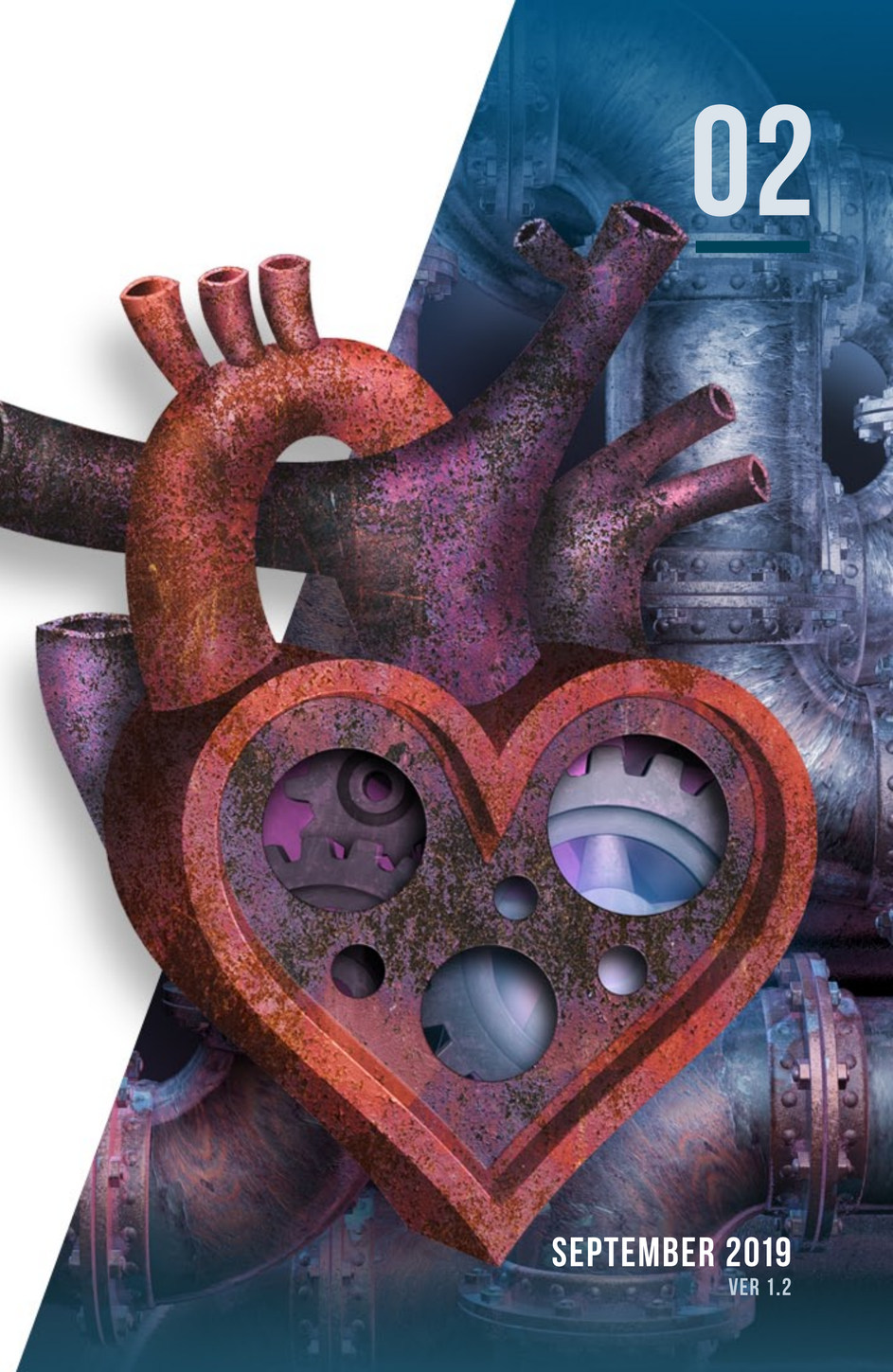
bpacnz
PRIMARY CARE
UPDATE SERIES

02

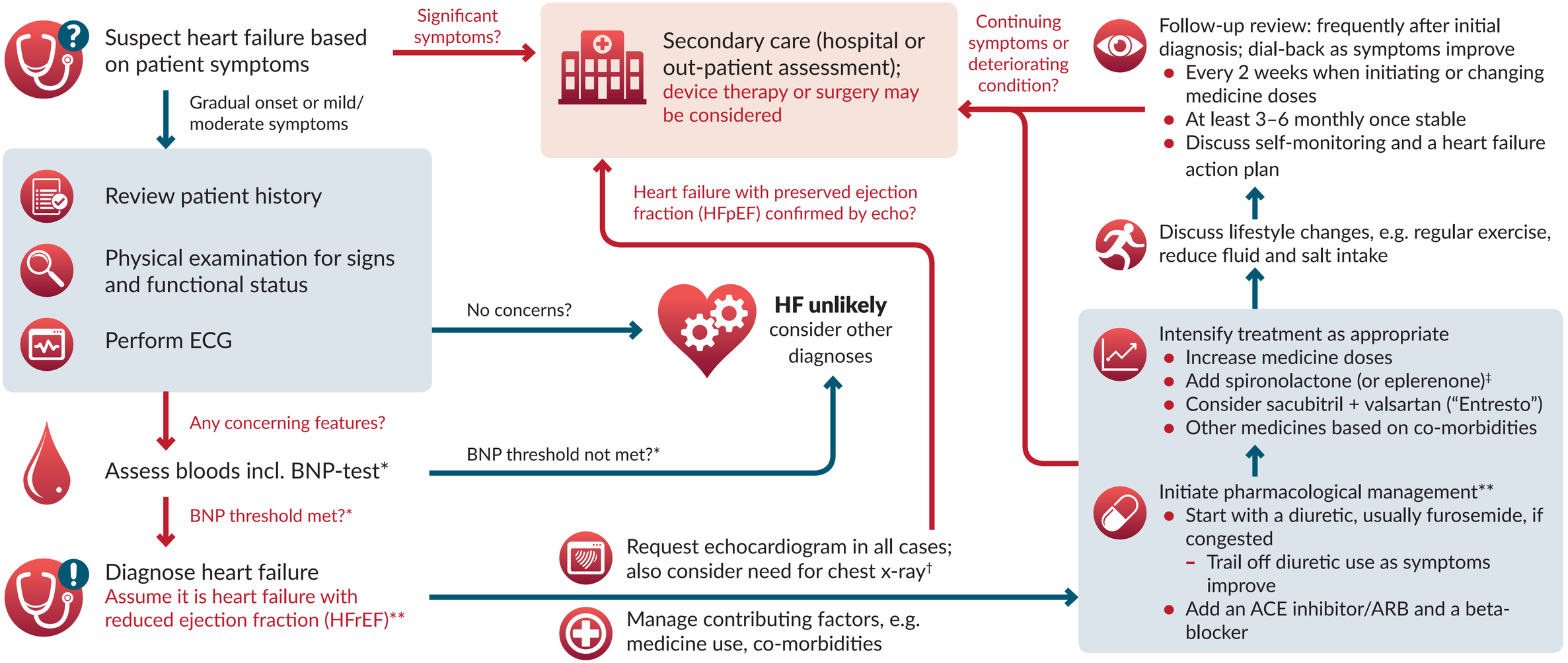
MANAGING HEART FAILURE IN PRIMARY CARE

Welcome to the next instalment of bpac[nz]'s primary care update series. Today we're going to take a look at another topic within our cardiovascular theme; heart failure. Following on from our update on atrial fibrillation, we are again fortunate enough to be able to draw on the expertise of **Associate Professor Gerry Wilkins**, who is a specialist in interventional cardiology from the Southern DHB.



SEPTEMBER 2019
VER 1.2

Overview: managing heart failure (HF) in primary care



* See the “practice tool” within this update for more information on the BNP (Brain natriuretic peptide) thresholds associated with diagnosing heart failure; † For example, if lung disease (e.g. COPD, asthma) is suspected as the cause of symptoms, or co-morbidities are present that may worsen HF; ** Immediate pharmacological treatment is required following a clinical diagnosis of heart failure. Treatment should proceed assuming the patient has heart failure with reduced ejection fraction (HFrEF) unless HFpEF is demonstrated using an