Integrated Heart Failure (HF) CoP Webinar:

The Role of NT-proBNP as a Screening Tool in Primary and Community Settings To Support Early Heart Failure Management

December 13th, 2024

Ontario Health

Land Acknowledgement

Agenda

TIME	TOPIC	NAME
12:00 pm	Land Acknowledgement	Grace Bannerman
12:05 pm	Welcome & Introductions Housekeeping	Colleen Lackey
12:10 pm	Everything You Wanted to Know About How to Diagnose and Manage Heart Failure	Dr. Stephanie Poon
12:40 pm	Q&A	All
12:55 pm	Wrap Up	Colleen Lackey

Objectives

1) Participants will gain an understanding of NT-pro BNP's role in early heart failure detection and management

2) Participants will learn practical applications on how to manage patients who are diagnosed with heart failure by utilizing clinical guidelines and emerging evidence

3) Our aim is to ensure that the participants can share their knowledge on this topic with their clinical champions and partners to support integrated clinical pathways for HF across OHT's

Housekeeping

- Please keep yourself on mute unless you are speaking.

- We encourage you to type your questions or comments in the chat box. The chat box is monitored throughout the webinar. Questions will be addressed directly in the chat box or in the discussion following the presentations.

- We also encourage you to share any suggestions/topics for future webinars.

- This meeting **will be recorded**. A copy of the webinar recording, and slides will be available on the virtual CoP shared space.

Poll #1

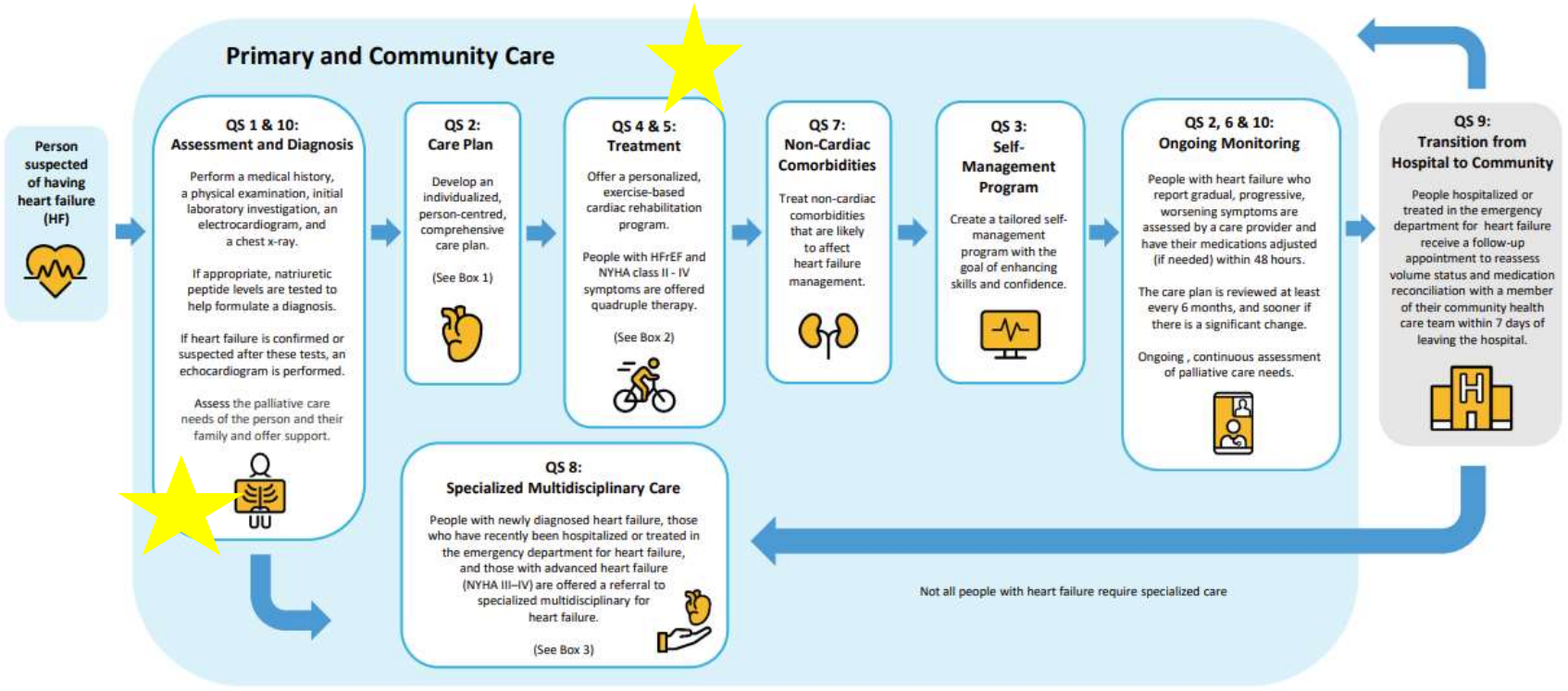
What is your role?

- ❑ Primary Care Provider
- ❑ Specialist
- ❑ Interprofessional Team Member
- ❑ OHT/PCN Clinical Lead
- ❑ OHT Backbone Team Member
- ❑ OHT Partner
- ❑ Planning and Operations
- ❑ Data Lead or Quality Specialists
- ❑ Patient, Family, and/or Caregiver
- ❑ OH/MOH/RISE
- ❑ Other

Heart Failure: Care in the Community for Adults

Ontario Health

A collaborative and community-based pathway outlining high-quality care based on the Ontario Health *Heart Failure* quality standard



Poll #2:

How would you rate your current knowledge of NT-proBNP?

1. Not familiar at all.
2. I have a vague understanding of its role in heart failure.
3. I know NT-proBNP is used in diagnosing heart failure but don’t know the details.
4. I have a good understanding of NT-proBNP's diagnostic role in heart failure.
5. I am very familiar with how NT-proBNP is used in diagnosing heart failure.

Speaker

Dr. Stephanie Poon

Cardiologist, Medical Director
Heart Function Clinic
Sunnybrook Health Sciences Centre

Stephanie.poon@sunnybrook.ca

The Role of NT-proBNP as a Screening Tool in Primary and Community Settings To Support Early Heart Failure Management

Everything You Wanted to Know About How to Diagnose and Manage Heart Failure

December 13, 2024

Integrated Heart Failure Care CoP Webinar Series

Dr. Stephanie Poon, MD, MSc, FRCPC

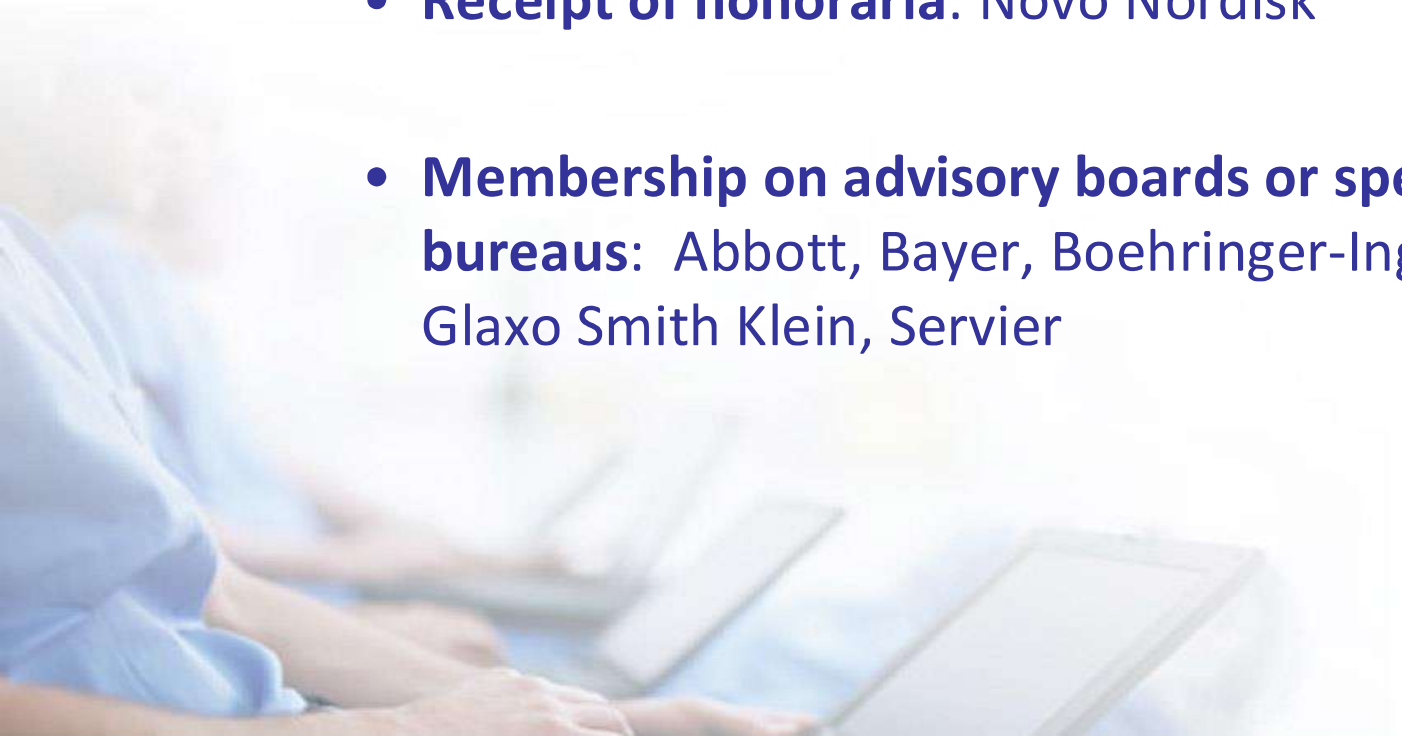
Associate Professor, University of Toronto

Cardiologist, Sunnybrook Health Sciences Centre

Medical Director, Sunnybrook Advanced Heart Function Clinic

Disclosures

- **Receipt of honoraria**: Novo Nordisk
- **Membership on advisory boards or speakers' bureaus**: Abbott, Bayer, Boehringer-Ingelheim, Glaxo Smith Klein, Servier



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Objectives

- How to utilize NT-pro BNP as a screening tool in primary and community care settings
- Discuss newer evidence-based strategies for the management of heart failure
- Examine practical approaches to heart failure medication management

Outline

- 1. Use of Natriuretic Peptides to Diagnose Heart Failure (HF)
- 2. Management of HFrEF
- 3. Management of HFpEF
- 4. Practical Medication Management

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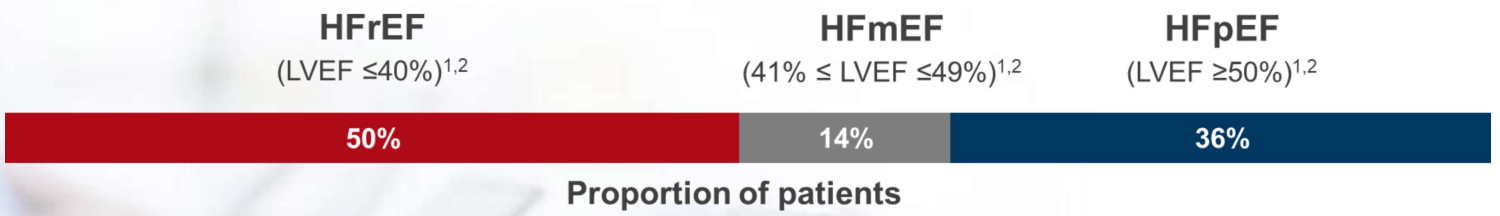
Part I:

DIAGNOSIS OF HEART FAILURE

Current Definition of HF

- HF is a complex clinical syndrome in which abnormal heart function results in, or increases the subsequent risk of, clinical symptoms and signs of reduced cardiac output and/or pulmonary or systemic congestions at rest
  or with stress1
- Categorized based upon ejection fraction (EF): ~50% have EF ≤40%, for which there are approved therapies, and ~50% have EF >40%



Echocardiography is the most accessible method to evaluate LVEF in Canada.[1]

EF, ejection fraction; HFmEF, heart failure with mid-range preserved ejection fraction; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction;
HHF, hospitalization for HF; LVEF, left ventricular ejection fraction

1. Ezekowitz JA et al. Can J Cardiol 2017;33(11):1342-1433; 2. Steinberg BA et al. Circulation 2012;126(1):65-75.

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Heart Failure is a Growing Epidemic in Canada

Ontario Health

Heart&Stroke

62% of patients presenting to ED with HF are admitted[1]

Length of stay for HF hospitalization average **8.9 days**[2]

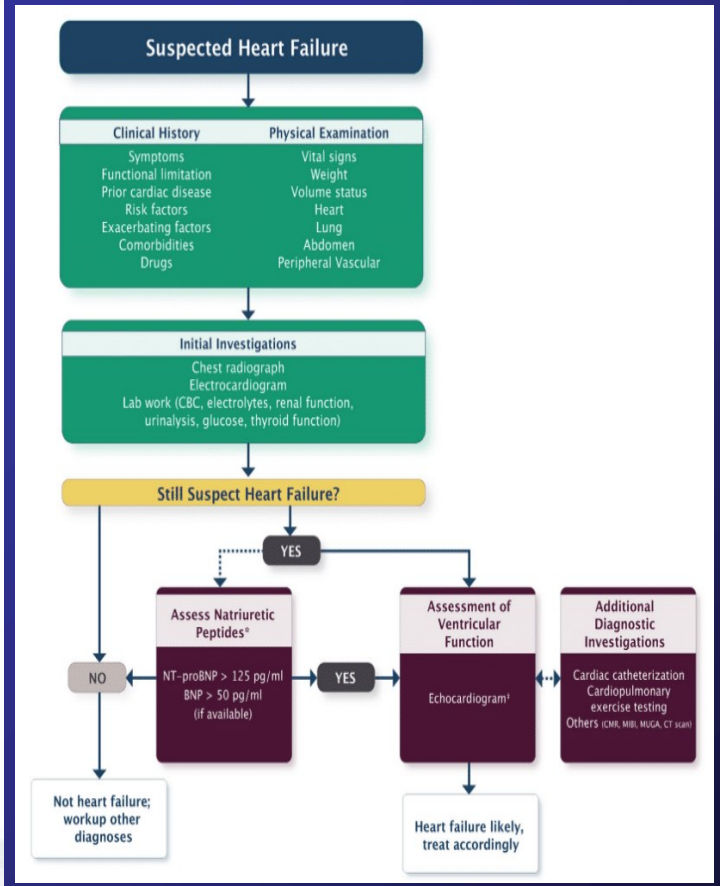
30-day readmission rates are **21%**[3]

- Significant predictors include: LTC residency status discharged from ED >2+ HHF in prior year +/- recipient of community care nursing services

$2,800,000,000
HEART FAILURE is estimated to cost more than **$2.8 billion** per year in Canada by 2030[4]

ED, emergency department; HHF, hypertensive heart failure; LTC, long-term care
1.Ontario Ministry of Health and Long-Term Care. Quality-Based Procedures: Clinical Handbook for Heart Failure (2015); 2. Canadian Institute for Health Information. Hospital Stays in Canada (2017–2018);
3. Heart and Stroke Foundation. 2016 Report on the Health of Canadians; 4. Tran DT et al. CMAJ Open 2016;4(3):E365-E370

