HEART FAILURE | DABIGATRAN | SMOKING CESSATION IN PREGNANCY

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Heart failure in primary care

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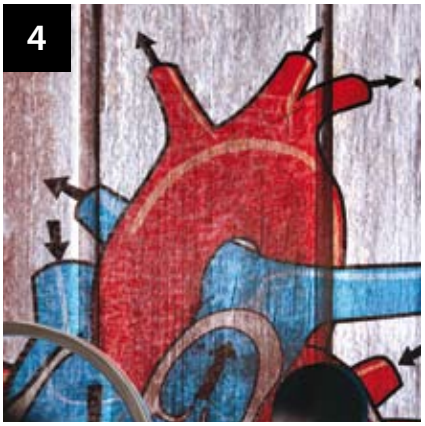

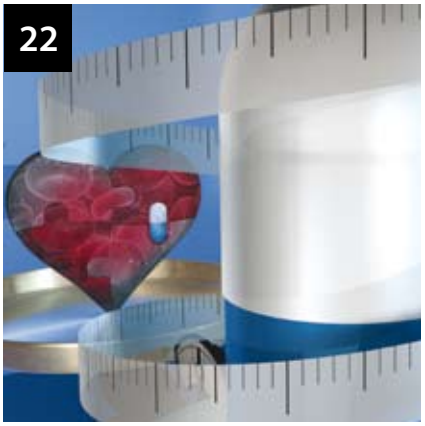

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Welcome to the 50th edition of Best Practice Journal

THIS MONTH MARKS OUR 50TH EDITION OF BEST PRACTICE JOURNAL. The Journal was first published in October 2006, and since then we have covered over 200 topics and sent out over 400 000 copies of the Journal. We currently distribute printed copies of Best Practice Journal to over 8000 General Practitioners, Nurse Practitioners, Practice Nurses, Community Pharmacists and Maori and Pacific health providers around New Zealand. The bpac^{nz} website, which contains online versions of Best Practice Journal, delivers over 100 000 page views each month.

We have an excellent in-house team of writers, clinicians, analysts and designers, along with the editorial staff, who all work tirelessly to produce eight editions of Best Practice Journal each year.

We are also grateful for the assistance of our external colleagues ("expert reviewers") and clinical advisory group who help to ensure that our content is clinically accurate and reflective of healthcare practice in New Zealand.

Finally, we thank you, our readers, for your ongoing support and endorsement.

"Today was good. Today was fun. Tomorrow is another one."
– DR SEUSS

REMINDER

It is now **time** to **change** your patient's **diabetes meter**

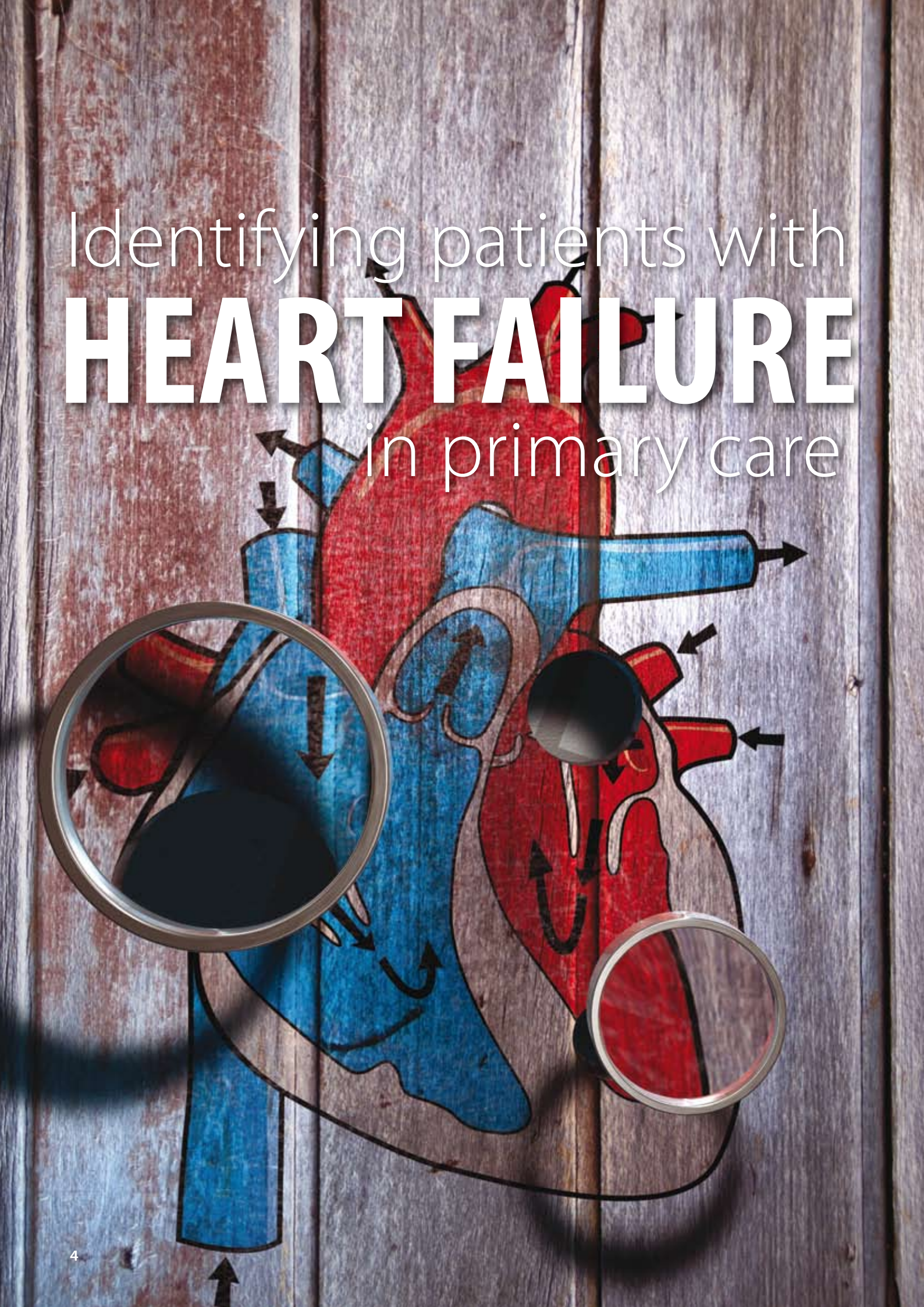
Contact information

Free phone help line for health professionals and to order sample meters – **0508 CARESENS** (0508 2273 7367)
Free phone help line for patients – **0800 GLUCOSE** (0800 458 2673)
CareSens information online – **www.caresens.co.nz**
Details of funding changes, seminars and general information – **www.pharmac.govt.nz**

