The Prince Charles Hospital

Heart and Lung Institute

innovation and collaboration

Queensland Government

Update on HF Guidelines

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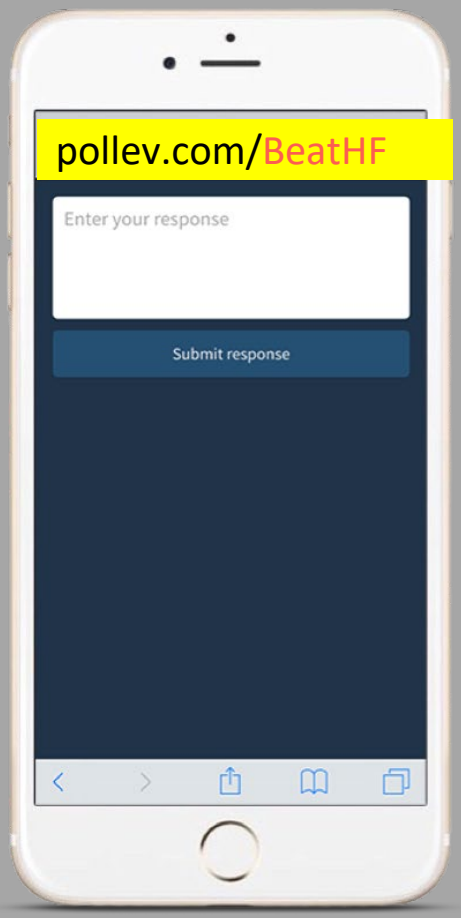
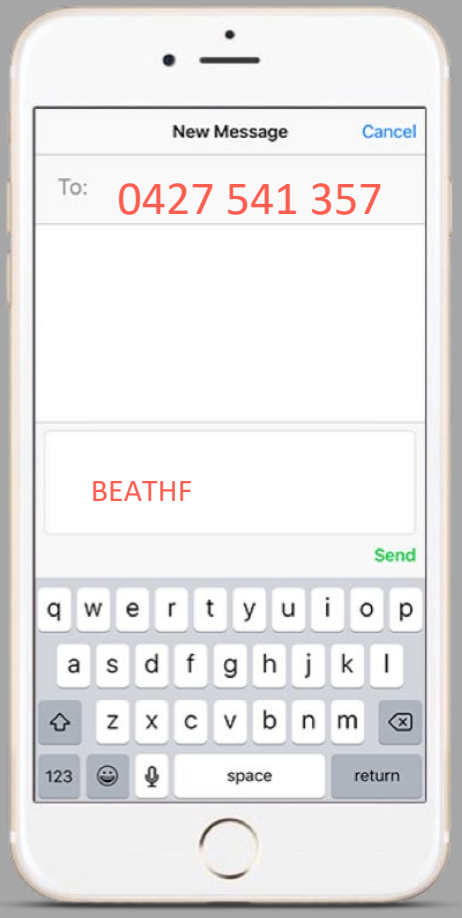
CARDIO-VASCULAR
MOLECULAR & THERAPEUTICS
Translation Research Group

How to respond to Poll Everywhere activities

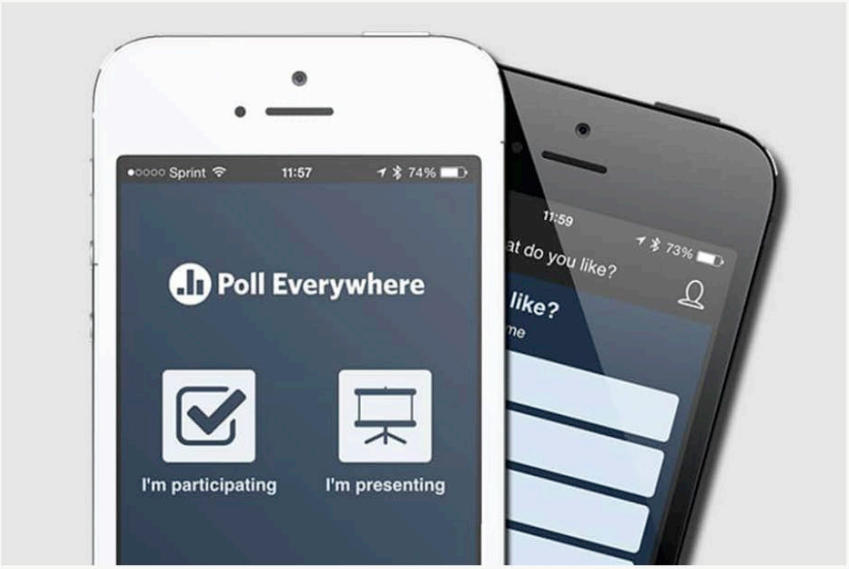




How to respond to Poll Everywhere activities

Poll Everywhere mobile app

For audience members and presenters



Now you really can poll everywhere!

The official Poll Everywhere app has landed.

Download on the App Store

GET IT ON Google play

pollev.com/BeatHF

Epidemiology

- HF is a developing global pandemic affecting 38 million world wide and ~480,000 adult Australia[1]
- Significant Healthcare burden
  - 2015-16 there were ~ 173,000 HF hospitalization, representing 1.6% of all hospitalization[2].
- Survival rate for acute HF at 1 month in contemporary studies – 80% and 57-80% at 1 year[3]
- Survival rates for chronic HF range 81-91% at 1 year and 52-63% at 5 years.

Figure 2.5a Trends in hospital separations for specific cardiovascular causes, men and boys, 1999–2000 to 2012–13

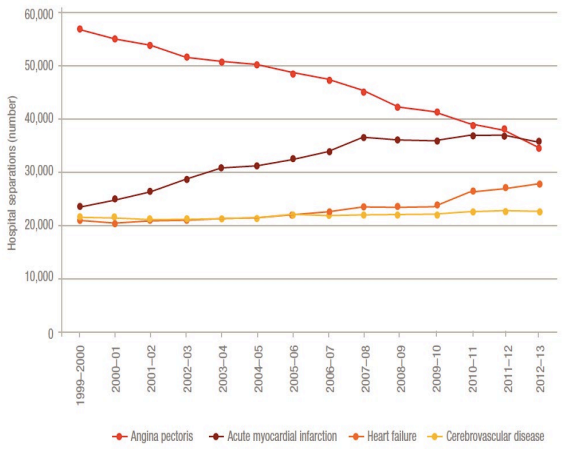
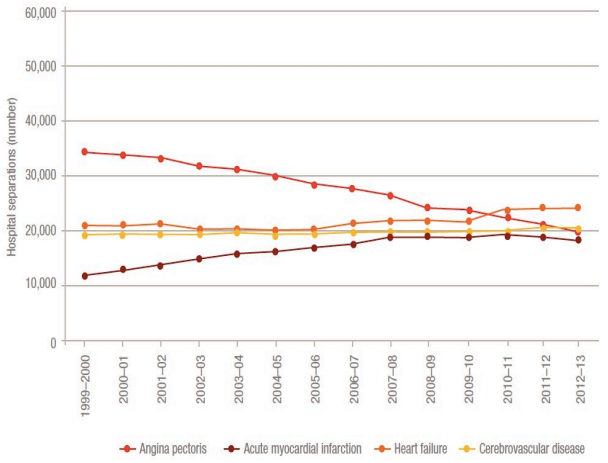


Figure 2.5b Trends in hospital separations for specific cardiovascular causes, women and girls, 1999–2000 to 2012–13



1 - Sahle, B.W., et al., BMC Cardiovasc Disord, 2016. **16**: p. 32.
2 - Ambrosy, A.P., et al, J Am Coll Cardiol, 2014. **63**(12): p. 1123-1133.
3 - Crespo-Leiro, M.G., et al., Eur J Heart Fail, 2016. **18**(6): p. 613-25.

