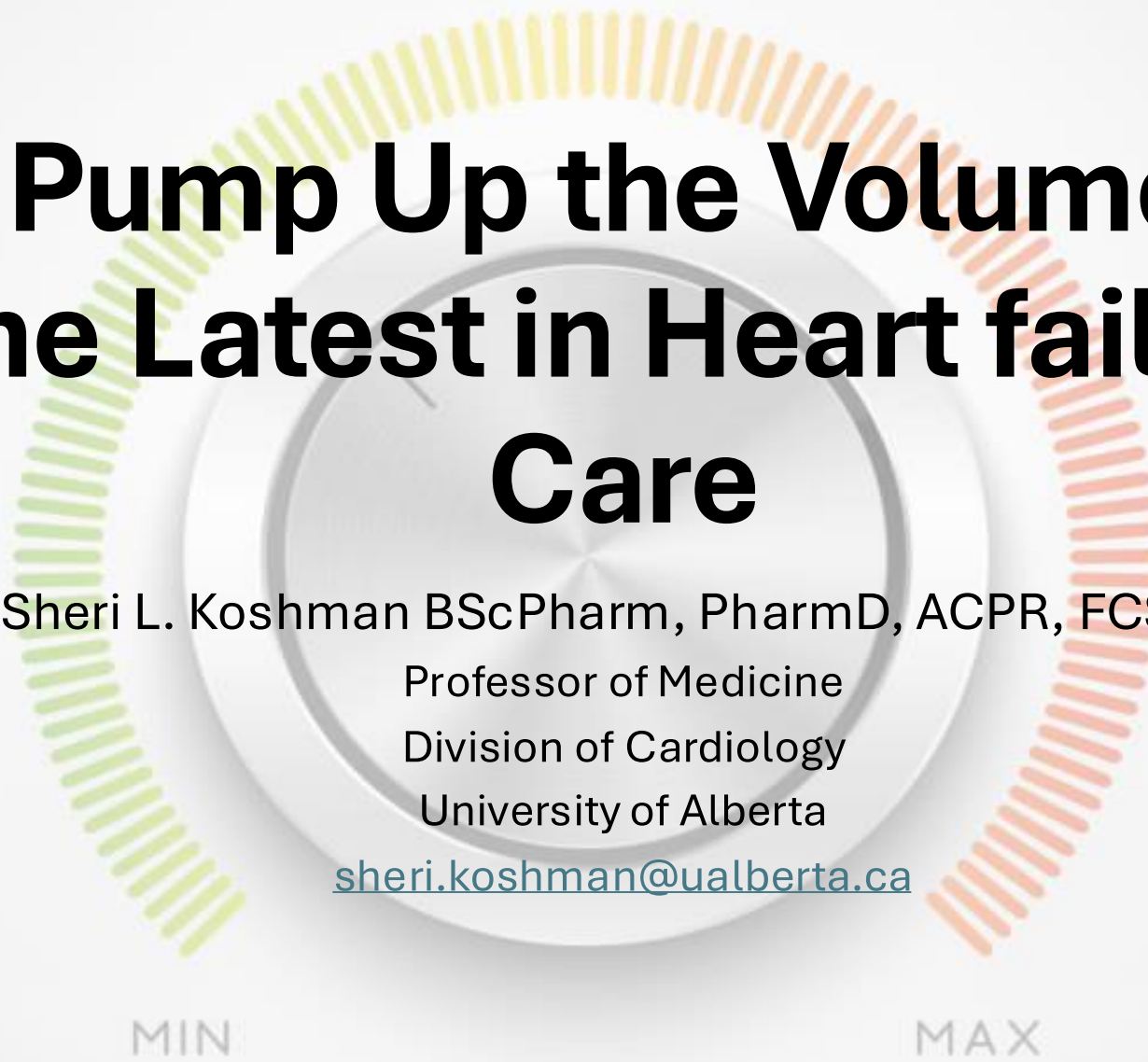




# **Pump Up the Volume: The Latest in Heart failure Care**

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# Presenter Disclosure



- I have the following relationships with these commercial interests:
  - Grants/Research Support: none
  - Speakers Bureau/Honoraria: Astra Zeneca, Bayer, GSK
  - Consulting Fees: none
  - Other: none
- I have received a speaker's fee from *the Alberta Pharmacists' Association* for this learning activity.

# Commercial Support Disclosure



- This program has received no financial or in-kind support from any commercial or other organization

# Bias Mitigation

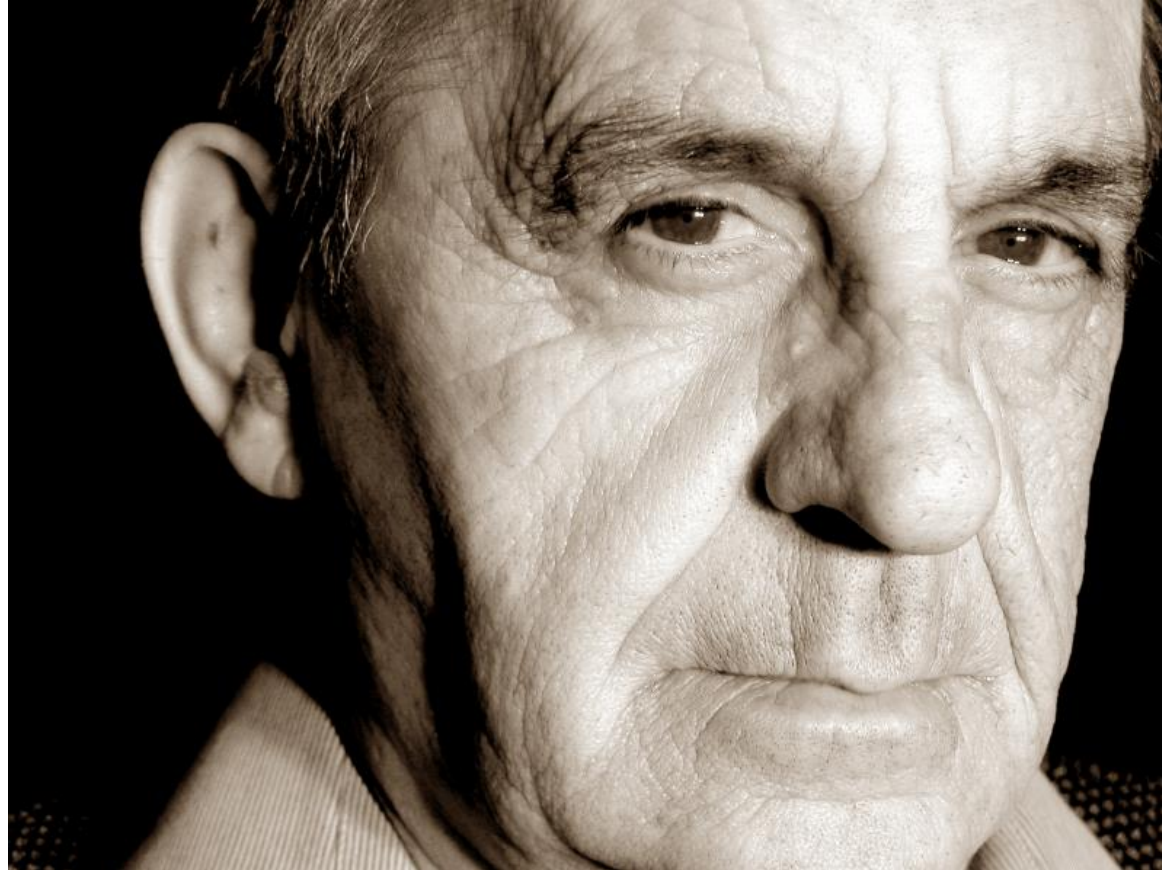


- I confirm that I have taken one or more of the following measures to ensure this learning activity is balanced and free from bias:
  - Conducted a comprehensive review of relevant literature
  - Supported the content and recommendations within by best available current evidence from the literature
  - Has a peer review conducted on my learning activity

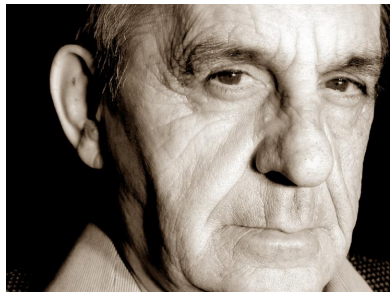
# Learning Objectives:

- By the end of the session, participants will be able to:
  - Classify heart failure phenotypes using correct and updated clinical nomenclature for your heart failure patients.
  - Formulate an evidence-based treatment plan incorporating the core pillars of guideline directed medical therapy (GDMT) in your practice.
  - Implement patient centred, multidisciplinary approaches to improve individualization, reduce readmissions and optimize long term care of patients in your practice.

# Mr. Smythe



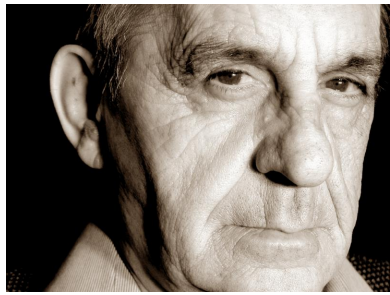
# Mr. Smythe



- Mr. Smythe is a 70 year old male well known to your PCN.
- He presents today for a refill on a prescription for furosemide 40mg BID.
- He tells you that he was just discharged from the emergency department one week ago.....

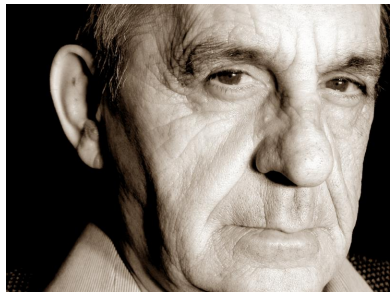


# Mr. Smythe



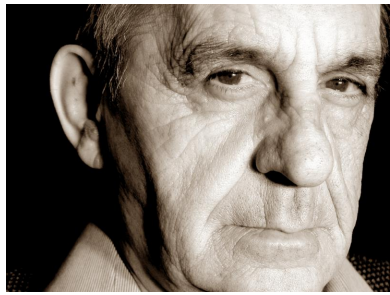
- He continues to tell you that over the past 2 months he has been feeling unwell.
- He first noticed being “short on air” while walking. He used to walk to his pharmacy and back (4 blocks), daily without stopping. A month ago, he had to stop 4 times and then stopped going.
- He also notes was avoiding the stairs in house because of SOB/OE.
- He has had 2 courses of antibiotics in the last month without any improvement as they thought it was pneumonia.

# Mr. Smythe



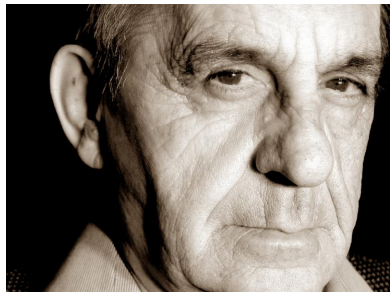
- He complains of being “low on energy”. You ask him how he is sleeping.....
- He says that he just can’t get comfortable in his recliner chair. When you ask him why he is sleeping in a chair, he reports that he is unable to lay flat as he “can’t breath”.
- He has been sleeping in the chair for the last week, prior to that he could sleep in bed as long as he had 3 large pillows under his head, for weeks prior.

# Mr. Smythe



- He has also noticed swelling in both of his ankles over the last month that has not gone away. He reports having swelling before, but usually only on hot days and if he stood too much and it would be gone the following day.
- He describes not having an appetite, but still continues to gain weight, about 15 pounds in the last month.

# Mr. Smythe



- When you ask what the doctors told him when his was in the emergency he states.....

*“They tell me that I am retaining fluid and they think that my heart is not pumping well. I have tests and an appointment with a heart doctor in 2 weeks. They also said something about heart failure. What is heart failure?”*

# What is heart failure (HF)?

- HF is a clinical syndrome with diverse causes
- Characterized by typical symptoms, physical examination signs and lab or imaging abnormalities suggestive of:
  - Pulmonary or systemic congestion  
OR
  - Changes in cardiac output attributed to underlying structural or functional cardiac abnormality
- Results in:
  - Decrease cardiac output
    - Unable to meet metabolic demands of the body
    - Only able to maintain cardiac output with abnormally high cardiac

# Phenotypes of HF

- Classification of HF by cause
- Classification of HF according to LVEF

**Table 3.** Proposed Universal Classification of HF by Cause

| Pathogenic group                                                       | Specific examples                                                                                                                                                                                 |
|------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Ischemic cardiomyopathy                                                | Ischemic heart disease, myocardial infarction, coronary artery disease                                                                                                                            |
| Hypertensive cardiomyopathy                                            | Hypertensive heart disease                                                                                                                                                                        |
| Valvular cardiomyopathy                                                | Structural valve disease: calcific aortic valve disease, degenerative mitral valve disease, other nonrheumatic and congenital valvular diseases, rheumatic heart disease                          |
| Arrhythmia-related cardiomyopathy                                      | Atrial fibrillation (uncontrolled), tachycardia, dyssynchrony, or premature ventricular contraction–induced cardiomyopathy, right ventricular pacing–induced cardiomyopathy, desmoplakin          |
| Infiltrative cardiomyopathy                                            | Cardiac amyloidosis, hemochromatosis, Fabry disease, glycogen storage disease, neoplastic/cancer-related infiltration                                                                             |
| Infective cardiomyopathy                                               | Viral myocarditis, Chagas disease, HIV, Lyme disease                                                                                                                                              |
| Inflammatory cardiomyopathy                                            | Autoimmune disease, sarcoidosis, hypersensitivity, desmoplakin                                                                                                                                    |
| Toxic cardiomyopathy                                                   | Medication-induced cardiotoxicity, substance use disorders, for example, alcohol, cocaine, amphetamine                                                                                            |
| Heritable cardiomyopathy                                               | Hypertrophic cardiomyopathy, dilated cardiomyopathy, restrictive cardiomyopathy, arrhythmogenic cardiomyopathy, nondilated left ventricular cardiomyopathy                                        |
| Pericardial disease                                                    | Constrictive and restrictive pericarditis                                                                                                                                                         |
| Metabolic disease and nutritional deficiency–associated cardiomyopathy | Obesity; diabetes; endocrine disorders, for example, thyroid disease; nutritional disease, for example, thiamine, vitamin B <sub>1</sub> , and selenium deficiencies; inborn errors of metabolism |
| Pregnancy-related cardiomyopathy                                       | Peripartum cardiomyopathy                                                                                                                                                                         |
| Stress-induced cardiomyopathy                                          | Takotsubo cardiomyopathy                                                                                                                                                                          |
| Pulmonary/right-sided heart disease                                    | Chronic obstructive pulmonary disease, interstitial lung disease, coal workers' pneumoconiosis, silicosis, asbestosis, other pneumoconiosis, pulmonary arterial hypertension                      |
| Congenital cardiomyopathy                                              | Systemic right ventricular failure, Fontan circulation, repaired tetralogy of Fallot                                                                                                              |
| High-output mediated cardiomyopathy                                    | Hemoglobinopathies, hemolytic anemias, atrioventricular malformations, endocrine causes (eg, pheochromocytoma)                                                                                    |
| Other causes                                                           | Other cardiovascular and systemic disorders, for example, neuromuscular disease, endomyocardial fibrosis, Loeffler endocarditis                                                                   |
| Idiopathic                                                             | Idiopathic cardiomyopathy                                                                                                                                                                         |

HF indicates heart failure.