echocardiogram, in which case cardiologist referral is recommended to guide treatment; ‡ Consider initiating spironolactone early alongside an ACE inhibitor and beta-blockers in patients with severe HF symptoms.

HF is a clinical syndrome

Patients present with varied symptoms and signs that indicate *something* is wrong with their heart

Clinical symptoms are often mild and non-specific

Presentations may differ based on age, weight, fitness and co-morbidities

Clinical suspicion of HF should be prompted by the patient's symptoms/signs in the context of their medical history

Symptoms suggestive of HF:

- Shortness of breath (dyspnoea)
- Swelling in the lower legs
- Fatigue, weakness, reduced exercise tolerance
- Orthopnoea
- Paroxysmal nocturnal dyspnoea
- Persistent cough/wheezing

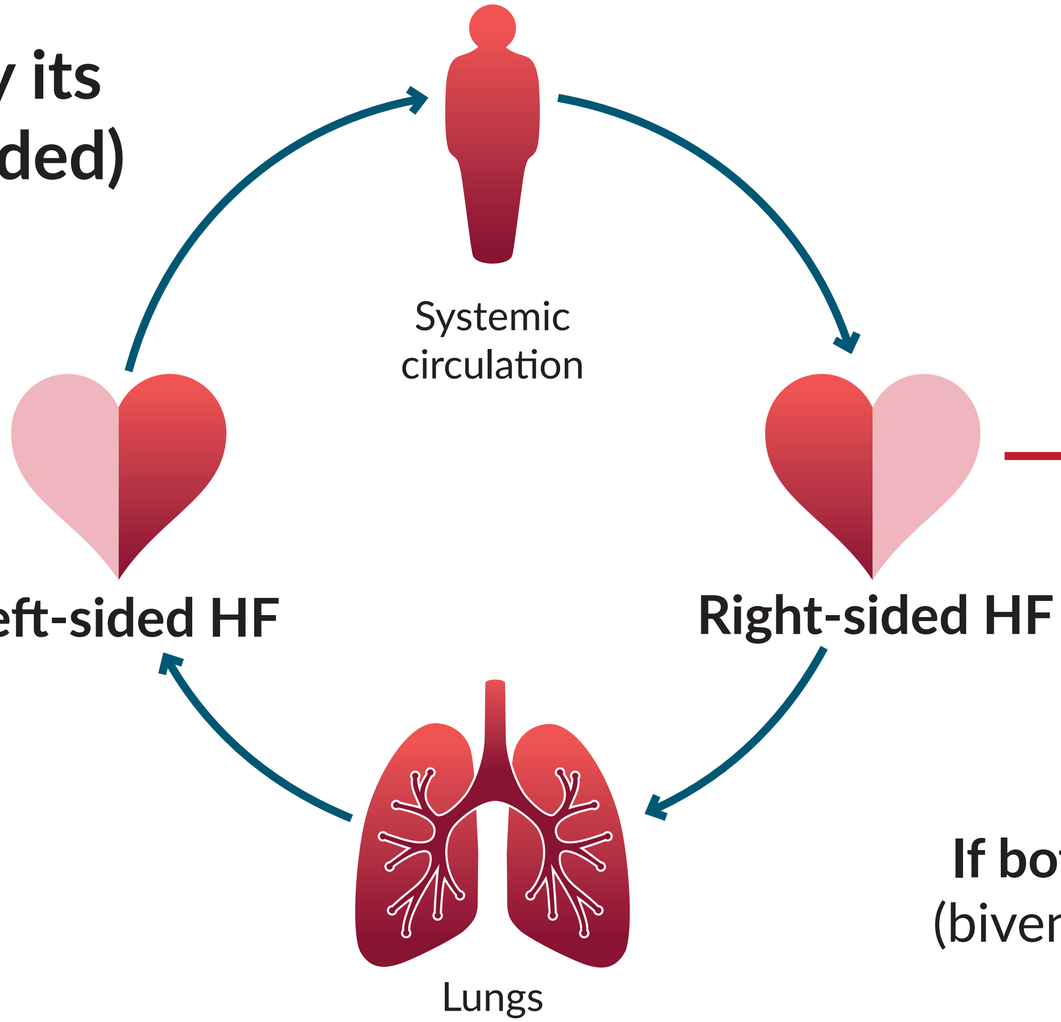
Signs suggestive of HF:

- Elevated jugular venous pressure
- Hepatojugular reflux
- Laterally displaced apical impulse
- Rapid or irregular heartbeat
- Pitting oedema
- Bibasilar crackles

1. Ponikowski P, Voors AA, Anker SD, et al. Eur J Heart Fail. 2016;18:891–975; 2. NHFA CSANZ Heart Failure Guidelines Working Group. Heart Lung Circ. 2018;27:1123–208.