Morbidity and mortality in Heart failure
HF is associated with significant mortality

Hospital

4-7%
in-hospital mortality rate‡[1–3]

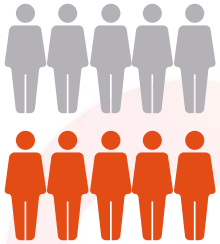
30 days

~10%
mortality after 30 days†[4]

1 year

~20%
mortality after 1 year‡[5]

5 years
post-diagnosis



Up to **50%**
mortality after 5 years§[6-8]

HF=heart failure

‡Data from European patients hospitalized for heart failure in the European Society of Cardiology Heart Failure (ESC-HF) Pilot study and EuroHeart Failure Survey (EHFS) II

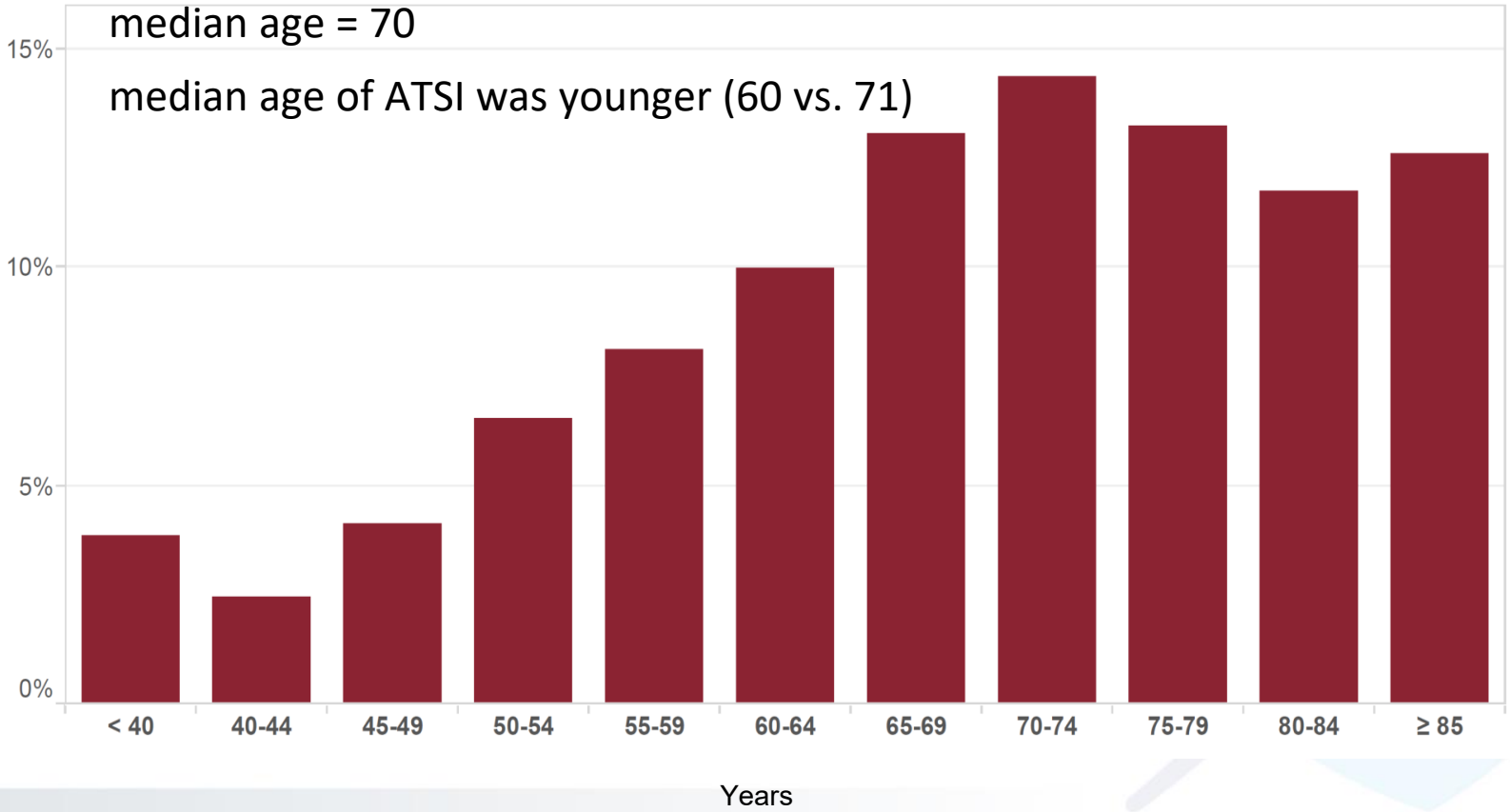
†Analysis of HF data from 1,282 incident cases of HF in the Atherosclerosis Risk in Communities (ARIC) population-based study of n=15,792 individuals from four communities in the USA (1987–2002)

§Reported rates vary but some publications include rates up to 50%6–8

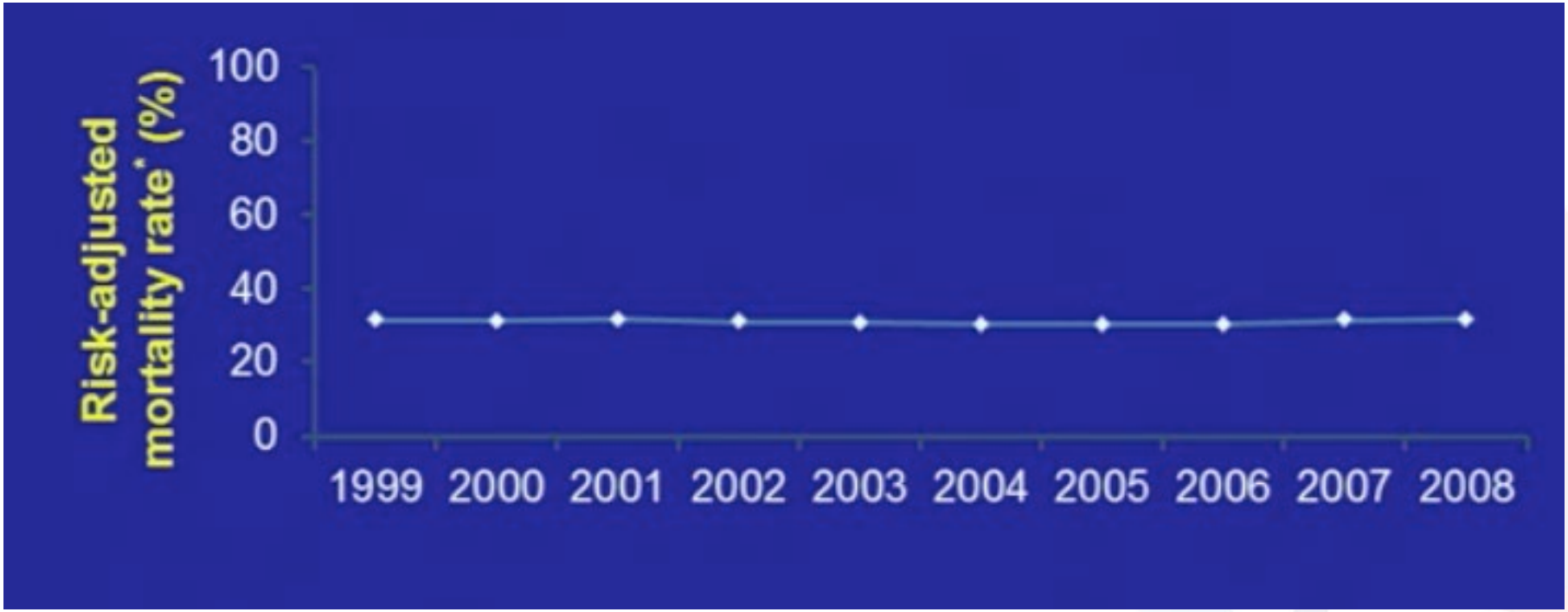
1.Maggioni et al. Eur J Heart Fail 2010;12:1076–84; 2. Nieminen et al. Eur Heart J 2006;27:2725–36;
3. Cleland et al. Eur Heart J 2003;24:442–636; 4. Loehr et al. Am J Cardiol 2008;101:1016–22;
5. Maggioni et al. Eur J Heart Fail 2013;15:808–17; 6. Roger et al. JAMA 2004;292:344–50;
7. Levy et al. N Engl J Med 2002;347:1397–402; 8. Askoxylakis et al. BMC Cancer 2010;10:105

Demographics of HF Patients in Qld

Percentage of HF Services Referral by Age – 2016
(N=4021)



1 Year Mortality Following Hospitalization for Acute Heart Failure



Chen. JAMA 2011;306:1669-1678

Publications

Full guideline in *Heart, Lung, and Circulation*

Heart, Lung and Circulation (2018) 27, 1123–1208
1443-9506/04/$36.00
https://doi.org/10.1016/j.hlc.2018.06.1042

GUIDELINES

National Heart Foundation of Australia and Cardiac Society of Australia and New Zealand: Guidelines for the Prevention, Detection, and Management of Heart Failure in Australia 2018

Contents

Executive summary in *Medical Journal of Australia*

National Heart Foundation of Australia and Cardiac Society of Australia and New Zealand: Australian clinical guidelines for the management of heart failure 2018

John J Atherton[1], Andrew Sindone[2], Carmine G De Pasquale[3], Andrea Driscoll[4,5], Peter S MacDonald[6], Ingrid Hopper[7], Peter Kistler[8], Tom G Briffa[9], James Wong[10], Walter P Abhayaratna[11], Liza Thomas[12], Ralph Audehm[13], Phillip J Newton[14], Joan O'Loughlin[15], Cia Connell[16], Maree Branagan[16]

The National Heart Foundation of Australia and the Cardiac Society of Australia and New Zealand have developed new guidelines to assist Australian clinicians in the care of adult patients with heart failure (HF). The guidelines are based on current evidence, and replace the 2011 guidelines for the prevention, detection and management of chronic HF in Australia.[1]

This executive summary provides important recommendations together with their strength of evidence and guidance for their implementation in clinical practice (practice points). The full clinical guidelines are available in *Heart, Lung and Circulation* at https://doi.org/10.1016/j.hlc.2018.06.1042.[2]

Definition of heart failure

HF is a complex clinical syndrome with typical symptoms and signs that generally occur on exertion but may also occur at rest (particularly when recumbent). HF is secondary to an abnormality of cardiac structure or function that impairs the ability of the heart to fill with blood at normal pressure or eject blood sufficient to fulfil the needs of the metabolising organs. Following clinical diagnosis, HF is generally categorised according to whether it is associated with a reduced left ventricular ejection fraction (LVEF) below 50% (heart failure with reduced ejection fraction [HFrEF]) or preserved LVEF of 50% or more (heart failure with preserved ejection fraction [HFpEF]) (Box 1).