2017 CCS HEART FAILURE GUIDELINES: ALGORITHM FOR THE DIAGNOSIS OF HEART FAILURE (HF)



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

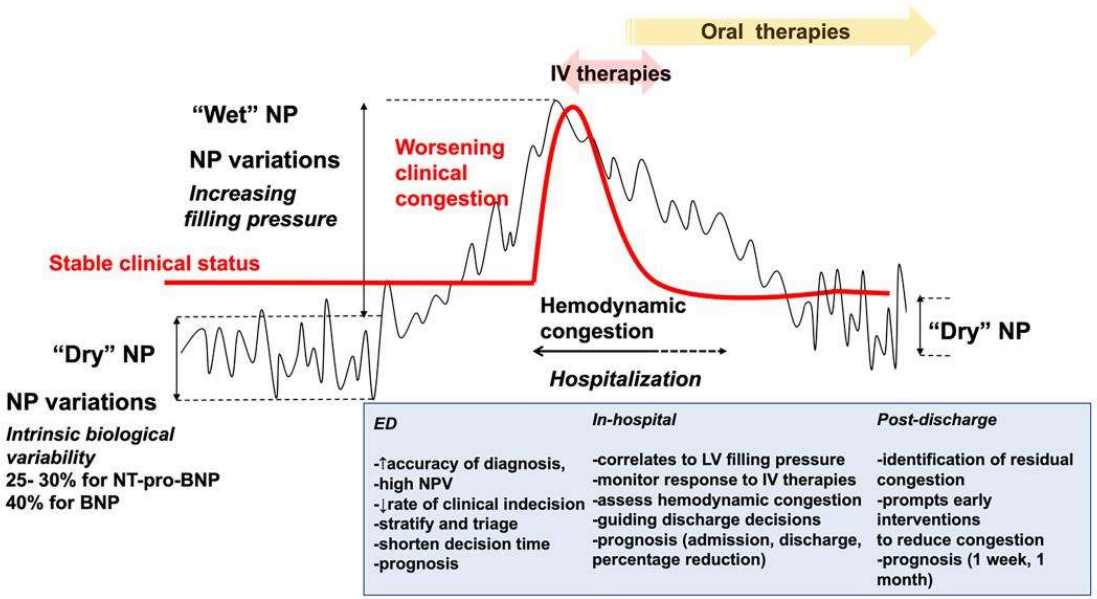
CCS HF GUIDELINES

Recommendation 21:

We recommend that BNP/NT-proBNP levels be measured to help confirm or rule out a diagnosis of HF in the acute or ambulatory care setting in patients in whom the cause of dyspnea is in doubt (Strong Recommendation; High-Quality Evidence).

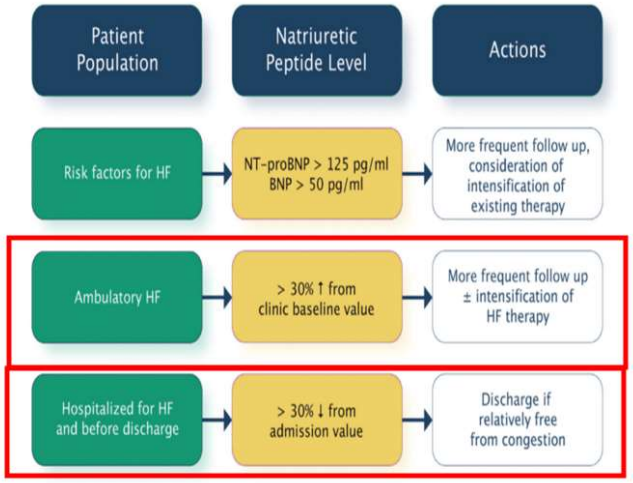
Ezekowitz JA et al. Can J Cardiol. 2017 Nov;33(11):1342-1433.

NP Trajectory Across the Spectrum of Acute HF Care

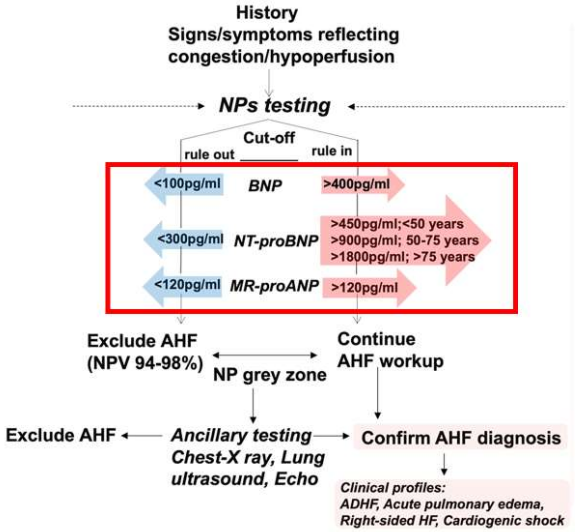


Tsutsui H et al. J Card Fail. 2023 May;29(5):787-804

Use of BNP/NT-pro BNP in Different Clinical Scenarios



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



Tsutsui H et al. J Card Fail. 2023 May;29(5):787-804

CCS HF GUIDELINES

Recommendation 24:

We suggest that measurement of BNP or NT-proBNP in patients hospitalized for HF should be considered before discharge, because of the prognostic value of these biomarkers in predicting rehospitalization and mortality (Strong Recommendation; Moderate-Quality Evidence).

Practical Tip:

For patients who are about to be discharged from the hospital after a HF hospitalization, the NP level should be lower than that on admission. If NP levels remain elevated, clinicians should re-evaluate the patient's condition and consider the possibility of delaying discharge from the hospital to optimize therapy and further reduce the NP level.

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

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Use of NP Testing in Adults with Suspected HF:

Recommendation (May 2021)

Ontario Health

Cost-effectiveness:

- "Our economic literature review found a total of 12 studies evaluating the cost effectiveness of BNP or NT-proBNP testing in people with suspected heart failure"
- "…found that BNP or NT-proBNP testing was highly likely to be cost effective in Ontario in the ED and community settings"
- "Over the next 5 y, publicly funding BNP and NT-proBNP testing would result in… savings of about $20 million in community care."

Final recommendation:

Ontario Health, based on guidance from the Ontario Health Technology Advisory Committee, recommends publicly funding natriuretic peptide (BNP or NT-proBNP) testing for the diagnosis of people with suspected heart failure in the community and emergency department settings.

https://hqontario.ca/Portals/0/Documents/evidence/reports/recommendation-use-of-b-type-natriuretic-peptide-and-n-terminal-probnp-as-diagnostic-tests-in-adults-with-suspected-heart-failure-en.pdf

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Part 2:

CONTEMPORARY MEDICAL MANAGEMENT OF HFrEF

Case: Ms. Wynded

- 75 year old woman
- DM2 treated with metformin 1000 mg BID and glyburide 5 mg BID
- History of HF due to previous MI
- LVEF 33%, declined ICD therapy
- Used to walk 30 min daily without shortness of breath
- Now NYHAIII for the past 2 weeks with orthopnea

- In clinic:
  - On perindopril 8 mg/day, bisoprolol 10 mg/day, spironolactone 12.5 mg/day
  - Creatinine 131 µmol/L, eGFR 36 mL/min/1.73 m2, K+ 5.2 mmol/L
  - HR 83 bpm, sinus
  - BP 120/78 mmHg

BID, twice a day; BP, blood pressure; EF, ejection fraction; eGFR, estimated glomerular filtration rate; HR, heart rate; ICD, implantable cardioverter defibrillator; K+, potassium; MI, myocardial infarction; NYHA, New York Heart Association Functional Classification; T2DM, type 2 diabetes mellitus

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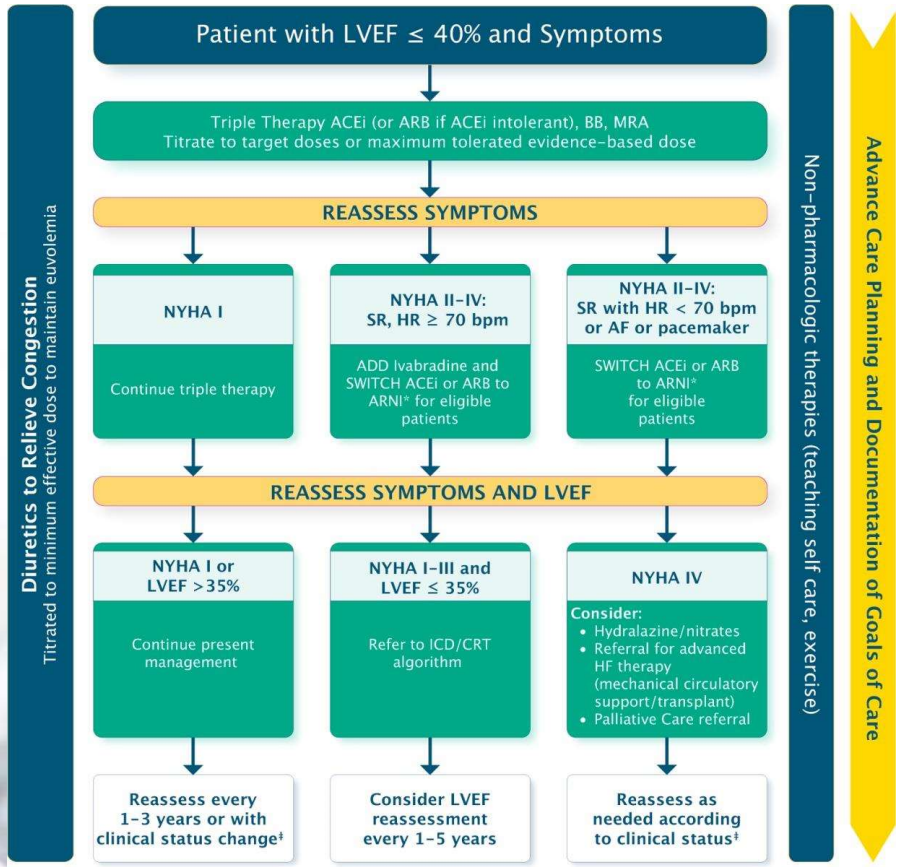
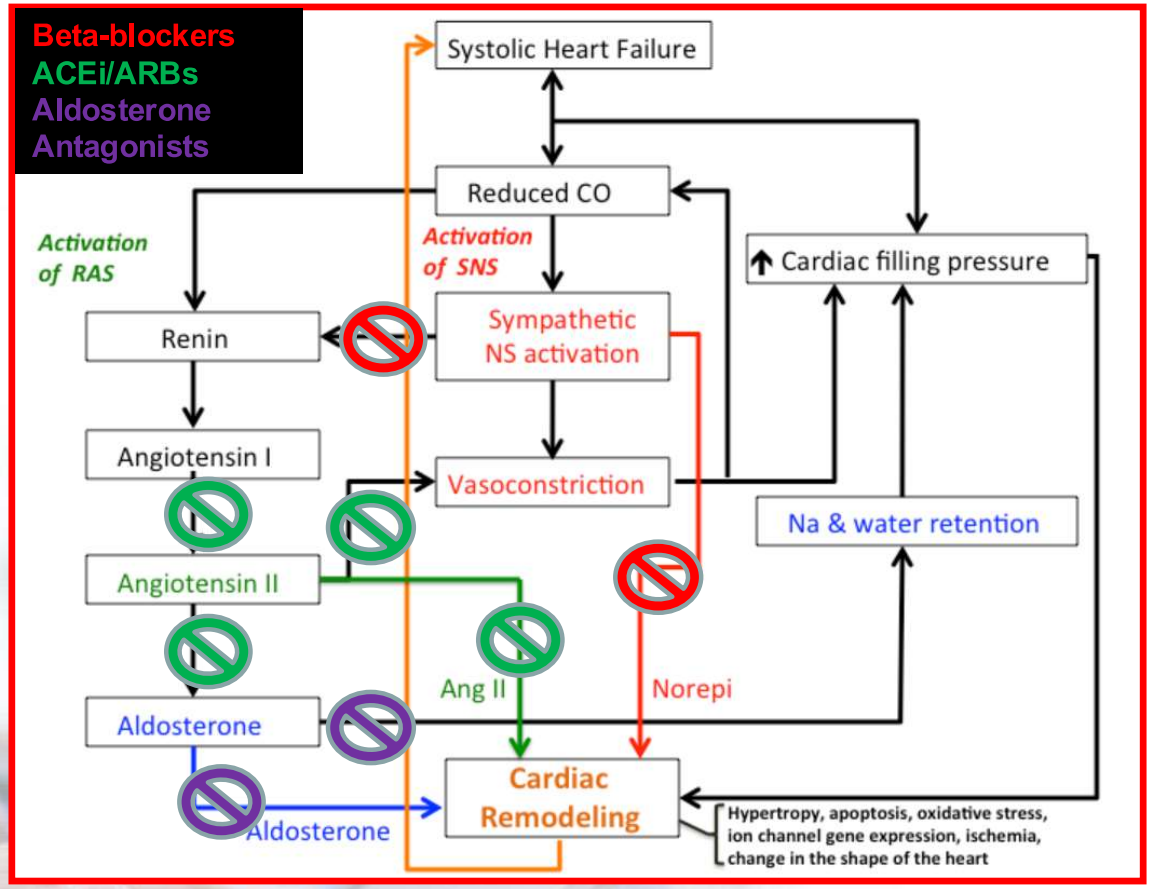
2017 CCS HF Guidelines



Mechanisms of HFrEF "triple therapy"