HF is a clinical syndrome

Defining heart failure by its features (left- vs right sided)



Blood backs up in pulmonary circulation

- Pulmonary oedema, bibasilar crackles
- Orthopnoea
- Paroxysmal nocturnal dyspnoea
- Gallop rhythm (S3)

Blood backs up in systemic circulation

- Systemic congestion
- Increased JVP
- Oedema – particularly feet and lower legs
- Hepatomegaly, ascites

If both occur: congestive (biventricular) heart failure

HF, heart failure; JVP, jugular venous pressure.

1. Ponikowski P, Voors AA, Anker SD, et al. Eur J Heart Fail. 2016;18:891–975; 2. NHFA CSANZ Heart Failure Guidelines Working Group. Heart Lung Circ. 2018;27:1123–208.

HF is a clinical syndrome

Defining heart failure by its mechanism (HFrEF vs HFpEF)

Refer patients with symptoms and signs of HF for an echocardiogram

LVEF <50%?

= heart failure with reduced ejection fraction (HFrEF)*

LVEF ≥50%?

and evidence of relevant structural heart disease† and/or diastolic dysfunction with high filling pressure

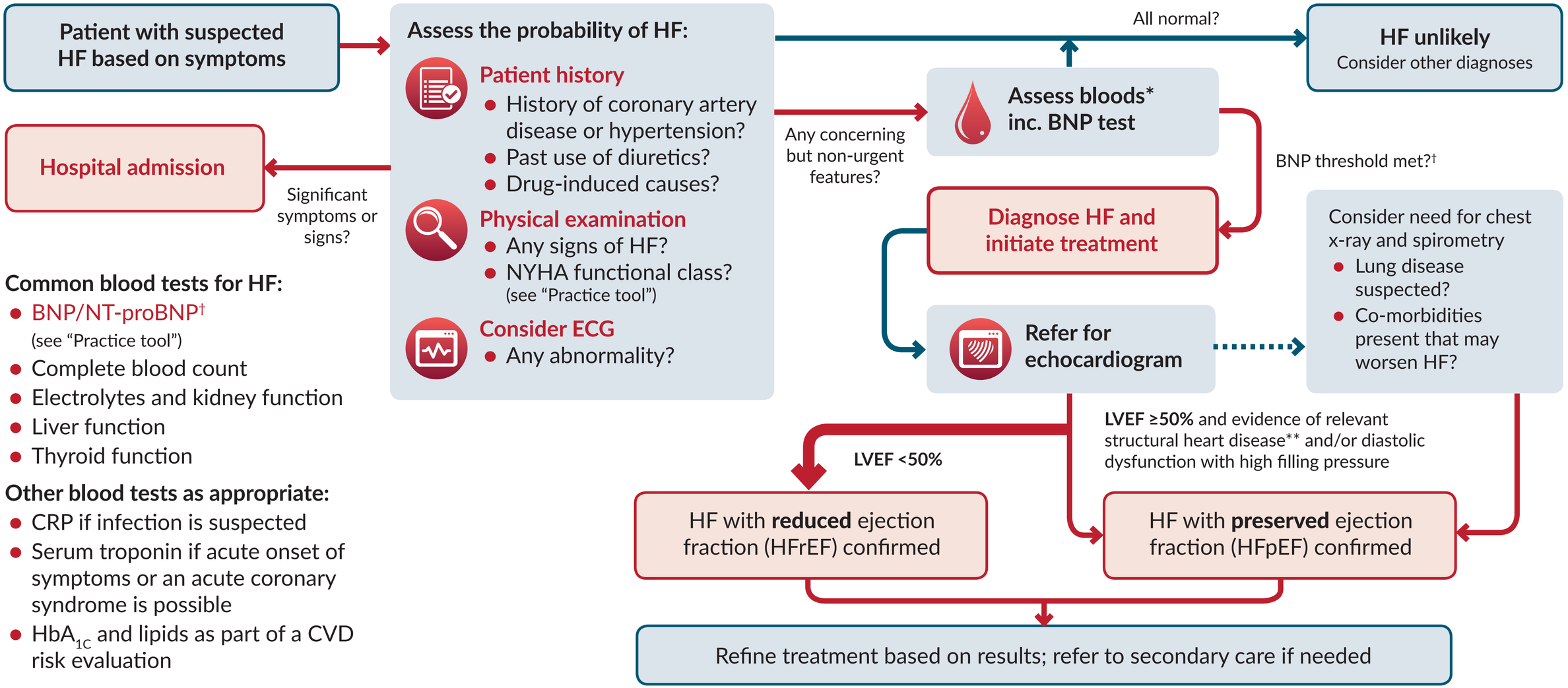
= heart failure with preserved ejection fraction (HFpEF)**

Results direct treatment decisions and may also reveal underlying causes

* Treatment recommendations are supported by an abundance of clinical trial data; † Such as left ventricular hypertrophy or left atrial enlargement; ** Treatment recommendations are poorly supported by clinical trial data.
HF, heart failure; LVEF, left ventricular ejection fraction

1. Ponikowski P, Voors AA, Anker SD, et al. Eur J Heart Fail. 2016;18:891–975; 2. NHFA CSANZ Heart Failure Guidelines Working Group. Heart Lung Circ. 2018;27:1123–208.

Diagnosing heart failure in primary care



Common blood tests for HF:

- BNP/NT-proBNP† (see "Practice tool")
- Complete blood count
- Electrolytes and kidney function
- Liver function
- Thyroid function

Other blood tests as appropriate:

- CRP if infection is suspected
- Serum troponin if acute onset of symptoms or an acute coronary syndrome is possible
- HbA_{1C} and lipids as part of a CVD risk evaluation

* See directly above for common blood tests; † Detection of elevated BNP levels are sufficient diagnose heart failure, however, an echocardiogram is still important for confirmation and for guiding long-term management (see the "practice tool" for more information) ** Such as left ventricular hypertrophy or left atrial enlargement.

1. Ponikowski P, Voors AA, Anker SD, et al. Eur J Heart Fail. 2016;18:891–975; 2 NHFA CSANZ Heart Failure Guidelines Working Group. Heart Lung Circ. 2018;27:1123–208.

Are there contributing factors that can be managed?