Method

The National Heart Foundation of Australia, in partnership with the Cardiac Society of Australia and New Zealand, appointed an expert writing group. The HF guideline development working group comprised an executive and four writing groups covering the topics of diagnosis; pharmacological management; devices and surgery; and non-pharmacological management. The working group comprised a broad mix of health professionals, including cardiologists (including an electrophysiologist), nurses, general practitioners, a clinical pharmacologist and general physician, an exercise health and professional epidemiologist, and a consumer representative.

In addition, a reference group including representatives from stakeholder groups, potential endorsing organisations and regional experts provided input into the scope and content of the

Abstract

Introduction: Heart failure (HF) is a clinical syndrome that is secondary to an abnormality of cardiac structure or function. These clinical practice guidelines focus on the diagnosis and management of HF with recommendations that have been graded on the strength of evidence and the likely absolute benefit versus harm. Additional considerations are presented as practice points.

Main recommendations:

- Blood pressure and lipid lowering decrease the risk of developing HF. Sodium–glucose cotransporter 2 inhibitors decrease the risk of HF hospitalisation in patients with type 2 diabetes and cardiovascular disease.
- An echocardiogram is recommended if HF is suspected or newly diagnosed.
- If an echocardiogram cannot be arranged in a timely fashion, measurement of plasma B-type natriuretic peptides improves diagnostic accuracy.
- Angiotensin-converting enzyme inhibitors, β-blockers and mineralocorticoid receptor antagonists improve outcomes in patients with HF associated with a reduced left ventricular ejection fraction. Additional treatment options in selected patients with persistent HF associated with reduced left ventricular ejection fraction include switching the angiotensin-converting enzyme inhibitor to an angiotensin receptor neprilysin inhibitor; ivabradine; implantable cardioverter defibrillators; cardiac resynchronisation therapy; and atrial fibrillation ablation.
- Multidisciplinary HF disease management facilitates the implementation of evidence-based HF therapies. Clinicians should also consider models of care that optimise medication titration (eg, nurse-led titration).

Changes in management as a result of the guideline: These guidelines have been designed to facilitate the systematic integration of recommendations into HF care. This should include ongoing audit and feedback systems integrated into work practices in order to improve the quality of care and outcomes of patients with HF.

A draft of the guideline was open for a 21-day period of public consultation in April 2018 to capture stakeholder views and facilitate engagement. Appropriate governance processes were followed to ensure transparency, minimise bias, manage conflict of interest and limit other influences during guideline

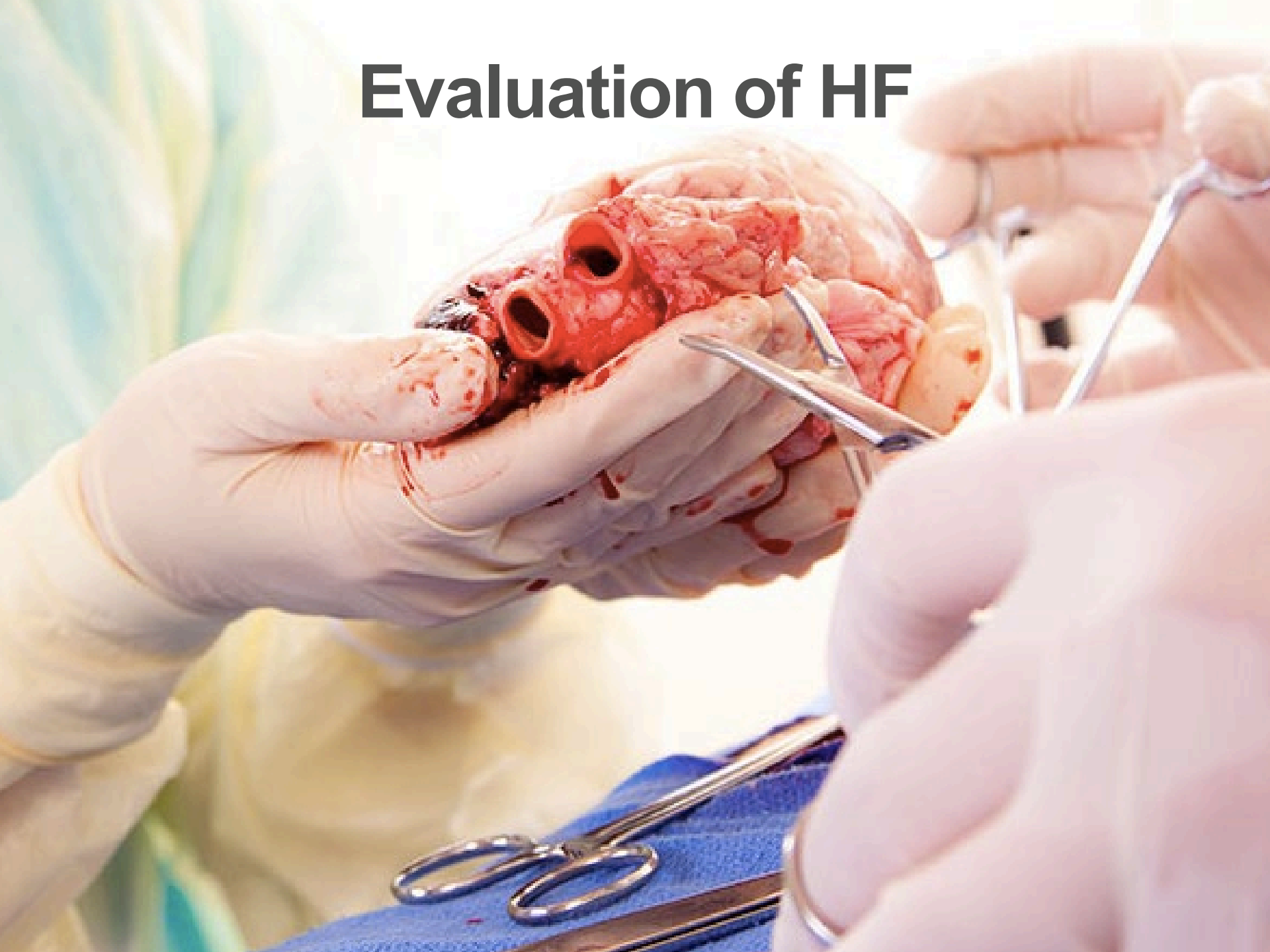
innovation and collaboration

Heart, Lung and Circulation 2018 27, 1123-1208DOI: (10.1016/j.hlc.2018.06.1042)

Areas of Change

- Diagnosis and Classification
  - HFrEF Vs HFpEF
  - Diagnostic algorithm
- Prevention
  - Updates
- Management
  - Guideline directed medical therapy (GDMT)
  - Angiotensin receptor neprilysin inhibitor (ARNI)
  - Education
- How to get patients to buy in.