# Classification: LVEF

|                                 | 2017<br>Canadian<br>Guidelines | 2021<br>First Universal<br>Definition | 2025<br>Canadian<br>Guidelines | 2026<br>Second Universal<br>Definition |
|---------------------------------|--------------------------------|---------------------------------------|--------------------------------|----------------------------------------|
| LVEF ≤40%                       | HFrEF                          | HFrEF                                 | HFrEF                          | HFrEF                                  |
| LVEF 41-49%                     | HFmrEF                         | HFmrEF                                | HFnrEF                         |                                        |
| LVEF ≥ 50%                      | HFpEF                          | HFpEF                                 |                                | HFpEF                                  |
| LVEF > 40%;<br>previously below | HFimpEF                        | HFimpEF                               | HFimpEF                        | HFimpEF                                |

Bozkurt B, et al. *J Card Fail.* 2021;27:387–413. doi: 10.1002/ejhf.2115

Virani S, et al. *Can J Cardiol* 2025: 1857-1874.

Ezekowitz JA et al.. *Can J Cardiol.* 2017 Nov;33(11):1342-1433.

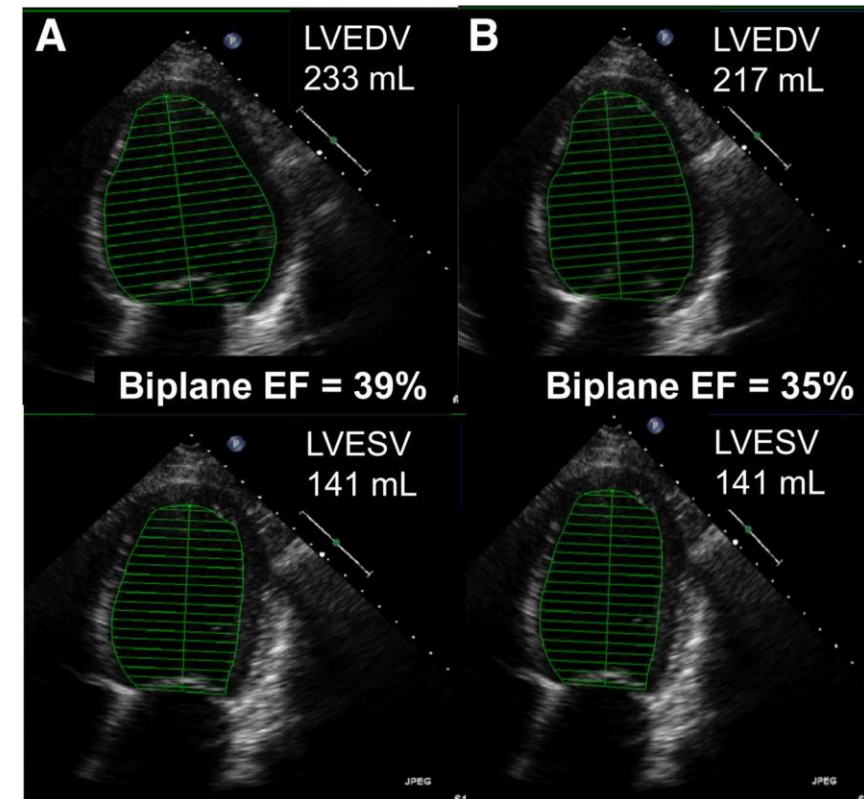
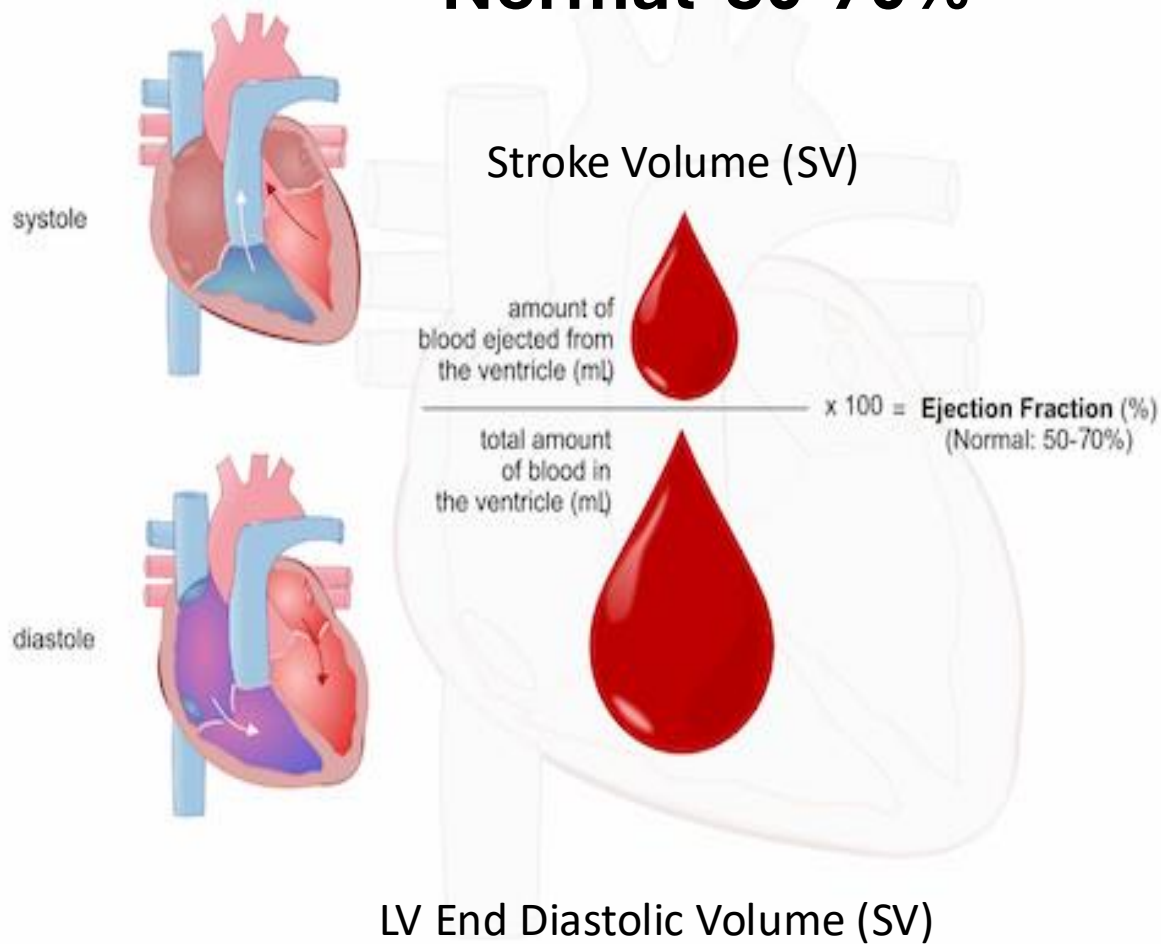
Walsh et al. *Circ* 2026; 154:<https://doi.org/10.1161/CIR.0000000000001455>

# Classification: LVEF

- Key criterion for HF trials for decades
  - Fundamental for extrapolating efficacy from clinical trials to clinical practice
  - Determining appropriate treatment
  - Understanding expected response to therapy
  - Monitoring individuals
- However.....
  - Cut-offs are arbitrary
  - Variability in measurement in echocardiography
  - Variability between imaging modalities
  - Debate on cut-offs for different patient groups

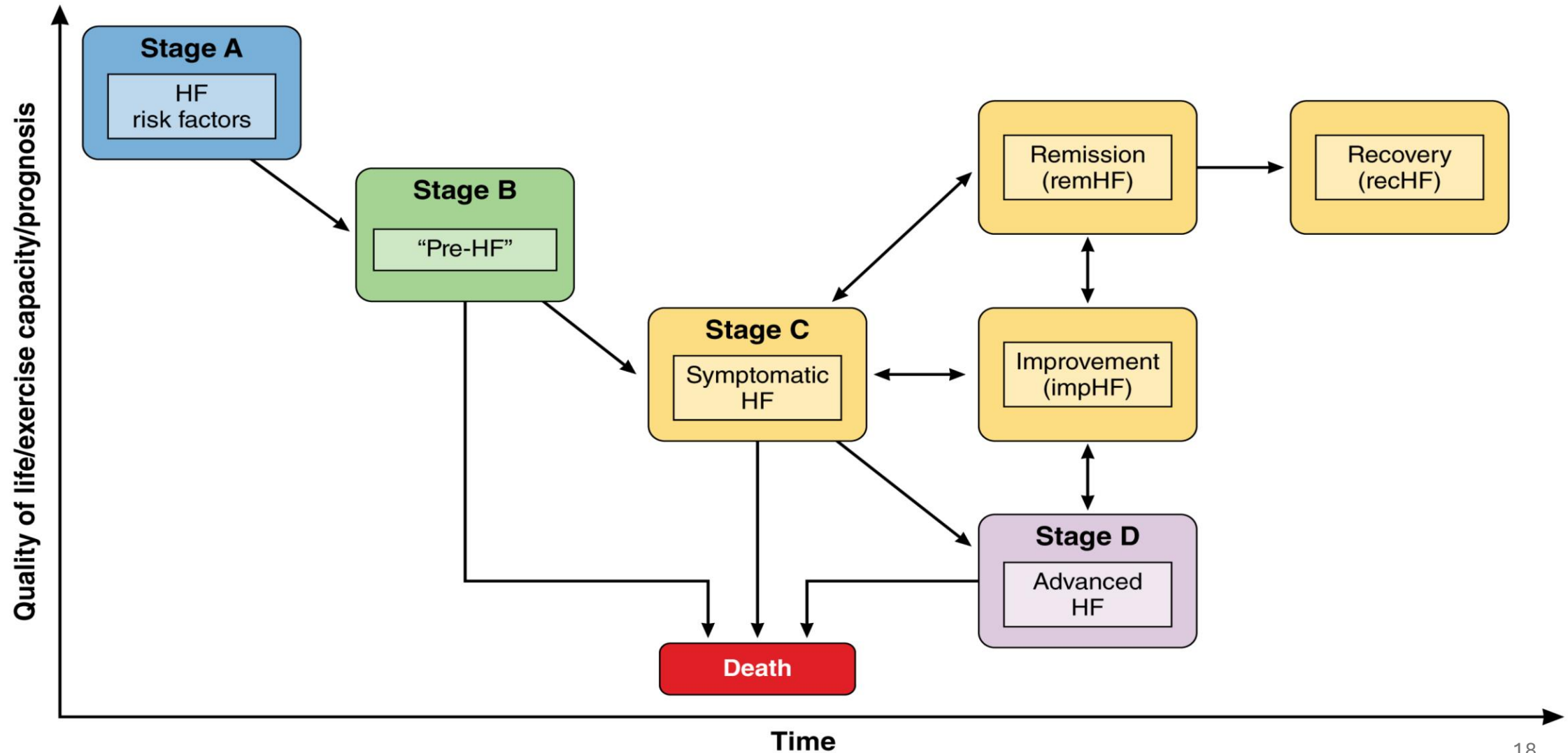
# Measurement of Left Ventricular Ejection Fraction (LVEF) is variable