Manage co-morbidities – possible contributors to HF include:

- Coronary artery disease (most common)
- Hypertension
- Chronic obstructive pulmonary disease
- Valvular disease
- Cardiac arrythmias, e.g. atrial fibrillation
- Cardiomyopathies, e.g. diabetic
- Thyrotoxicosis (can cause high output failure)
- Infection

1. Ponikowski P, Voors AA, Anker SD, et al. Eur J Heart Fail. 2016;18:891–975; 2. NHFA CSANZ Heart Failure Guidelines Working Group. Heart Lung Circ. 2018;27:1123–208; 3 Potentially harmful drugs to avoid in heart failure. Heart Online. Available at: http://www.heartonline.org.au/media/DRL/Potentially_harmful_drugs_to_avoid_in_heart_failure.pdf (accessed Sep, 2019); 4 NZ Formulary. NZF v87. 2019. Available at: www.nzf.org.nz (Accessed Sep, 2019)

Are there contributing factors that can be managed?

Medicines to use with caution or avoid (if possible):

Note: This is not an exhaustive list; see footnotes for contraindications

Medicine	Adverse effect(s) when used in patients with HF
Corticosteroids	Sodium and water retention
Most NSAIDs* (inc. COX-2 inhibitors†)	Sodium and water retention; increased vasoconstriction; impaired response to diuretics and ACE inhibitors
Thiazolidinediones e.g. pioglitazone†	Sodium and water retention; avoid in patients with symptomatic HF
Non-dihydropyridine CCBs e.g. diltiazem and verapamil**	Negative inotropy
Some antiarrhythmic medicines	
e.g. Sotalol‡	Proarrhythmic properties
Flecainide†	Negative inotropy
Disopyramide*	Negative inotropy
Some antidepressants	
e.g. Tricyclic	Negative inotropy
Citalopram	Dose-dependent QT prolongation
Venlafaxine	Hypertension; dose-dependent tachycardia and QT prolongation
Amphetamines	Sympathetic agonist activity; tachyarrhythmias; tachycardia; hypertension

* Contraindicated in patients with severe HF (unless secondary to arrhythmia for disopyramide);

† Contraindicated in patients with symptomatic HF;

** Contraindicated in HF with a significantly impaired left ventricular function, but may be useful in HF with preserved ejection fraction;

‡ Contraindicated in patients with uncontrolled HF.

ACE, angiotensin converting enzyme; CCBs, calcium channel blockers; HF, heart failure; LVEF, left ventricular ejection fraction; MDMA, 3,4-Methylenedioxymethamphetamine; NSAIDs, non-steroidal anti-inflammatory drugs.

1. Ponikowski P, Voors AA, Anker SD, et al. Eur J Heart Fail. 2016;18:891–975; 2. NHFA CSANZ Heart Failure Guidelines Working Group. Heart Lung Circ. 2018;27:1123–208; 3 Potentially harmful drugs to avoid in heart failure. Heart Online. Available at: http://www.heartonline.org.au/media/DRL/Potentially_harmful_drugs_to_avoid_in_heart_failure.pdf (accessed Sep, 2019); 4 NZ Formulary. NZF v87. 2019. Available at: www.nzf.org.nz (Accessed Sep, 2019)

Managing heart failure

Goals of pharmacological HF treatment:

1. Improve symptoms and signs, functional capacity and quality of life
2. Decrease hospital admissions
3. Improve longevity

Treatment should be individualised

Treatment should be prompt

Proceed with the assumption you are treating **HFrEF** until proven otherwise

Patients with **HFpEF** are generally referred to a cardiologist to refine their management (see later slide)

HF, heart failure; HFpEF, HF with preserved ejection fraction; HFrEF, HF with reduced ejection fraction.

1. Ponikowski P, Voors AA, Anker SD, et al. Eur J Heart Fail. 2016;18:891–975; 2. NHFA CSANZ Heart Failure Guidelines Working Group. Heart Lung Circ. 2018;27:1123–208.

Managing heart failure

Is the patient congested or breathless?

Start with a diuretic (loop) to reduce fluid overload/retention if needed, e.g. furosemide

- Weigh the patient first; monitor weight/blood pressure throughout treatment
- Treat assertively in the short-term; adjust dose to reduce fluid overload without causing hypovolaemia*
- **Do not** continue long-term unless the patient remains symptomatic; taper use over time

* Within recommended dose range. See final two slides or the management summary for dosing regimens.

1. Ponikowski P, Voors AA, Anker SD, et al. Eur J Heart Fail. 2016;18:891–975; 2. NHFA CSANZ Heart Failure Guidelines Working Group. Heart Lung Circ. 2018;27:1123–208.

Managing heart failure

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- **Do not** continue long-term unless the patient remains symptomatic; taper use over time

Add an ACE inhibitor (or ARB if an ACE inhibitor is not tolerated)†

- Up-titrate to max tolerated dose*

Add a beta-blocker once the patient stops displaying symptoms of fluid overload**

- Start low, go slow; up-titrate to max tolerated dose*

Start both as soon as practically possible

* Within recommended dose range. See final two slides or the management summary for dosing regimens; † An ACE inhibitor can be initiated immediately alongside the diuretic; ** If the patient does not have symptoms of congestion, then a beta-blocker may be initiated at the same time as the ACE inhibitor. ACE, angiotensin converting enzyme; ARB, angiotensin II receptor blocker; HF, heart failure.

1. Ponikowski P, Voors AA, Anker SD, et al. Eur J Heart Fail. 2016;18:891–975; 2. NHFA CSANZ Heart Failure Guidelines Working Group. Heart Lung Circ. 2018;27:1123–208

Managing heart failure

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- Up-titrate to max tolerated dose*

Add a beta-blocker once the patient stops displaying symptoms of fluid overload**

- Start low, go slow; up-titrate to max tolerated dose*

Start both as soon as practically possible

Add spironolactone if the patient is still symptomatic despite ACE inhibitor/beta-blocker*

- Consider an ACE inhibitor, beta-blocker and spironolactone concomitantly straight away in patients with severe symptoms
- Closely monitor serum potassium and renal function due to risk of hyperkalaemia 1–2 weeks after initiation or up-titration

* Within recommended dose range. See final two slides or the management summary for dosing regimens; † An ACE inhibitor can be initiated immediately alongside the diuretic; ** If the patient does not have symptoms of congestion, then a beta-blocker may be initiated at the same time as the ACE inhibitor.ACE, angiotensin converting enzyme; ARB, angiotensin II receptor blocker; HF, heart failure.