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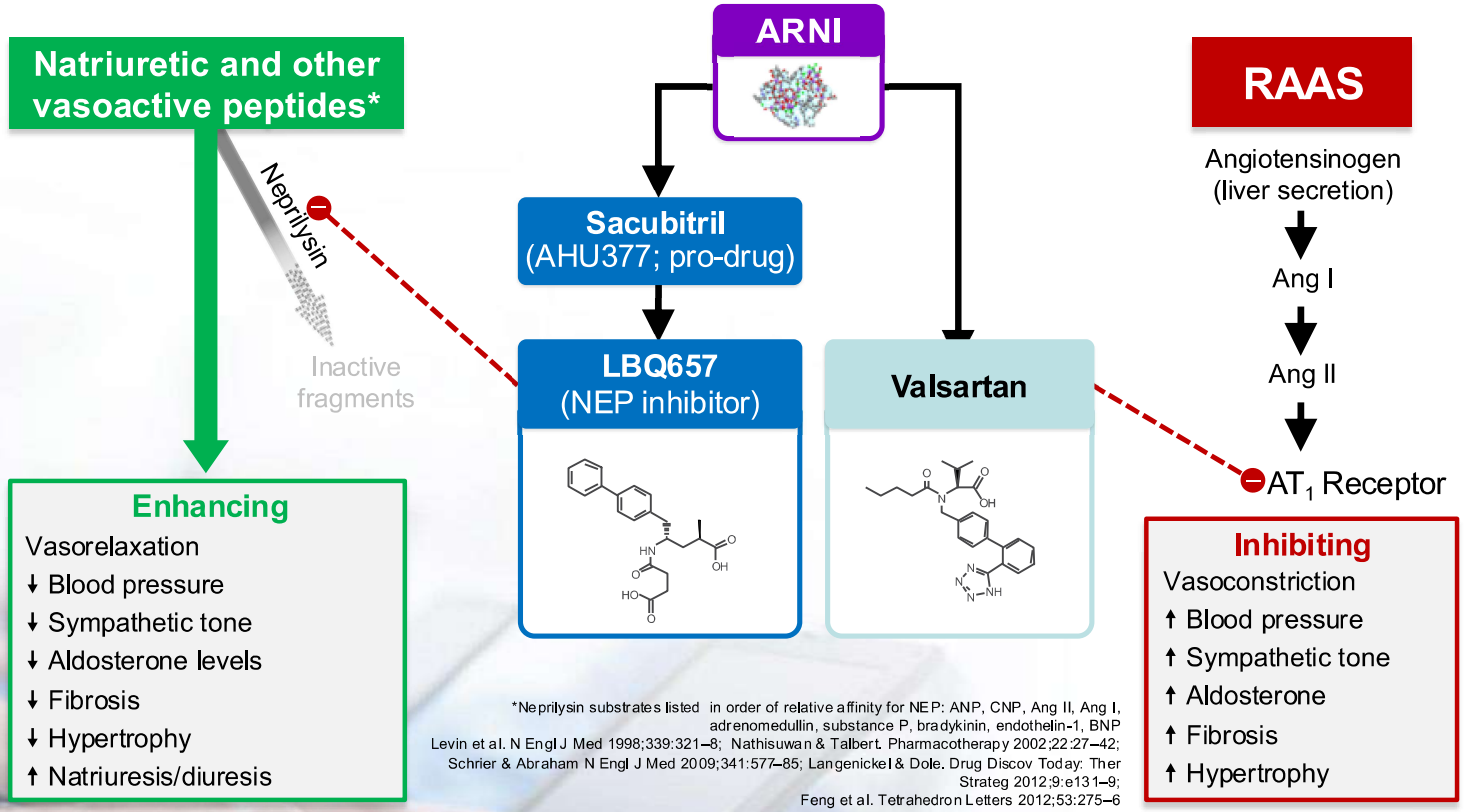
Sacubitril/valsartan simultaneously promotes the NP pathway and inhibits the RAAS pathway

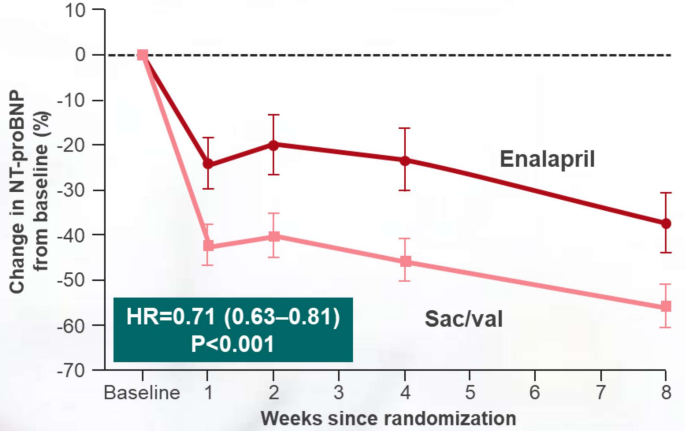


*Neprilysin substrates listed in order of relative affinity for NEP: ANP, CNP, Ang II, Ang I, adrenomedullin, substance P, bradykinin, endothelin-1, BNP

Levin et al. N Engl J Med 1998;339:321–8; Nathisuwan & Talbert. Pharmacotherapy 2002;22:27–42; Schrier & Abraham N Engl J Med 2009;341:577–85; Langenickel & Dole. Drug Discov Today: Ther Strateg 2012;9:e131–9; Feng et al. Tetrahedron Letters 2012;53:275–6

Sacubitril/Valsartan: Early separation in HFrEF and acute decompensated HF

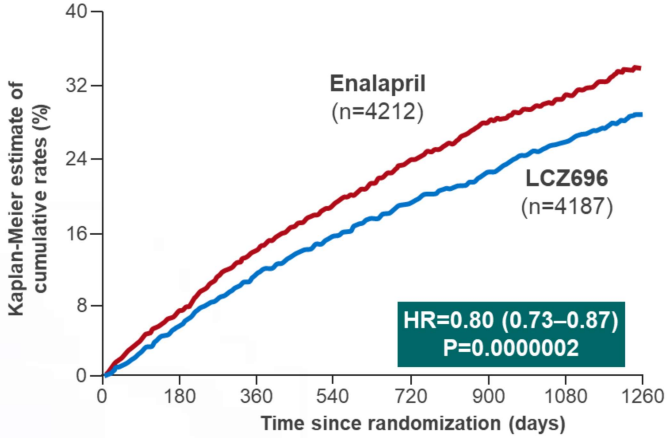
PIONEER-HF (acute decompensated inpatients): Primary efficacy outcome (change in the NT-proBNP concentration)[2]



No. at risk

Sac/val	397	355	363	365	349
Enalapril	394	359	351	350	348

PARADIGM-HF (outpatients): Primary endpoint (CV death or HF hospitalization)[1]



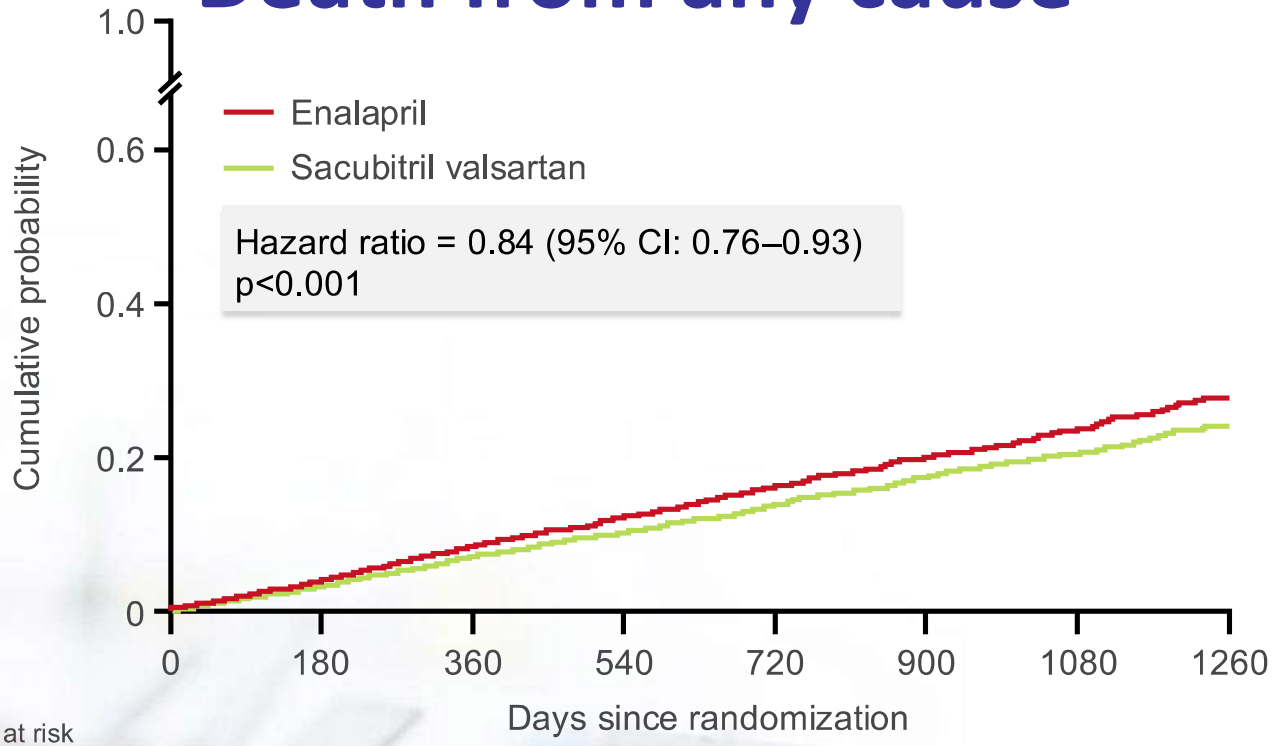
Patients at risk

LCZ696:	4187	3822	3663	3018	2257	1544	896	249
Enalapril:	4212	3883	3579	2922	2123	1488	853	236

CV, cardiovascular; HR, hazard ratio; NT-pro-BNP, N-terminal pro b-type natriuretic peptide; sac/val, sacubitril/valsartan

1. McMurray JJ et al. N Eng J Med 2014;371(11):993-1004; 2. Velazquez EJ et al. N Eng J Med 2019;280(6): 539-548.

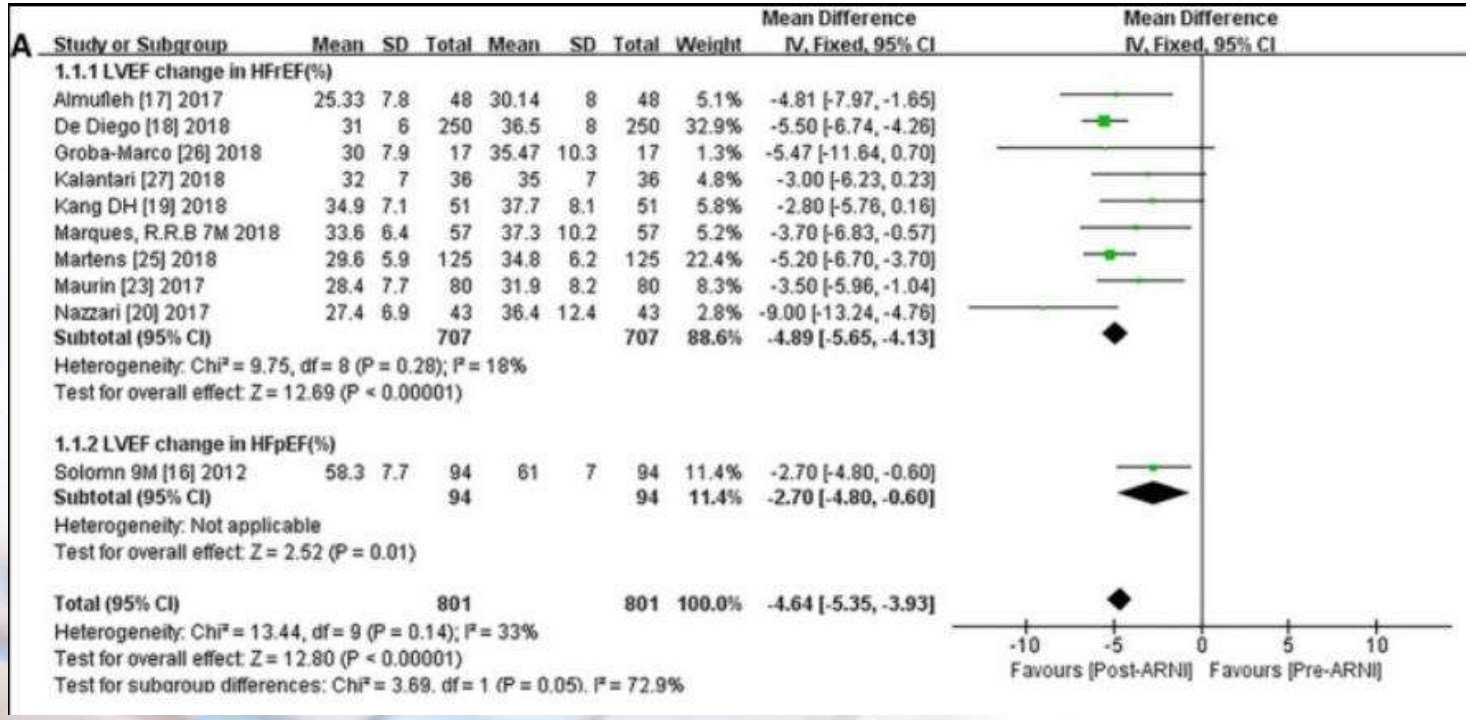
Death from any cause



No at risk								
LCZ696	4187	4056	3891	3282	2478	1716	1005	280
Enalapril	4212	4051	3860	3231	2410	1726	994	279

McMurray et al. N Engl J Med 2014;371:993–1004

ARNI outperformed ACEi/ARBs in terms of cardiac reverse remodelling (CRR) indices



Wang Y et al. *J Am Heart Assoc*. 2019;8:e012272.

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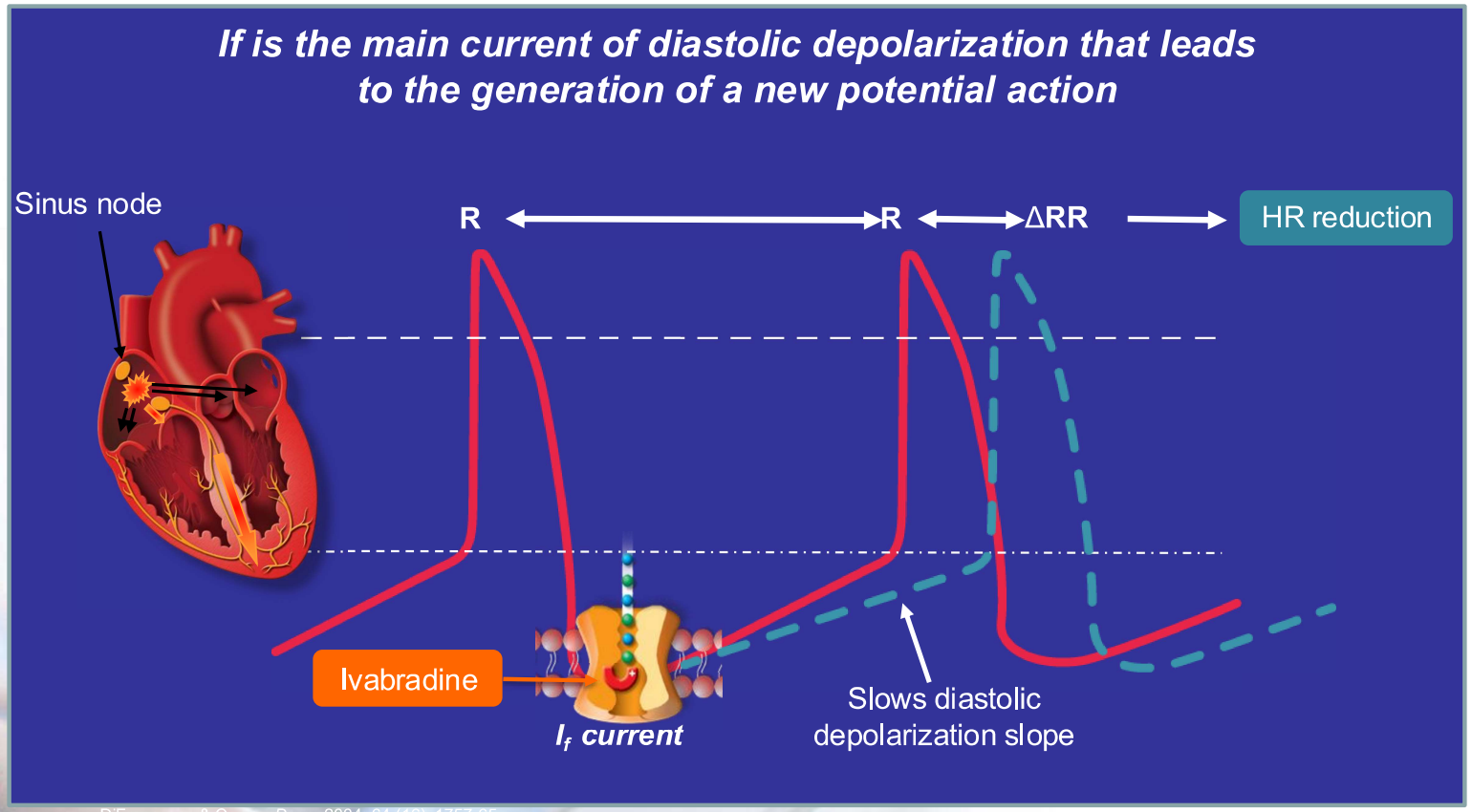
Ivabradine is a medication that slows down heart rate



DiFrancesco & Camm. *Drugs* 2004; 64 (16): 1757-65.