**Normal 50-70%**



Results may vary by up to 10%  
LVEF 40% versus 35-40% or 40-45%  
versus 35-45%

# Trajectories of HF



Ejection fraction can change over time

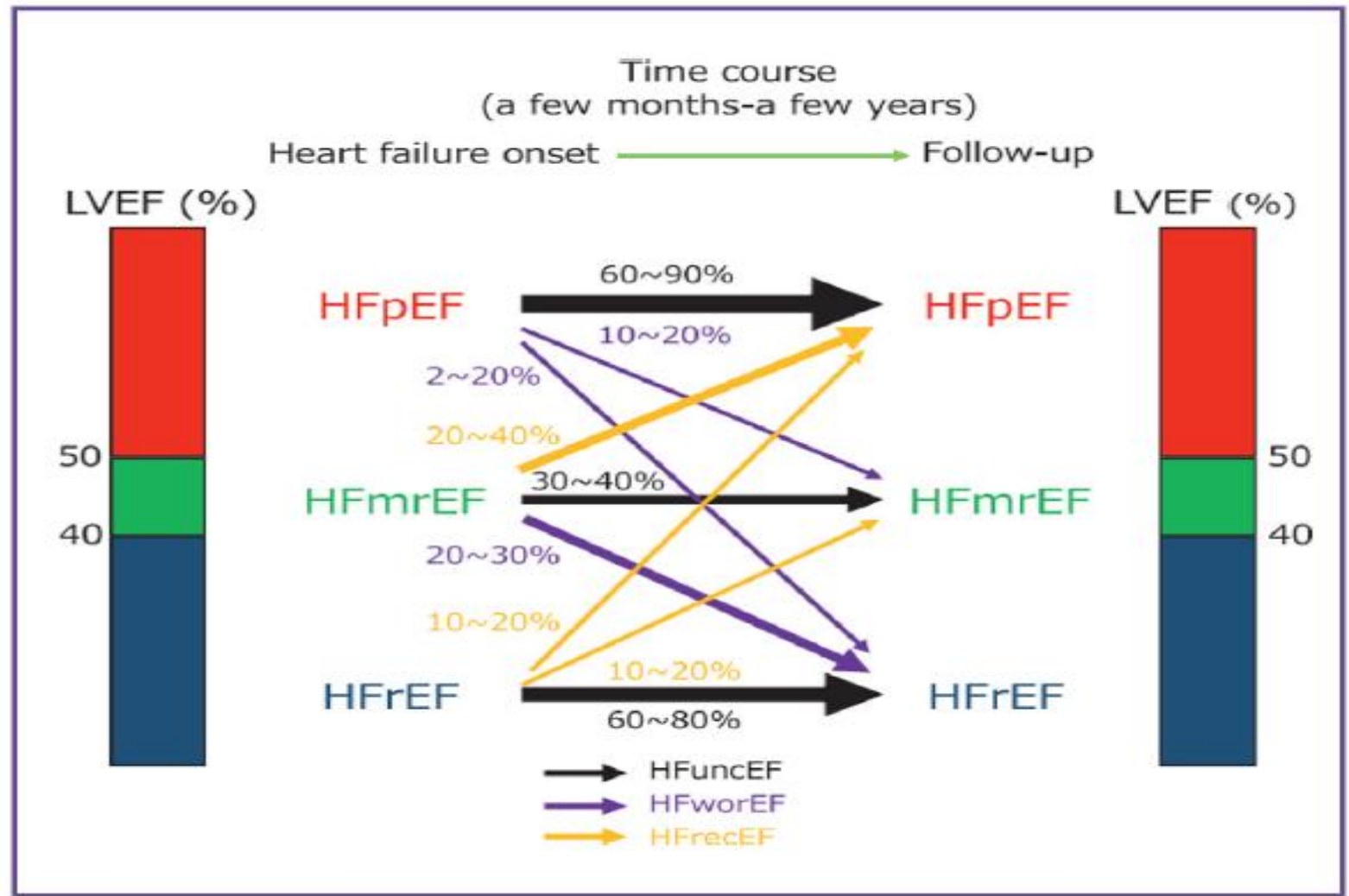
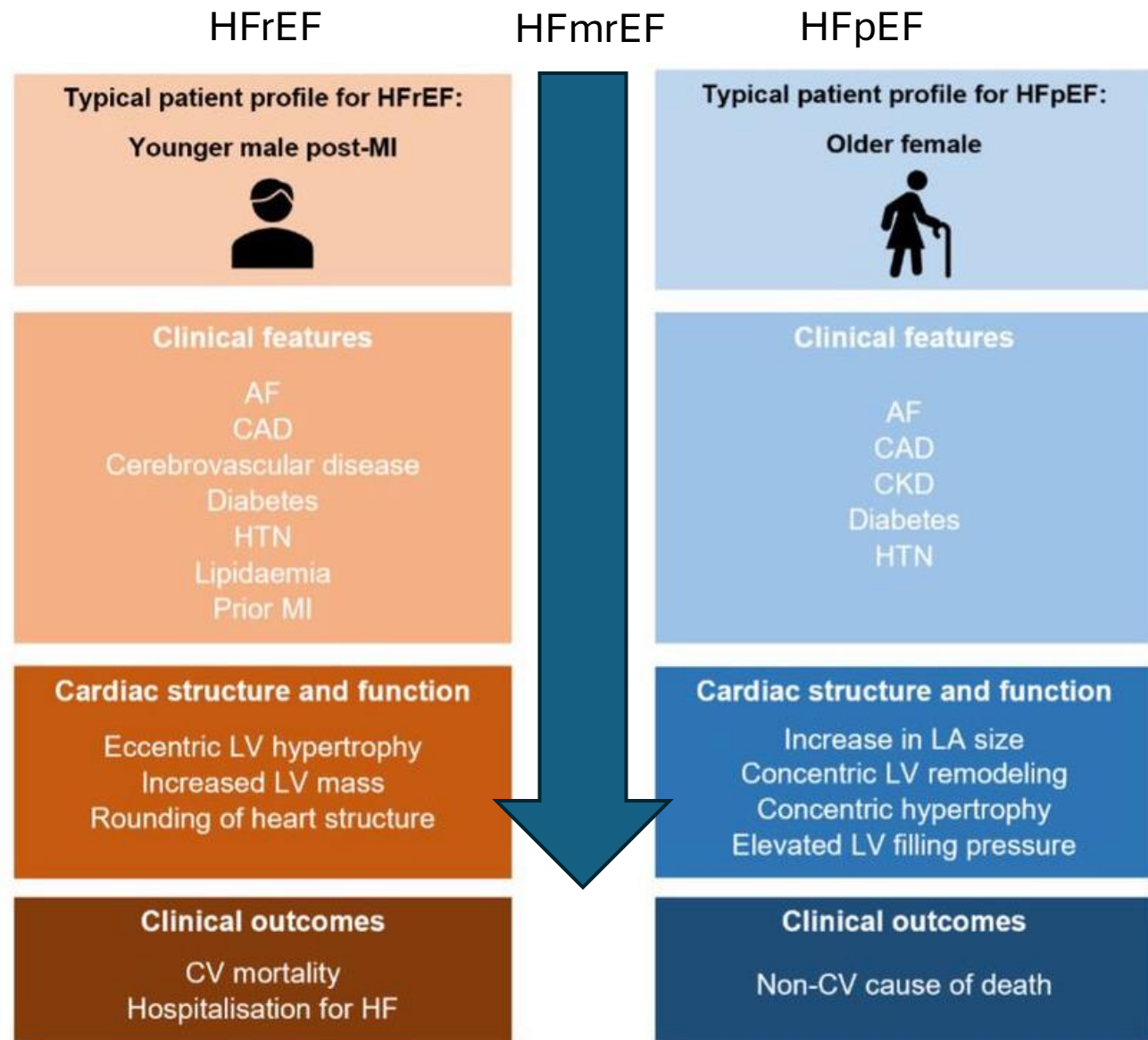
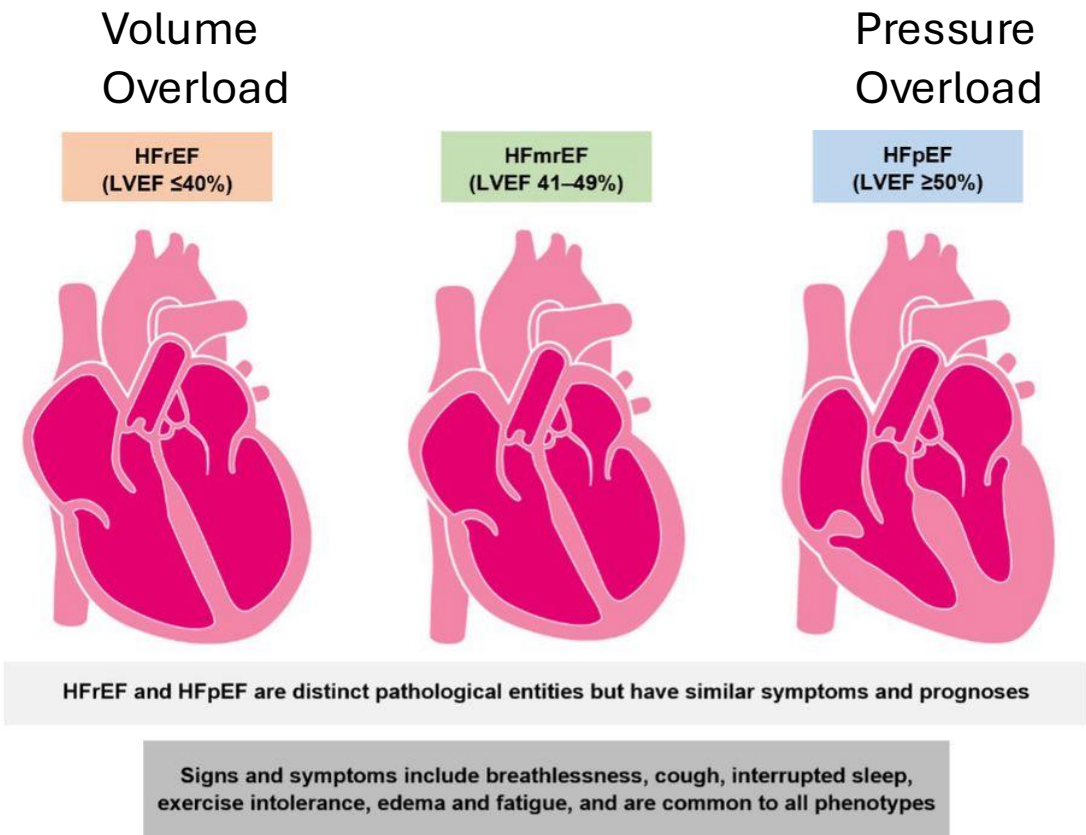


**Figure 1.** Guideline-defined trajectory in left ventricular ejection fraction (LVEF).<sup>25</sup> HFmrEF, heart failure with mildly reduced ejection fraction; HFpEF, heart failure with preserved ejection fraction; HFrecEF, heart failure with recovered ejection fraction; HFrEF, heart failure with reduced ejection fraction; HFuncEF, heart failure with unchanged ejection fraction; HFworEF, heart failure with worsening ejection fraction.



# General Approach to the patient with HF

## 1. Fluid assessment

- Wet? Dry? Euvolemic?
- Goals of therapy
  - Symptoms

## 2. Disease modification

- Goals of therapy
  - Morbidity
  - Mortality
- Correct medications
- Target doses

## 3. Risk reduction

- Evaluate and manage reversible causes
- Manage risk factors
- Self-care: daily weights, self-monitoring, salt and fluids

Priority will change  
depending on where  
they are in disease  
trajectory

Disease  
modification will  
depend on the type  
of HF

TREAT COMORBIDITIES PER CCS HF RECOMMENDATIONS (INCL. AF, FUNCTIONAL MR, IRON DEF, CKD, DM)  
 DIURETICS TO RELIEVE CONGESTION (TITRATED TO MINIMUM EFFECTIVE DOSE TO MAINTAIN EUVOLEMIA)

## HFrEF: LVEF $\leq$ 40% AND SYMPTOMS

### Initiate Standard Therapies

**ARNI or ACEi/ARB**  
then substitute **ARNI**

**BETA BLOCKER**

**MRA**

**SGLT2 INHIBITOR**



### Assess Clinical Factors for Additional Interventions

HR >70 bpm and sinus rhythm  
 • Consider ivabradine\*

Recent HF hospitalization  
 • Consider vericiguat \*\*

Black patients on optimal GDMT, or patients unable to tolerate ARNI/ACEi/ARB  
 • Consider combination hydralazine-nitrates

Suboptimal rate control for AF, or persistent symptoms despite optimized GDMT  
 • Consider digoxin

*Initiate standard therapies as soon as possible and titrate every 2-4 weeks to target or maximally tolerated dose over 3-6 months*



### Reassess LVEF, Symptoms, Clinical Risk



**NYHA III/IV, Advanced HF or High-Risk Markers**

#### CONSIDER

- Referral for advanced HF therapy (mechanical circulatory support/transplant)
- Referral for supportive/palliative care



**LVEF  $\leq$  35% and NYHA I-IV (ambulatory)**

Refer to CCS CRT/ICD recommendations



**LVEF > 35%, NYHA I, and Low Risk**

Continue present management, reassess as needed

NON-PHARMACOLOGIC THERAPIES (EDUCATION, SELF-CARE, EXERCISE)