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Managing heart failure

PHARMAC now funds an alternative to spironolactone: Eplerenone

Dose equivalent to spironolactone; similar rates of hyperkalaemia

Special Authority approval required

- Patients must have a LVEF <40%; and
  - Be intolerant to optimal dosing of spironolactone; or
  - Have experienced a clinically significant adverse effect while on an optimal dose of spironolactone

Offers similar rates of cardiovascular protection, with reduced rates gynaecomastia or breast tenderness

* Within recommended dose range. See final two slides or the management summary for dosing regimens; † An ACE inhibitor can be initiated immediately alongside the diuretic; ** If the patient does not have symptoms of congestion, then a beta-blocker may be initiated at the same time as the ACE inhibitor.ACE, angiotensin converting enzyme; ARB, angiotensin II receptor blocker; HF, heart failure.

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Managing heart failure

Start with a diuretic (loop) to reduce fluid overload/retention if needed, e.g. furosemide

- Weigh the patient first; monitor weight/blood pressure throughout treatment
- Treat assertively in the short-term; adjust dose to reduce fluid overload without causing hypovolaemia*
- **Do not** continue long-term unless the patient remains symptomatic; taper use over time

~~**Add an ACE inhibitor** (or ARB if an ACE inhibitor is not tolerated)†~~

~~- Up-titrate to max tolerated dose*~~

STOP

Add a beta-blocker once the patient stops displaying symptoms of fluid overload**

- Start low, go slow; up-titrate to max tolerated dose*

Add spironolactone if the patient is still symptomatic despite ACE inhibitor/beta-blocker*

- Consider an ACE inhibitor, beta-blocker and spironolactone concomitantly straight away in patients with severe symptoms
- Closely monitor serum potassium and renal function due to risk of hyperkalaemia 1–2 weeks after initiation or up-titration
- Trial **eplerenone**‡ if needed

Consider sacubitril+valsartan (Entresto)‡ if the patient is still symptomatic (**stop ACE inhibitor/ARB** – allow washout period)

START

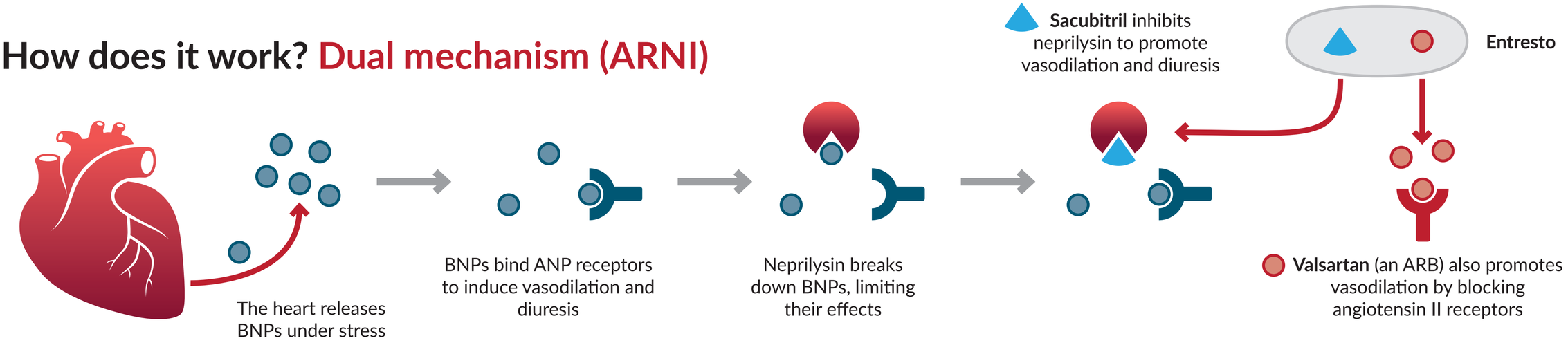
* Within recommended dose range. See final two slides or the management summary for dosing regimens; † An ACE inhibitor can be initiated immediately alongside the diuretic; ** If the patient does not have symptoms of congestion, then a beta-blocker may be initiated at the same time as the ACE inhibitor. ‡ Special authority approval required ACE, angiotensin converting enzyme; ARB, angiotensin II receptor blocker; HF, heart failure.

1. Ponikowski P, Voors AA, Anker SD, et al. Eur J Heart Fail. 2016;18:891–975; 2. NHFA CSANZ Heart Failure Guidelines Working Group. Heart Lung Circ. 2018;27:1123–208.

A new medicine for chronic heart failure: sacubitril+valsartan (“Entresto”)

Available fully funded with Special Authority approval in patients with chronic symptomatic (NYHA Class II-IV) (LVEF ≤ 35%) who are receiving concomitant optimal standard treatment*

How does it work? Dual mechanism (ARNI)



Do not use sacubitril+valsartan concurrently with an ACE inhibitor or ARB; initiate at least 36 hours after the final ACE inhibitor or when the next ARB dose is due

- **Three strengths available**; titrate upwards to maximum tolerated dose
- Do not initiate if SBP <100 mmHg or serum potassium >5.4 mmol/L
- **Review two weeks after initiation or up-titration**; check the patient’s blood pressure, renal function and serum potassium

* Optimal standard treatment must include an ACE inhibitor (or ARB) and a beta-blocker at the maximum tolerated dose (unless contraindicated) but does not need to include spironolactone/eplerenone.

ACE, angiotensin converting enzyme; ANP, atrial natriuretic peptide; ARB, angiotensin II receptor blocker; ARNI, angiotensin receptor neprilysin inhibitor; BNPs, brain natriuretic peptides; HFrEF, HF with reduced ejection fraction; NYHA, New York Heart Association; SBP, systolic blood pressure. 1. Ponikowski P, Voors AA, Anker SD, et al. Eur J Heart Fail. 2016;18:891–975; 2. NHFA CSANZ Heart Failure Guidelines Working Group. Heart Lung Circ. 2018;27:1123–208; NZ Formulary. 3. NZF v87. 2019. Available at: www.nzf.org.nz (Accessed Sep, 2019)

A new medicine for chronic heart failure: sacubitril+valsartan (“Entresto”)

PARADIGM-HF trial (N=8442)

Patients with **HFrEF** receiving a **beta-blocker** and an **ACE inhibitor** (or **ARB**) +/- **spironolactone**

Single-blind run-in period
(6–8 weeks)

Patient’s ACE inhibitor or ARB switched to **enalapril**, then to **Entresto** to ensure tolerance

Double-blind treatment period
(duration was event driven; median follow-up 27 months)

Entresto 97/103 mg BD
N=4209

1:1 randomisation

Enalapril 10 mg BD
N=4233

Composite endpoint: cardiovascular death or hospitalisation for HF occurred in:

- 21.8% with Entresto (ARNI)
- 26.5% with enalapril (ACE inhibitor)

(HR, 0.80; 95% CI, 0.73–0.87; p<0.001)

NNT*=21

* To prevent one death over five-years with Entresto versus enalapril. ACE, angiotensin converting enzyme; ARB, angiotensin II receptor blocker; ARNI, angiotensin receptor neprilysin inhibitor; BD, twice daily; CI, confidence interval; HF, heart failure; HFrEF, HF with reduced ejection fraction; HR, hazard ratio; NNT, number needed to treat.