Evaluation of HF



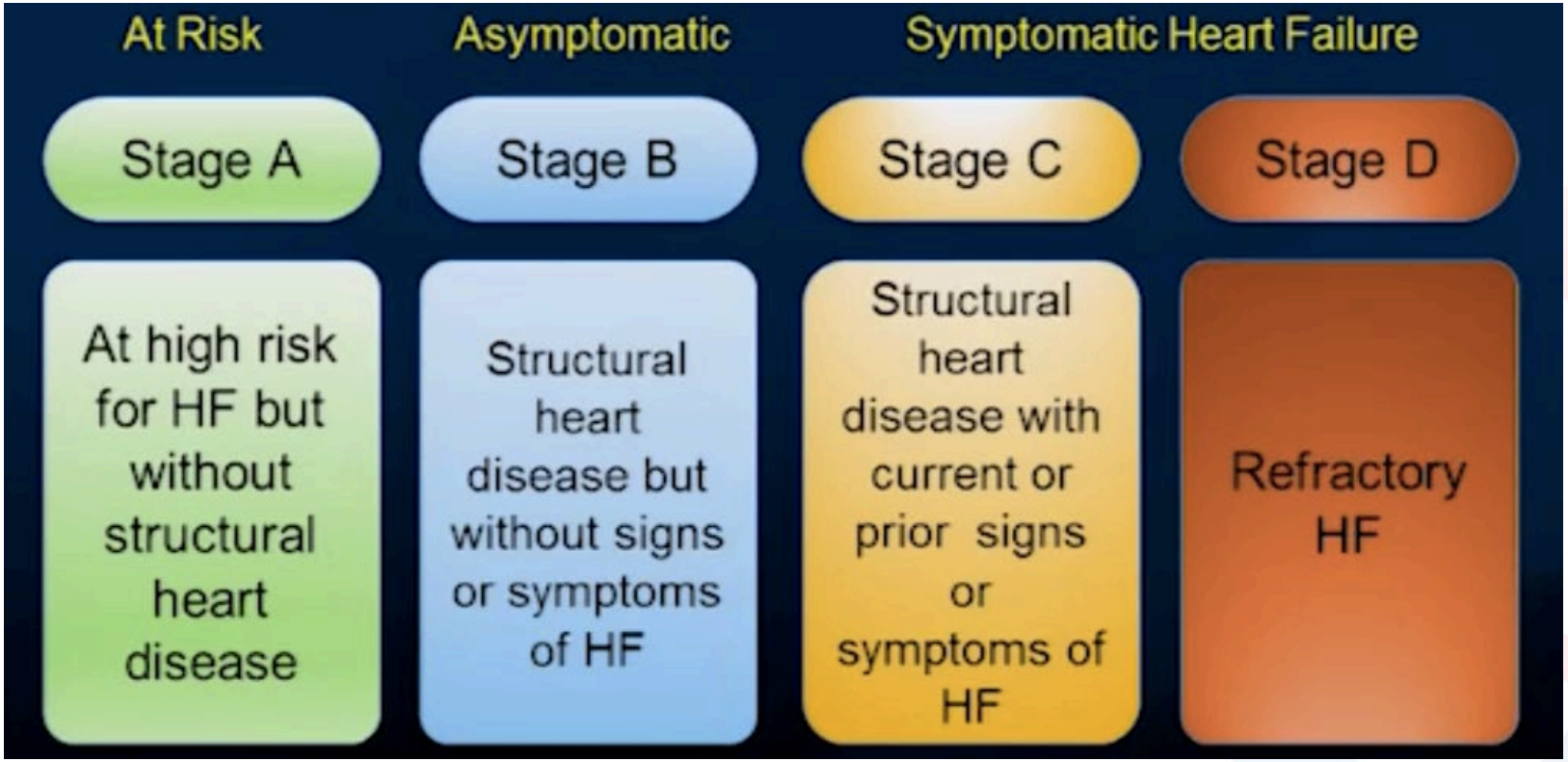
Definition of Heart Failure

3.2. Definition

Heart failure is a **complex clinical syndrome** with **typical symptoms and signs** that generally occur on **exertion**, but can also occur at **rest** (particularly when **recumbent**). It is secondary to an **abnormality of cardiac structure or function** that **impairs the ability of the heart to fill with blood at normal pressure** or **eject blood sufficient** to fulfil the needs of the metabolising organs.

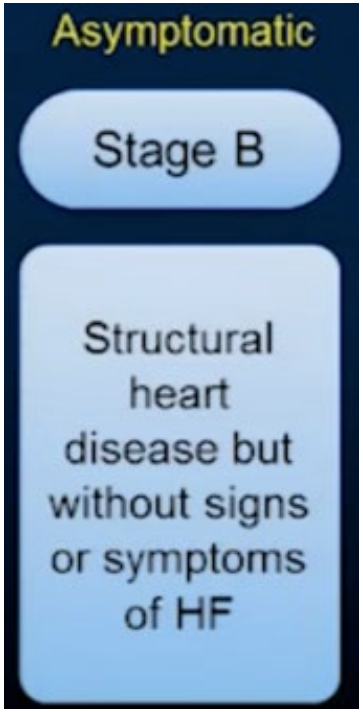
- Following clinical diagnosis, Hf generally categorized according to:
  - **Reduced** left ventricular ejection fraction (**LVEF**) - **<50%** (HFrEF)
  - **Preserved** LVEF **≥ 50%** (**HFpEF**)

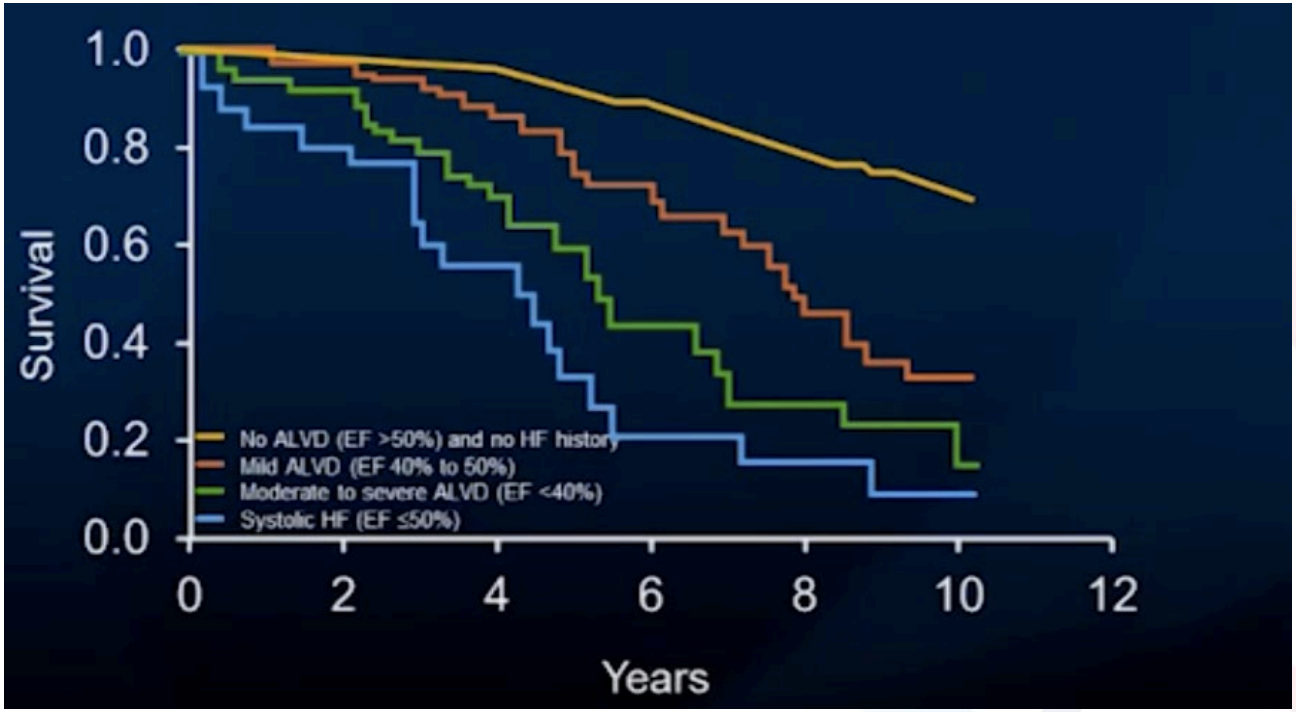
ACC/AHA Stages of Heart Failure



Lee R. Goldberg, and Mariell Jessup Circulation. 2006;113:2851-2860

Importance of Asymptomatic with Structural Heart Disease





Weng et al. Circulation 2003

Heart Failure: Diagnostic criteria

Heart failure diagnostic criteria	
HFrEF	**HFpEF**
• Symptoms ± signs of heart failure **and** • LVEF <50%*	• Symptoms ± signs of heart failure **and** • LVEF ≥50% **and** • Objective evidence of: ○ Relevant structural heart disease (LV hypertrophy, left atrial enlargement) **and/or** ○ Diastolic dysfunction, with high filling pressure demonstrated by any of the following: ▪ invasive means (cardiac catheterisation) ▪ echocardiography ▪ biomarker (elevated BNP or NT proBNP) ▪ exercise (invasive or echocardiography)

Heart, Lung and Circulation 2018 27, 1123-1208DOI: (10.1016/j.hlc.2018.06.1042)