See www.bpac.org.nz for a full version of this information sheet

Key dates for changes to diabetes management products

- 1 September 2012 – CareSens range of blood glucose meters and testing strips listed on the Pharmaceutical Schedule
- 1 December 2012 – CareSens range of blood glucose meters now the only meters subsidised
- **1 March 2013 – only CareSens range of testing strips will be subsidised**



Identifying patients with HEART FAILURE in primary care

Heart failure is now described as either heart failure with reduced ejection fraction (HF-REF) or heart failure with preserved ejection fraction (HF-PEF). Identifying people with suspected heart failure in primary care is often based on the patient's presenting symptoms and signs. Ideally, a formal diagnosis should always be made with echocardiography, however, referring every patient with suspected heart failure is likely to be impractical, given resource limitations. Other investigations such as BNP and ECG can assist in making a diagnosis.

Getting to the heart of the matter

In developed countries the prevalence of heart failure among adults is approximately 1–2%, although the prevalence may be more than 10% among older adults (≥ 70 years).[1] A typical primary care clinician, caring for 2000 patients, is therefore likely to have approximately 40 patients with heart failure, and more if their patient population is older.[2] In addition, approximately five patients will be newly diagnosed with heart failure each year and the condition suspected in three times as many patients as this.[1] The number of people with heart failure will inevitably increase in New Zealand in the future. This is attributed to people living longer, more effective treatments for coronary heart disease and a reduction in mortality from acute coronary events.[3, 4] An increase in prevalence of cardiovascular risk factors such as diabetes and obesity is also contributing to the increasing prevalence of heart failure.[5]

People with heart failure often have a reduction in quality of life, require frequent hospital admissions and have a poor prognosis. Although there have been improvements in the clinical outcomes for patients over the last two decades, such as fewer admissions, a reduced length of hospital stay and longer survival out of hospital, mortality from heart failure remains high.[6, 7] In the first year after diagnosis, 30 – 40% of patients die, however, this decreases to 10% per year thereafter.[7]

Mortality rates are highest for patients who have heart failure associated with an acute myocardial infarction or arrhythmia, those who are hypotensive (i.e. in cardiogenic shock), those with more severe symptoms (NYHA Class IV, Page 11) and patients who have repeated hospitalisations for heart failure.[8,9]

There is some evidence that heart failure is likely to affect males more than females, although females with heart failure are more likely to:[3, 10]

- Be older than males when they develop heart failure
- Have heart failure with a preserved ejection fraction (Page 7)
- Live longer than males with heart failure
- Have more pronounced symptoms of heart failure than males

Defining heart failure

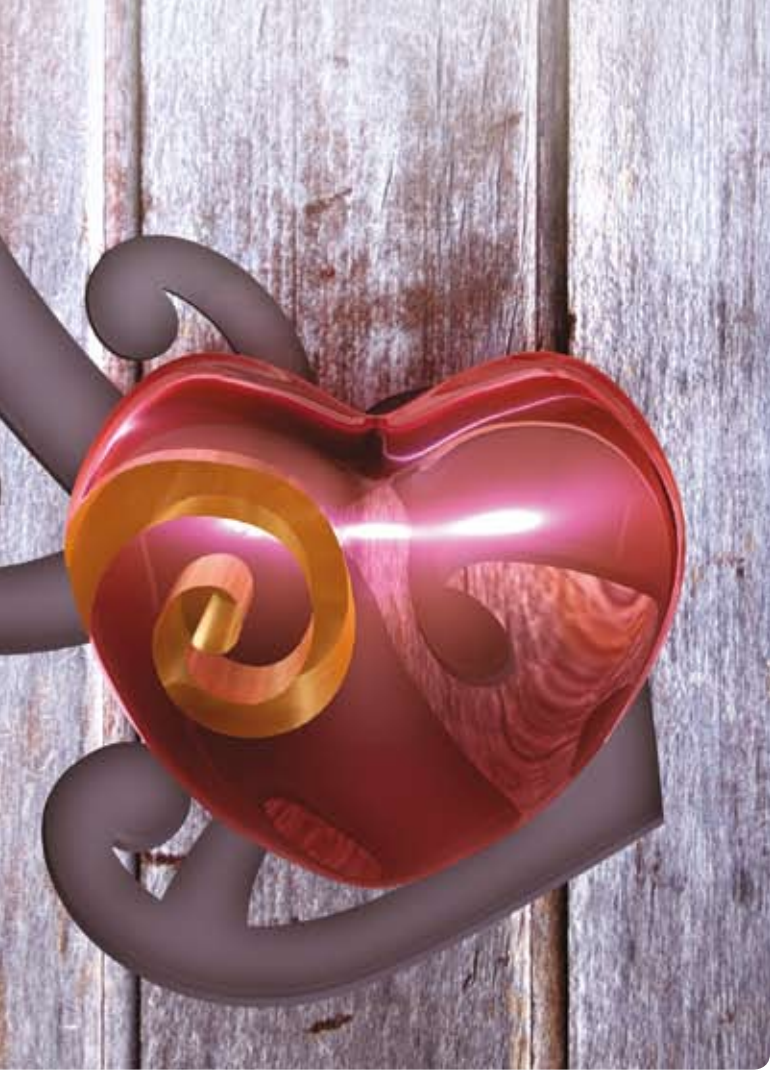
Heart failure can be defined as an abnormality of the structure or function of the heart that leads to a failure of the heart to deliver sufficient oxygen to the metabolising tissues (or when the heart can only do so with elevated diastolic filling pressures).[1] Compensatory mechanisms, e.g. an increase in heart rate, cardiac muscle mass, cardiac filling pressures and blood volume, work to maintain the ability of the heart to pump effectively, however, over time the heart progressively fails.