Canadian Cardiovascular Society Heart Failure Companion 2016

- *"Resting heart rate is directly related to mortality in patients with heart failure".*
- *"Decrease of an initially increased HR is associated with improved mortality.."*
- *Most clinicians target a resting heart rate of 50-60 beats/min or as low as tolerated*

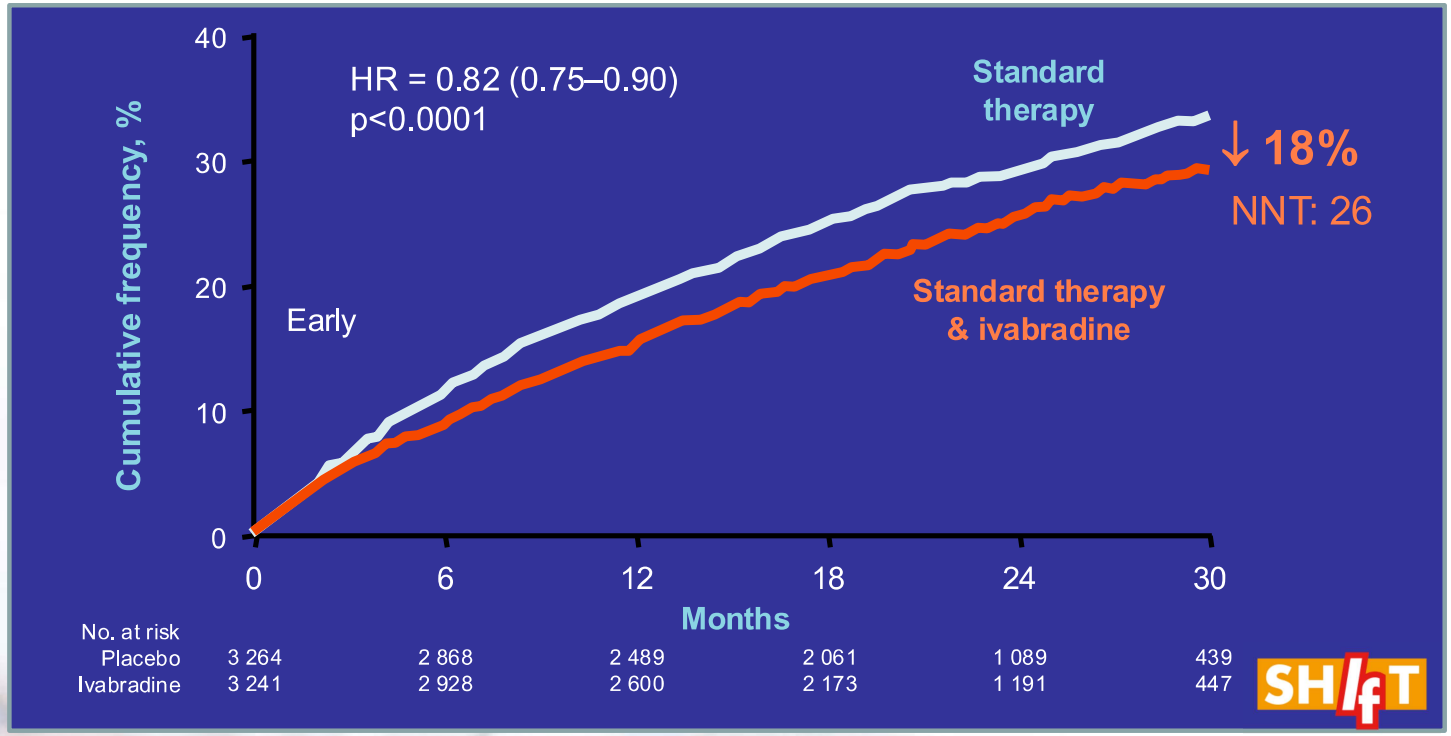
Howlett et al. *Can J Cardiol* 2016; 32: 296-310

Ivabradine and outcomes in chronic heart failure (SHIFT): a randomised placebo-controlled study

*Karl Swedberg, Michel Komajda, Michael Böhm, Jeffrey S Borer, Ian Ford, Ariane Dubost-Brama, Guy Lerebours, Luigi Tavazzi, on behalf of the SHIFT Investigators**

- 6505 patients with LVEF ≤ 35%, NYHA II-IV, HR ≥70 bpm, sinus rhythm, on optimal medical therapy
- Ivabradine 5-7.5 mg po bid vs placebo
- Median study duration: 23 months
- Median heart rate: 77 bpm

CV mortality and HF hospitalization benefits



- The curves for ivabradine and placebo begin to diverge at 3 months, and the difference is statistically significant at 6 months

Swedberg et al. *Lancet* 2010; 376: 875-85.

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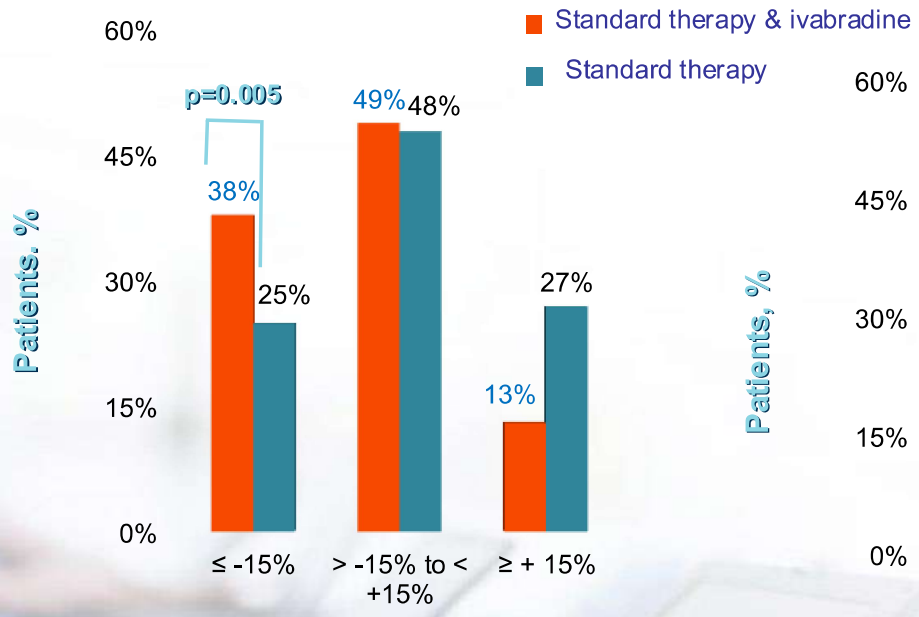
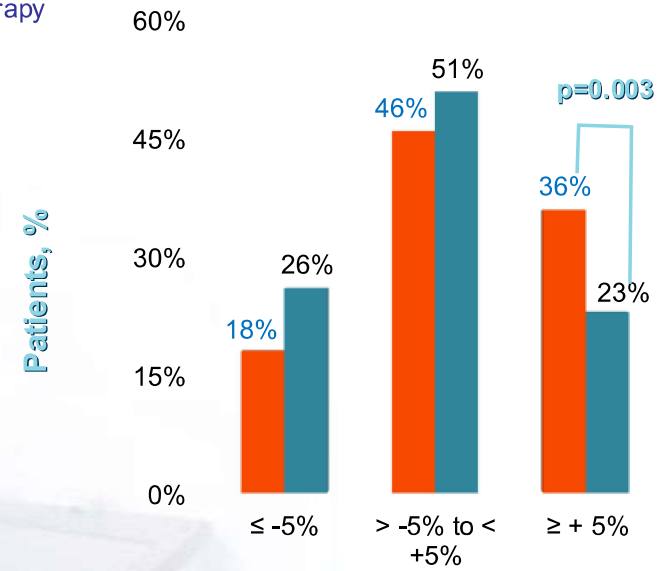
Ivabradine reversed cardiac remodeling on top of recommended therapy within 8 months



Relative change in LVESVI



Relative change in LVEF

Tardif et al. *Eur Heart J* 2011; 32: 2507-15.

SGLT2 inhibitors in HFrEF

	DAPA-HF	EMPEROR-Reduced
SGLT2 inhibitor	Dapagliflozin 10 mg daily	Empagliflozin 10 mg daily
No. of patients	4,744	3,730
Inclusion criteria	LVEF ≤40% +/-DM (42%)	LVEF ≤40% +/-DM (50%)
eGFR	>30	>20
Median follow-up	18.2 months	16 months
Primary outcome	CV death + HF composite (HF hosp + urgent HF visit)	CV death + HF hosp
Results	HR 0.74 (0.65-0.85); P<0.001	HR 0.75 (0.65-0.86); P<0.001

Consistent regardless of DM status, age, sex, baseline ARNI

McMurray JJV et al. *N Engl J Med*. 2019;381:1995-2008.
Packer M et al. *N Engl J Med*. 2020;383:1413-1424.

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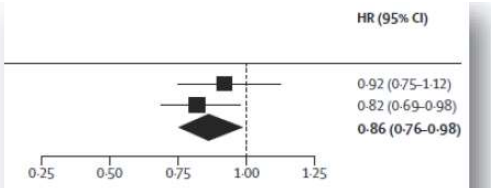
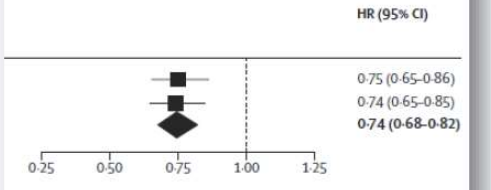
SGLT2i in HFrEF: DAPA-HF + EMPEROR-Reduced

CV Death
EMPEROR-Reduced
DAPA-HF



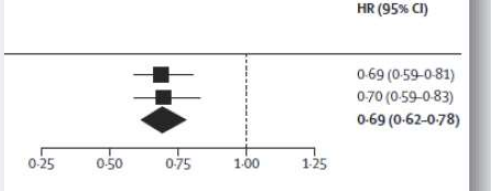
↓14%

CV Death + HF Hosp
EMPEROR-Reduced
DAPA-HF



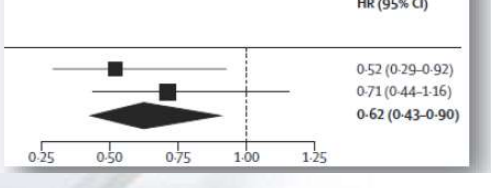
↓26%

HF Hosp
EMPEROR-Reduced
DAPA-HF



↓31%

Kidney Composite*
EMPEROR-Reduced
DAPA-HF

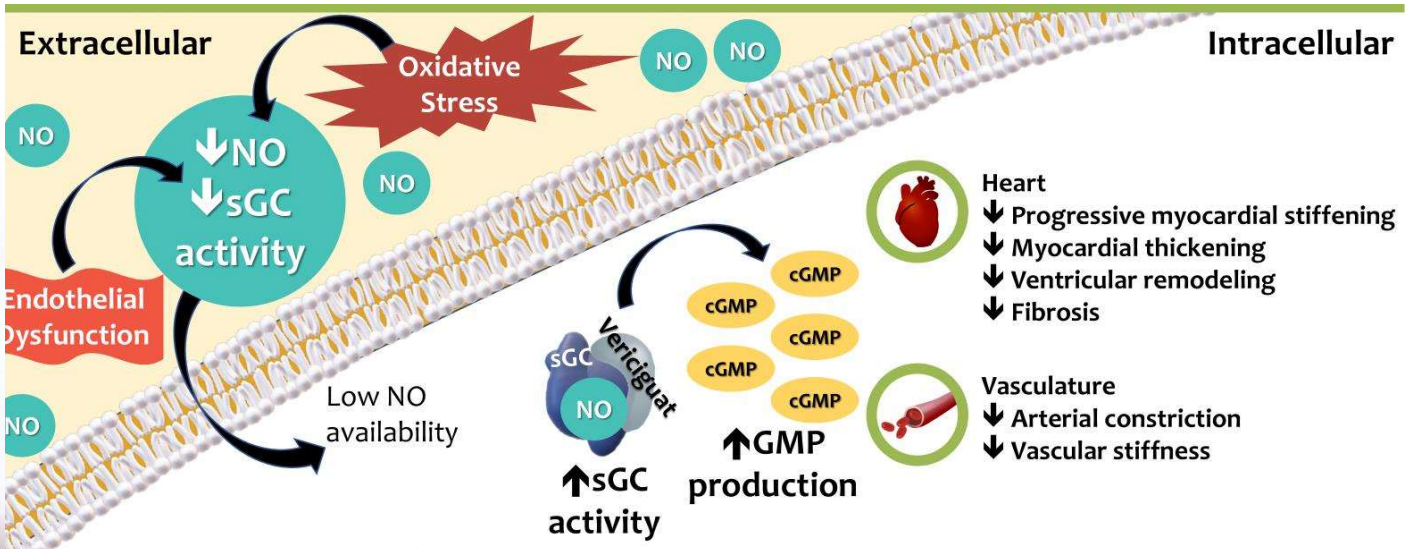


↓38%

*↓GFR 50%, ESRD, renal death

Zannad F et al. *Lancet*. 2020;396:819-829

Vericiguat increases soluble guanylate cyclase to improve myocardial and vascular function



cGMP, cyclic guanosine monophosphate; HF, heart failure; NO, nitric oxide; sGC, soluble guanylate cyclase.
Mann D et al. Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine (10th Ed) 2014 Saunders; Felker GM, Mann D. Heart Failure: A Companion to Braunwald's Heart Disease (4th Ed) 2019 Elsevier; Breitenstein S et al. Handb Exp Pharmacol. 2017;243:225-247; Gheorghiade M et al. Heart Fail Rev. 2013;18:123-34; Boerrigter G et al. Handb Exp Pharmacol. 2009;191:485-506.