Heart Failure: Diagnostic criteria

Heart failure diagnostic criteria	
HFrEF	**HFpEF**
• Symptoms ± signs of heart failure **and** • LVEF <50%* **If LVEF mildly reduced (LVEF 41-49%), additional criteria required (e.g. signs of heart failure; diastolic dysfunction with high filling pressure demonstrated by invasive means or echocardiography or biomarker testing)*	• Symptoms ± signs of heart failure **and** • LVEF ≥50% **and** • Objective evidence of: ○ Relevant structural heart disease (LV hypertrophy, left atrial enlargement) **and/or** ○ Diastolic dysfunction, with high filling pressure demonstrated by any of the following: ▪ invasive means (cardiac catheterisation) ▪ echocardiography ▪ biomarker (elevated BNP or NT proBNP) ▪ exercise (invasive or echocardiography)

Heart, Lung and Circulation 2018 27, 1123-1208DOI: (10.1016/j.hlc.2018.06.1042)

Prevention

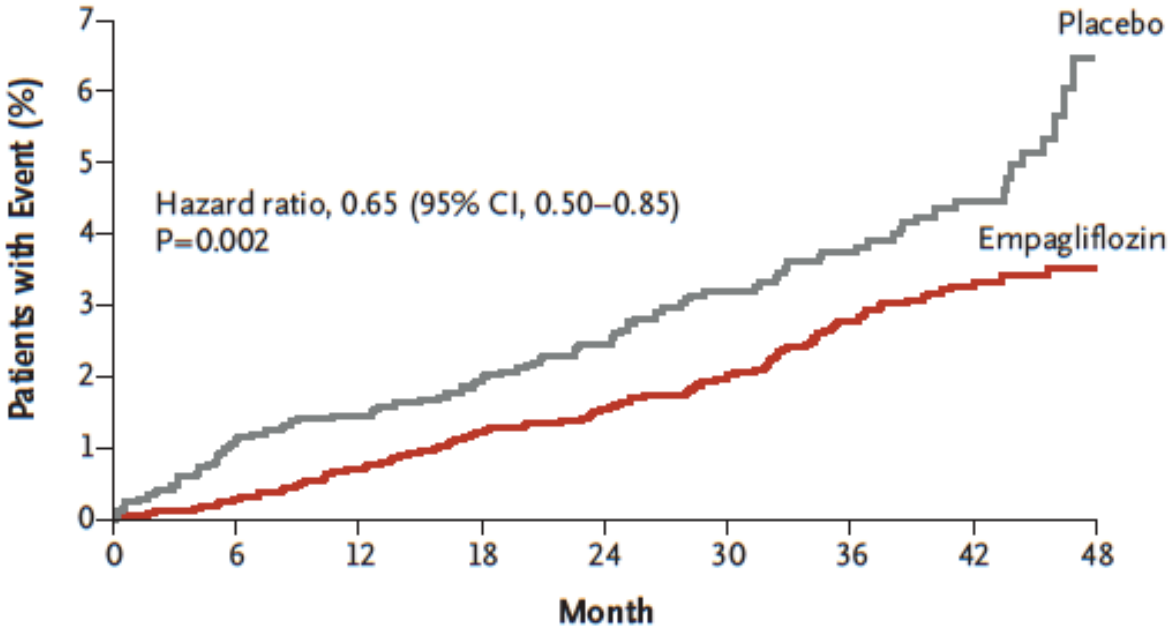
Recommendation	GRADE strength of recommendation	GRADE quality of evidence
Blood pressure[1] and lipid lowering[2] according to published guidelines are recommended, to decrease the risk of cardiovascular events and the risk of developing HF.	Strong	High
Sodium-glucose cotransporter 2 (SGLT2) inhibitors are recommended in patients with type 2 diabetes mellitus associated with cardiovascular disease and insufficient glycaemic control despite metformin, to decrease the risk of cardiovascular events and decrease the risk of HF hospitalisation[3]	Strong	High
Angiotensin converting enzyme (ACE) inhibitors are recommended in patients with LV systolic dysfunction to decrease the risk of developing HF.[4]	Strong	High

1. Ettehad D, et al. Lancet. 2016;387 (10022):957-67
2. Preiss D, et al. Eur Heart J. 2015;36(24):1536-46
3. Zhang XL, et al. J Am Heart Assoc. 2018;7(2).
4. The SOLVD Investigator. N Engl J Med 1992;327:685-91

Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes

Bernard Zinman, M.D., Christoph Wanner, M.D., John M. Lachin, Sc.D., David Fitchett, M.D., Erich Bluhmki, Ph.D., Stefan Hantel, Ph.D., Michaela Mattheus, Dipl. Biomath., Theresa Devins, Dr.P.H., Odd Erik Johansen, M.D., Ph.D., Hans J. Woerle, M.D., Uli C. Broedl, M.D., and Silvio E. Inzucchi, M.D., for the EMPA-REG OUTCOME Investigators