Heart failure can be regarded as a complex clinical syndrome with typical symptoms and signs that develops as a result of a large number of diverse cardiac and non-cardiac abnormalities.[14] There are multiple risk factors for heart failure, which include:[5, 14, 15]

- Coronary heart disease – ischaemic heart disease (IHD) leading primarily to left ventricular dysfunction; the most significant risk factor for heart failure in developed countries

Ethnic disparities in morbidity and mortality from heart failure in New Zealand

The mortality rate from heart failure for Māori aged over 65 years in New Zealand is significantly higher than for non-Māori for both males and females (RR 2.80 for males; RR 1.70 for females).[11] Rates of hospitalisation for heart failure amongst Māori in this age group are also significantly higher than for non-Māori (RR 4.73 for males; RR 4.85 for females).[11] It is reported that the differences between mortality rates from heart failure between Māori and non-Māori are even more pronounced in younger age groups (45 – 65 years), and heart failure occurs approximately 10 – 15 years earlier in Māori compared to non-Māori. Māori are significantly younger on admission to hospital for heart failure than New Zealand Europeans (age 62 compared to age 78 years).[12] Morbidity and mortality from heart failure for Pacific peoples is approximately twice as high compared to the total population.[13]



- Hypertension – 75% of patients with heart failure have a history of hypertension[16]
- Valvular heart disease, including valvular damage from rheumatic fever
- Abnormalities of rhythm (e.g. atrial fibrillation) or conduction (e.g. left bundle branch block)
- Cardiomyopathy, e.g. idiopathic, viral, alcoholic, toxic, peripartum
- Diabetes – independent risk factor for coronary heart disease but also increases the risk of heart failure directly
- Male gender
- Excessive alcohol use – increasing cardiovascular risk and as a direct cardiotoxin
- Smoking – increasing cardiovascular risk and as a direct cardiotoxin
- Obesity – increasing cardiovascular risk and an independent risk factor
- Dyslipidaemia
- Respiratory conditions, e.g. COPD, obstructive sleep apnoea
- Thyroid disorders – both hypo- and hyperthyroidism
- Medicines e.g. NSAIDs, pioglitazone (see Box below)
- Cardiotoxins e.g. chemotherapy medicines, cocaine
- Infections or inflammation – leading to myocarditis or cardiomyopathy
- Congenital heart disease

Medicines that can worsen heart failure

Medicines that may worsen heart failure in symptomatic patients include:[1]

- NSAIDs including COX-2 inhibitors because they may cause renal impairment and sodium and water retention
- Pioglitazone due to dose related fluid retention
- Most calcium channel blockers in patients with HF-REF (with the exception of amlodipine and felodipine) due to their negative inotropic effect
- The combination of an ACE inhibitor AND an angiotensin-II receptor blocker (ARB) AND a mineralcorticoid antagonist (e.g. spironolactone) because this combination can worsen renal function which in turn may render loop diuretics ineffective and cause hypokalaemia or hyperkalaemia

Heart failure with reduced or preserved ejection fraction

Heart failure has, in the past, been predominately thought of in terms of systolic dysfunction of the left ventricle, i.e. a reduction in left ventricular ejection fraction. Clinical trials, however, have found that left ventricular failure can develop in patients who have an essentially normal ejection fraction and that this is a separate clinical syndrome.[17] This has led to the adoption of the terms **heart failure with reduced ejection fraction (HF-REF,** previously referred to as systolic heart failure) and **heart failure with preserved ejection fraction (HF-PEF**, previously referred to as diastolic heart failure). Although, the terms systolic and diastolic heart failure remain in use in the literature there is now a preference for the terms HF-REF and HF-PEF.[1,17] Up to 50% of people with symptoms and signs of heart failure have been shown to have preserved or relatively preserved (≥45 – 50%) left ventricular ejection fraction.[8, 17] The underlying causative conditions and the treatment of each type of heart failure differ.

Heart failure with reduced ejection fraction (HF-REF) – i.e. impaired left ventricular systolic function, is typically seen in patients with structural heart disease, e.g. ischaemic heart disease.[17] Many other causative factors may contribute to HF-REF, including hypertension, diabetes and idiopathic dilated cardiomyopathy.[1]

The majority of research into effective, evidence-based treatment strategies for heart failure has been based on patients who have HF-REF.

Heart failure with preserved ejection fraction (HF-PEF) – i.e. impaired diastolic function (such as impaired diastolic relaxation and filling due to stiffening of the ventricles) is more frequently seen in older people, females and people who are obese. People with HF-PEF are also more likely to have atrial fibrillation and to be more hypertensive.[8, 17] In addition, other underlying causes include constrictive pericarditis or cardiomyopathy, hypertrophic cardiomyopathy and restrictive cardiomyopathy, e.g. from amyloidosis or sarcoidosis.

Making a diagnosis

Identifying people with suspected heart failure in primary care is often based on the patient's presenting symptoms and signs.[18] Ideally a formal diagnosis should always be made with echocardiography, however, availability of services may be a barrier in some areas.