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Key **Inclusion and Exclusion Criteria** for the VICTORIA Trial

Inclusion Criteria

"Chronic HF" **after** **"Worsening Event"**

- NYHA class II to IV
- LVEF <45%
- Guideline-based HF therapies

- Recent HFH or iv diuretic use
- Very elevated BNP or NT-proBNP

BNP ≥300 and NT-proBNP ≥1,000 pg/mL NSR
BNP ≥500 and NT-proBNP ≥1,600 pg/mL AF

Participants may have been randomized as an inpatient or an outpatient but must have met criteria for clinical stability

Exclusion Criteria

- Long-acting nitrates, PDE5 inhibitors, riociguat
- Awaiting heart transplantation, continuous iv inotropes, or has/anticipates ventricular assist device
- eGFR <15 mL/min/1.73m^2 or chronic dialysis
- Severe pulmonary disease
- Severe hepatic insufficiency
- Correctable cardiac comorbidities

BNP, brain natriuretic peptide; eGFR, estimated glomerular filtration rate; HF, heart failure; HFH, hospitalization for heart failure; LVEF, left ventricular ejection fraction; NT-proBNP, N-terminal pro-brain natriuretic peptide; PDE5, phosphodiesterase type 5; NYHA, New York Heart Association.

Armstrong PW et al. N Engl J Med. 2020; 382:1883-1893.

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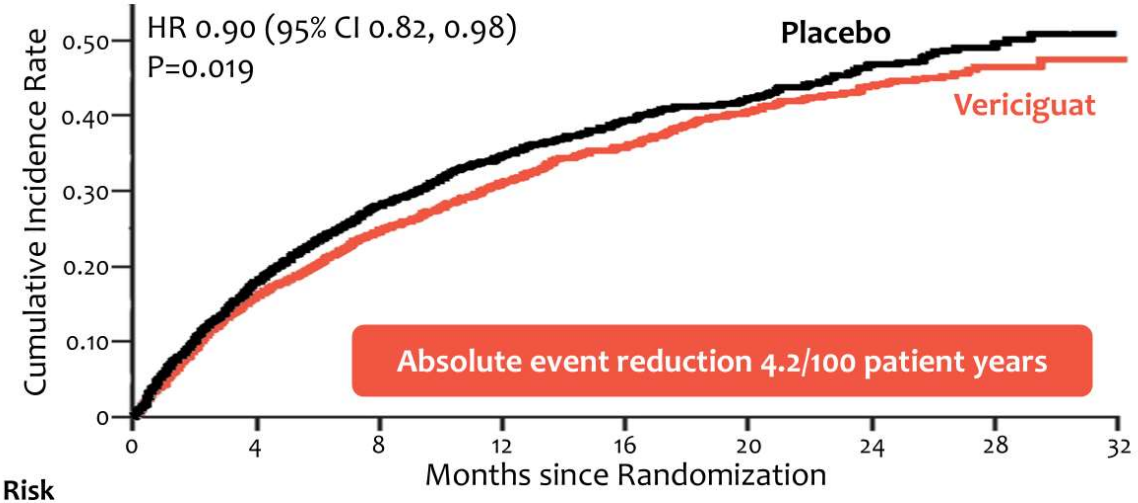
Primary Endpoint of the VICTORIA Trial

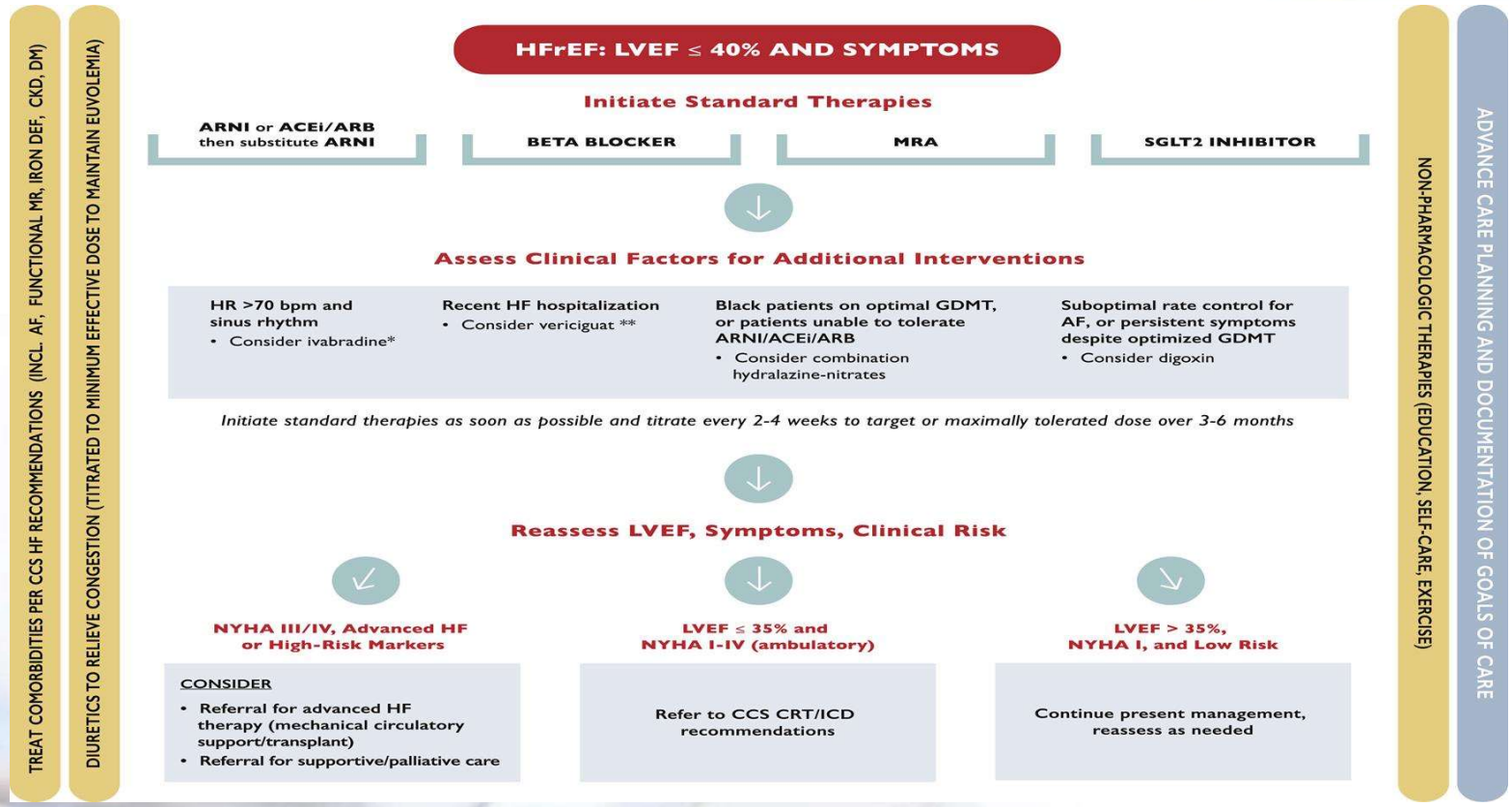
Time to Cardiovascular Death or First Heart Failure Hospitalization



Number at Risk									
Placebo	2,524	2,053	1,555	1,097	772	559	324	110	0
Vericiguat	2,526	2,099	1,621	1,154	826	577	348	125	1

Adapted from Armstrong PW et al. N Engl J Med. 2020; 382:1883-1893.

Figure 1



Canadian Journal of Cardiology 2021 37531-546DOI: (10.1016/j.cjca.2021.01.017)

Summary: Management of HFrEF

RECAP:

- 75 year old woman
- DM2 treated with metformin 1000 mg BID and glyburide 5 mg BID
- History of HF due to previous MI
- LVEF 33%, declined ICD therapy
- Used to walk 30 min daily without shortness of breath
- Now NYHAIII for the past 2 weeks with orthopnea
- In clinic:
  - On perindopril 8 mg/day, bisoprolol 10 mg/day, spironolactone 12.5 mg/day
  - Creatinine 131 µmol/L, eGFR 36 mL/min/1.73 m2, K+ 5.2 mmol/L
  - HR 83 bpm, sinus
  - BP 120/78 mmHg

BID, twice a day; BP, blood pressure; EF, ejection fraction; eGFR, estimated glomerular filtration rate; HR, heart rate; ICD, implantable cardioverter defibrillator; K+, potassium; MI, myocardial infarction; NYHA, New York Heart Association Functional Classification; T2DM, type 2 diabetes mellitus

MANAGEMENT STRATEGIES:

- Contemporary strategies that would be appropriate in this patient:
  - Switch ACEI to sac/val
  - Switch sulfonylurea to SGLT2i
  - Add ivabradine
- Don't forget nonpharmacologic interventions:
  - Exercise rehabilitation
  - Lifestyle modifications
  - Discuss device therapies
  - Discuss end of life when appropriate

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Part 3:

MANAGEMENT OF HFpEF

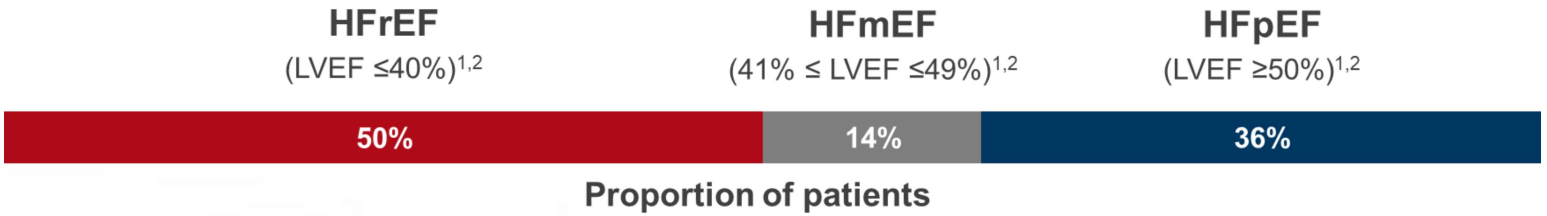
Case: What if this was HFpEF?

- 75 year old woman
- DM2 treated with metformin 1000 mg BID and glyburide 5 mg BID
- **AF for 5 yrs on apixaban**
- **Hypertension for past 15 years, variable control**
- **Remote MI, treated with two vessel PCI without subsequent angina**
- **Ischemic heart disease, no chest pain**
- History of HF **with unchanged LVEF 54% since January 2020**
- **History of osteoarthritis**

- Presents with:
  - **Worsening symptoms x2 weeks, NYHA Class III**
  - **EF 52%**
  - **Creatinine 141 µmol/L, eGFR 34 mL/min/1.73 m^2, K^+ 4.8 mmol/L**
  - **HR 92, irregular**
  - **Arterial BP 154/94 mmHg**

AF, atrial fibrillation; BID, twice a day; BP, blood pressure; EF, ejection fraction; eGFR, estimated glomerular filtration rate; HFpEF, heart failure with preserved ejection fraction; HR, heart rate; K+, potassium; MI, myocardial infarction; NYHA, New York Heart Association Functional Classification; PCI, percutaneous coronary intervention; T2DM, type 2 diabetes mellitus

Current definition of HFpEF



- HFpEF is a clinical syndrome that evolves from a combination of risk factors and comorbidities including:[3]
  - Advanced age
  - Female sex
  - Obesity
  - Systemic arterial hypertension
  - Diabetes
  - Renal dysfunction
  - Anemia, iron deficiency
  - Sleep disorders
  - COPD

HFpEF "masqueraders" that should be excluded:

- CAD
- Valvular heart disease
- Arrhythmias
- Pericardial constriction

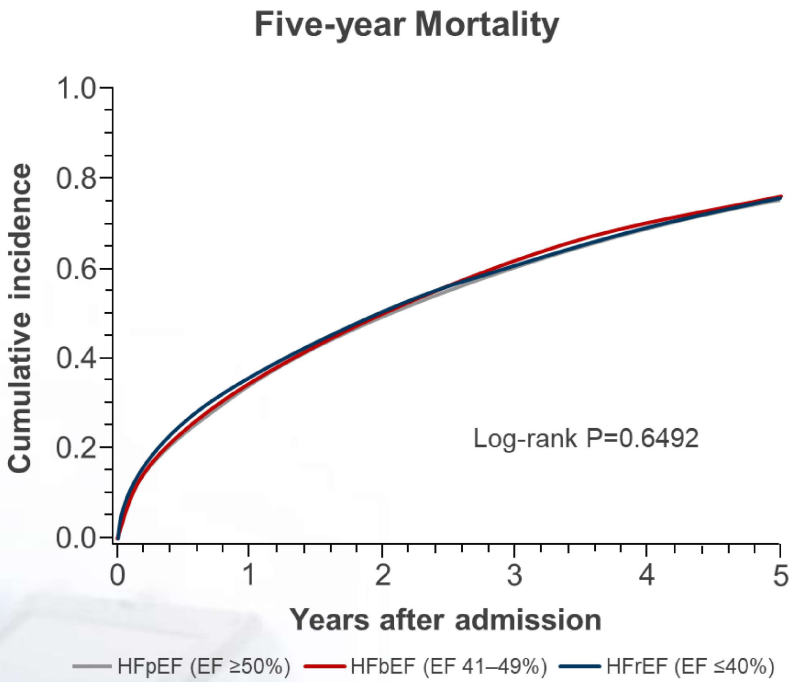
Echocardiography is the most accessible method to evaluate LVEF in Canada.[2]

CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; EF, ejection fraction; HFmEF, heart failure with mid-range preserved ejection fraction; HFpEF, heart failure with preserved ejection fraction;
HFrEF, heart failure with reduced ejection fraction; LVEF, left ventricular ejection fraction

1. Steinberg BA et al. Circulation 2012;126(1):65-75. 2. Ezekowitz JA et al. Can J Cardiol 2017;33(11):1342-1433; 3. Pieske B et al. Eur Heart J 2019;40(40):3297-3317.

Poor prognosis in HFpEF

- ~50% die from non-CV causes
- Similar 30-day and 1-year rehospitalization rates as HFrEF
- Risk factors for mortality in HFpEF:
  - Increasing age, male sex
  - Higher NP levels, higher NYHA class
  - CAD or PVD
  - Diabetes, CKD
  - Lower EF, restrictive filling pattern on Doppler echocardiography
  - Low and very high BMI

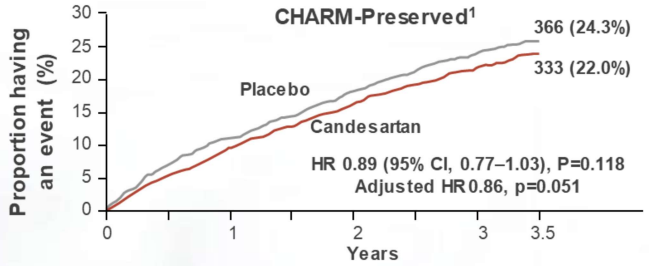


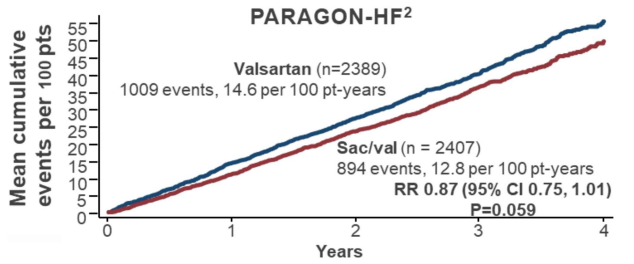
BMI, body mass index; CAD, coronary artery disease; CKD, chronic kidney disease; CV, cardiovascular; EF, ejection fraction; HFbEF, heart failure with borderline ejection fraction; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; NP, natriuretic peptide; NYHA, New York Heart Association Functional Classification; PVD, peripheral vascular disease

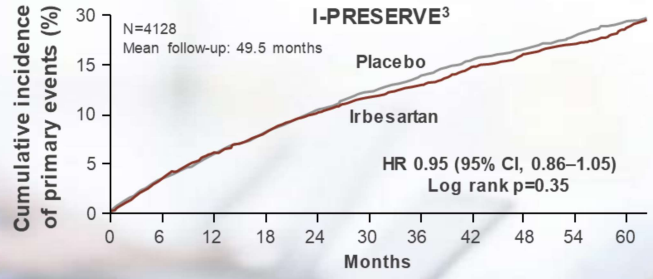
Shah KS et al. J Am Coll Cardiol. 2017;70(20):2476-2486.