1. McMurray JJ, Packer M, Desai AS, et al. N Eng J Med. 2014;371:993–1004; 2. Sauer, AJ, Cole, R, Jensen, BC, *et al*. Heart Fail Rev. 2019;24:167–76.

Other medicines to consider as appropriate

Digoxin

- Only use in patients who have atrial fibrillation in addition to heart failure that is not controlled with a beta-blocker

Anticoagulants

- If the patient is at risk of stroke

Does your patient have type 2 diabetes and CVD? – consider an SGLT2 inhibitor

(dapagliflozin; unsubsidised)

Reduces HF-hospitalisation in patients with T2D and HF by almost one-third compared with placebo

- The reason for this benefit on HF outcomes is still unclear and their usefulness is still being assessed in clinical trials

Consider discussing use with patients that have T2D and a high risk of HF (or established HF) and insufficient glycaemic control

- Costs approximately $90/month

ACE, angiotensin converting enzyme; ARB, angiotensin II receptor blocker; CVD, cardiovascular disease; HF, heart failure; HFrEF, HF with reduced ejection fraction; SGLT2, sodium glucose cotransporter-2; T2D, type 2 diabetes. 1. Ponikowski P, Voors AA, Anker SD, et al. Eur J Heart Fail. 2016;18:891–975; 2. NHFA CSANZ Heart Failure Guidelines Working Group. Heart Lung Circ. 2018;27:1123–208; 3. Fitchett DH, Udell JA, Inzucchi SE. Eur J Heart Fail. 2017;19:43–53; 4. Wiviott SD, Raz I, Bonaca MP, et al. N Engl J Med. 2019;380:347-357.

How does management differ for patients with HFpEF?

Generally discuss with or refer to a cardiologist to refine management if HFpEF is suspected or known

Diuretics are important to control fluid balance; to be used carefully at the lowest possible dose

Treatment is largely influenced by the management of associated conditions and symptoms

Use **ACE inhibitors** and **beta-blockers** as required – no need to maximise doses as for HFrEF

- **Diltiazem** and **verapamil** can be considered as an alternative to beta-blockers for rate control
- Low-dose **spironolactone** can be considered to reduce hospitalisation for HF (low level evidence)

Consider **digoxin** and **anticoagulants** if the patient also has AF

ACE, angiotensin converting enzyme; AF, atrial fibrillation; HF, heart failure; HFpEF, HF with preserved ejection fraction; HFrEF, HF with reduced ejection fraction.
1. Ponikowski P, Voors AA, Anker SD, *et al*. Eur J Heart Fail. 2016;18:891–975; 2. NHFA CSANZ Heart Failure Guidelines Working Group. Heart Lung Circ. 2018;27:1123–208; 3. Pitt B, Pfeffer MA, Assmann SF, *et al*. N Engl J Med. 2014;370:1383–92.

Lifestyle changes to consider once heart failure medicines have been initiated

Reduce sodium intake*
(<3 g/day is best; no more than 5 g/day)

- Regular physical exercise as appropriate
- Cardiac rehabilitation

Weight loss if the patient is overweight

Encourage pneumococcal and annual influenza vaccination

- Patients with HF have worse outcomes if they experience these infections

Consume an adequate – but not excessive – amount of fluid daily (e.g. 1.5–2L per day)

Reduce alcohol intake

Stop smoking

* Evidence for the benefit of reducing salt intake is limited in the context of HF, but this modification constitutes part of a healthy overall diet so should be encouraged regardless. HF, heart failure.

1. Ponikowski P, Voors AA, Anker SD, *et al*. Eur J Heart Fail. 2016;18:891–975; 2. NHFA CSANZ Heart Failure Guidelines Working Group. Heart Lung Circ. 2018;27:1123–208; 3. Bhatt AS, DeVore AD, Hernandez AF, *et al*. JACC Heart Fail. 2017;5:194–203

Ongoing review of patients with HF

Just diagnosed? – review at least weekly (more often if clinically indicated);
dial-back frequency as symptoms improve

Adjusting medicine dose? – review after two weeks

- Clinical review: any symptoms (check exercise tolerance), any clinical signs (check weight, blood pressure, heart rate/rhythm, chest auscultation), routine blood tests (e.g. electrolytes and kidney function)
- Some medicine combinations should be monitored closely, e.g. patients receiving an ACE inhibitor + spironolactone may require review one week after initiation or up-titration due to the risk of hyperkalaemia

Stable HF? – clinical review every three to six months

- Consider serial BNP testing in some patients*

Some patients may need more frequent follow-up,
e.g. those who are frail or that are at an increased risk of decompensation

* Particularly if the BNP testing was a good marker for heart failure during diagnosis. See the practice tool for more information.

ACE, angiotensin converting enzyme; BNP, brain natriuretic peptide; HF, heart failure 1. Ponikowski P, Voors AA, Anker SD, *et al*. Eur J Heart Fail. 2016;18:891–975; 2. NHFA CSANZ Heart Failure Guidelines Working Group. Heart Lung Circ. 2018;27:1123–208; 3. Fitchett DH, Udell JA, Inzucchi SE. Eur J Heart Fail. 2017;19:43–53.