ADVANCE CARE PLANNING AND DOCUMENTATION OF GOALS OF CARE



## HFrEF: LVEF $\leq$ 40% AND SYMPTOMS

### Initiate Standard Therapies

**ARNI or ACEi/ARB**  
then substitute **ARNI**

**BETA BLOCKER**

**MRA**

**SGLT2 INHIBITOR**

|      |                                                                  |
|------|------------------------------------------------------------------|
| ACEI | captopril<br>enalapril<br>lisinopril<br>ramipril<br>trandolapril |
| ARB  | candesartan<br>valsartan                                         |
| ARNI | sacubitril /<br>valsartan                                        |

bisoprolol  
carvedilol  
metoprolol

eplerenone  
spironolactone

dapagliflozin  
empagliflozin

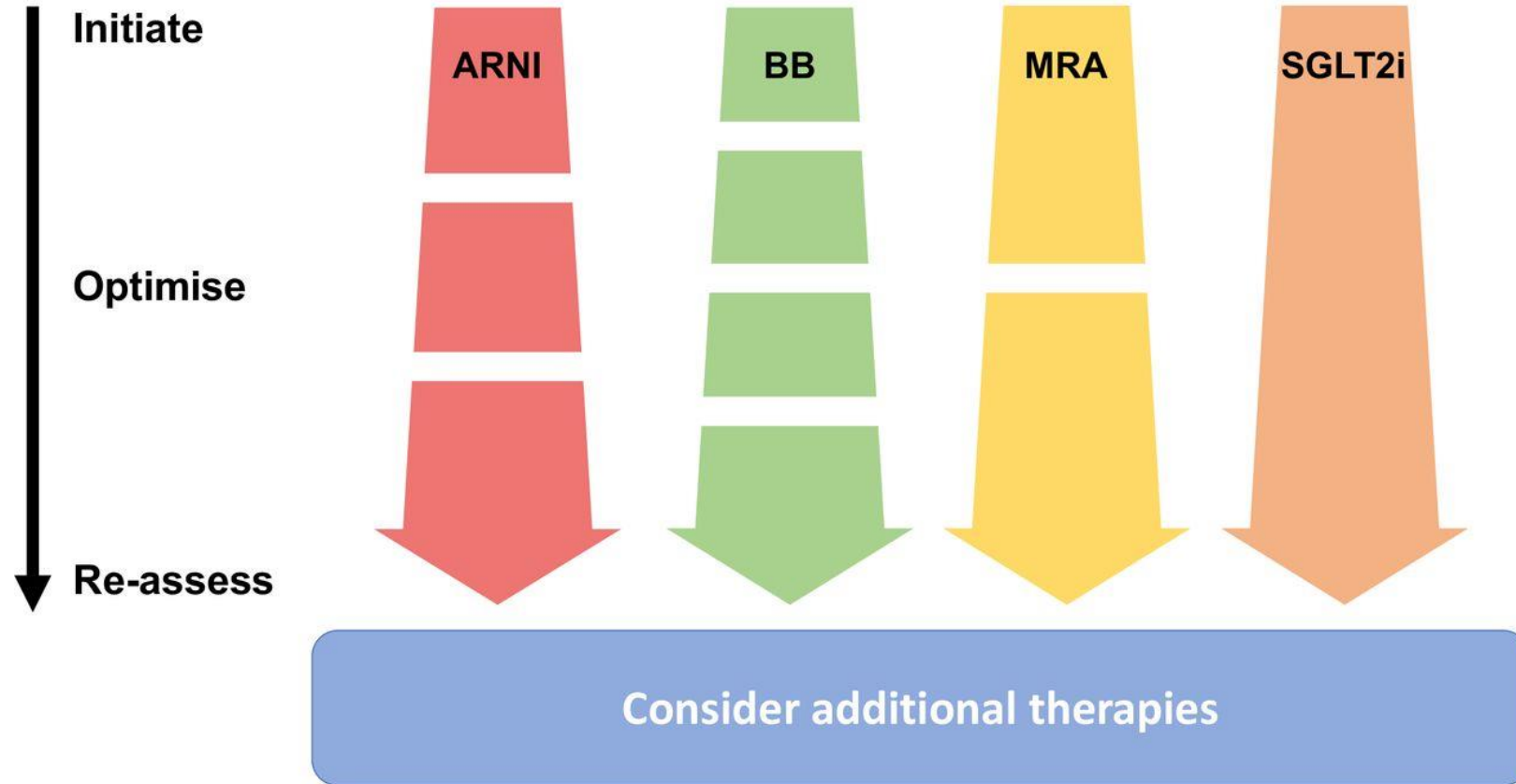
### BENEFITS:

- ↓ risk of mortality
- ↓ risk of HF hospitalizations
- improve HF symptoms

Strive to initiate the above agents within 3 to 6 months after diagnosis, and titrate to target or maximally tolerated doses.

Quadruple Therapy (Strong Recommendation, Moderate Quality Evidence)  
Target or maximum tolerated dose (Strong Recommendation, High Quality Evidence)

# The Four Pillars of Heart Failure

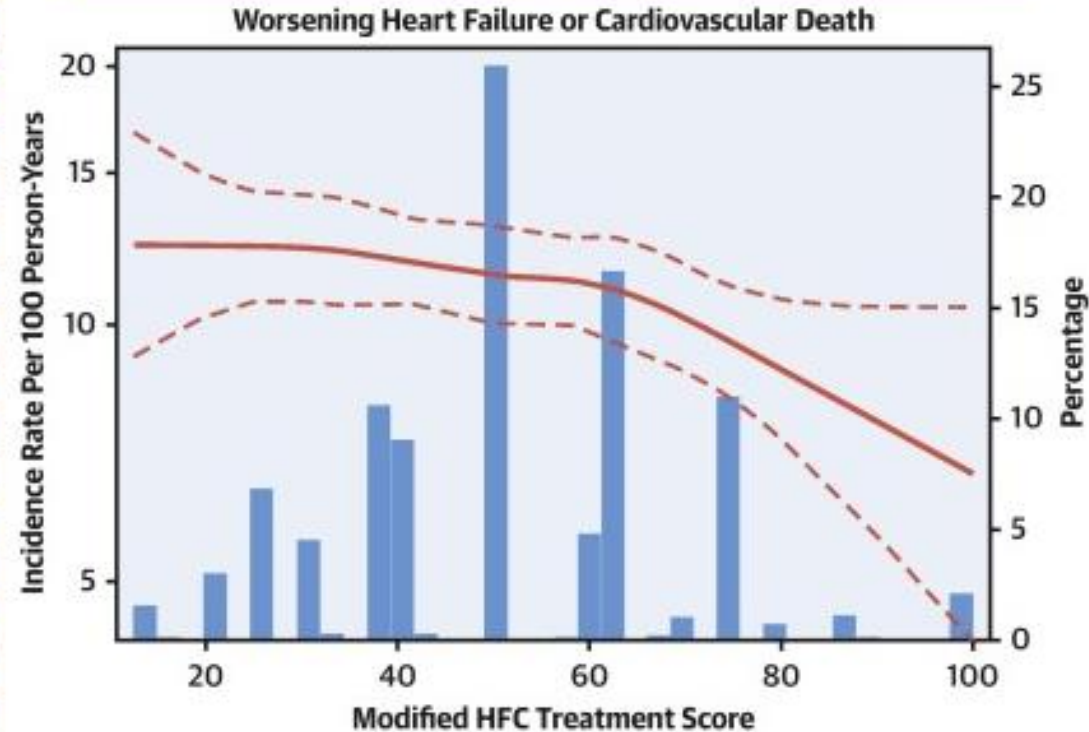


## CENTRAL ILLUSTRATION: Components of the Modified HFC Treatment Score and Effect of Dapagliflozin According to a Modified HFC Treatment Score

DAPA-HF  
Post-hoc

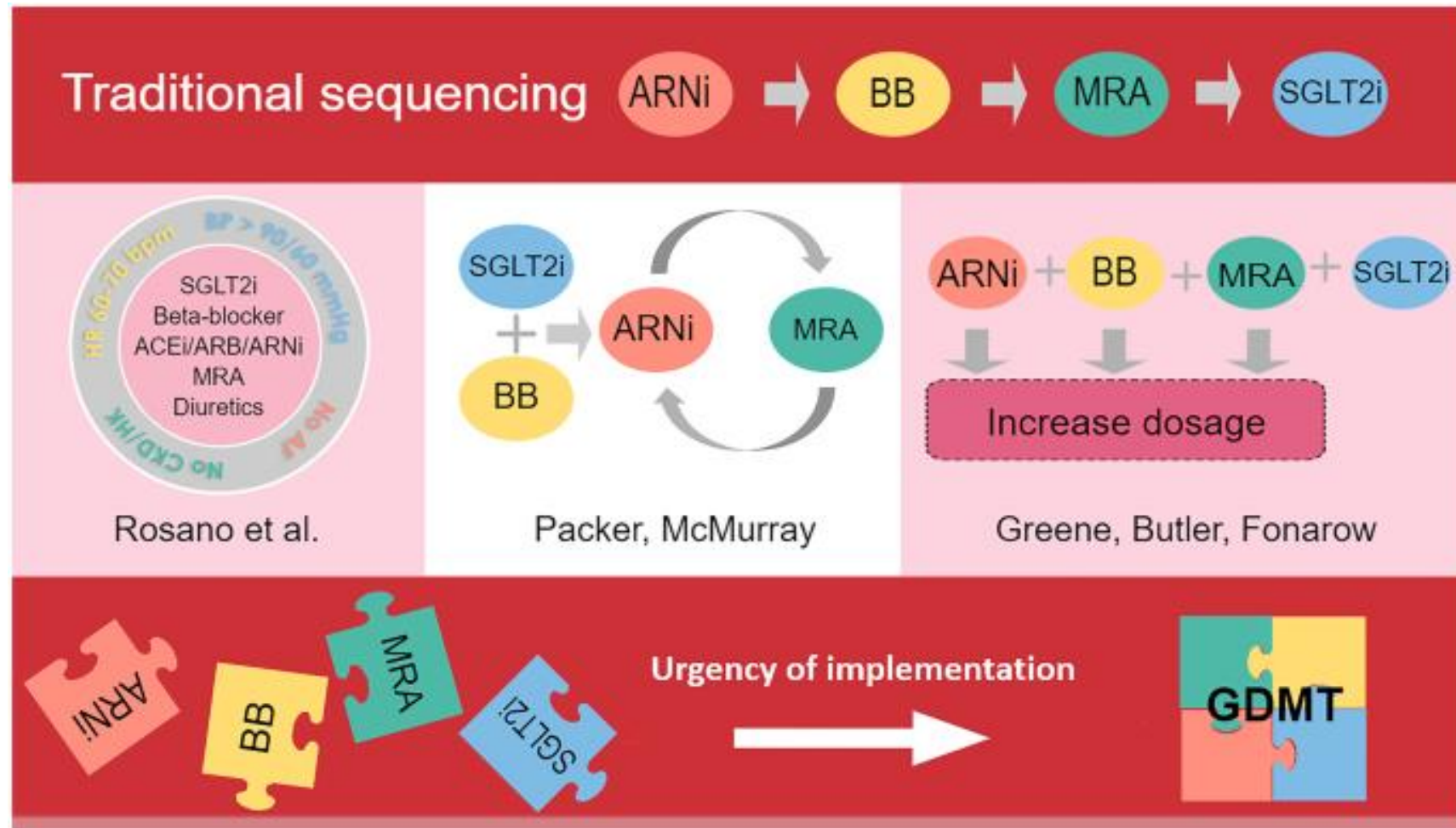
| Components of the Modified HFC Treatment Score                                           |       |
|------------------------------------------------------------------------------------------|-------|
| Modified HFC score = $\frac{\text{Total score}}{\text{Total possible score}} \times 100$ |       |
| Therapy                                                                                  | Score |
| Beta-blocker                                                                             |       |
| <50% of target daily dose                                                                | 1     |
| ≥50% of target daily dose                                                                | 2     |
| ACEI/ARB/ARNI (valsartan part)                                                           |       |
| <50% of target daily dose                                                                | 1     |
| ≥50% of target daily dose                                                                | 2     |
| ARNI (sacubitril part)                                                                   |       |
| <50% of target daily dose                                                                | 1     |
| ≥50% of target daily dose                                                                | 2     |
| Mineralocorticoid-receptor antagonist                                                    |       |
| <50% of target daily dose                                                                | 1     |
| ≥50% of target daily dose                                                                | 2     |
| Ivabradine*                                                                              |       |
| <50% of target daily dose                                                                | 1     |
| ≥50% of target daily dose                                                                | 2     |
| Hydralazine**                                                                            |       |
| <50% of target daily dose                                                                | 1     |
| ≥50% of target daily dose                                                                | 2     |

A Higher Modified HFC Treatment Score (Indicating More Optimal Therapy) Was Associated With a Lower Risk of Adverse Outcomes