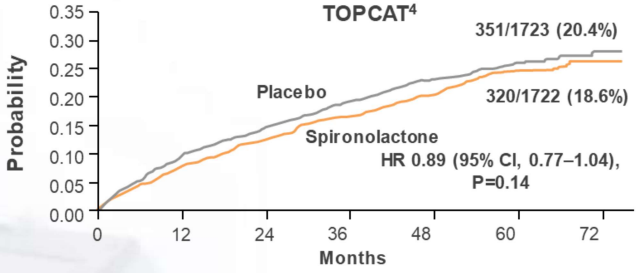
All previous HFpEF trials had failed to find an effective therapy: Primary outcome CV death or HHF

Treatment in HFpEF is focused on diuresis and treatment of comorbidities, such as CAD, AF and HTN









AF, atrial fibrillation; CAD, coronary artery disease; CI, confidence interval; CV, cardiovascular; HFpEF, heart failure with preserved ejection fraction; HHF, hospitalization for HF; HR, hazard ratio; HTN, hypertension; RR, relative risk; sac/val, sacubitril/valsartan

1. Yusuf S et al. Lancet 2003;362(9386):777-781; 2. Solomon SD et al. N Engl J Med 2019;381(17):1609-1620; 3. Massie BM et al. New Eng J Med 2008;359(23):2456-2467;
4. Pitt B et al. New Eng J Med 2014;370(15):1383-1392.

Two trials demonstrated a reduction in hospitalization for HF (HHF)

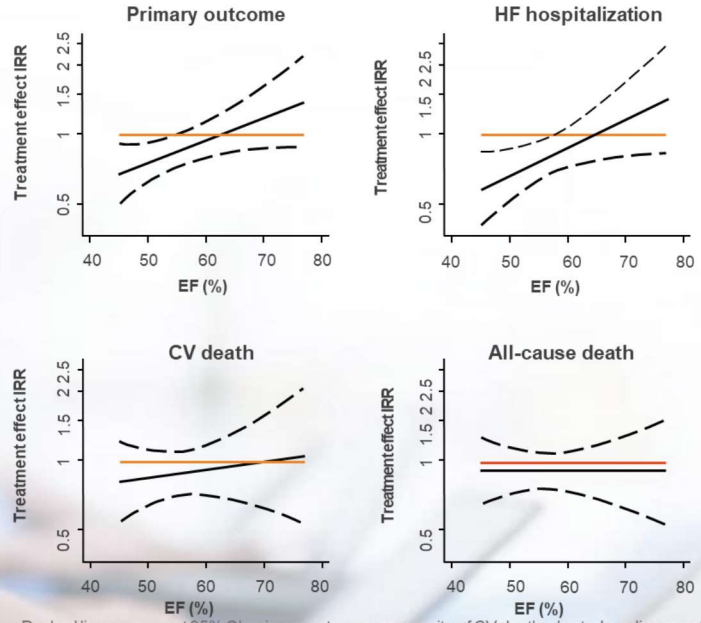
	HR (95% CI)	P Value
CHARM-Preserved[1]	0.84 (0.70–1.00)	0.047
PARAGON-HF[2]	0.85 (0.72–1.00)	N/A
I-PRESERVE[3]	0.95 (0.81–1.10)	0.50
TOPCAT[4]	0.83 (0.69–0.99)	0.04

CI, confidence interval; HR, hazard ratio

1. Yusuf S et al. Lancet 2003;362(9386):777-781; 2. Solomon SD et al. N Engl J Med 2019;381(17):1609-1620; 3. Massie BM et al. New Eng J Med 2008;359(23):2456-2467; 4. Pitt B et al. New Eng J Med 2014;370(15):1383-1392.

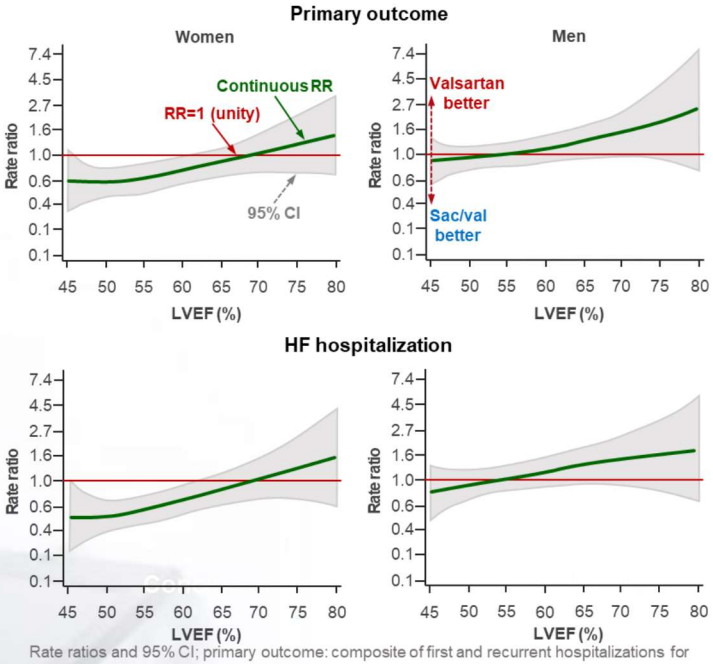
Clinical efficacy of HF therapies across the LVEF spectrum is not homogeneous

Post hoc analysis of the TOPCAT study[1]



Dashed lines represent 95% CI; primary outcome: composite of CV death, aborted cardiac arrest or hospitalization for HF

Post hoc analysis of PARAGON-HF[2]



Rate ratios and 95% CI; primary outcome: composite of first and recurrent hospitalizations for HF and death from CV causes

CI, confidence interval; CV, cardiovascular; EF, ejection fraction; HFpEF, heart failure with preserved ejection fraction; IRR, incidence rate ratio; LVEF, left ventricular ejection fraction; RR, relative risk; sac/val, sacubitril/valsartan 1. Solomon SD et al. Eur Heart J 2016;37(5):455-462. 2. McMurray JJV et al. Circulation 2020;141(5):338-351.

HFpEF phenotypes/clusters

A heterogeneous condition and will likely require further subcategorization for treatment

B	A	D	E	C	F
96% women	100% men	100% women	100% men	Men or women	Mostly women (77.5%)
65 years	65 years	73 years	75 years	70 years	82 years
Low rates of AF, renal dysfunction, and valvular disease	Low rates of AF, renal disease, valvular disease	Average rates of diabetes, hyperlipidemia, obesity, renal insufficiency	Lower BMI, +AF, +CAD	Obesity, diabetes, CAD, anemia	Lower BMI, +AF, valvular disease, renal dysfunction, anemia
No difference in symptoms, SBP, BNP across groups					

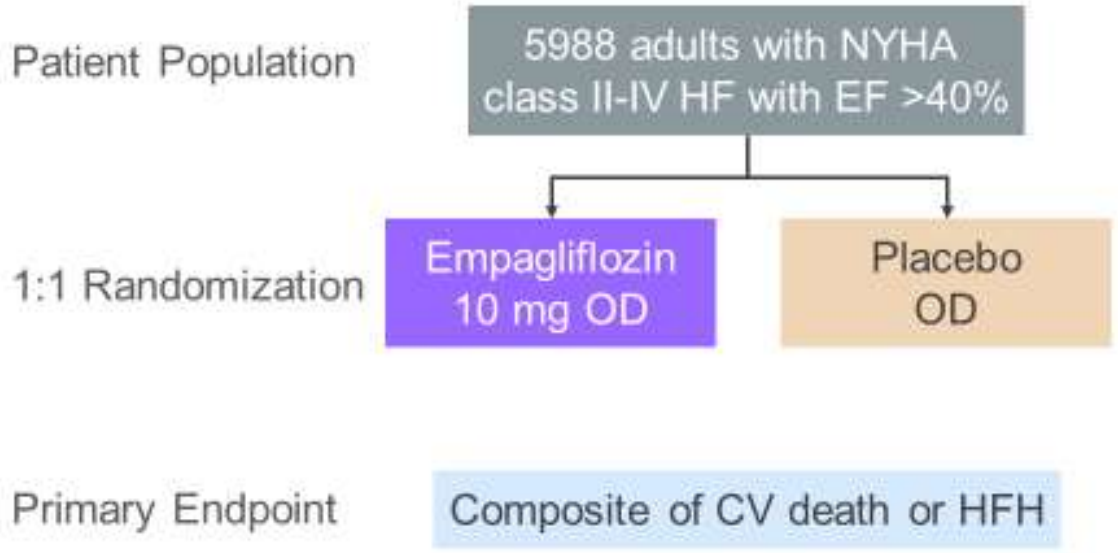
Retrospective, exploratory analysis of I-PRESERVE: Latent class analysis (LCA) was applied to clinical profiles of enrolled patients to identify prevalent HFpEF subgroups and differences in outcomes. Quintile of survival by subgroup from highest (left) to lowest (right).

AF, atrial fibrillation; BMI, body mass index; BNP, B-type natriuretic peptide; CAD, coronary artery disease; HFpEF, heart failure with preserved ejection fraction; SBP, systolic blood pressure. Adapted from Kao DP et al. Eur J Heart Fail 2015;17(9):925-935.

EMPEROR-Preserved:

Phase III Empagliflozin RCT

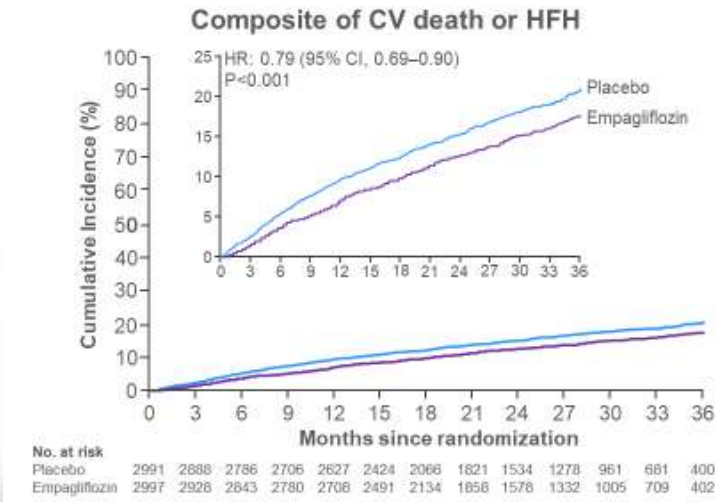
Multicentre, international, double-blind, placebo-controlled



Abbreviations: CV, cardiovascular; EF, ejection fraction; HFH, heart failure hospitalization, NYHA, New York Heart Association; q.d., once daily
Anker SD et al. N Engl J Med. 2021;14;385(16):1451-1461.

EMPEROR-Preserved:
Reduction of CV Death and HFH

- Risk of CV death and HFH were reduced with empagliflozin in patients with HFpEF
- Successfully shown that a therapy can cut the risk of hospitalization and CV death for patients with HF with preserved ejection fraction (HFpEF)

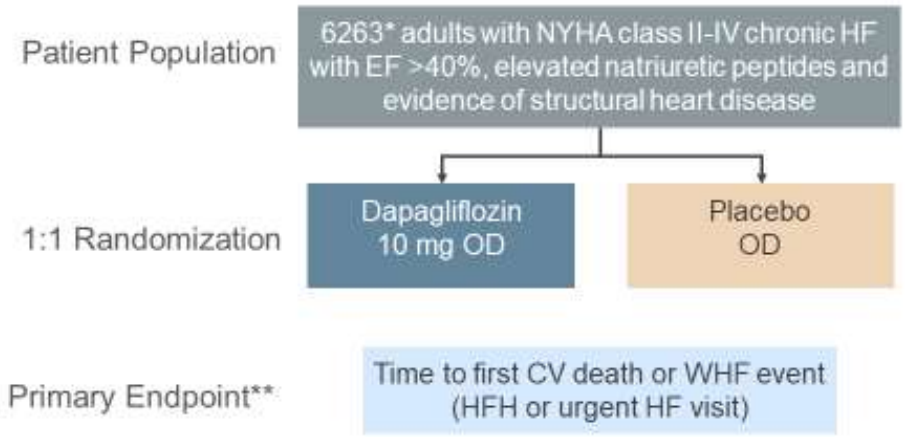


Anker SD et al. N Engl J Med. 2021;14;385(16):1451-1461.

DELIVER

International, multicentre, parallel-group, event-driven, randomized, double-blind, placebo-controlled study in HFpEF patients.

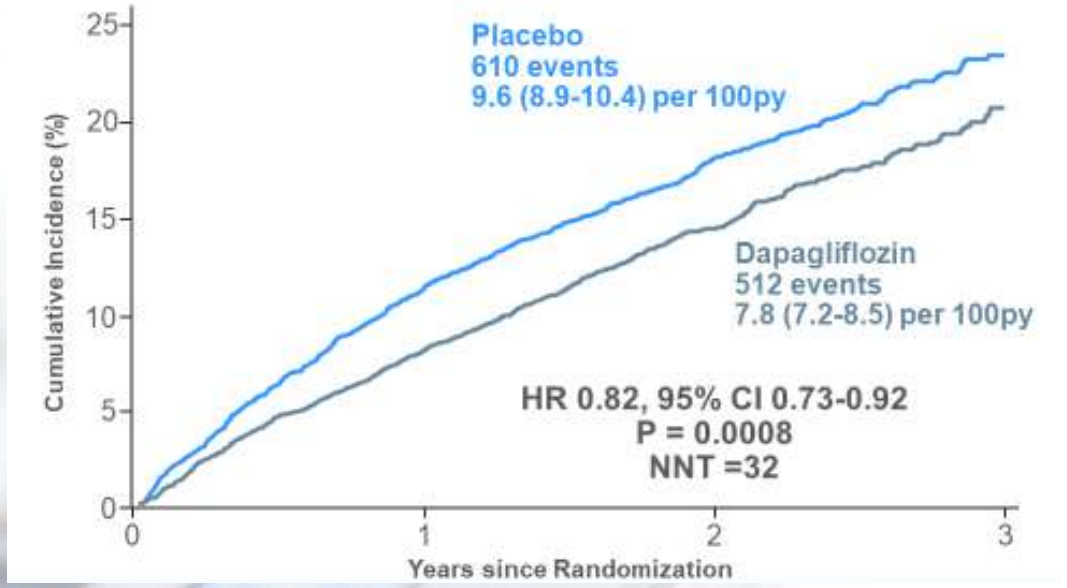
- Evaluating the effect of dapagliflozin 10 mg vs. placebo
- Given once daily in addition to background regional standard of care therapy, including treatments to control comorbidities, in reducing the composite of CV death or HF events



*Total number of randomized patients.
**Will be assessed in the full study population and separately in patients with LVEF <60%.
Solomon SD et al. Eur J Heart Fail. 2021;23(7):1217-1225.