Patient self-management of heart failure

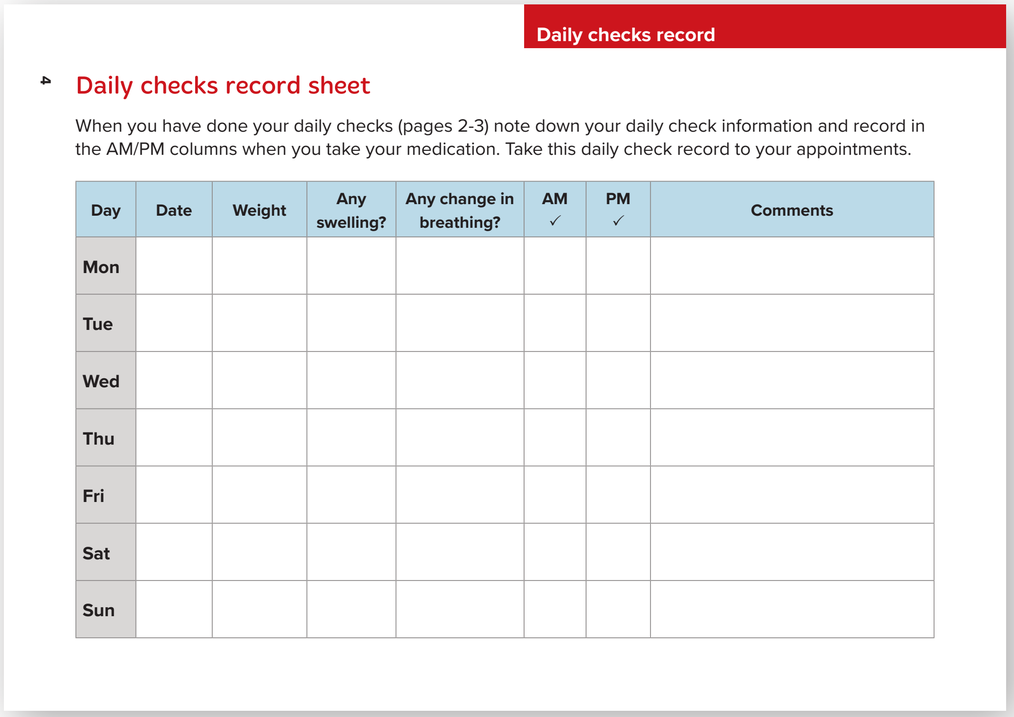
Discuss a heart failure action plan and advise the patient to monitor daily changes in:

- Weight
- Swelling, e.g. in lower legs, fingers, waist
- Breathlessness, incl. at night

This can facilitate:

- Better self-management and adherence to medicines
- Self-adjustments in diuretic dosing
- Prompt identification of worsening heart failure between appointments

For more information on daily checks and the action plan, see: **www.heartfoundation.org.nz/resources/heart-failure-action-plan**



Daily checks record

Daily checks record sheet

When you have done your daily checks (pages 2-3) note down your daily check information and record in the AM/PM columns when you take your medication. Take this daily check record to your appointments.

Day	Date	Weight	Any swelling?	Any change in breathing?	AM ✓	PM ✓	Comments
Mon							
Tue							
Wed							
Thu							
Fri							
Sat							
Sun							

1. NHFA CSANZ Heart Failure Guidelines Working Group. Heart Lung Circ. 2018;27:1123–208;
2. Heart failure – daily checks record. National Heart Foundation of New Zealand. Available at: www.heartfoundation.org.nz/resources/heart-failure-action-plan (accessed Sep, 2019).

Secondary care for heart failure

Cardiologist and/or emergency involvement will likely be required at some stage for most patients with heart failure

Device therapy

- Implantable cardioverter defibrillator (ICD)
- Cardiac resynchronisation therapy (CRT)
- CRT-Defibrillator (CRT-D)

Surgery

- Depending on underlying cardiac pathology
- Heart transplantation, though uncommon, can be highly effective

1. Ponikowski P, Voors AA, Anker SD, *et al*. Eur J Heart Fail. 2016;18:891–975;
2. NHFA CSANZ Heart Failure Guidelines Working Group. Heart Lung Circ. 2018;27:1123–208.

Treatment options for patients with HF (main options)

Symptom relief

Reducing hospitalisation and mortality

Class	Medicine	Usual dose range for HF	Notes
Loop Diuretic	Furosemide	Initially 20–40 mg daily; for resistant oedema, up-titrate in 20–40 mg increments to the min dose that improves symptoms and achieves a weight loss of approximately 1 kg/day with a return to dry body weight; the frequency of up-titration will depend on patient response and the severity of congestion (weekly is common); usual dose range in primary care is 40–240 mg daily	Monitor serum potassium and renal function according to the patients clinical status; usually weekly during titration, then every three months Use alongside fluid restriction (1.5–2L/day)
ACE inhibitors*	Cilazapril	Initially 0.5 mg daily; double dose at intervals of at least 2 weeks if tolerated to 5 mg daily (otherwise use highest tolerated dose)	Generally discontinue potassium-supplements and -sparing diuretics before introducing an ACE inhibitor; however, low dose MRAs may be used for HF if serum potassium is closely monitored Monitor patient response to first dose closely (particularly if taking ≥80 mg furosemide); monitor blood pressure, renal function and serum potassium with every dose increase
	Enalapril	Initially 2.5 mg BD; double dose at intervals of at least 2 weeks to 10 mg BD (or 20 mg once daily) if tolerated (otherwise use highest tolerated dose); higher doses indicated in some patients, e.g. 40 mg daily, for those with co-existing hypertension	
	Quinapril	Initially 2.5 mg BD; double dose at intervals of at least 2 weeks to 10 mg BD (or 20 mg once daily) if tolerated (otherwise use highest tolerated dose); higher doses indicated for some patients, e.g. 40 mg daily, such as for those with co-existing hypertension	
Beta-blocker	Carvedilol	Initially 3.125 mg BD; double dose at intervals of at least 2 weeks if tolerated to 25 mg BD in patients with severe heart failure or body-weight less than 85 kg and 50 mg BD in patients over 85 kg (otherwise use highest tolerated dose)	Use alongside an ACE inhibitor (or ARB) If the patient has an acute fluid overload, initiate use only once the fluid has reduced If a beta-blocker is initiated before an ACE inhibitor, e.g. for arrhythmias or angina without acute fluid overload, the dose should be increased to mid-range and before an ACE inhibitor started Some patients may require slower titration
	Bisoprolol	Initially 1.25 mg daily; double dose at intervals of at least 2 weeks if tolerated to 10 mg daily (otherwise use highest tolerated dose)	
	Metoprolol succinate (MR)	Initially 23.75 mg daily double dose at intervals of at least 2 weeks if tolerated to 190 mg daily (otherwise use highest tolerated dose)	

* The beneficial effect of ACE inhibitor treatment in patients with heart failure is likely a class effect, so other options not listed here can be considered as appropriate, e.g. lisinopril, perindopril.

ACE, angiotensin converting enzyme; ARB, angiotensin II receptor blocker; BD, twice daily; HF, heart failure; MR, modified release; MRA, mineralocorticoid receptor antagonist.