More comprehensive treatment  
= less HHF + CV death

# Practical Approach



# Individualization is key.....

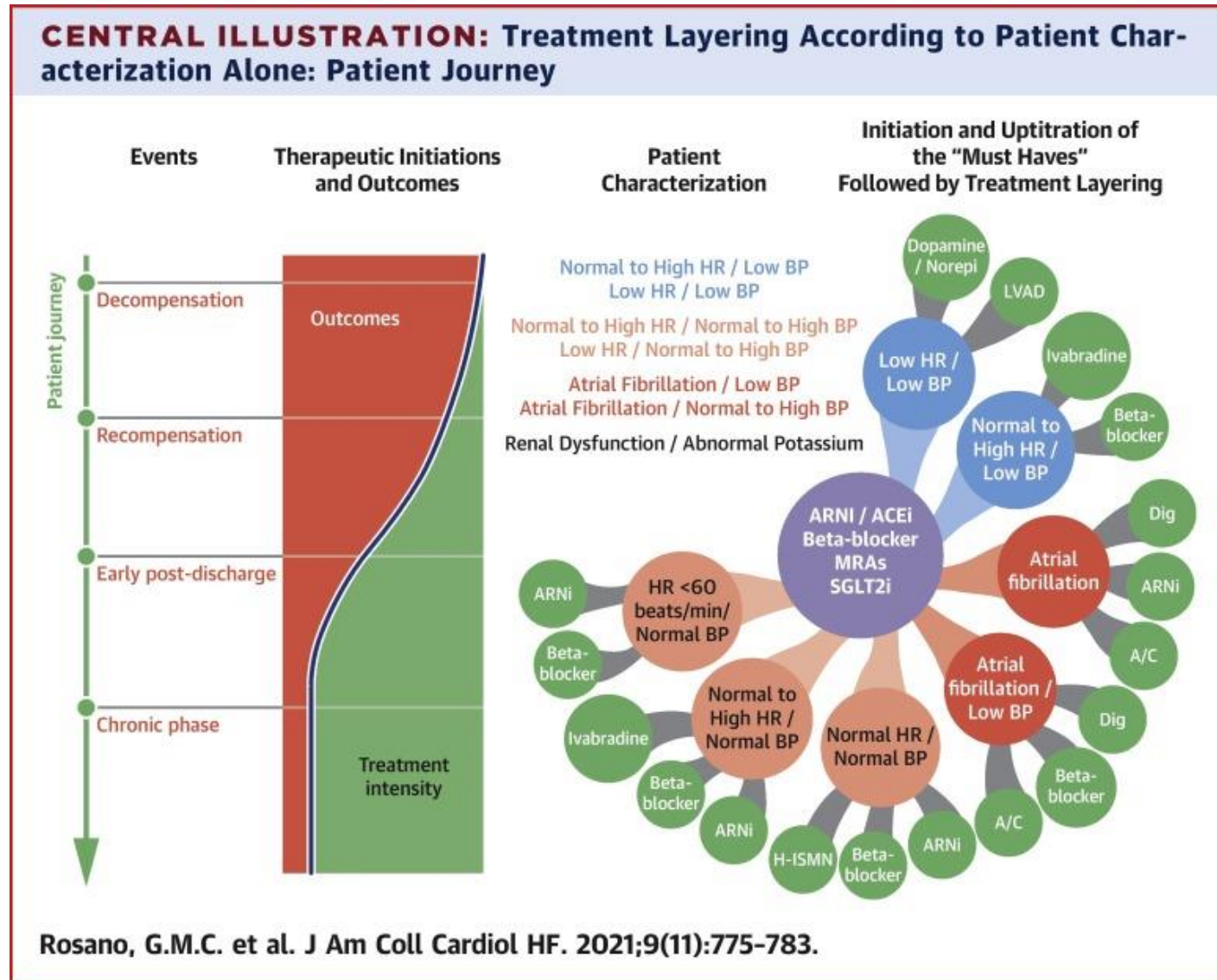


**Table 4** Key monitoring parameters for heart failure pharmacologic therapy

| Drug class        | BP                                                                                                                                                                             | HR                                          | Serum potassium                                                                                    | SCr | Other                                                   |
|-------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------|----------------------------------------------------------------------------------------------------|-----|---------------------------------------------------------|
|                   | Monitor for low systolic BP (<90 mmHg), orthostatic hypotension (systolic BP drop of $\geq 20$ mmHg with postural change), and symptoms of hypotension (e.g., lightheadedness) | Monitor for marked bradycardia (HR <50 bpm) | Monitor renal function (SCr) and serum potassium 1–2 weeks after initiating or increasing the dose |     |                                                         |
| RAAS inhibitors*  | ✓                                                                                                                                                                              | –                                           | ✓                                                                                                  | ✓   | Cough (ACEI >> ARNI)                                    |
| Beta-blockers     | ✓                                                                                                                                                                              | ✓                                           | –                                                                                                  | –   | Fatigue, exercise intolerance                           |
| MRAs              | ✓ (less)                                                                                                                                                                       | –                                           | ✓                                                                                                  | ✓   | Gynecomastia (spironolactone)                           |
| SGLT2 inhibitors  | ✓ (minimal)                                                                                                                                                                    | –                                           | –                                                                                                  | ✓   | Genital infection (yeast infection, UTI)                |
| Incretin mimetics | –                                                                                                                                                                              | –                                           | –                                                                                                  | –   | GI effects (nausea, vomiting, diarrhea, abdominal pain) |

✓/known adverse effect—monitor closely.

ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ARNI, angiotensin receptor-neprilysin inhibitor; BP, blood pressure; bpm, beats per minute; HR, heart rate; GI, gastrointestinal; MRA, mineralocorticoid receptor antagonist; RAAS, renin–angiotensin–aldosterone system; SBP, systolic blood pressure; SCr, serum creatinine; SGLT2, sodium-glucose cotransporter-2; UTI, urinary tract infection.

\*In the PARADIGM-HF trial, hypotension was more common with ARNI vs ACEI, while elevated serum creatinine ( $\geq 221 \mu\text{mol/L}$ ) and severe hyperkalemia ( $>6.0 \text{ mmol/L}$ ) were less common with ARNI vs ACEI.



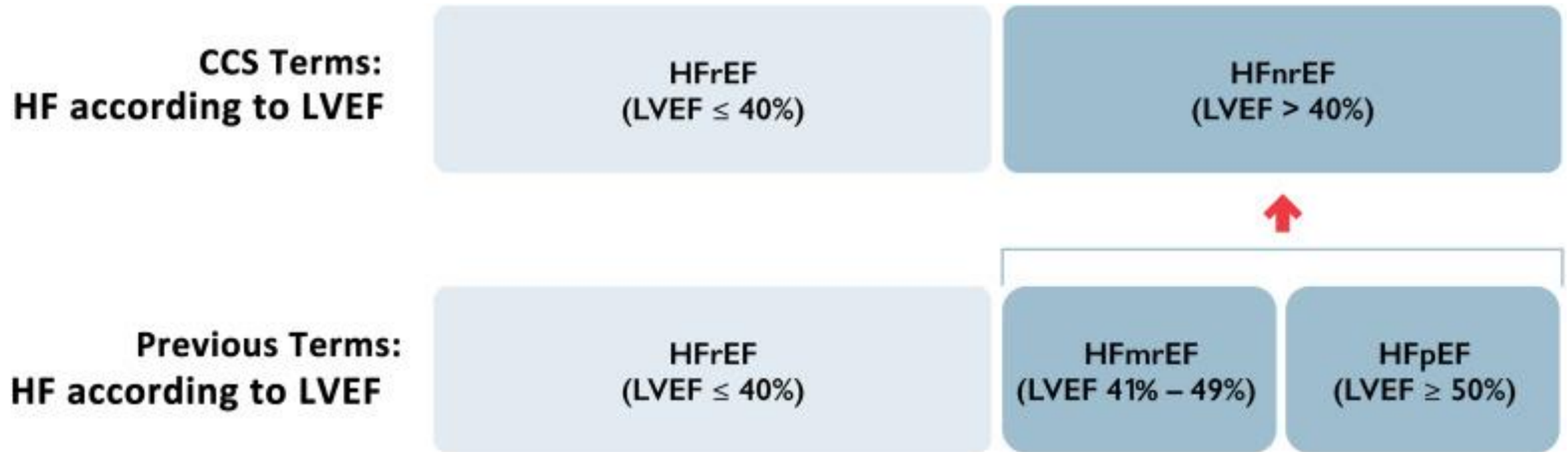
Canadian Journal of Cardiology 41 (2025) 1857–1874

## Guidelines

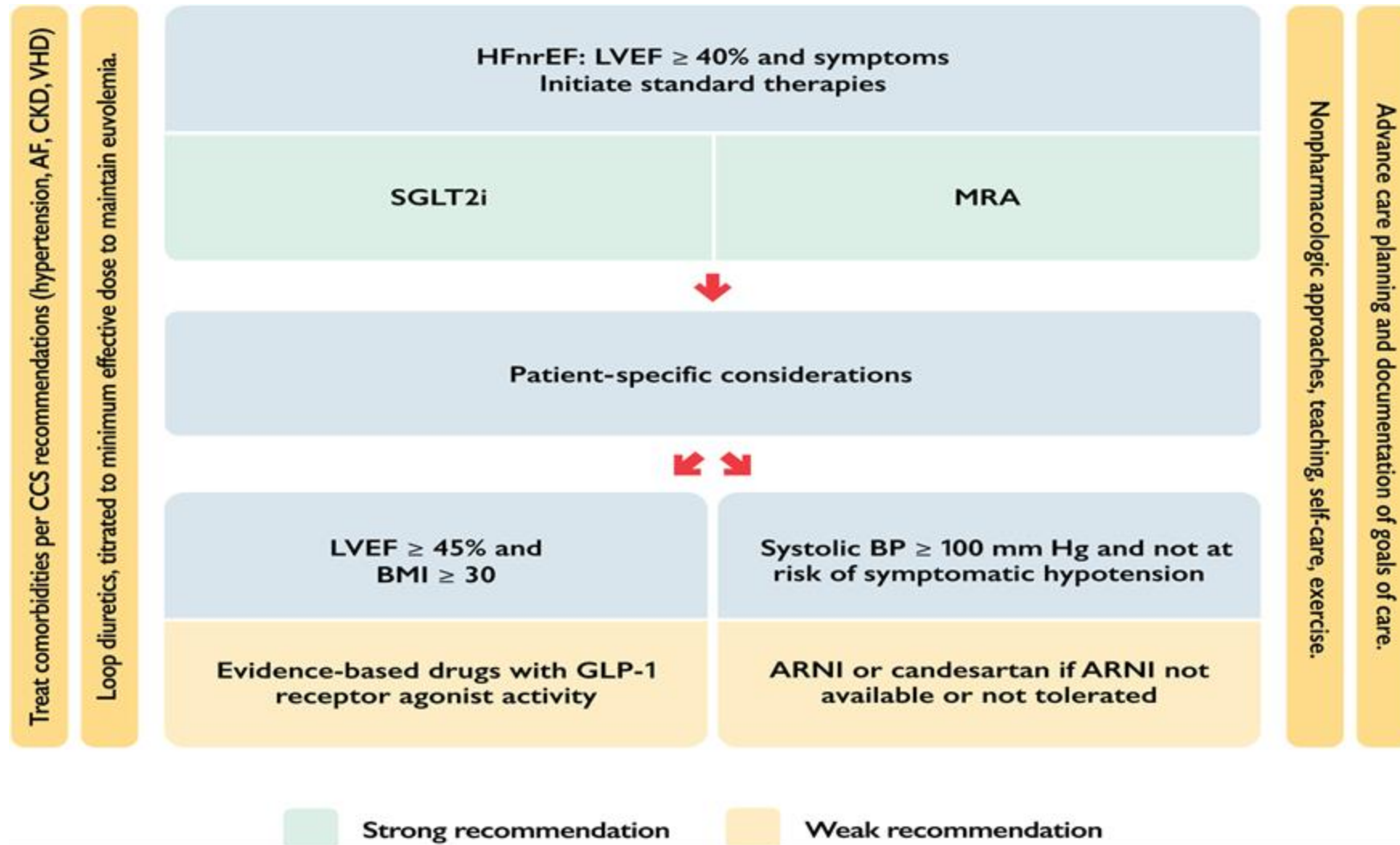
# Canadian Cardiovascular Society/Canadian Heart Failure Society 2025 Guideline Update for Pharmacologic Management of Heart Failure With Nonreduced Ejection Fraction (LVEF > 40%)

**Primary Panel:** Sean Virani, MD, (Co-chair),<sup>a</sup> Shelley Zieroth, MD, (Co-chair),<sup>b</sup> Natasha Aleksova, MD,<sup>c</sup> Kim Anderson, MD, MSc,<sup>d</sup> Brian Clarke, MD,<sup>a</sup> Anique Ducharme, MD,<sup>e</sup> Justin A. Ezekowitz, MBBCh,<sup>f</sup> Farid Foroutan, HBS, PhD,<sup>g</sup> Nadia Giannetti, MD,<sup>h</sup> Rahul Jain, MD,<sup>i</sup> Douglas Lee, MD, PhD,<sup>c</sup> Serge Lepage, MD,<sup>j</sup> Kristin Lyons, MDCM,<sup>k</sup> Michael McDonald, MD,<sup>c</sup> Caroline McGuinty, MD,<sup>l</sup> Lisa Mielniczuk, MD,<sup>l,m</sup> Eileen O'Meara, MD,<sup>e</sup> Stephanie Poon, MD,<sup>i</sup> Kyla Siatecki, MN, NP,<sup>b</sup> Elizabeth Swiggum, MD,<sup>n</sup> Mustafa Toma, MD,<sup>a</sup> Ricky D. Turgeon, PharmD,<sup>o</sup>

# New Definition



# 2025 CCS / CHFS Guidelines



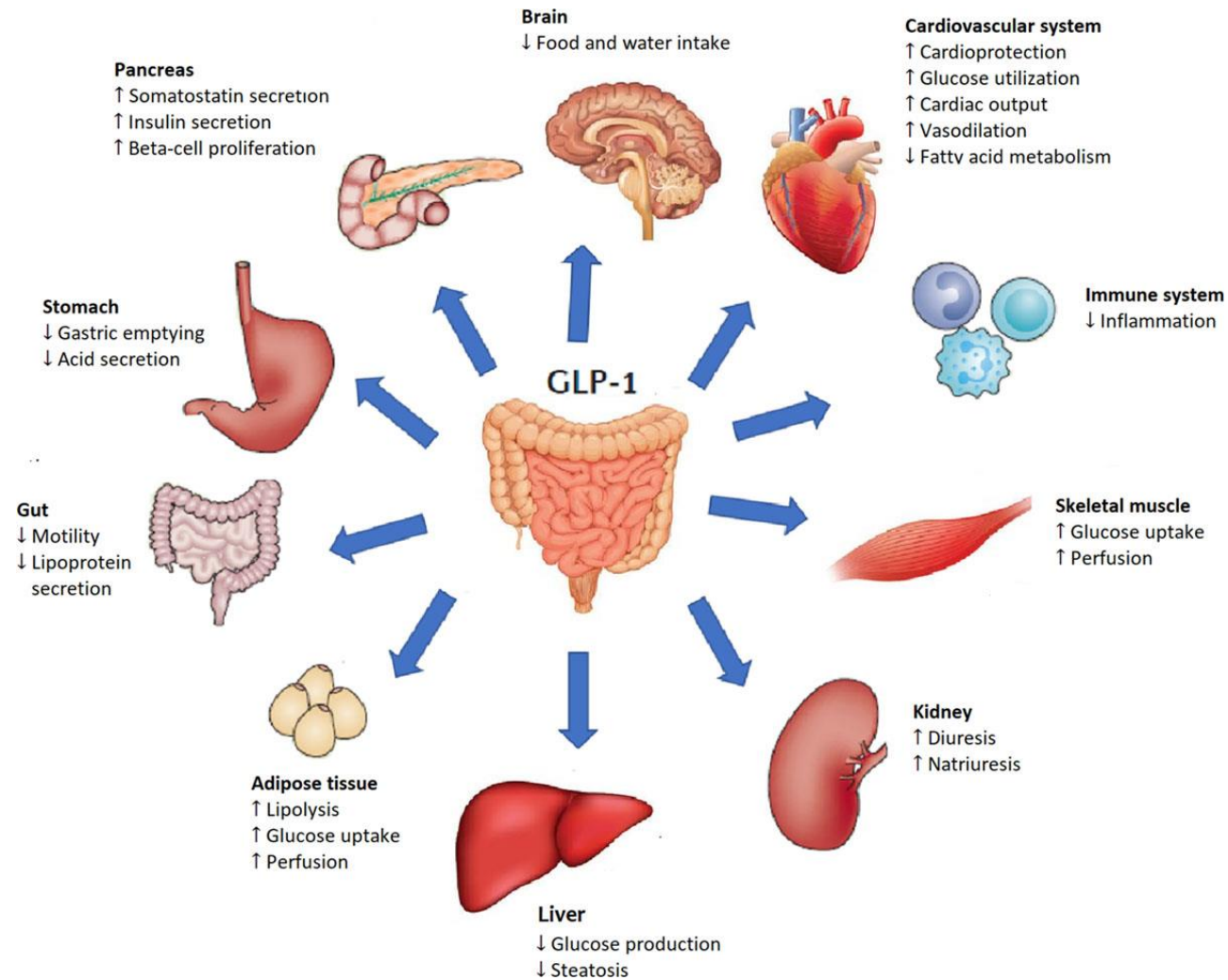
|        | Trial (Years)                    | Population                           | N    | Primary Endpoint                      | Relative Effect     | ARR / NNT*    | Key Takeaway                                                 |
|--------|----------------------------------|--------------------------------------|------|---------------------------------------|---------------------|---------------|--------------------------------------------------------------|
| SGLT2i | EMPEROR-Preserved<br>(2017–2020) | Symptomatic HF LVEF >40% ↑ NT-proBNP | 5988 | CV death or <u>HF hospitalization</u> | HR 0.79 (0.69–0.90) | 3.3% → NNT 30 | Consistent ↓ HF hospitalizations No clear CV death reduction |
|        | DELIVER<br>(2018–2022)           | Symptomatic HF LVEF >40% ↑ BNP       | 6263 | CV death or <u>worsening HF</u>       | HR 0.82 (0.73–0.92) | 3.1% → NNT 32 | Confirms SGLT2 class effect                                  |