D Hospitalization for Heart Failure

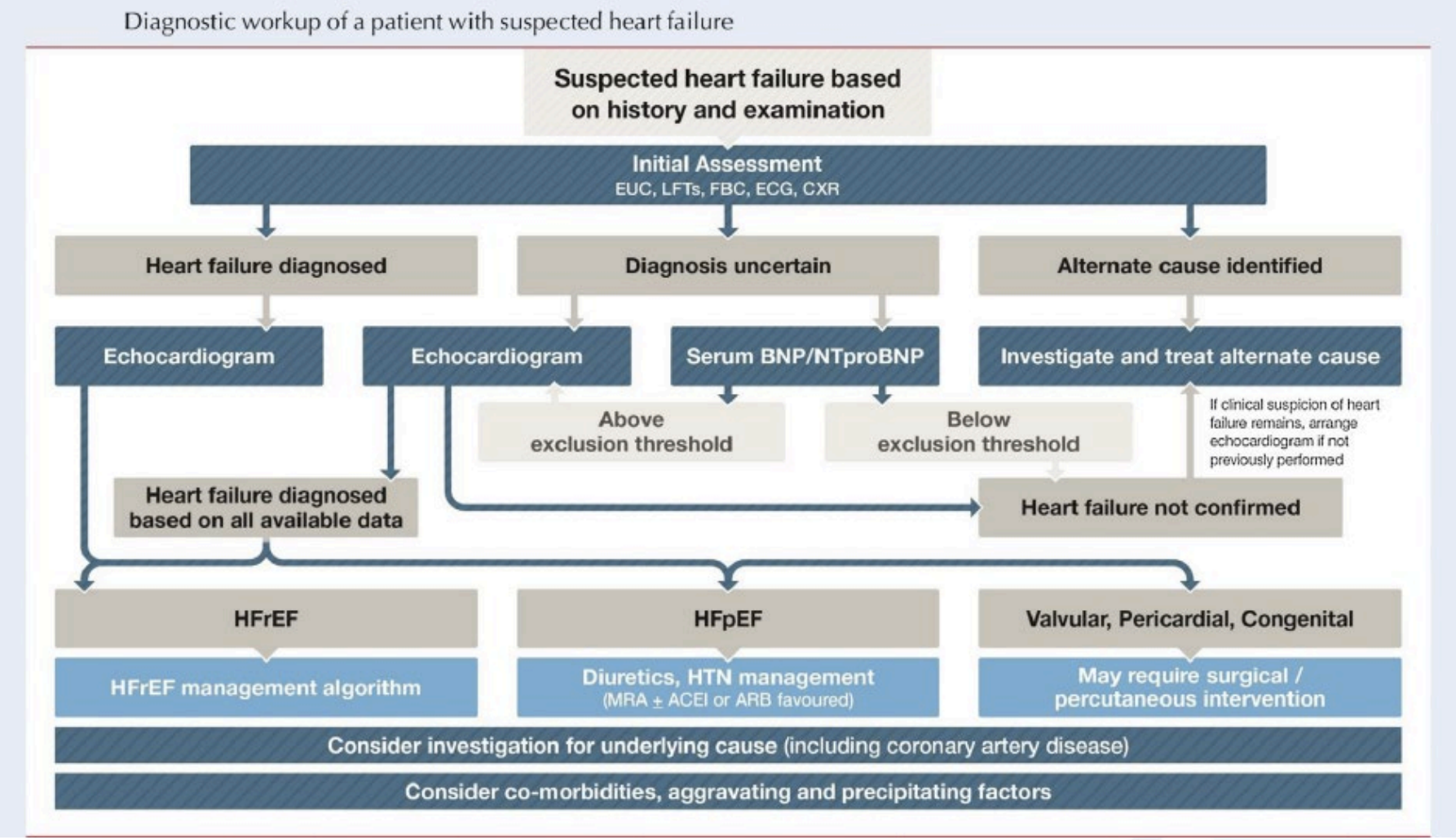


No. at Risk

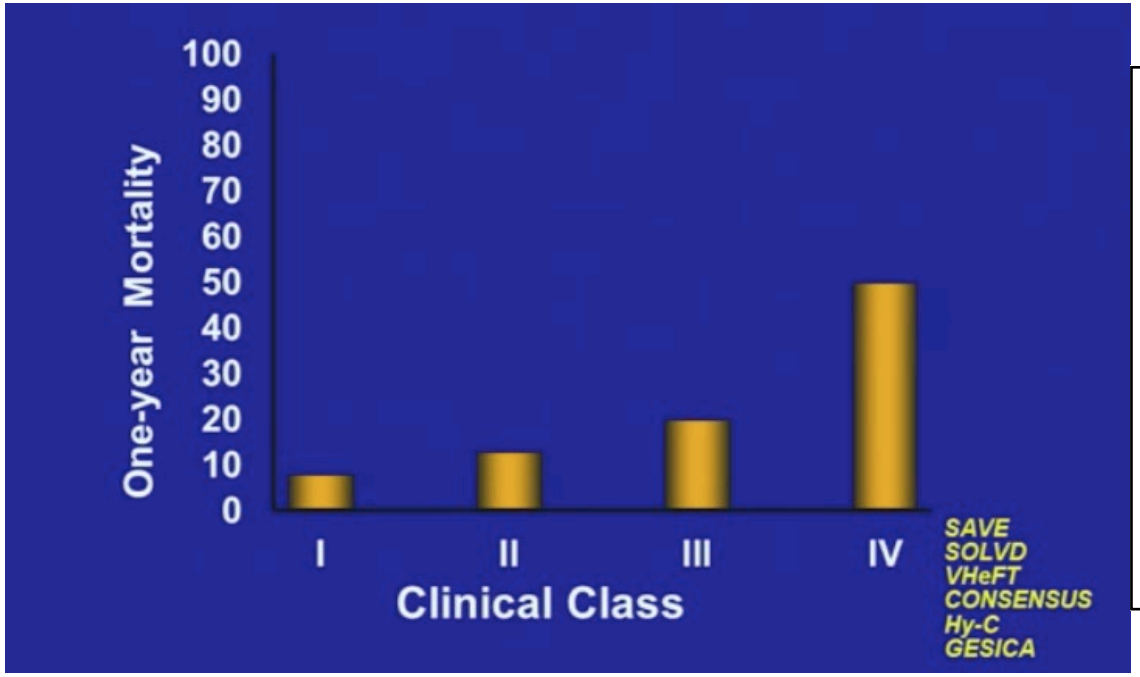
Empagliflozin	4687	4614	4523	4427	3988	2950	2487	1634	395
Placebo	2333	2271	2226	2173	1932	1424	1202	775	168

1. Zinman et al, N Engl J Med 2015;327:685-91

Diagnostic Work Up



Clinical class remain the #1 predictor of mortality in HF



Classification of HF by Symptoms (NYHA)

- Must Identify NYHA class II

NYHA classes			
NYHA class I	**NYHA class II**	**NYHA class III**	**NYHA class IV**
No limitation of physical activity	Slight limitation of physical activity	Marked limitation of physical activity	Unable to carry on any physical activity without discomfort
No overt symptoms	Comfortable at rest, but ordinary physical activity causes symptoms of heart failure	Comfortable at rest, but less than ordinary activity causes symptoms of heart failure	May have symptoms even at rest which increases with any activity

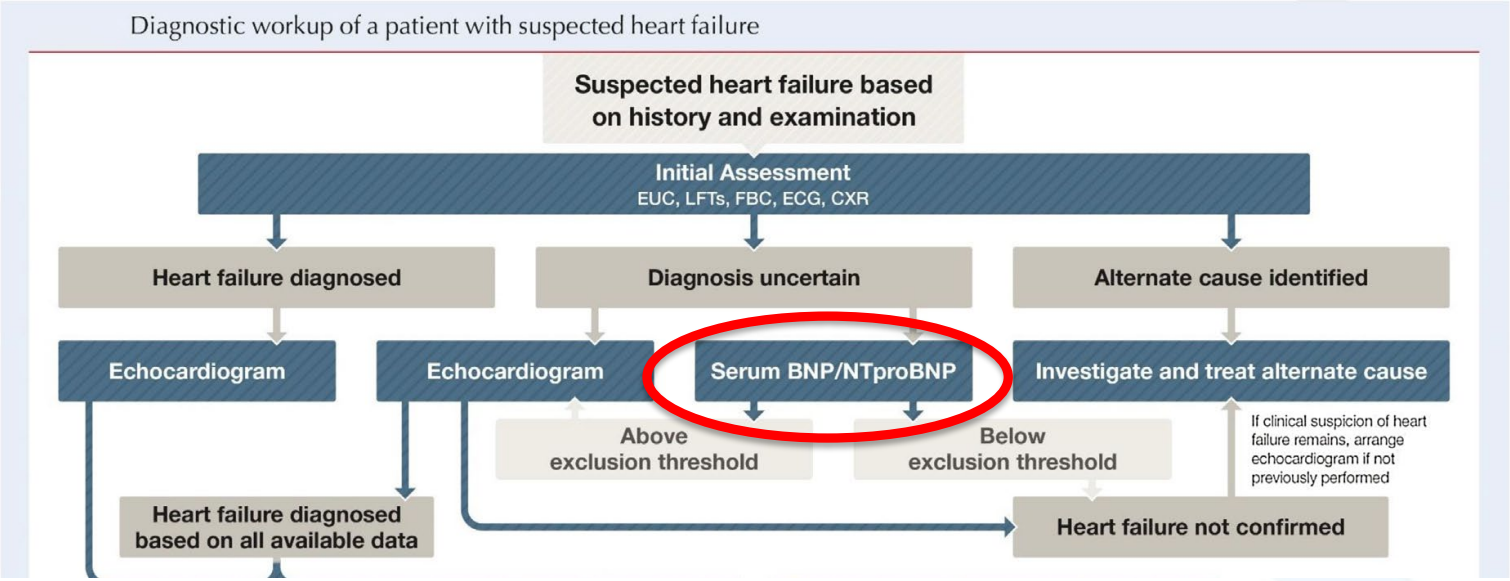
McMurray JJ *et al*. *Eur Heart J* 2012;33:1787–847

Diagnostic Tests: BNP

Recommendation	GRADE strength of recommendation	GRADE quality of evidence
Plasma B-type natriuretic peptide (**BNP**) or N-terminal proBNP (**NT proBNP**) levels are recommended for diagnosis in patients with suspected HF, when the diagnosis is uncertain.	Strong	High
A transthoracic **echocardiogram** is recommended in patients with suspected HF, to improve diagnostic accuracy, and in patients with a new diagnosis of HF, to assess cardiac structure and function (including the measurement of LVEF), assist in classification and therefore guide management.	Strong	Low

Views on BNP

- HF is a clinical diagnosis
- BNP < 100 ng/L and an NT proBNP < 300 ng/L for rule-out.
- Affected by individual patient characteristics.
- Levels can be elevated in PAH, AF, ACS, PE, CTEPH



Aetiology

Recommendation	GRADE strength of recommendation	GRADE quality of evidence
Invasive coronary angiography should be considered in patients with HF associated with refractory angina, resuscitated cardiac arrest, sustained ventricular arrhythmias, or with evidence of IHD on other investigations, or an intermediate-to-high pre-test probability for coronary artery disease, to determine the need for coronary revascularisation.	Strong	Low
Either computed tomography (**CT**) **coronary angiography** or cardiac magnetic resonance imaging (**CMR**) with late gadolinium enhancement (LGE) may be considered in patients with HF who have a **low-to-intermediate** pre-test probability of coronary artery disease, to distinguish ischaemic and non-ischaemic causes of ventricular dysfunction.	Weak	Low
Non-invasive functional testing – stress echocardiography, single-photon emission CT scan (SPECT), positron emission tomography (PET) and CMR with LGE – may be considered in patients with heart failure and established coronary artery disease, for the **assessment of myocardial ischaemia and viability** to determine the need for coronary revascularisation.	Weak	Very Low

Management

Treatment (HFrEF ≤ 40%)

Recommendation	GRADE strength of recommendation	GRADE quality of evidence
An ACE inhibitor is recommended in all patients with HFrEF associated with an LVEF less than or equal to 40% unless contraindicated or not tolerated to decrease mortality and decrease hospitalisation.[1]	Strong	High
A beta-blocker (specifically bisoprolol, carvedilol, controlled or extended release metoprolol or nebivolol) is recommended in all patients with HFrEF associated with an LVEF less than or equal to 40% unless contraindicated or not tolerated, and once stabilised with no or minimal clinical congestion on physical examination, to decrease mortality and decrease hospitalisation.[2-5]	Strong	High
A mineralocorticoid receptor antagonist (MRA) is recommended in all patients with HFrEF associated with an LVEF less than or equal to 40% unless contraindicated or not tolerated, to decrease mortality and decrease hospitalisation for HF.[6, 7]	Strong	High

Treatment (HFrEF ≤ 35 - 40%)