Diagnosis of heart failure (adapted from ESC)[1]

HF-REF – To make a diagnosis of HF-REF the patient must have:

1. Symptoms typical of heart failure
2. Signs typical of heart failure
3. Evidence of reduced left ventricular ejection fraction on echocardiography

HF-PEF – To make a diagnosis of HF-PEF the patient must have:

1. Symptoms typical of heart failure
2. Signs typical of heart failure
3. Normal or only mildly reduced left ventricular ejection fraction and no left ventricular dilatation
4. Relevant structural heart disease such as left ventricular hypertrophy or left atrial enlargement and/or diastolic dysfunction

Making a diagnosis of HF-PEF is essentially one of exclusion after other potential non-cardiac causes for the patient's symptoms, e.g. anaemia, respiratory disease, are ruled out.[1]

Symptoms and signs of heart failure

Patients with heart failure present with a variable combination of symptoms and signs (Table 1, over page), each of which influence the level of clinical suspicion and help guide the investigations and initial management. Patients may present (either as a first presentation or with a known history of heart failure) with a sudden onset of acute symptoms consistent with heart failure or have symptoms that have developed more gradually.

Symptoms typically include dyspnoea, orthopnoea, fatigue, reduced exercise tolerance and ankle oedema, however, many of the symptoms are not necessarily specific to heart failure and vary with the acuteness of the condition.[3] The significance of symptoms and signs may be more difficult to interpret in people who are older, obese or those with co-morbidities such as chronic obstructive pulmonary disease (COPD).

Peripheral oedema is a non-specific symptom that may be seen frequently but can be due to other reasons such as varicose veins, medicines (e.g. calcium channel blockers) or decreased mobility. Crepitations in the chest on auscultation

Table 1: Symptoms and signs of heart failure[1]

Symptoms	
Typical	**Less typical**
■ Dyspnoea – progressing in severity from dyspnoea on exertion, to dyspnoea at rest ■ Orthopnoea ■ Paroxysmal nocturnal dyspnoea ■ Reduced exercise tolerance ■ Fatigue, weakness, more time needed to recover after exercise ■ Ankle oedema	■ Nocturnal cough ■ Wheezing ■ Weight gain of > 2kg/ week (although weight loss in severe heart failure) ■ Bloated feeling ■ Anorexia, nausea ■ Cerebral symptoms secondary to reduced cardiac output, e.g. confusion, anxiety, memory impairment, headaches, insomnia ■ Depression ■ Palpitations, chest pain or pressure ■ Syncope
Signs	
More specific	**Less specific**
■ Elevated jugular venous pressure ■ Prolonged hepatojugular reflux (distension of the neck veins with application of pressure to the liver) ■ Third heart sound (gallop rhythm) ■ Lateral displacement of the apex beat ■ Cardiac murmur	■ Peripheral oedema of the ankles, sacrum or scrotum ■ Crepitations on auscultation of the chest ■ Decreased air entry and dullness to percussion at the lung bases (pleural effusion) ■ Tachycardia ■ Irregular pulse ■ Tachpnoea (> 16 breaths/ min) ■ Hepatomegaly (with ascites in patients with severe heart failure) ■ Cachexia – in patients with long-term heart failure

are also a non-specific sign and may confound the presentation, especially if the patient has an existing respiratory condition. The presence of orthopnoea and paroxysmal nocturnal dyspnoea are more specific symptoms of heart failure but are less often reported at presentation and tend to be associated with more severe heart failure.[1] Clinical signs that are more specific to heart failure, e.g. increased jugular venous pressure and displacement of the apex beat, can be difficult signs to detect accurately.[1] These factors, therefore, can make a clinical diagnosis of heart failure difficult, particularly in a primary care setting.

Echocardiography is the gold standard investigation

Depending on the findings from history and examination, a number of investigations may be required in a patient with suspected heart failure (Table 2). Some tests may support or rule out a clinical suspicion, other investigations are required for identification of a reversible cause, e.g. thyroid dysfunction, and for ongoing monitoring of the patient's progress and medicine use.

Ideally all patients with suspected heart failure require echocardiography for an accurate diagnosis to be made. Referring every patient with suspected heart failure, however, is likely to be impractical, given resource limitations. To help identify which symptomatic patients require echocardiography, use the results from an ECG and brain natriuretic peptide (BNP) test – patients with either an abnormal ECG or an increased BNP level are likely to have heart failure and require referral for echocardiography.[1] Guidance from NICE suggests that the timeframe required for further assessment with echocardiogram is within two weeks if the patient has a history of a previous myocardial infarction (MI) and an elevated BNP, and within six weeks if there is no history of MI and a moderately raised BNP.[7]

The role of BNP in the diagnosis of heart failure

Laboratory assessment of BNP or N-terminal pro-BNP (NT-proBNP), depending on the laboratory, may provide additional information for some patients, where the diagnosis is uncertain. If BNP is normal (<30 pmol/L), a diagnosis of heart failure is unlikely.[20] The cut-off values in patients presenting with a more gradual onset of symptoms may be lower.[1] Laboratories around New Zealand differ in their recommendations for cut-off values for using BNP or NT ProBNP for diagnosing heart failure, therefore it is best to check with your local laboratory or discuss the results with a clinical biochemist. Table 3, over page, gives an example of cut-off values.