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| MRA    | TOPCAT<br>(2006–2012)            | Symptomatic HF LVEF ≥45%<br>Spironolactone 45mg daily | 3445 | CV death, aborted arrest, or HF hospitalization | HR 0.89 (0.77–1.04) | 1.8% → NNT 56   | Regional heterogeneity<br>Possible benefit (Americas)        |
|        | FINE-ARTS-HF<br>(2020–2023)      | Symptomatic HF LVEF ≥40%<br>Finereone 20-40mg daily   | 6001 | <u>Total worsening HF events</u> + CV death     | RR 0.84 (0.74–0.95) | ~2.4% → NNT ~42 | ↓ Worsening HF events. Mortality unchanged                   |

|        | Trial (Years)                    | Population                                                        | N    | Primary Endpoint                                        | Relative Effect        | ARR / NNT*          | Key Takeaway                                                       |
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| GLP-1  | SUMMIT<br>(2021–2024)            | HFpEF + Obesity LVEF ≥50%<br>Tirzepatide 15mg sc weekly           | ~731 | 1) CV death or <u>worsening HF</u><br>2) 2) KCCQ change | ~HR 0.62†              | ~4–5% → NNT ~20–25† | First obesity-focused trial showing benefit on hard outcomes + QoL |
|        | STEP-HFpEF<br>(2020–2022)        | HFpEF + Obesity LVEF ≥45% BMI ≥30<br>Semaglutide 2.4mg sc qweekly | 529  | KCCQ-CSS change                                         | +7.8 points (4.8–10.9) | —                   | Major symptom improvement ~13% weight loss<br>Not event-driven     |

# GLP-1



# GLP-1: SUMMIT Trial



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ORIGINAL ARTICLE



## Tirzepatide for Heart Failure with Preserved Ejection Fraction and Obesity

**Authors:** Milton Packer, M.D. , Michael R. Zile, M.D., Christopher M. Kramer, M.D., Seth J. Baum, M.D., Sheldon E. Litwin, M.D., Venu Menon, M.D., Junbo Ge, M.D., , for the SUMMIT Trial Study Group\* [Author Info & Affiliations](#)

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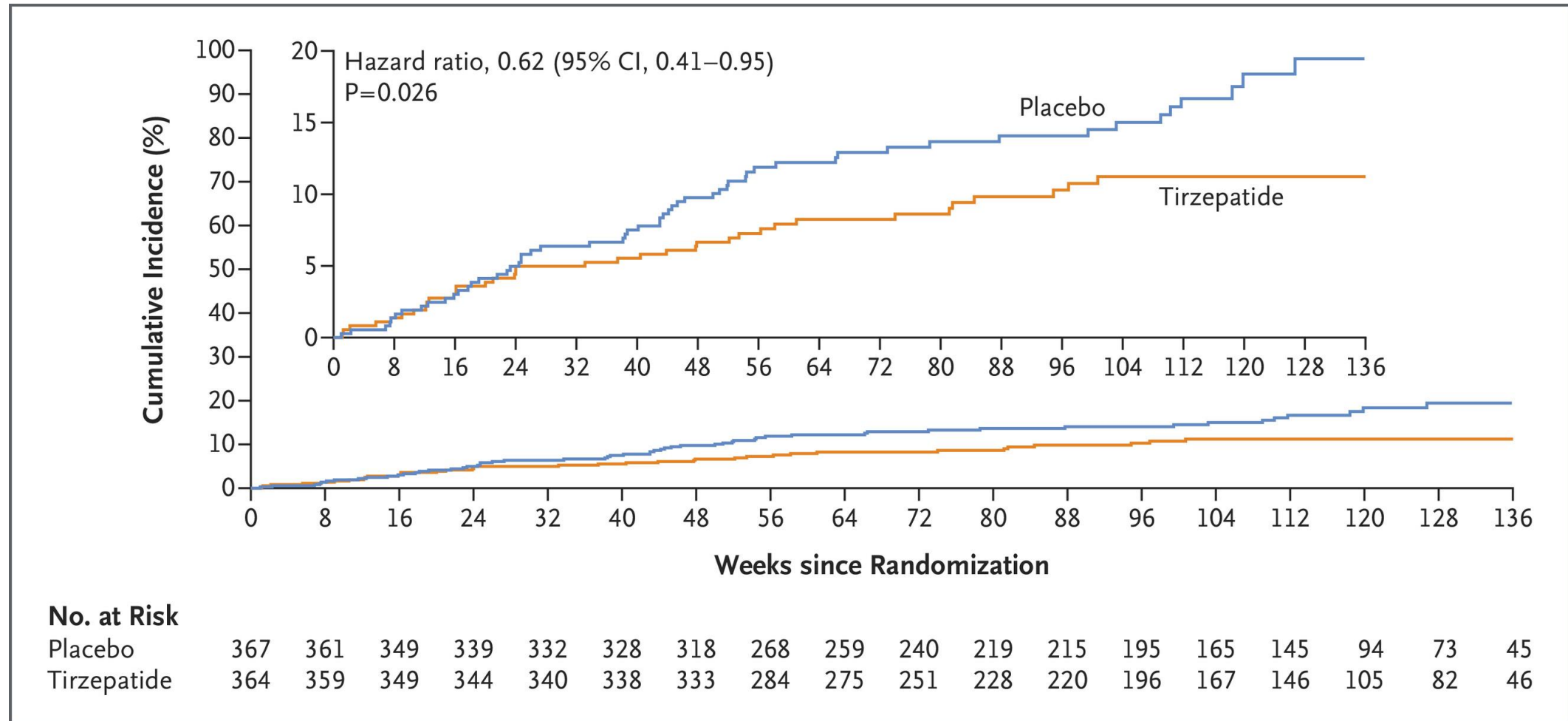
# SUMMIT Trial

|   | International, DB, R, PC                                                                                                                                                                                                                                                                                                                                       |
|---|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| P | <p>HFpEF LVEF &gt; 50%; BMI &gt; 30; NYHA II-IV</p> <p>Enrichment criteria (at least 1):</p> <ul style="list-style-type: none"> <li>• NTpBNP &gt; 200 pg/mL (or &gt; 600 if AF)</li> <li>• LA enlargement</li> <li>• elevated filling pressures</li> <li>• HF decompensation with 12 mos</li> <li>• eGFR &lt; 70ml/min at baseline</li> </ul>                  |
| I | Tirzepatide 15mg weekly (GLP-1 / GIP) (n=364) (up-titrate 2.5mg q4 weeks)                                                                                                                                                                                                                                                                                      |
| C | Placebo (n=367)                                                                                                                                                                                                                                                                                                                                                |
| O | <p>Adjudicated death from cardiovascular causes or a worsening heart-failure event (assessed in a time-to-first-event analysis) <u>and</u></p> <p>the change from baseline to 52 weeks in the Kansas City Cardiomyopathy Questionnaire clinical summary score (KCCQ-CSS; scores range from 0 to 100, with higher scores indicating better quality of life)</p> |

# SUMMIT Trial

|   | Results                                                                                                                                                                                                                        |
|---|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| P | Age : 65<br>Female: 53%<br>White: 70%<br>NYHA II: 72%<br>Weight: 102kg / BMI 38<br>LVEF = 60%<br>NTpBNP = 180<br>Hosp with 12 mos: 48%<br>Meds: <ul style="list-style-type: none"><li>- MRA 35%</li><li>- SGLT2i 17%</li></ul> |
| I | Tirzepatide: 72% at target dose; 19.2% discontinued; 4% for GI discomfort                                                                                                                                                      |
| C | Placebo: 79% ; 21.3% discontinued                                                                                                                                                                                              |

# SUMMIT trial



Death for CV cause or worsening HF event

# SUMMIT Trial

| Key secondary end points                                                    |           |   |           |   |                         |         |
|-----------------------------------------------------------------------------|-----------|---|-----------|---|-------------------------|---------|
| Change at 52 weeks in 6-minute walk distance — m                            | 26.0±3.8  | — | 10.1±3.9  | — | 18.3 (9.9 to 26.7)‡     | <0.001§ |
| Percent change at 52 weeks in body weight — %                               | −13.9±0.4 | — | −2.2±0.5  | — | −11.6 (−12.9 to −10.4)  | <0.001  |
| Percent change at 52 weeks in high-sensitivity C-reactive protein level — % | −38.8±4.5 | — | −5.9±5.3  | — | −34.9 (−45.6 to −22.2)¶ | <0.001  |
| Adjusted change at 52 weeks in physiological and laboratory measurements    |           |   |           |   |                         |         |
| NT-proBNP — ratio of geometric means                                        | 0.93±0.04 | — | 1.04±0.04 | — | 0.90 (0.79 to 1.01)¶    |         |
| Systolic blood pressure — mm Hg                                             | −4.6±0.8  | — | 0.1±0.8   | — | −4.7 (−6.8 to −2.5)     |         |
| Heart rate — beats/min                                                      | 3.0±0.5   | — | 0.3±0.5   | — | 2.8 (1.3 to 4.3)        |         |

# Conclusion

- Tirzepatide decreases worsening HF events, improves symptoms and QOL (and reasonably well tolerated)
- Proposed mechanisms
  - Decrease fat mass = decrease inflammation (decrease CRP) / plasma volume
  - Reverse pro-inflammatory pathways independent of weight loss
  - Decrease BP
- Outstanding questions
  - Target dose or target weight
  - Duration of therapy
  - Impact on lean muscle mass
- Practical issues
  - No indication for HF for either tirzepatide or semaglutide
  - GDMT may need to be adjusted with large weight loss

# Practically speaking.....

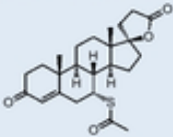
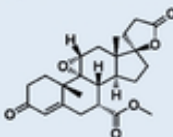
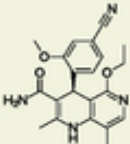
- ARNIs
  - No Canadian indication currently
  - Not covered by public plans for HF
- MRAs
  - Spironolactone
    - Data less robust in HFnrEF
  - Finerenone
    - Indication: reducing risks in adults with heart failure with a left ventricular ejection fraction (LVEF) of 40% or greater
    - Not covered by public plans for HF (only DM+CKD)
    - Added benefits in CKD +/-DM
- Is it a class effect??

# MRAs

\$0.05

\$1.37

\$3.26

|  | Distinct properties from steroidal MRA                                                                                                                                     |                                                                                                                                                                              |                                                                                                                                                                              |
|-----------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                   | Steroidal MRA                                                                                                                                                              |                                                                                                                                                                              | Non-steroidal MRA                                                                                                                                                            |
|                                                                                   | Spironolactone<br>                                                                       | Eplerenone<br>                                                                            | Finerenone<br>                                                                            |
| MR selectivity                                                                    | +                                                                                                                                                                          | ++                                                                                                                                                                           | +++                                                                                                                                                                          |
| MR potency                                                                        | +++                                                                                                                                                                        | +                                                                                                                                                                            | +++                                                                                                                                                                          |
| MR cofactor recruitment                                                           | Partial agonist                                                                                                                                                            | Partial agonist                                                                                                                                                              | Inverse agonist                                                                                                                                                              |
| Tissue distribution                                                               |  >>  |  >>  |  ==  |
| $t_{1/2}$                                                                         | >20 hours                                                                                                                                                                  | 4–6 hours                                                                                                                                                                    | 2–3 hours                                                                                                                                                                    |
| Structure                                                                         | Flat                                                                                                                                                                       | Flat                                                                                                                                                                         | Bulky                                                                                                                                                                        |