Recommendation	GRADE strength of recommendation	GRADE quality of evidence
An angiotensin receptor blocker (ARB) is recommended in patients with HFrEF associated with an LVEF less than or equal to 40% if an ACE inhibitor is contraindicated or not tolerated, to decrease the combined endpoint of cardiovascular mortality and HF hospitalisation.[1]	Strong	Moderate
An angiotensin receptor neprilysin inhibitor (ARNI) is recommended as a replacement for an ACE inhibitor (with at least a 36-hour washout window) or an ARB in patients with HFrEF associated with an LVEF of less than or equal to 40% despite receiving maximally tolerated or target doses of an ACE inhibitor (or ARB) and a beta-blocker (unless contraindicated), with or without an MRA, to decrease mortality and decrease hospitalisation.[2]	Strong	High
Ivabradine should be considered in patients with HFrEF associated with an LVEF of less than or equal to 35% and with a sinus rate of 70 bpm and above, despite receiving maximally tolerated or target doses of an ACE inhibitor (or ARB) and a beta-blocker (unless contraindicated), with or without an MRA, to decrease the combined endpoint of cardiovascular mortality and HF hospitalisation.[3]	Strong	High

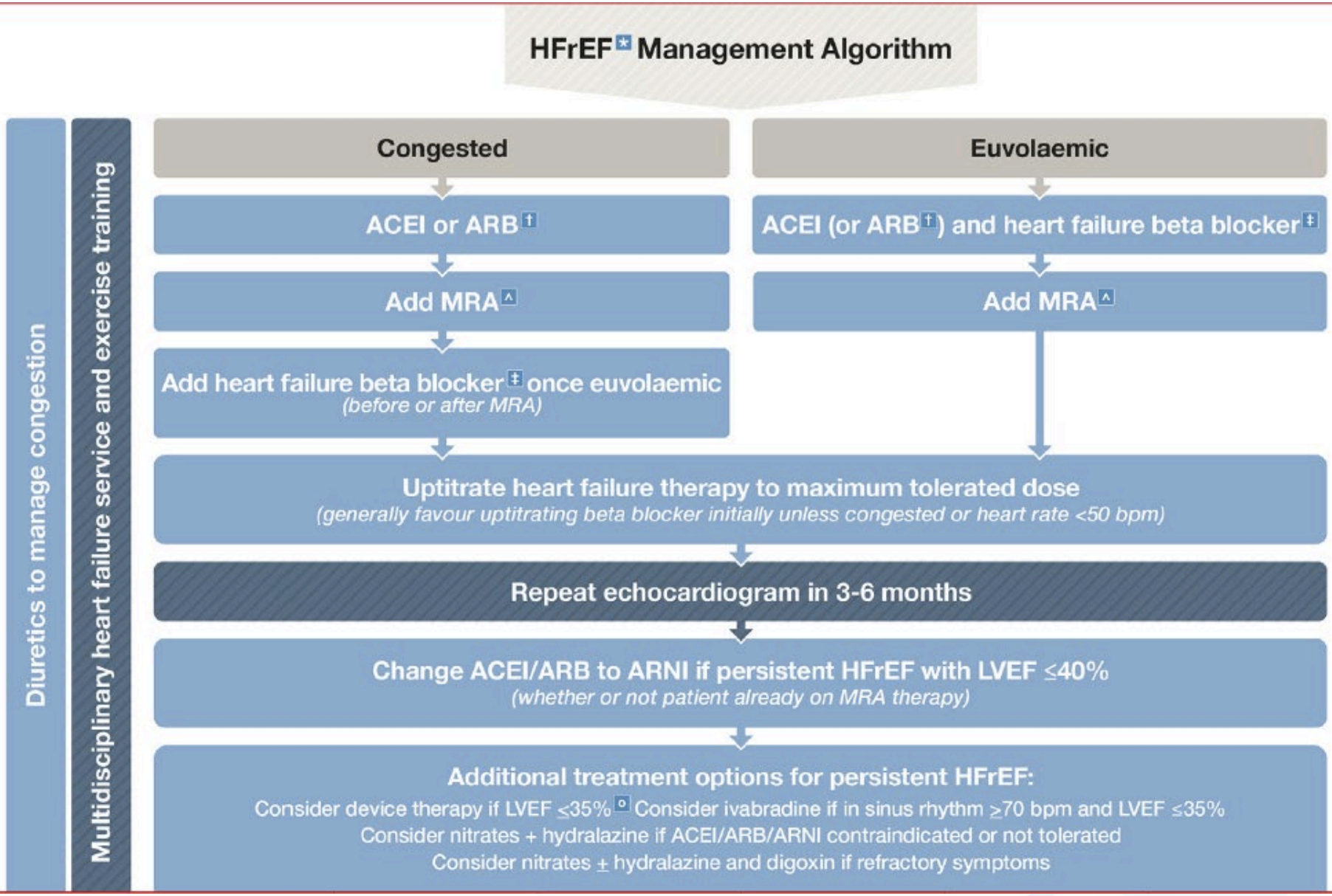
1 – GrangerCB, et al. Lancet. 2003;362(9386):772-6.
2 – McMurray JJ, et al. N Engl J Med. 2014;371(11):993-1004
3 – Swedberg K et al. Lancet. 2010 ;376(9744)875-885

Treatment (HF with EF 41-49%)

Recommendation	GRADE strength of recommendation	GRADE quality of evidence
An ACE inhibitor may be considered in patients with HFrEF associated with a mild reduction in LVEF (LVEF 41-49%) unless contraindicated or not tolerated to decrease mortality and decrease hospitalisation.	Weak	Low
A beta-blocker (specifically bisoprolol, carvedilol, controlled or extended release metoprolol or nebivolol) may be considered in patients with HFrEF associated with a mild reduction in LVEF (LVEF 41-49%) unless contraindicated or not tolerated, and once stabilised with no or minimal clinical congestion on physical examination to decrease mortality and decrease hospitalisation.	Weak	Low
An MRA may be considered in patients with HFrEF associated with a mild reduction in LVEF (LVEF 41-49%) unless contraindicated or not tolerated, to decrease mortality and decrease hospitalisation for heart failure.	Weak	Low
An ARB may be considered in patients with HFrEF associated with a mild reduction in LVEF (LVEF 41-49%) if an ACE inhibitor is contraindicated or not tolerated, to decrease the combined endpoint of cardiovascular mortality and hospitalisation for heart failure.	Weak	Low

EF and Starting Meds

- HFrEF < 40%
  - Strong evidence for medical treatment
- HFrEF < 41-49
  - Weak evidence
  - Patient needs investigating
- HFpEF > 50%
  - Treat Co-morbidities


HFrEF* Management Algorithm
Diuretics to manage congestion
Multidisciplinary heart failure service and exercise training
Congested
Euvolaemic
ACEI or ARB†
ACEI (or ARB†) and heart failure beta blocker‡
Add MRA^
Add MRA^
Add heart failure beta blocker‡ once euvolaemic
(before or after MRA)
Uptitrate heart failure therapy to maximum tolerated dose
(generally favour uptitrating beta blocker initially unless congested or heart rate <50 bpm)
Repeat echocardiogram in 3-6 months
Change ACEI/ARB to ARNI if persistent HFrEF with LVEF ≤40%
(whether or not patient already on MRA therapy)
Additional treatment options for persistent HFrEF:
Consider device therapy if LVEF ≤35%°
Consider ivabradine if in sinus rhythm ≥70 bpm and LVEF ≤35%
Consider nitrates + hydralazine if ACEI/ARB/ARNI contraindicated or not tolerated
Consider nitrates ± hydralazine and digoxin if refractory symptoms

Stopping Treatment

- HFrEF which has now recovered and patient has been stable.

Withdrawal of pharmacological treatment for heart failure in patients with recovered dilated cardiomyopathy (TRED-HF): an open-label, pilot, randomised trial

Brian P Halliday, Rebecca Wassall, Amrit S Lota, Zohya Khalique, John Gregson, Simon Newsome, Robert Jackson, Tsveta Rahneva, Rick Wage, Gillian Smith, Lucia Venneri, Upasana Tayal, Dominique Auger, William Midwinter, Nicola Whiffin, Ronak Rajani, Jason N Dungu, Antonis Pantazis, Stuart A Cook, James S Ware, A John Baksi, Dudley J Pennell, Stuart D Rosen, Martin R Cowie, John G F Cleland, Sanjay K Prasad

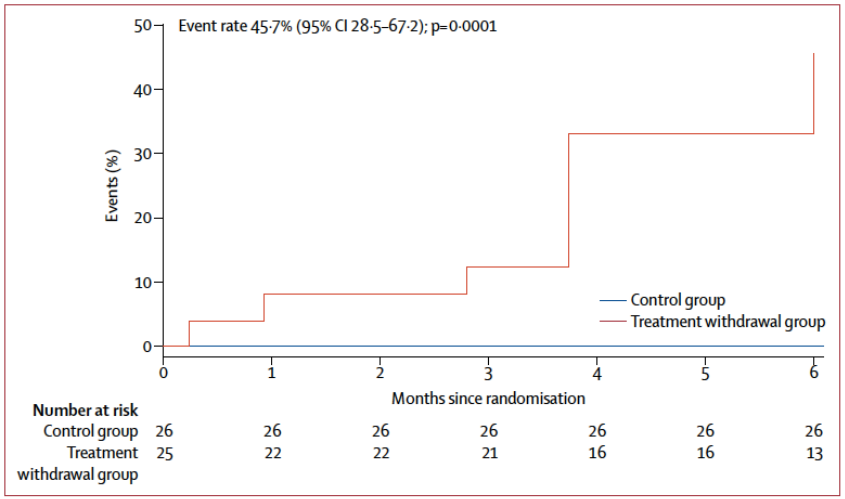


Figure 3: Kaplan-Meier curve of time to primary endpoint in randomised phase, according to treatment group
One patient dropped out at 7 days.