Table 2: Investigations for diagnosis and monitoring of patients with heart failure[1]

Investigation	Comment
Echocardiography and Doppler	The gold standard test for heart failure that ideally should be used in every patient with suspected heart failure. Ventricular and valvular function can be assessed. Echocardiography can confirm a diagnosis of heart failure, can distinguish between HF-REF and HF-PEF and guide management options. An echocardiogram is also often useful if the patient has unexplained symptoms of shortness of breath or fatigue. Echocardiography is also used to follow a patient's progress once treatment is initiated. It can provide a sequential assessment of the response to treatment, of ejection fractions, left atrial remodelling and filling pressures. Echocardiography can also be used to assess for dyssynchrony for cardiac resynchronisation therapy (CRT).
Brain natriuretic peptide (BNP) or NT-proBNP*	BNP is most useful in ruling out heart failure in a patient with an atypical presentation or a patient with respiratory co-morbidities. BNP is released from the cardiac ventricles in response to increases in ventricular volume and pressures. BNP is regarded as a good "rule out test" for heart failure, but should be interpreted in view of the clinical features of the patient. BNP cannot be used to differentiate between HF-REF and HF-PEF. BNP can also be useful for monitoring treatment and has prognostic implications – high levels are associated with a poorer prognosis.
Electrocardiography (ECG)	Long-term left ventricular dysfunction will usually result in left atrial enlargement and left ventricular hypertrophy which will be apparent on ECG. If an ECG is normal this usually rules out heart failure. If there is uncertainty, consider discussing the interpretation of the ECG with a cardiologist. An ECG is useful for assessing other cardiac pathology, e.g. arrhythmia, cardiac ischaemia which may cause or aggravate heart failure.
Chest x-ray (CXR)	A CXR is most useful in a patient who is acutely unwell with pulmonary oedema. In primary care, a CXR is generally of limited value but can show enlargement of the heart and pulmonary congestion, and help assess possible alternative respiratory causes of dyspnoea.
Spirometry	This may be helpful to assess respiratory causes of dyspnoea but does not assist in the diagnosis of heart failure.
Full blood count (FBC)	Severe anaemia may cause or aggravate heart failure. Rarely, a raised white cell count may indicate infection as a possible precipitating cause of acute heart failure.
Thyroid function	Hyperthyroidism or hypothyroidism can precipitate heart failure and are potentially reversible forms of heart failure.
Renal function	An assessment of renal function is important to provide a baseline prior to treatment, to guide medicine choice and to monitor changes once treatment is initiated, especially if the patient is prescribed diuretics or angiotensin-converting enzyme (ACE) inhibitors.
Liver function tests	Elevated liver enzymes may indicate hepatic congestion associated with heart failure. Acute hepatic venous congestion can increase bilirubin levels and in some patients cause jaundice. Abnormal LFTs usually resolve with successful treatment of heart failure. Patients with long term heart failure may have low albumin levels as a result of decreased albumin synthesis which may in turn aggravate fluid retention.
Other tests	HbA_{1c} and lipids should be requested as part of a cardiovascular work-up depending on the patient's cardiovascular risk. Consider troponin to investigate cardiac ischaemia in a patient where symptoms are atypical or presentation has been delayed. N.B. if symptoms and ECG findings are suggestive of MI, immediate referral to secondary care is recommended.
Other secondary care investigations	Other investigations that may be requested, usually in secondary care, include tests such as stress echocardiography, nuclear perfusion scan, cardiac catheter, cardiac MRI or CT angiogram and rarely, cardiac biopsy, and genetic testing in patients with a family history of cardiomyopathy.

* Depending on the laboratory, BNP or N-terminal pro-BNP (NT-proBNP) may be measured. The normal ranges for each test are different (although provide similar information) and may also vary between laboratories. BNP can be affected by factors such as age, gender, obesity and renal impairment.

Table 3: Suggested cut-off values for BNP in the diagnosis of heart failure[20]

	Heart failure unlikely (rule out test)	Heart failure likely (rule in test)
BNP	< 30 pmol/L (approximately < 100 pg/mL)	>145 pmol/L (approximately > 500 pg/mL)
NT-proBNP	< 35 pmol/L (approximately < 300 pg/mL)	■ Age <50 years – > 50 pmol/L (> 450 pg/mL) ■ Age 50–70 years – >100 pmol/L (> 900 pg/mL) ■ Age > 75 years – > 210 pmol/L (> 1800 pg/mL)

Notes:
For indeterminate values, e.g. BNP > 30 pmol/L but < 145 pmol/L, clinical assessment is the key factor for interpretation
To covert BNP from pmol/L to pg/mL, multiply by 3.47
To convert NT-ProBNP from pmol/L to pg/mL, multiply by 8.46

The MICE rule[2,19]

The MICE rule is a clinical decision rule for use in primary care, developed in the United Kingdom because of concerns about the accuracy and lack of sensitivity of ECG and BNP for diagnosing heart failure.[2,19] This rule relies on the use of a number of clinical features to increase the diagnostic value of BNP and therefore to guide decisions about the need for referral for echocardiography.

The clinical features are:[19]

- **M**ale gender
- **I**nfarction (history of myocardial infarction)
- **C**repitations (basal crepitations on auscultation)
- **E**dema (peripheral oedema)

Symptomatic patients, who have either crepitations or a history of a previous myocardial infarction, or are male and have ankle oedema should be referred for echocardiography without the need for a BNP. For all other patients, arrange a BNP test and refer for echocardiography depending on the results of the BNP test.

Studies are underway to validate the use of this clinical rule in primary care.[19]

Other conditions can also increase BNP, e.g. myocardial ischaemia, atrial fibrillation, therefore a raised BNP does not necessarily mean that heart failure is the only, or even the main, cause of the patient's symptoms.

A clinical decision tool has been developed that incorporates the use of BNP and the patient's clinical features to help guide diagnosis and referral for echocardiography (see "The MICE rule").[2, 19]

Differential diagnosis of heart failure

Symptoms that may be suggestive of heart failure, e.g. dyspnoea can be caused by conditions other than heart failure. These include:

- Non-cardiac causes of dyspnoea such as respiratory infections, COPD, pulmonary embolism, adult respiratory distress syndrome
- Other cardiac causes such as myocardial ischaemia, atrial fibrillation, pericardial disease

Functional classification of heart failure

People with heart failure can be classified into functional groups depending on the amount of exertion needed to bring on symptoms such as dyspnoea, fatigue and palpitations (Table 4).