Primary Endpoint:
CV Death or Worsening HF

Risk of CV death and WHF were reduced with dapagliflozin in patients with HFpEF



Solomon SD et al. Eur J Heart Fail. 2021;23(7):1217-1225.

2017 CCS Guidelines for Pharmacological Management of HFpEF

We suggest candesartan be considered to reduce HF hospitalizations in patients with HFpEF **(Weak recommendation; Moderate-Quality Evidence)**

We suggest that in individuals with HFpEF, serum potassium <5.0 mmol/L, and an eGFR >30 mL/min, an MRA such as spironolactone should be considered, with close surveillance of serum potassium and creatinine **(Weak Recommendation; Moderate-Quality Evidence)***

Summary: Management of HFpEF

RECAP:

- 75 year old woman
- DM2 treated with metformin 1000 mg BID and glyburide 5 mg BID
- **AF for 5 yrs on apixaban**
- **Hypertension for past 15 years, variable control**
- **Remote MI, treated with two vessel PCI without subsequent angina**
- **Ischemic heart disease, no chest pain**
- History of HF **with unchanged LVEF 54% since January 2020**
- **History of osteoarthritis**
- Presents with:
  - **Worsening symptoms x2 weeks, NYHA Class III**
  - **EF 52%**
  - **Creatinine 141 µmol/L, eGFR 34 mL/min/1.73 m^2, K^+ 4.8 mmol/L**
  - **HR 92, irregular**
  - **Arterial BP 154/94 mmHg**

MANAGEMENT STRATEGIES:

- To improve symptoms, consider:
  - Starting diuretic
  - Optimizing HR control
  - Controlling BP
  - Replacing glyburide with SGLT2i
- Don't forget non-pharmacologic therapies:
  - Exercise rehabilitation
  - Lifestyle modifications

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Proposed Algorithm for Treating HFpEF

	Kidney dysfunction ↓ ACEI/ARBs SGLT2i Salt reduction	Obesity and deconditioning ↓ Caloric restriction Exercise	Iron deficiency ↓ IV iron supplementation	CAD/ischemia ↓ ASS Statins Revascularization
Therapy of comorbidities/ risk factors	Diabetes ↓ Metformin Incretins SGLT2i Diet Exercise	AF ↓ Anticoagulation Beta-blockers Digitalis glycosides Catheter ablation?	Pulmonary hypertension ↓ Diuretics sGC stimulators/activators Inorganic nitrites/nitrates PDESi Prostaglandin derivatives	Hypertension ↓ ACEI/ARBs CCBs Diuretics Beta-blockers MRAs Salt reduction
Reduction in symptoms and HF hospitalization	Diuretics		Remote monitoring, if available	
Evidence-based therapy to reduce CV mortality and HFH – all patients	Empagliflozin, dapagliflozin			
Evidence-based therapy to reduce CV mortality and HFH – selected patients	Sacubitril/Valsartan → Individual decision after thorough diagnostic process			

Abbreviations: ACEI angiotensin-converting enzyme inhibitor, ARB angiotensin receptor blocker, ASS, acute splanchnic syndrome; CAD coronary artery disease, CCB calcium channel blocker, iv intravenous, MRA mineralocorticoid receptor antagonist, PDE5i phosphodiesterase type 5 inhibitor, sGC soluble guanylate cyclase, SGLT2i sodium-glucose cotransporter 2 inhibitor

Wirtwich J et al. Herz. 2022; 6:1–8. doi: 10.1007/s00059-022-05119-5. Epub ahead of print.

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Part 3:

PRACTICAL MANAGEMENT TIPS: PUTTING IT ALL TOGETHER

Case: Recap of Mrs. Wynded

- 75 year old woman
- DM2 treated with metformin 1000 mg BID and glyburide 5 mg BID
- History of HF due to previous MI
- LVEF 33%, declined ICD therapy
- Used to walk 30 min daily without shortness of breath
- Now NYHAIII for the past 2 weeks with orthopnea

- In clinic:
  - On perindopril 8 mg/day, bisoprolol 10 mg/day, spironolactone 12.5 mg/day
  - Creatinine 131 µmol/L, eGFR 36 mL/min/1.73 m2, K+ 5.2 mmol/L
  - HR 83 bpm, sinus
  - BP 120/78 mmHg

Potential management options?
- ARNI instead of ACEI
- SGLT2i instead of sulfonylurea
- Add ivabradine

ACEI, angiotensin-converting enzyme inhibitor; ARNI, angiotensin receptor neprilysin inhibitor; BID, twice a day; BP, blood pressure; EF, ejection fraction; eGFR, estimated glomerular filtration rate; HFrEF, heart failure with reduced ejection fraction; HR, heart rate; ICD, implantable cardioverter defibrillator; K+, potassium; MI, myocardial infarction; NYHA, New York Heart Association Functional Classification; T2DM, type 2 diabetes mellitus

Example of Sacubitril/Valsartan treatment implementation

First dose of sacubitril/valsartan

	S	M	T	W	T	F	S
AM	ACEi	ACEi	---				
PM	ACEi	ACEi	---				

Last dose of ACEi. 36 hours wash-out required

How to Follow Up a Patient Initiated on Sacubitril Valsartan

✓	**Do replace ACE or ARB in the management of HFrEF**	• Leverage both suppression of RAAS pathway and increased NP levels • Stop ACE for 36 hours (if ARB, start at next dose) • Start sac/val at 49/51 mg (or 24/26 mg based on patient profile) • Increase dose 4 weeks after initiation if labs/BP adequate* • If ARNI, ACE/ARB inadequate, try nitrates + hydralazine
✓	**Do watch K^+/Cr for 2–3 weeks post initiation**	• Cut down if hyperkalemia or significant rise in Cr occurs • Recall that with ACE/ARB/diuretic or sac/val – ↑ Cr of 30% is acceptable* • No visit with specialist or GP required
✓	**Do follow BP for 2–3 weeks post initiation**	• Anticipate BP-lowering effect • No visit with specialist or GP required
! CAUTION	**Use caution if SBP <100 mmHg and/or eGFR <30 mL/min/1.73 m^2**	PARADIGM-HF trial excluded patients with eGFR <30 mL/min/1.73 m^2 or symptomatic hypotension with SBP <100 mmHg
✗	**Do NOT start an ACE when already on sac/val**	Risk of angioedema with combined use
✗	**Do NOT start an ARB when already on sac/val**	Redundant, as there is ARB already in it

*If initial dose is 24/26 mg, add one addition step during the titration

ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; ARNI, angiotensin receptor neprilysin inhibitor; BP, blood pressure; CR, creatinine; eGFR, estimated glomerular filtration rate; HFrEF, heart failure with reduced ejection fraction; K+, potassium; NP, natriuretic peptide; RAAS, renin-angiotensin-aldosterone system; sac/val, sacubitril/valsartan; SBP, systolic blood pressure

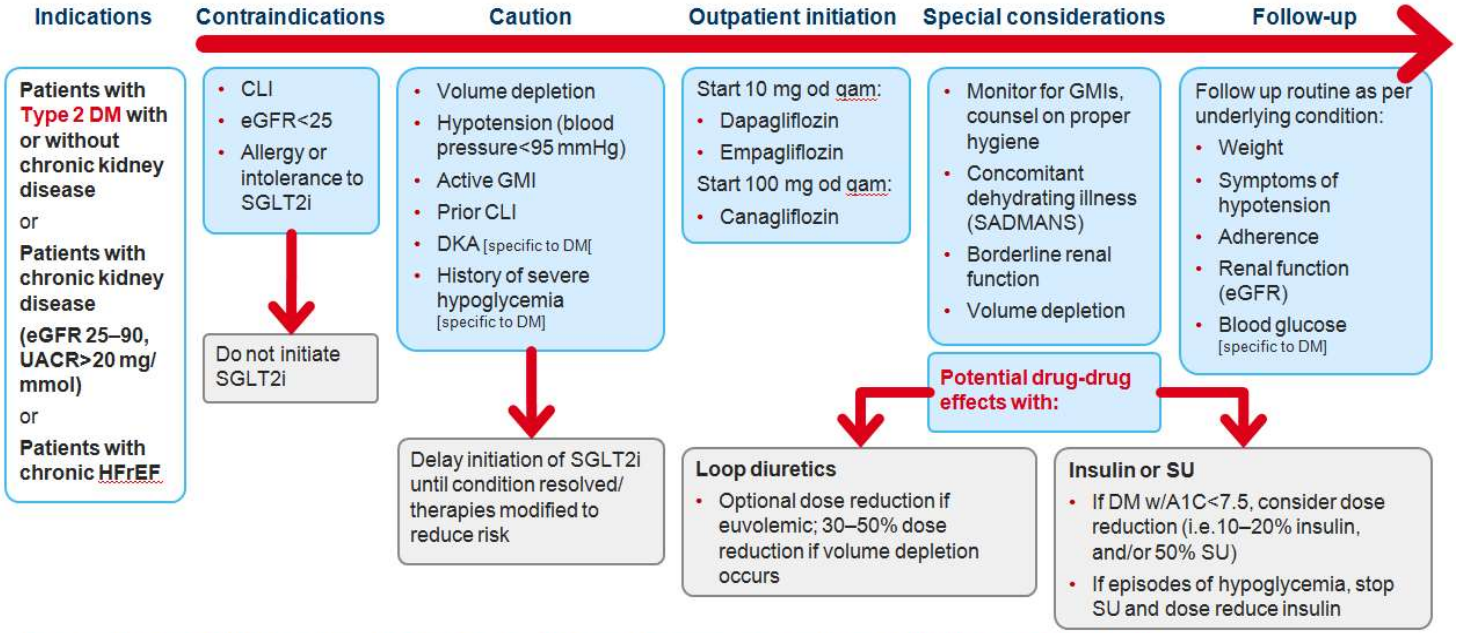
Howlett JG. Can J Cardiol 2015;32(3):296-310. Consult product monograph.

How to Follow Up a Patient Initiated on Ivabradine

✓	**Do try to achieve target doses of BBs prior to initiation**	• If HR remains ≥70 bpm, consider initiation of ivabradine
✓	**Do start with low dose and modify dose based on patient's resting HR**	• In patients >75 years of age, 2.5 mg BID starting dose may be used • Aim for targeted dose, or highest tolerated dose based on resting HR (50–60 bpm target) • Titration can usually be accomplished in 2–4 weeks
✓	**Do follow-up with 12-lead ECG**	• HR fluctuates considerably over time • Assess HR prior to dose modifications
! CAUTION	**Use with caution if symptomatic hypotension (<90/50 mmHg)**	While ivabradine has no effect on BP, caution is advised when used in patients with BP <90/50 mmHg
✗	**Do NOT use if HR <70 bpm or not in sinus rhythm prior to treatment**	Titrate dose downward if bradycardia develops (HR <50 bpm) or patient experiences symptoms of dizziness, fatigue or hypotension
✗	**Do NOT use if severe cirrhosis**	Titrate dose downward if bradycardia develops (HR <50 bpm) or patient experiences symptoms of dizziness, fatigue or hypotension

BB, beta-blocker; BID, twice a day; BP, blood pressure; bpm, beats per minute; ECG, electrocardiogram; HR, heart rate
Howlett JG. Can J Cardiol 2015;32(3):296-310; Ponikowski P et al. Eur Heart J. 2016;37(27):2129-2200. Consult product monograph.

Algorithm for Use of SGLT2is in HF



This tool is available for download in the Initiatives & Programs section at: www.heartfailure.ca

CLI, critical limb ischemia; DM, diabetes mellitus; DKA, diabetic ketoacidosis; eGFR, estimated glomerular filtration rate; GMI, genital mycotic infections; HFrEF, heart failure with reduced ejection fraction; OD, once a day; QAM, every morning; SGLT2i, sodium-glucose cotransporter 2 inhibitor; SU, sulfonylurea; UACR: urine albumin to creatinine ratio
Adapted from the Canadian Heart Failure Society's "Practical approach to SGLT2 inhibitors for treatment of cardiovascular disease" document

Sick Day/Dehydrating illness management

S sulfonylureas

A ACEIs/angiotensin or angiotensin neprilysin inhibitors

D diuretics, direct renin inhibitors

M metformin

A angiotensin receptor blockers

N nonsteroidal anti-inflammatory

S SGLT2is

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Safety and Tolerability
of Vericiguat in the VICTORIA Trial

Symptomatic hypotension and syncope tended to be more common with vericiguat

More anemia developed with **vericiguat (7.6%)** than with **placebo (5.7%)**

Frequencies of **SAEs** were balanced: **vericiguat (32.8%)** and **placebo (34.8%)**

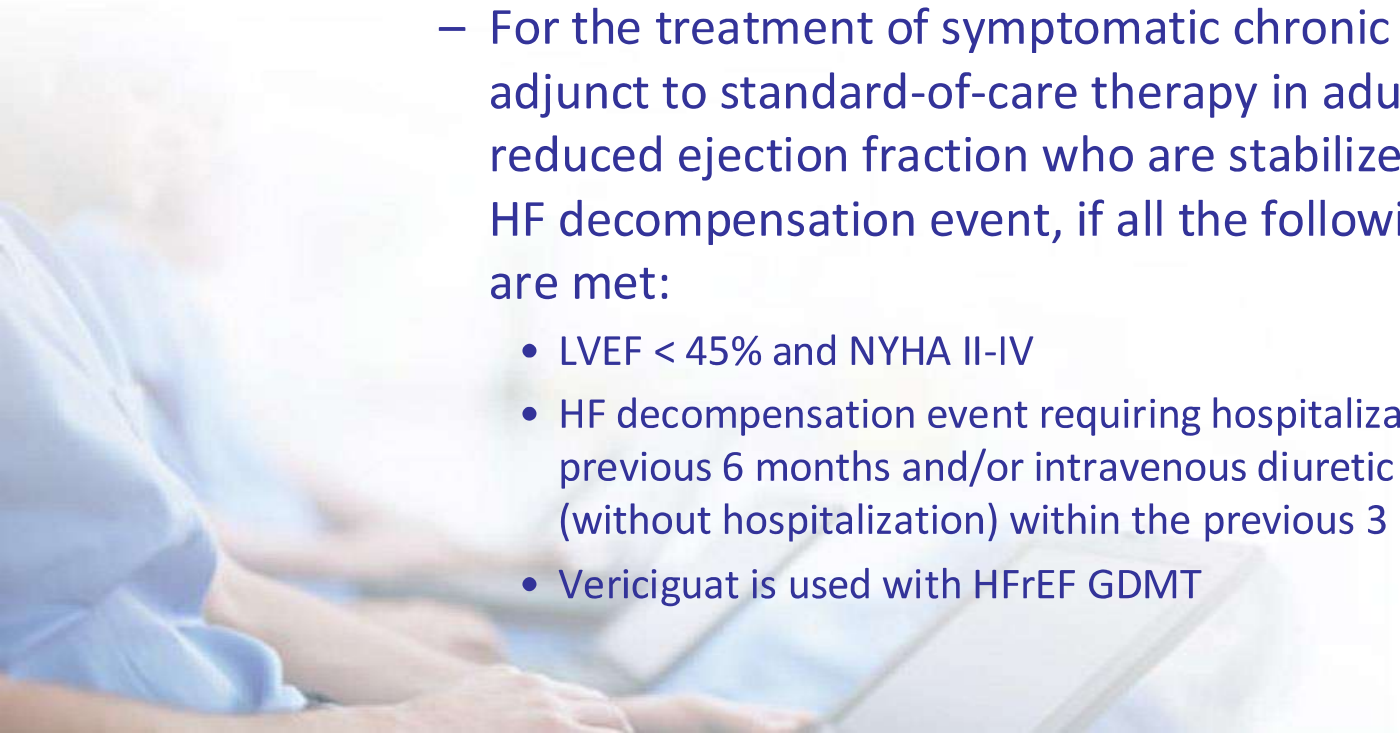
No adverse effects of vericiguat on either electrolytes or kidney function

After 12 months, 89.2% of those randomized to vericiguat
and 91.4% of those assigned to placebo achieved the 10 mg target dose

SAE, serious adverse event.
Armstrong PW et al. N Engl J Med. 2020; 382:1883-1893.