Findings Between April 21, 2016, and Aug 22, 2017, 51 patients were enrolled. 25 were randomly assigned to the treatment withdrawal group and 26 to continue treatment. Over the first 6 months, 11 (44%) patients randomly assigned to treatment withdrawal met the primary endpoint of relapse compared with none of those assigned to continue treatment (Kaplan-Meier estimate of event rate 45·7% [95% CI 28·5–67·2]; p=0·0001). After 6 months,

Non-Pharmacological Management

Recommendation	GRADE strength of recommendation	GRADE quality of evidence
Nurse-led medication titration is recommended in patients diagnosed with HFrEF who have not achieved maximum tolerated doses of ACE inhibitors, ARBs, ARNIs, beta-blockers or MRAs, to decrease hospitalisation.[1]	Strong	High
Regular performance of up to moderate intensity (i.e. breathe faster but hold conversation) continuous exercise is recommended in patients with stable chronic HF, particularly in those with reduced LVEF, to improve physical functioning and quality of life, and to decrease hospitalisation.[2]	Strong	High

1 – Driscoll A et al. Cochrane database Syst Rev. 2015 (12)
2 – Sagar VA et al open Heart 2015

Education

- Sodium restrict to < 2 grams per day
- Fluid restrict < 2 L a day
- Exercise - 30minutes 5 times a week
- ETOH – ideally abstain
- Work out goals and wishes including NFR

Devices

- **Key Points**
  - **LBBB**
  - **LVEF ≤ 35% on Guideline directed therapy (GDMT)**

- **CRT**
  - **Grade 1A – allowed in NYHA class III-IV**
    - Sinus rhythm, LVEF <35%, QRS >150, despite GDMT
    - Consider 130-150
  - **CRT and ICD**
    - **Patients for CRT also candidates for ICD**
- **ICD**
  - **Ischaemic Heart disease with LVEF ≤ 35% on OMT**
  - **Weaker evidence if non ischaemic**

HF and Atrial Fibrillation

Recommendation	GRADE strength of recommendation	GRADE quality of evidence
Pharmacological therapy aiming for a resting ventricular rate of 60–100 bpm should be considered in patients with heart failure associated with AF and a rapid ventricular response.[1]	Strong	Low
Catheter ablation for AF (either paroxysmal or persistent) should be considered in patients with HFrEF associated with an LVEF of less than or equal to 35%, who present with recurrent symptomatic AF, to decrease mortality and hospitalisation for HF.[2]	Strong	Moderate

- Rate Control Strategy
  - Beta Blocker, Digoxin
- Rhythm Control Strategy

Anemia/Iron Deficiency

Recommendation	GRADE strength of recommendation	GRADE quality of evidence
Erythropoietin should not be used routinely for the treatment of anaemia in patients with HF because of an increased risk of thromboembolic adverse events.[1]	Strong AGAINST	Moderate
In patients with HFrEF associated with persistent symptoms despite optimised therapy, iron studies should be performed and, if the patient is iron deficient (i.e. ferritin <100 µg/L, or ferritin 100–300 µg/L with transferrin saturation <20%), intravenous iron should be considered, to improve symptoms and quality of life.[2]	Strong	Moderate

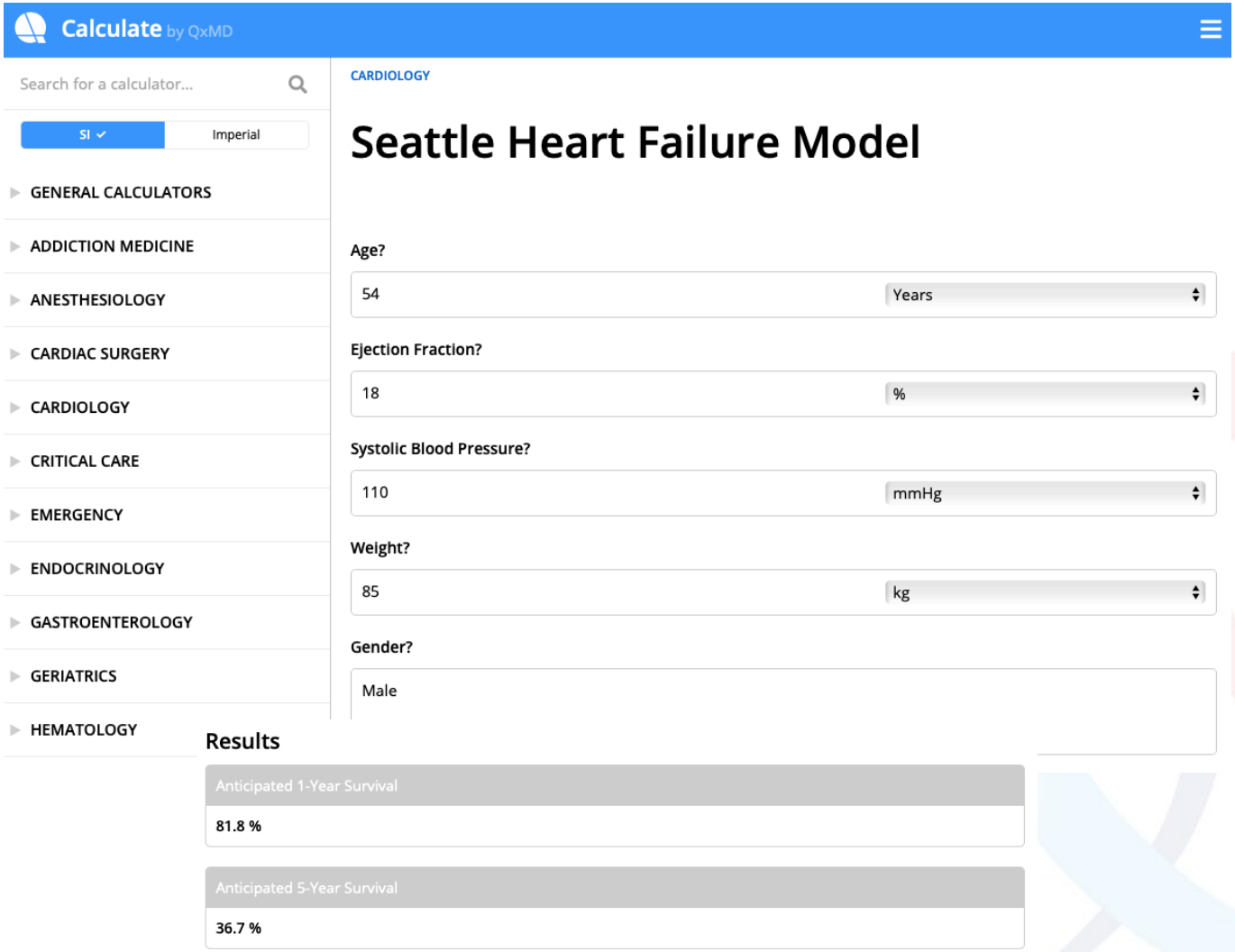
- IV Iron

Pressure monitoring: coming to you soon

Recommendation	GRADE strength of recommendation	GRADE quality of evidence
Implantable pulmonary arterial pressure monitoring may be considered in patients who have been previously hospitalised for heart failure associated with a reduced or preserved LV ejection fraction with persistent moderate (NYHA functional class III) heart failure symptoms, despite optimal care, to decrease hospitalisation for heart failure, provided systems are in place to ensure daily upload and at least weekly review of pressure monitoring data.	Weak	Low

How Do You Get Your Patients to Buy into Your Management ?

Seattle Heart Failure Model



In Conclusion

- HF reduced Ejection Fraction (EF) - <50%
- NYHA class – Look out for Class II
- All EF < 40 % should be on GDMT
- Sacubitril/Valsartan- Cohort mainly NYHA II
- Maximum tolerated dose
- Seattle HF model


Questions