A functional assessment can be useful in people with an established diagnosis of heart failure but it is not disease-specific and does not help make a formal diagnosis. Although

this type of functional classification is often used to select patients for clinical trials, it does not group patients in terms of the cause of the heart failure or take into account any underlying abnormalities of the heart that may contribute to heart failure. Its value in primary care is that the classes (as they increase) are associated with a worsening prognosis. Patients, however, may move between classes, e.g. they may present acutely unwell (Class IV) but after treatment become asymptomatic (Class I), or a stable patient with mild symptoms (Class II) may have a sudden onset of dyspnoea at rest due to arrhythmia (Class IV).[1, 2, 21]

This form of classification for heart failure is also subject to other limitations such as variability between clinicians in detecting clinical signs and interpretation of terms such as "ordinary", "slight" and "marked".

Table 4: New York Heart Association functional classification of heart failure[1, 3]

Class I	Asymptomatic – no limitation of physical activity. The patient does not develop undue dyspnoea, fatigue or palpitations with ordinary physical activity
Class II	Mild symptoms – slight limitation of physical activity. The patient is comfortable at rest, but develops dyspnoea, fatigue or palpitations with ordinary physical activity
Class III	Moderate symptoms – marked limitation of physical activity. The patient is comfortable at rest, but develops dyspnoea, fatigue or palpitations with less than ordinary physical activity
Class IV	Severe symptoms – unable to do any physical activity without discomfort. The patient may have symptoms at rest and if any physical activity is undertaken, the level of discomfort is increased

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The importance of primary prevention

Cardiovascular risk assessment may help identify people who are at risk of heart failure. Identification and treatment of patients with hypertension, diabetes, dyslipidaemia and encouraging smoking cessation is important for prevention of ischaemic cardiovascular disease and therefore also to minimise the risk of development and progression of heart failure.[22] In some older people, however, heart failure can still develop due to age-related cardiovascular changes alone.[5]

Factors that significantly increase the risk of heart failure include older age, a history of IHD or valvular heart disease, long-term hypertension or diabetes, presence of left ventricular hypertrophy on ECG or cardiomegaly on chest x-ray. Family history of cardiovascular disease or diabetes also increases the risk of underlying conditions which can cause heart failure. Currently routine screening of at-risk patients for asymptomatic left ventricular (LV) dysfunction is not recommended primarily because there is no widely available, cost effective and safe screening test.[22]

For patients with known LV dysfunction who are asymptomatic (Class I) but at high risk of heart failure, managing risk factors may slow progression to symptomatic heart failure.[22]

Ensure that:

- Hypertension, if present, is treated, e.g. with an ACE inhibitor
- Hyperlipidaemia, if present, is treated
- Smoking cessation is encouraged
- Regular exercise is encouraged
- The patient is aware of safe levels of alcohol intake
- Medicines or other drugs that can precipitate heart failure are avoided

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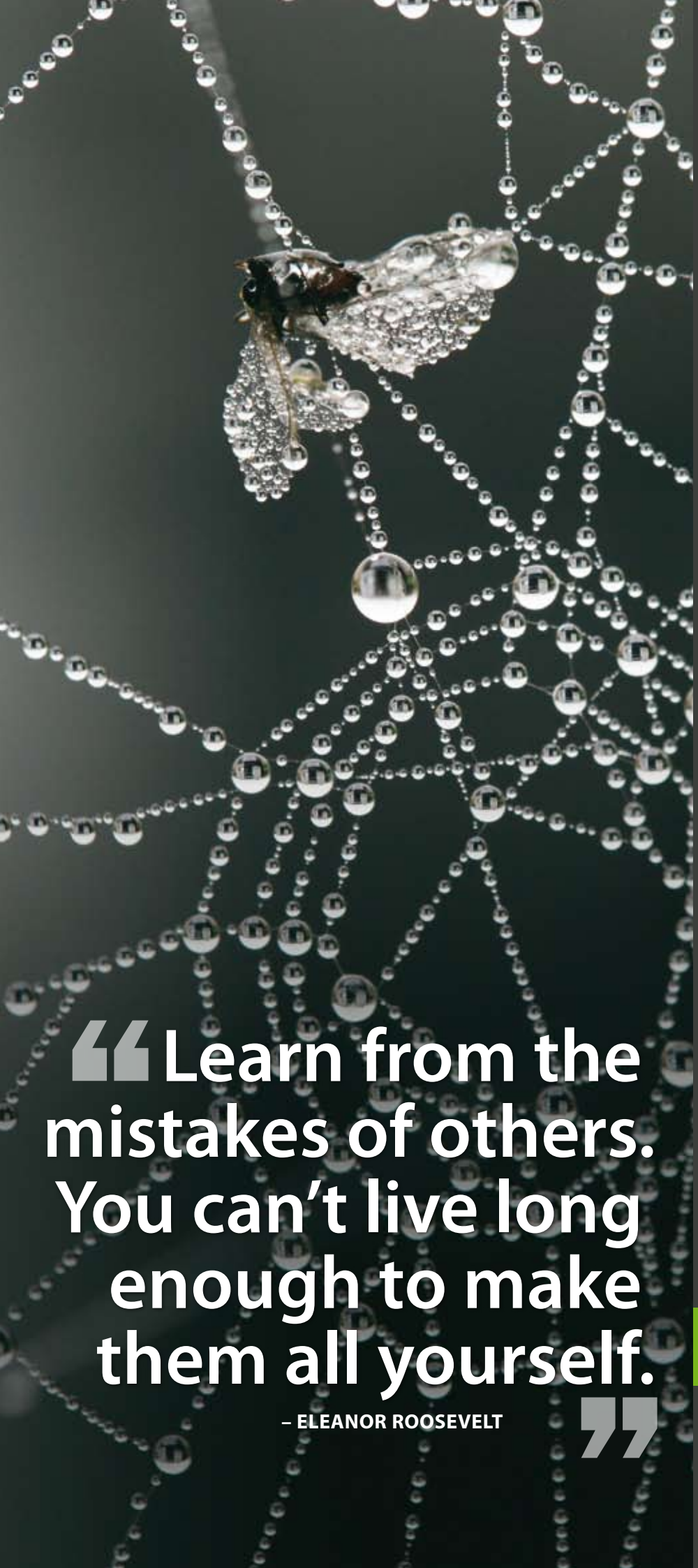