Vericiguat Now Available on ODB!!

- LU Code 685 (as of October 2024):
  - For the treatment of symptomatic chronic HF as an adjunct to standard-of-care therapy in adult patients with reduced ejection fraction who are stabilized after a recent HF decompensation event, if all the following conditions are met:
    - LVEF < 45% and NYHA II-IV
    - HF decompensation event requiring hospitalization within the previous 6 months and/or intravenous diuretic treatment for HF (without hospitalization) within the previous 3 months
    - Vericiguat is used with HFrEF GDMT



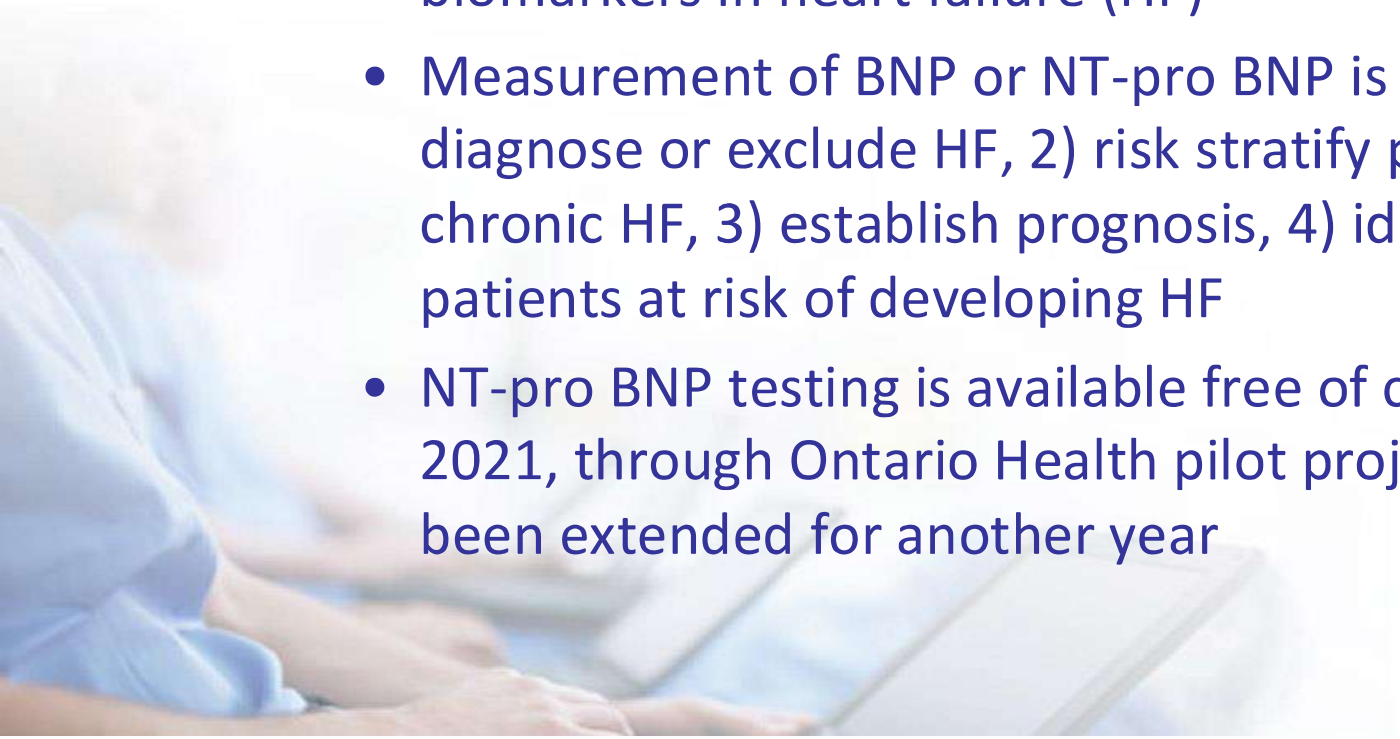
Nonpharmacologic Strategies for All HF Patients

- Typical sodium intake ≤2000 mg/day
- Fluid restriction in selected patients
- Daily weight monitoring with diuretic sliding scale
- Regular exercise may improve quality of life
- Achieving and maintaining healthy body weight
- Smoking cessation
- Annual influenza, periodic pneumococcal pneumonia immunizations and current/future vaccines relevant to this high-risk population (e.g. COVID-19)
- Close follow-up and disease management
- Patient and caregiver education

TAKEAWAY MESSAGES

Conclusions

- Natriuretic peptides are the gold standard for biomarkers in heart failure (HF)
- Measurement of BNP or NT-pro BNP is useful to: 1) diagnose or exclude HF, 2) risk stratify patients with chronic HF, 3) establish prognosis, 4) identify patients at risk of developing HF
- NT-pro BNP testing is available free of charge since 2021, through Ontario Health pilot project which has been extended for another year



CCS/CHFS 2021 HF Guidelines

- We recommend that in the absence of contraindications, patients with HFrEF be treated with combination therapy including 1 evidence-based medication from each of the following categories *(Strong Recommendation; Moderate-Quality Evidence)*:
  - **a.** ARNI (or ACEI/ARB);
  - **b.** β-blocker;
  - **c.** MRA; and
  - **d.** SGLT2 inhibitor.
- *The Committee acknowledges lack of evidence favouring one particular titration strategy for guideline-directed medical therapy (GDMT) over another.*

2017 CCS Guidelines for Pharmacological Management of HFpEF

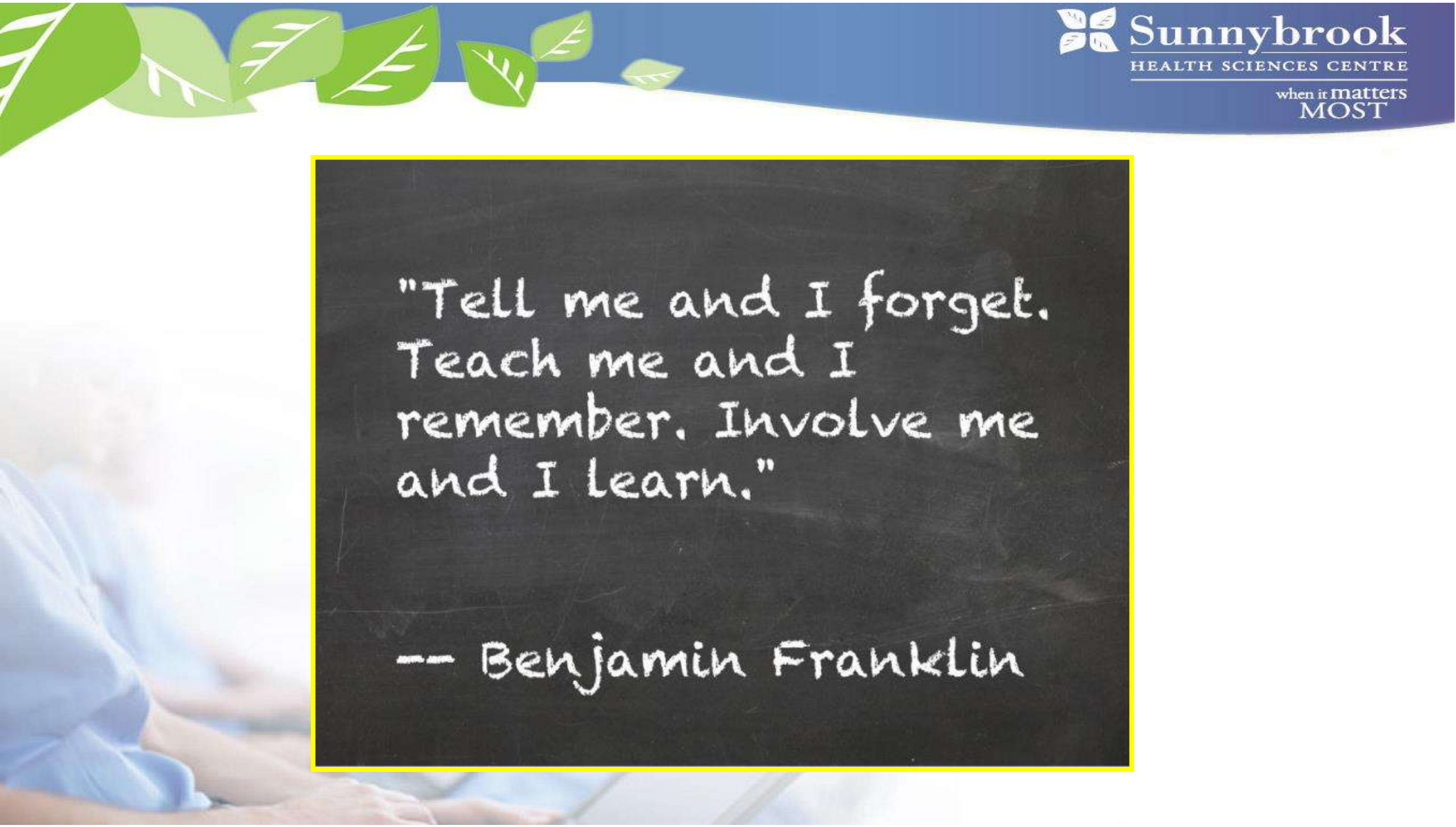
We suggest candesartan be considered to reduce HF hospitalizations in patients with HFpEF **(Weak recommendation; Moderate-Quality Evidence)**

We suggest that in individuals with HFpEF, serum potassium <5.0 mmol/L, and an eGFR >30 mL/min, an MRA such as spironolactone should be considered, with close surveillance of serum potassium and creatinine **(Weak Recommendation; Moderate-Quality Evidence)***

What does successful treatment include?

- An effective treatment plan will include:[1–3]
  - Lifestyle management advice
  - Ongoing patient education
  - Pharmacological and/or nonpharmacological interventions
- A treatment strategy should:
  - Be tailored to individual patients
  - Be frequently reviewed
  - Have well-defined treatment goals

1. McMurray JJ et al. Eur Heart J 2012;33(14):1787-1847. 2. Grady KL et al. Circulation 2000;102(19):2443-2456. 3. NICE clinical guideline [CG187]. 2014. Acute heart failure: diagnosis and management.
Available at: https://www.nice.org.uk/guidance/cg187.


"Tell me and I forget. Teach me and I remember. Involve me and I learn."
-- Benjamin Franklin

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Thank you

Questions & Discussion

Poll #3:

How would you rate your knowledge of NT-proBNP after attending this session?

1. Not familiar at all.
2. I have a vague understanding of its role in heart failure.
3. I know NT-proBNP is used in diagnosing heart failure but don’t know the details.
4. I have a good understanding of NT-proBNP's diagnostic role in heart failure.
5. I am very familiar with how NT-proBNP is used in diagnosing heart failure.

Join the…

Integrated Heart Failure Care Community of Practice

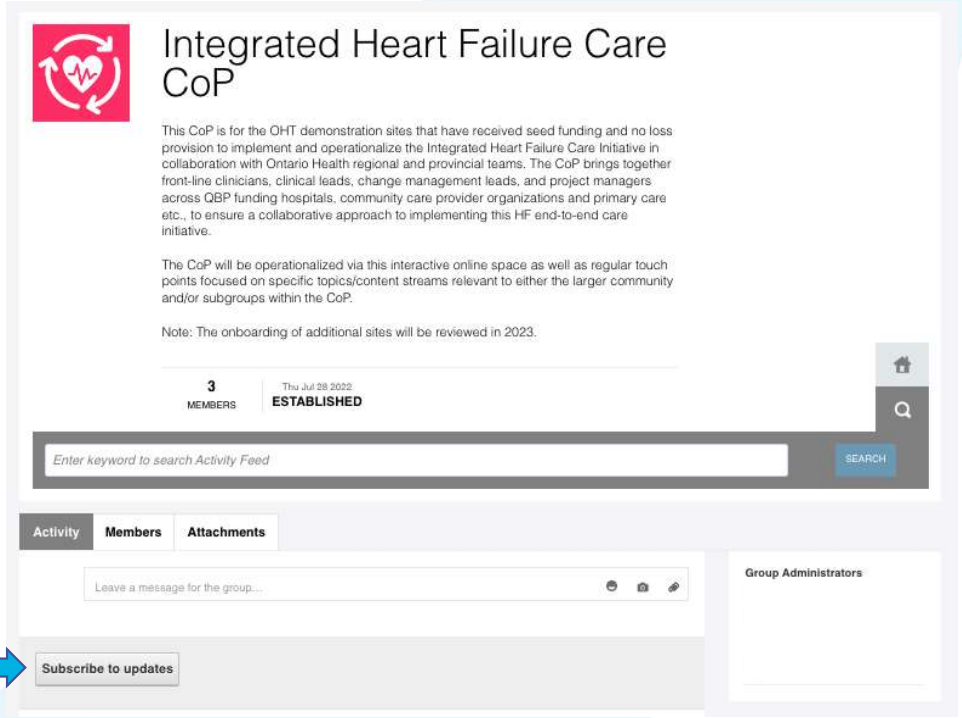
Joining is as easy as 1,2,3

1. Visit the OHT Shared Space and click “SIGN UP” to create your account.

2. Visit the Integrated Heart Failure Care CoP and click the “JOIN GROUP” button. You will receive an email notification when you’ve been accepted into the group.

   Note: *You are automatically accepted into the “General Discussion” Group.*

3. Don’t forget to click on the “Subscribe to Updates” button once you’ve been accepted into your CoP!



Any questions/concerns? Contact the OH ICP Project Team at OHTSupport@OntarioHealth.ca

Thank You

OH HF Project Team