HFrEF

HFrEF

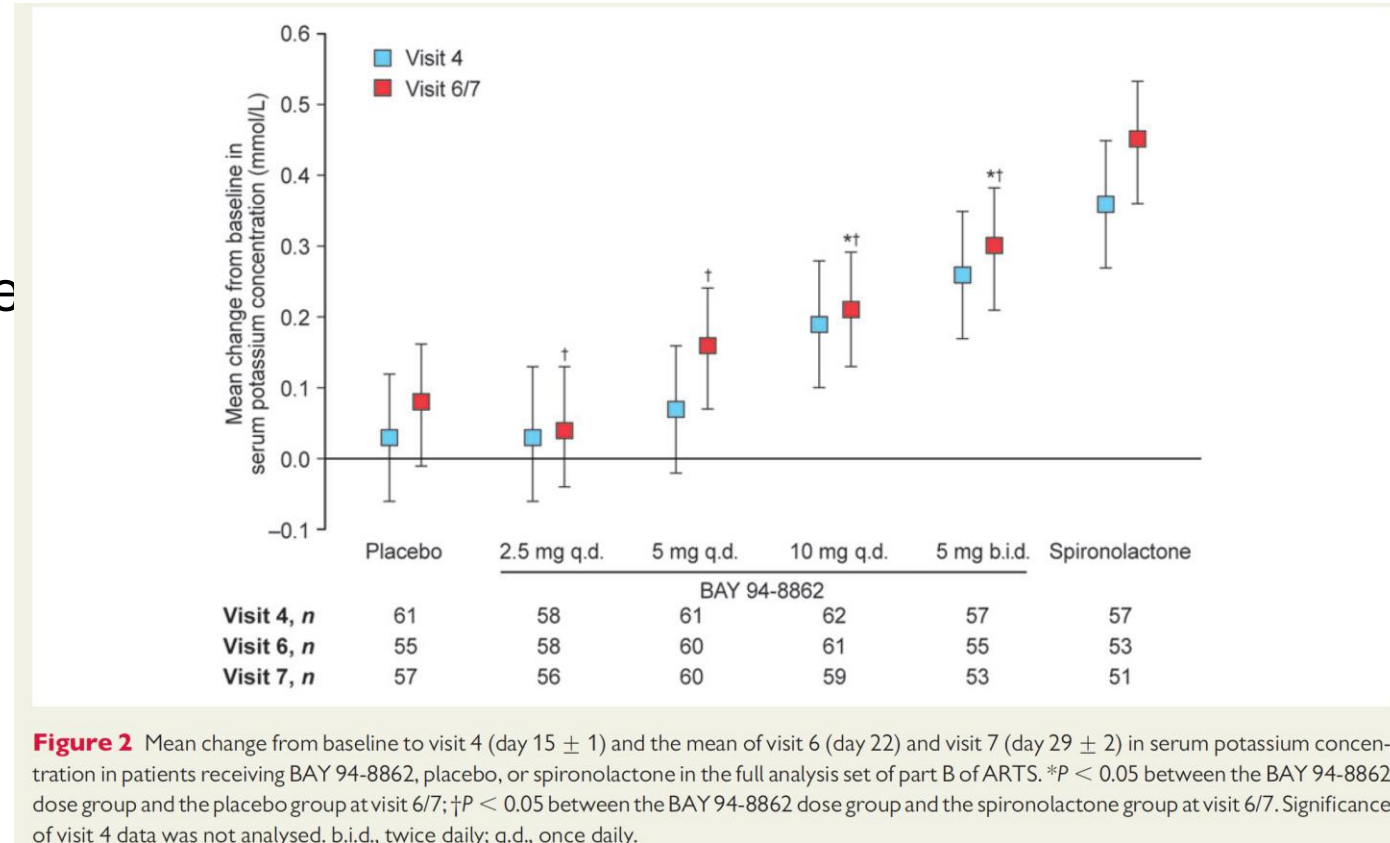
HFnrEF

HFnrEF

HFrEF: HF with reduced HF  
HFnrEF: HF with non-reduced HF

# What about ADE?

- ARTS
  - Phase IIb
  - Finerenone 2.5, 5, 10mg vs Spironolactone 25-50mg (open label)
  - HFrEF + CKD (eGFR 90-60 ml/min)
  - 1 mos follow-up



# What about ADE?

- ARTS-HF
  - Phase 2b
  - n= 1066
  - HFrEF + T2DM and/or CKD
  - Finerenone 2.5, 5, 7.5, 10 or 15mg; up-titrated to 5, 10, 15, 20mg (day 30) vs eplerenone 25mg q2d, 25mg daily (day 30); 50mg (day 90)
  - 40% on MRA previously

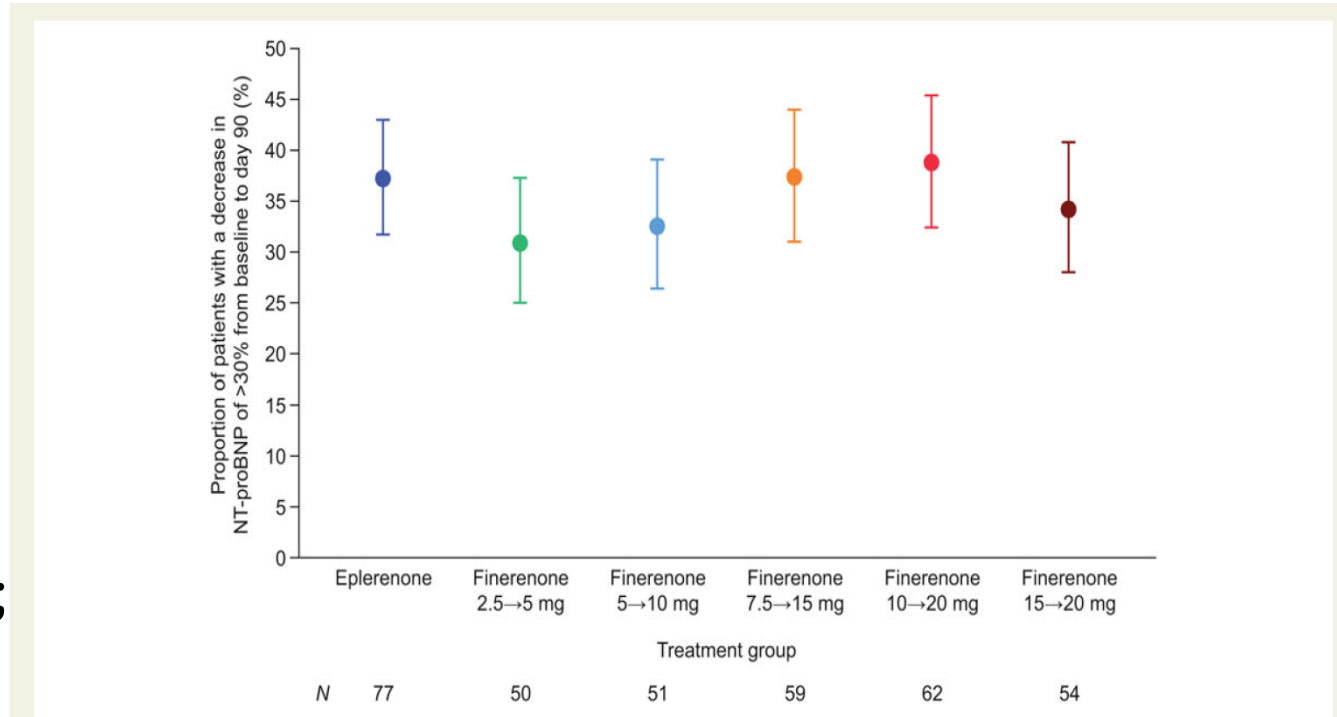


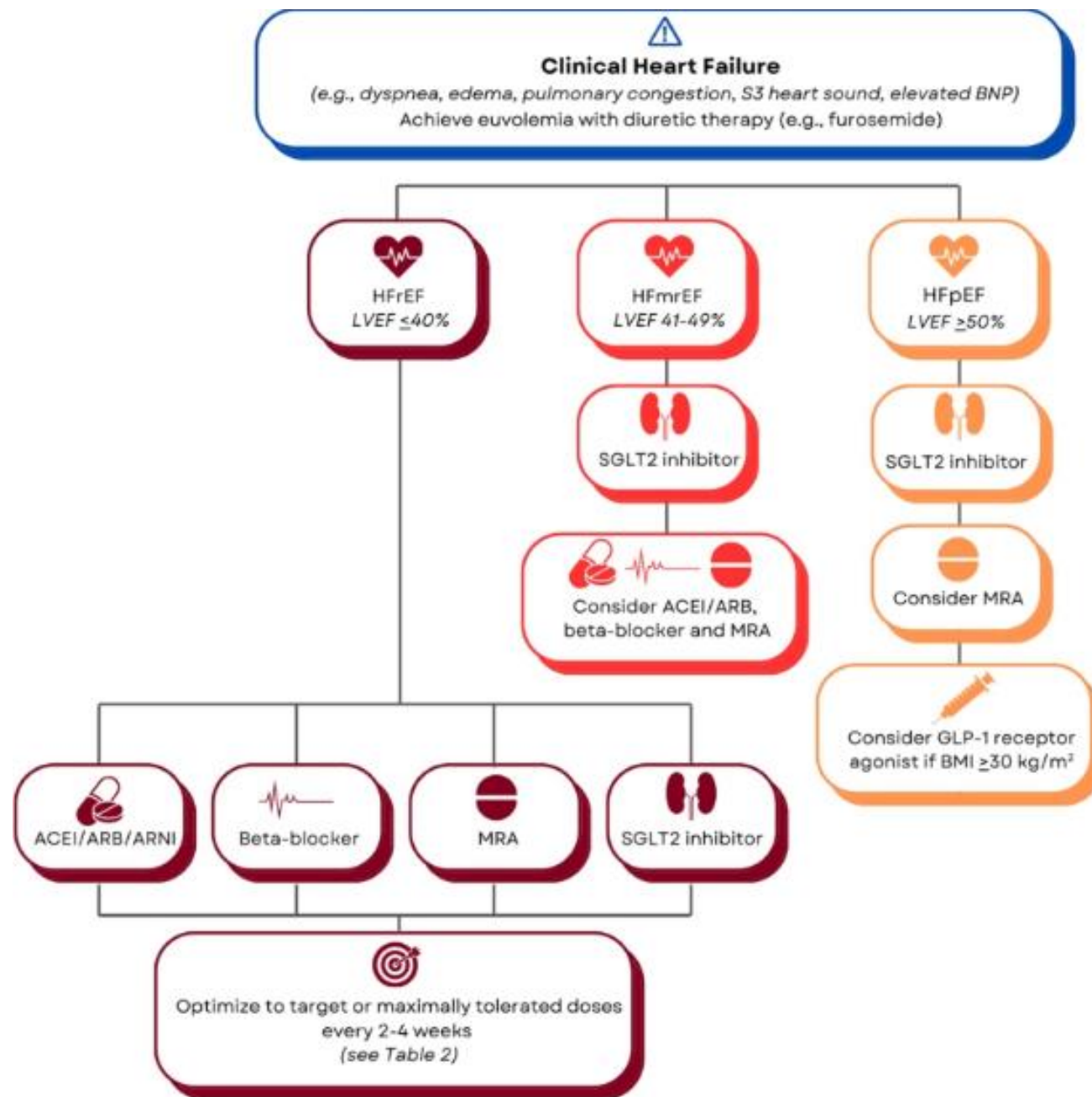
**Figure 2** Proportion of patients with a decrease of >30% in plasma N-terminal pro-B-type natriuretic peptide concentration from baseline at Day 90 (full-analysis set). Patients who died prior to Day 90 or who experienced permanent ( $\geq 5$  consecutive days) withdrawal of study drug after a cardiovascular hospitalization or emergency presentation for worsening chronic heart failure were counted as nonresponders for the primary efficacy analysis.

|              | HFmrEF/ HFpEF Guideline recommendations |                  |              |                       |                |
|--------------|-----------------------------------------|------------------|--------------|-----------------------|----------------|
|              | Canadian<br>2025                        | European<br>2023 |              | American<br>2022/2023 |                |
|              | HFnrEF                                  | HFmrEF           | HFpEF        | HFmrEF                | HFpEF          |
| Beta-blocker | -                                       | Yes (weak)       | -            | Yes (weak)            | -              |
| ARB          | Yes (weak)                              | Yes (weak)       | -            | Yes (weak)            | Yes (weak)     |
| MRA          | Yes (strong)                            | Yes (weak)       | -            | Yes (weak)            | Yes (weak)     |
| ARNI         | Yes (weak)                              | Yes (weak)       | -            | Yes (weak)            | Yes (weak)     |
| SGLT2i       | Yes (strong)                            | Yes (strong)     | Yes (strong) | Yes (moderate)        | Yes (moderate) |
| GLP-1        | Yes – BMI > 30; LVEF > 45% (weak)       | pre-data         |              | pre-data              |                |

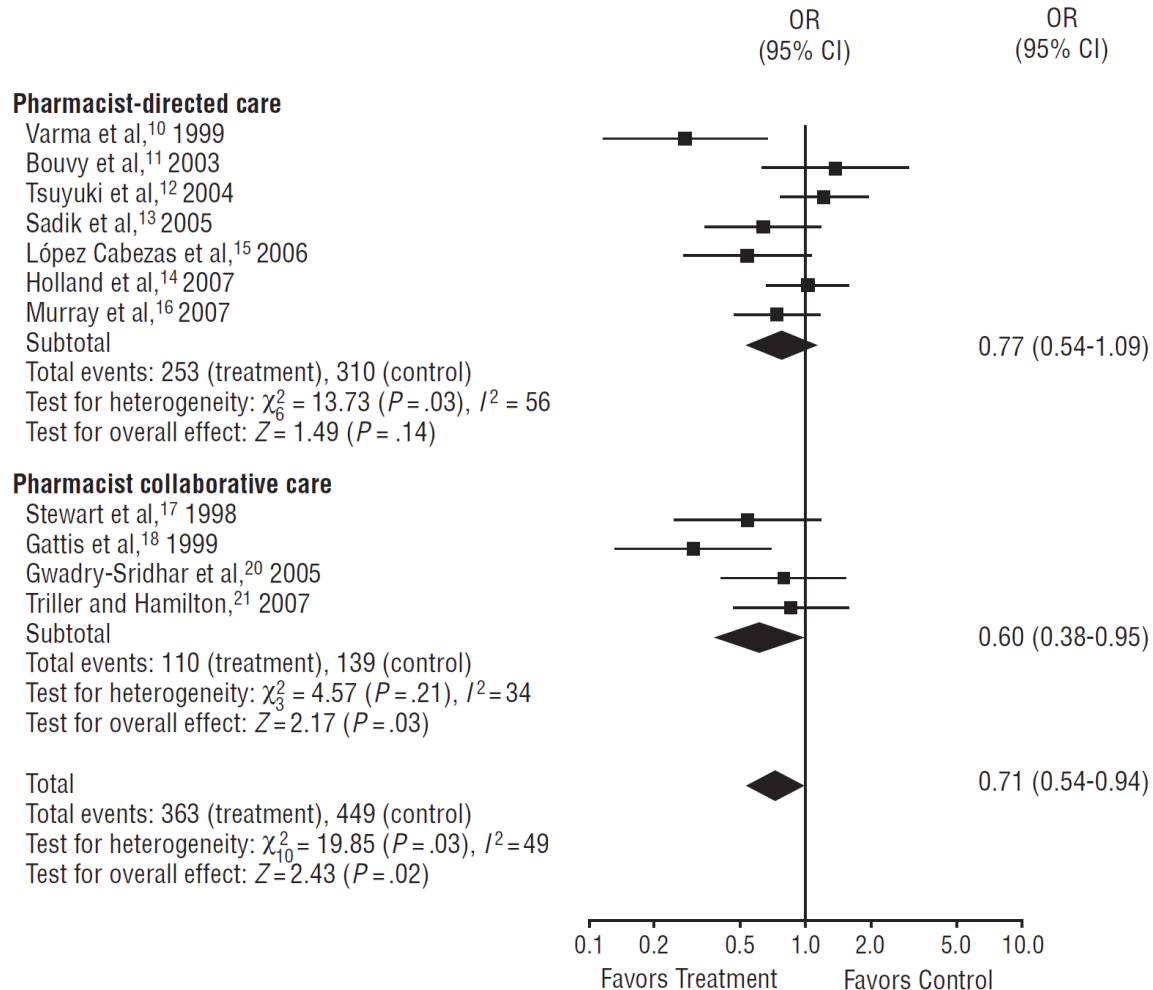
# Putting it all together.....