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– ELEANOR ROOSEVELT

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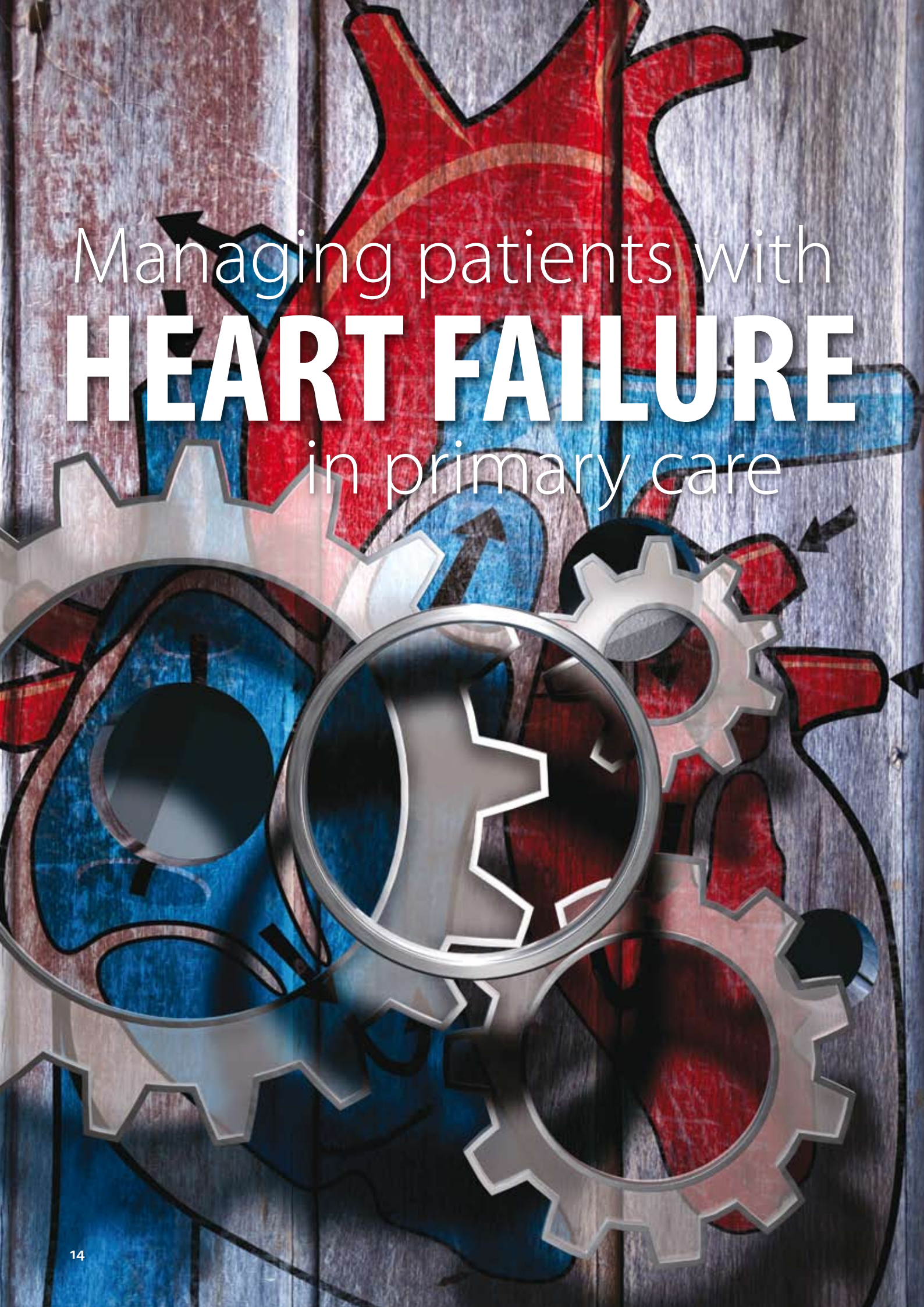


Managing patients with HEART FAILURE in primary care

Once heart failure has been diagnosed, the goal of treatment is to improve symptoms and signs and avoid or reduce hospital admissions. In the majority of patients with symptomatic heart failure, a diuretic is used first-line to reduce fluid overload. An ACE inhibitor and beta-blocker are then added, followed by spironolactone if the patient is still symptomatic. An angiotensin-II receptor blocker, digoxin and anticoagulants can be added as appropriate. Surgical interventions may be considered for some patients.

The general principles of management

The goal of pharmacological treatment in patients with heart failure is to improve symptoms and signs, decrease hospital admission (particularly for patients with established heart failure) and improve longevity. The initial aim of pharmacological treatment is to relieve symptoms. Medicines should then be up-titrated to doses that will improve long-term clinical outcomes by slowing or preventing progressive deterioration of heart failure.[1]

Management of patients with suspected heart failure

Patients who present with an acute onset of significant symptoms suggestive of a new diagnosis of heart failure usually require referral for hospital admission, especially if the patient has a history of ischaemic heart disease (IHD). Some people may present with a more gradual onset of symptoms and the findings from the history, examination, and in some cases brain natriuretic peptide (BNP) test results, will help guide the need for community or hospital management.