1. Ponikowski P, Voors AA, Anker SD, et al. Eur J Heart Fail. 2016;18:891–975; 2. NHFA CSANZ Heart Failure Guidelines Working Group. Heart Lung Circ. 2018;27:1123–208; 3. NZ Formulary. NZF v87. 2019. Available at: www.nzf.org.nz (Accessed Sep, 2019).

Treatment options for patients with HF (main options)

	Class	Medicine	Usual dose range for HF	Notes
Symptom relief	Loop Diuretic	Furosemide	Initially 20–40 mg daily; for resistant oedema, up-titrate in 20–40 mg increments to the min dose that improves symptoms and achieves a weight loss of approximately 1 kg/day with a return to dry body weight; the frequency of up-titration will depend on patient response and the severity of congestion (weekly is common); usual dose range in primary care is 40–240 mg daily	Monitor serum potassium and renal function according to the patients clini Use
Reducing hospitalisation and mortality	ACE inhibitors*	Cilazapril	Initially 0.5 mg daily; double dose at intervals of at least 2 weeks if tolerated to 5 mg daily (otherwise use highest tolerated dose)	Gen intro if se Mon furos with
		Enalapril	Initially 2.5 mg BD; double dose at intervals of at least 2 weeks to 10 mg BD (or 20 mg once daily) if tolerated (otherwise use highest tolerated dose); higher doses indicated in some patients, e.g. 40 mg daily, for those with co-existing hypertension	
		Quinapril	Initially 2.5 mg BD; double dose at intervals of at least 2 weeks to 10 mg BD (or 20 mg once daily) if tolerated (otherwise use highest tolerated dose); higher doses indicated for some patients, e.g. 40 mg daily, such as for those with co-existing hypertension	
	Beta-blocker	Carvedilol	Initially 3.125 mg BD; double dose at intervals of at least 2 weeks if tolerated to 25 mg BD in patients with severe heart failure or body-weight less than 85 kg and 50 mg BD in patients over 85 kg (otherwise use highest tolerated dose)	Use If the has r If a b angi rang Some patients may require slower titration
		Bisoprolol	Initially 1.25 mg daily; double dose at intervals of at least 2 weeks if tolerated to 10 mg daily (otherwise use highest tolerated dose)	
		Metoprolol succinate (MR)	Initially 23.75 mg daily double dose at intervals of at least 2 weeks if tolerated to 190 mg daily (otherwise use highest tolerated dose)	

For more information on using ACE inhibitors in patient with HF, see: www.saferx.co.nz/assets/Documents/c4aeb520bc/ACE_Inhibitor_titration.pdf

For more information on using beta-blockers in patient with HF, see: www.saferx.co.nz/assets/Documents/771173e260/Beta_blocker_titration.pdf

* The beneficial effect of ACE inhibitor treatment in patients with heart failure is likely a class effect, so other options not listed here can be considered as appropriate, e.g. lisinopril, perindopril.

ACE, angiotensin converting enzyme; ARB, angiotensin II receptor blocker; BD, twice daily; HF, heart failure; MR, modified release; MRA, mineralocorticoid receptor antagonist.

1. Ponikowski P, Voors AA, Anker SD, et al. Eur J Heart Fail. 2016;18:891–975; 2. NHFA CSANZ Heart Failure Guidelines Working Group. Heart Lung Circ. 2018;27:1123–208; 3. NZ Formulary. NZF v87. 2019. Available at: www.nzf.org.nz (Accessed Sep, 2019).

Additional treatment options for patients with HF (to be considered as appropriate)

Symptom relief

Reducing hospitalisation and mortality

Class	Medicine	Usual dose range for HF	Notes
ARB*	**Losartan**	Initially 12.5 mg daily; double dose at intervals of 2 weeks if tolerated to 150 mg daily (otherwise use highest tolerated dose)	To be used if an ACE inhibitor is not tolerated (same monitoring applies)
MRA	**Spironolactone**	Initially 25 mg daily; increased after 4–8 weeks to 50 mg daily if tolerated	Use if patients remain symptomatic despite max tolerated doses of ACE inhibitor/ARB and beta-blocker; consider immediate use in patients with severe symptoms Contraindicated if eGFR <30 mL/min/1.73m^2 Monitor renal function and serum potassium 1–2 weeks after initiating or up-titrating Trial spironolactone before eplerenone†
MRA	**Eplerenone†**	Initially 25 mg daily, increased within 4 weeks to 50 mg daily if tolerated	
ARNI	**Sacubitril + valsartan (Entresto)** Do not use concurrently with an ACE inhibitor or ARB	**If patient is currently taking an ACE inhibitor/ARB:** • Initially 49 mg/51 mg BD for 2–4 weeks; increase if tolerated to 97 mg/103 mg BD; consider starting dose of 24 mg/26 mg if SBP <110 mmHg or patient aged ≥75 years **If patient is not taking an ACE inhibitor/ARB, or stabilised on low doses of either:** • Initially 24 mg/26 mg BD for 2–4 weeks; increase if tolerated to 49 mg/51 mg BD for 2–4 weeks, then increased if tolerated to 97 mg/103 mg BD	Special Authority approval required (valid 12 months); For patients with symptomatic HFrEF <35% that are receiving concomitant optimal standard treatment (maximum tolerated dose of an ACE inhibitor/ARB and beta-blocker with/without an MRA) Initiate ≥36 hours after last dose of ACE inhibitor; or for an ARB when next dose is due
Other options	**Digoxin**	If the patient has AF: 0.75–1.5 mg over 24 hours in divided doses (loading dose); usual maintenance dose 62.5–250 micrograms daily (e.g. according to renal function, clinical response, drug concentration monitoring)	Consider for patients with HF and AF if max tolerated dose of ACE inhibitor/ARB and beta-blocker does not control symptoms
	Anticoagulants, e.g. dabigatran, rivaroxaban, warfarin		Assess need for patients with HF and AF based on CHA_2DS_2-VASc score; see AF update or NZF

* Candesartan is an alternative and equal choice of ARB for managing heart failure (see NZF for more details); † Special Authority approval required. Patients must have a LVEF <40% and be intolerant to optimal dosing of spironolactone or have experienced a clinically significant adverse effect while on an optimal dose of spironolactone.

1. Ponikowski P, Voors AA, Anker SD, *et al.* Eur J Heart Fail. 2016;18:891–975; 2. NHFA CSANZ Heart Failure Guidelines Working Group. Heart Lung Circ. 2018;27:1123–208; 3. NZ Formulary. NZF v87. 2019. Available at: www.nzf.org.nz (Accessed Sep, 2019).