|                   | HFrEF (LVEF ≤40%)                      | HFmrEF (LVEF 41%-49%)               | HFpEF (LVEF ≥50%)                    |
|-------------------|----------------------------------------|-------------------------------------|--------------------------------------|
| ARNIs             | +                                      | +/-                                 | +/-                                  |
| ACEIs             | +                                      | +/-                                 | +/-                                  |
| ARBs              | +                                      | + (candesartan)                     | + (candesartan)                      |
| Beta-blockers     | + (bisoprolol, carvedilol, metoprolol) | +/-                                 | +/-                                  |
| MRAs              | + (eplerenone, spironolactone)         | + (finerenone) +/- (spironolactone) | + (finerenone) +/- (spironolactone)  |
| SGLT2 inhibitors  | + (dapagliflozin, empagliflozin)       | + (dapagliflozin, empagliflozin)    | + (dapagliflozin, empagliflozin)     |
| Incretin mimetics | ?                                      | +/- (semaglutide)                   | + (tirzepatide)<br>+/- (semaglutide) |

+ denotes a beneficial effect (lower risk of death and/or heart failure hospitalization); +/- denotes an inconclusive or unclear effect; ? denotes unknown effect. ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ARNI, angiotensin receptor-neprilysin inhibitor; HFmrEF, heart failure with mildly reduced ejection fraction; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; LVEF, left ventricular ejection fraction; MRA, mineralocorticoid receptor antagonist; SGLT2, sodium-glucose cotransporter-2.



# Would you use this drug in HF??



**Absolute risk reduction  
6.2%, NNT=17 at 6-12  
months**

**1 HF patient avoids  
hospitalization over 6-12  
months for every 17 HF  
patients treated by a  
pharmacist**

# Pharmacists improve HF outcomes

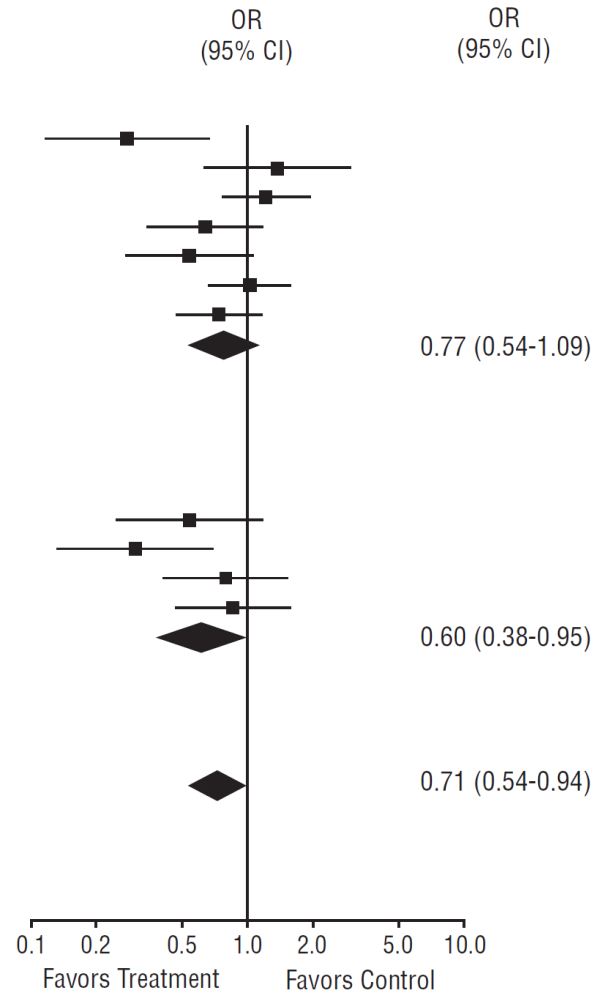
## Pharmacist-directed care

Varma et al,<sup>10</sup> 1999  
 Bouvy et al,<sup>11</sup> 2003  
 Tsuyuki et al,<sup>12</sup> 2004  
 Sadik et al,<sup>13</sup> 2005  
 López Cabezas et al,<sup>15</sup> 2006  
 Holland et al,<sup>14</sup> 2007  
 Murray et al,<sup>16</sup> 2007  
 Subtotal  
 Total events: 253 (treatment), 310 (control)  
 Test for heterogeneity:  $\chi^2_6 = 13.73$  ( $P = .03$ ),  $I^2 = 56$   
 Test for overall effect:  $Z = 1.49$  ( $P = .14$ )

## Pharmacist collaborative care

Stewart et al,<sup>17</sup> 1998  
 Gattis et al,<sup>18</sup> 1999  
 Gwadry-Sridhar et al,<sup>20</sup> 2005  
 Triller and Hamilton,<sup>21</sup> 2007  
 Subtotal  
 Total events: 110 (treatment), 139 (control)  
 Test for heterogeneity:  $\chi^2_3 = 4.57$  ( $P = .21$ ),  $I^2 = 34$   
 Test for overall effect:  $Z = 2.17$  ( $P = .03$ )

Total  
 Total events: 363 (treatment), 449 (control)  
 Test for heterogeneity:  $\chi^2_{10} = 19.85$  ( $P = .03$ ),  $I^2 = 49$   
 Test for overall effect:  $Z = 2.43$  ( $P = .02$ )



**Absolute risk reduction  
 6.2%, NNT=17 at 6-12  
 months**

**1 HF patient avoids  
 hospitalization over 6-12  
 months for every 17 HF  
 patients treated by a  
 pharmacist**

# Rx interventions that improve HF outcomes

- Educate patients & colleagues
- BPMH, med rec at transitions of care
- Prevent, identify & treat adverse drug events
- Prevent, identify drug interactions
- Improve adherence & access
- **Optimize (start & titrate) pharmacotherapy**

# Resources



[Heart Failure](#) [My Treatments](#) [My Medications](#) [Steps I Can Take](#) [Living My Life](#) [Resources](#)

## Living My Life

*Discover how to balance daily life while managing heart failure.*



[Heart Failure](#) [My Treatments](#) [My Medications](#) [Steps I Can Take](#) [Living My Life](#) [Resources](#)

## My Heart Failure Medications

*Heart failure medications are a key part of treating heart failure.*

*These medicines work together to help your heart pump better, protect it from further damage, reduce symptoms and ultimately help you live longer.*

On this page

# Resources

| What medicines am I taking for my heart function? |                                                                                     |                                                                                          |                                                                          |                                                        |                                                                         |                                                                                       |
|---------------------------------------------------|-------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------|--------------------------------------------------------------------------|--------------------------------------------------------|-------------------------------------------------------------------------|---------------------------------------------------------------------------------------|
| Type of medicine                                  | ONE of each of these medicines                                                      |                                                                                          |                                                                          |                                                        | For some people                                                         |                                                                                       |
|                                                   | ARNI /ACEI / ARB                                                                    | Beta Blocker                                                                             | MRA                                                                      | SGLT2 Inhibitor                                        | Sinus Node Inhibitor                                                    | Diuretic (water pill)                                                                 |
| Common names                                      | ARNI: sacubitril + valsartan (Entresto™)                                            | bisoprolol<br>carvedilol                                                                 | spironolactone<br>eplerenone                                             | empagliflozin (Jardiance™)<br>dapagliflozin (Forxiga™) | ivabradine (Lancora™)                                                   | furosemide (Lasix™)                                                                   |
|                                                   | ACEI: ramipril, lisinopril, perindopril                                             | metoprolol                                                                               |                                                                          |                                                        |                                                                         |                                                                                       |
|                                                   | ARB: candesartan, valsartan                                                         |                                                                                          |                                                                          |                                                        |                                                                         |                                                                                       |
| How it works                                      | Helps the heart work better and stops heart function from getting worse             |                                                                                          |                                                                          |                                                        |                                                                         | Removes fluid                                                                         |
|                                                   | Opens up blood vessels to make it easier for your heart to pump blood to your body. | Blocks adrenaline and slows your heart rate so your heart does not have to work as hard. | Blocks stress hormones that make the heart stiff and can cause scarring. | Works in many ways to help lower stress on your heart. | Slows your heart rate, so your heart can relax and fill up more easily. | Gets rid of extra fluid and lowers swelling by making you pass more urine (pee more). |
| How do these medicines help me?                   |                                                                                     |                                                                                          |                                                                          |                                                        |                                                                         |                                                                                       |
| Feel better                                       | ✓                                                                                   | ✓                                                                                        | ✓                                                                        | ✓                                                      | ✓                                                                       | ✓                                                                                     |
| Live longer                                       | ✓                                                                                   | ✓                                                                                        | ✓                                                                        | ✓                                                      |                                                                         |                                                                                       |
| Fewer hospital visits                             | ✓                                                                                   | ✓                                                                                        | ✓                                                                        | ✓                                                      | ✓                                                                       | ✓                                                                                     |

Created by: Felicia Yang, Sheri Koshman - Reviewed by: Lynette Kosar, Ricky Turgeon  
Version Date: July 22, 2021

| What do I need to watch out for? |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                                                                                                |                                                                                                                     |                                                                                                                                  |                                                                                                   |                                                                                                                    |
|----------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------|
|                                  | *ARNI/ACEI/ ARB                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Beta Blocker                                                                                                                                   | *MRA                                                                                                                | *SGLT2 Inhibitor                                                                                                                 | Sinus Node Inhibitor                                                                              | *Diuretic                                                                                                          |
| Kidney function (blood work)     | ✓                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                                                                                                                | ✓                                                                                                                   | ✓                                                                                                                                |                                                                                                   | ✓                                                                                                                  |
| Potassium (blood work)           | ✓<br>risk of high potassium                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                                | ✓<br>risk of high potassium                                                                                         |                                                                                                                                  |                                                                                                   | ✓<br>risk of low potassium                                                                                         |
| Symptoms of low blood pressure   | ✓                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | ✓                                                                                                                                              |                                                                                                                     |                                                                                                                                  |                                                                                                   | ✓                                                                                                                  |
| Symptoms of low heart rate       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | ✓                                                                                                                                              |                                                                                                                     |                                                                                                                                  | ✓                                                                                                 |                                                                                                                    |
| Other side effects               | <p>ACEI: May cause a dry cough (2 in 10 people), which is reversible.</p> <p>Swelling of the tongue, lips, and throat (very rare). Stop the medicine and get help right away.</p>                                                                                                                                                                                                                                                                                                                                                                    | <p>You may feel tired (low energy) when you first start this medicine.</p> <p>This will get better as your body gets used to the medicine.</p> | <p>Spironolactone: Your breasts may get larger, and/ or they feel tender, especially in males (1 in 10 people).</p> | <p>Genital yeast infection (less than 1 in 10 people).</p> <p>You can prevent this by keeping yourself clean.</p>                | <p>Vision changes such as halos around bright lights that go away over time (1 in 50 people).</p> | <p>Dehydration (thirsty, dry mouth).</p> <p>Sun sensitivity (wear sunscreen).</p> <p>Gout</p>                      |
| Tips for taking each medicine    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Do not stop this medicine suddenly unless your healthcare provider tells you to. Your heart may race if you stop it suddenly                   |                                                                                                                     | This medicine is also used to treat diabetes. Your other diabetes medicines may need to be adjusted when you take this medicine. | Take this medicine with food.                                                                     | Take the medicine earlier in the day, before 2 p.m. This lowers your chance of having to get up and pee overnight. |
| General tips                     | <ul style="list-style-type: none"> <li>Low blood pressure: You may feel lightheaded, faint, or nearly faint, especially when you stand or sit up suddenly.</li> <li>Low heart rate: You may feel tired, lightheaded, or faint or nearly fainting.</li> <li>If you are vomiting, have diarrhea, or are dehydrated: You may need to stop taking some (* above) of these medicines for a short time (see sick day management sheet).</li> <li>Talk to your healthcare provider about your medicines when you have any questions or concerns.</li> </ul> |                                                                                                                                                |                                                                                                                     |                                                                                                                                  |                                                                                                   |                                                                                                                    |

Created by: Felicia Yang, Sheri Koshman - Reviewed by: Lynette Kosar, Ricky Turgeon  
Version Date: July 22, 2021

# Learning Objectives:

- By the end of the session, participants will be able to:
  - Reclassify heart failure phenotypes using correct, updated clinical nomenclature and diagnostic criteria.
  - Formulate an evidence based treatment plan incorporating the core pillars of guideline directed medical therapy (GDMT)
  - Implement patient centred, multidisciplinary approaches to improve individualization, reduce readmissions and optimize long term care.

# Thank you for your attention