Management of patients with known chronic heart failure

Patients with known heart failure who present with symptoms reflecting a gradual deterioration of a previously stable situation are generally able to be managed in the community. Patients who have an established diagnosis of heart failure may also present acutely due to decompensation (see "Decompensation in a previously stable, compensated patient", over page). Although many of these patients are admitted to hospital, primarily for intravenous diuretics, there is increasing agreement among clinicians that community management may be appropriate for some patients who are at lower risk, determined by their clinical features, the results of investigations, e.g. BNP, the presence of co-morbidities and their social circumstances.[2,3] Repeated hospitalisations in a patient with heart failure are associated with a poorer prognosis.[4]

Treatment of patients with heart failure with reduced ejection fraction: HF-REF

1. Start with a diuretic

In the majority of patients with symptomatic heart failure, the first-line medicine used is a **diuretic**, which will work to reduce fluid overload to improve the patient's symptoms, however, there is no evidence that diuretics improve mortality.[1]

A loop diuretic such as furosemide is recommended as these are usually more effective than thiazide diuretics. A reasonable starting dose of oral furosemide for a patient in a community setting is 20 – 40 mg, once daily. Subsequent doses are then determined by the response to treatment – an improvement in symptoms and a weight loss of approximately 1.0 kg/day. Bumetanide (fully subsidised) is an alternative for patients who do not respond to adequate doses of furosemide. The recommended starting dose for oedema is 0.5 – 1 mg, once daily. In severe cases, the dose may be increased up to 5 mg per day.[7]

Decompensation in a previously stable, compensated patient

Episodes of decompensation leading to acute heart failure can occur in patients with known heart failure who have been well and stable on treatment. Some patients, despite treatment, are prone to recurrent episodes of decompensation. A number of factors can result in decompensation including:[1]

- Alterations to the patient's medicine regimen, e.g. reduction in dose of diuretic, addition of a new medicine – including over-the-counter items
- Poor adherence to medicines
- Uncontrolled hypertension
- Cardiac arrhythmia (most often atrial fibrillation)
- Changes in diet (primarily affecting sodium) and fluid intake
- Changes in exercise levels
- Cardiac ischaemia
- Systemic infection (secondary to increased haemodynamic demand on the heart)
- Cardiac infection or inflammation
- Conditions that result in a high-output state, e.g. severe anaemia, thyrotoxicosis, multiple myeloma, pregnancy, cor pulmonale
- Physical or mental exhaustion, e.g. from prolonged travel, an emotional crisis

Doses of diuretic that are too low will not clear the fluid overload effectively, and may reduce the patient's response to an ACE inhibitor when started and also can increase the risk of decompensation when a beta-blocker is initiated. Doses that are too high may lead to removal of too much fluid, which increases the risk of hypotension and renal impairment, particularly when an ACE inhibitor is started.

2. Add an ACE inhibitor and beta-blocker

The next step after the use of a diuretic is the addition of an **ACE inhibitor** (or an angiotensin-II receptor blocker – ARB) to reduce symptoms and a **beta-blocker** to improve ventricular function. There is good evidence that ACE inhibitors and beta-blockers improve both morbidity and mortality for patients with HF-REF.[1]

Guidelines vary as to which of these medicines should be initiated first as they are regarded as complementary.[1, 8] If a patient has acute fluid overload, a beta-blocker may not be tolerated until the fluid is reduced, although an ACE inhibitor can be initiated. Ideally both should be started as soon as practical after a diagnosis of HF-REF is made, with an aim of achieving an ejection fraction of > 40% as this is associated with improved prognosis. ACE inhibitors assist with LV re-modelling and beta-blockers can markedly improve the ejection fraction.[1]

Any medicine from the ACE inhibitor class can be used, e.g. cilazapril. ACE inhibitors tend to give effective control of blood pressure and are generally well tolerated. If postural hypotension or other adverse effects occur, this is usually at low doses and increasing the dose does not tend to significantly change the incidence or severity of adverse effects. Initiation of an ACE inhibitor may result in an increase in potassium and creatinine. If the potassium is < 5.5 mmol/L and the increase in creatinine is no more than 50% above baseline, these changes are acceptable. If potassium or creatinine rises excessively, reduce the dose of the diuretic if there are no signs of congestion and stop nephrotoxic medicines such as NSAIDs. If potassium or creatinine remain raised, the dose of ACE inhibitor should be halved and the creatinine and electrolytes checked in one to two weeks. Discussion with a cardiologist is recommended as the ACE inhibitor may need to be stopped.[1,9]

N.B. Guidelines for use of ACE inhibitors in people with chronic kidney disease take a more conservative approach and suggest altering the dose of ACE inhibitor if creatinine rises > 30%.[10]

If an ACE inhibitor is not tolerated, an ARB can be substituted. Losartan is the only fully subsidised ARB available. Candesartan

is available under Special Authority (criteria are persistent ACE-inhibitor induced cough, history of angioedema or inadequate control on maximum tolerated dose of ACE inhibitor). Adverse effects from ARBs are usually mild and transient but may include headache, dizziness and gastrointestinal effects.

Beta-blockers approved for use in New Zealand for heart failure include metoprolol, carvedilol, and bisoprolol (see "Bisoprolol – newly funded beta-blocker"). There is no clear evidence that any one of these medicines is superior to another, but specific patient factors may guide the choice.[11] For example, bisoprolol and metoprolol CR are once daily dosing, which may be more convenient for some patients. Bisoprolol may be preferable in patients with atrial fibrillation as it reduces heart rate more than other beta-blockers, but it also increases susceptibility to bradycardia. Bisoprolol may be preferable in people with COPD compared to carvedilol as it is more cardio-selective.

When initiating a beta-blocker the recommendation is to start at a low dose, increase slowly and aim for the highest tolerated dose ("go slow, aim high"). If a beta-blocker is initiated before an ACE inhibitor, e.g. in a patient with arrhythmia or angina but without acute fluid overload, the dose should be increased to mid-range and then an ACE inhibitor started.

3. Add spironolactone if still symptomatic

The use of **spironolactone** (the only subsidised aldosterone receptor antagonist), is recommended for patients who remain symptomatic, or who have an ejection fraction < 35%, despite maximal doses of an ACE inhibitor and a beta-blocker. If the patient's LV function has improved somewhat with the use of an ACE inhibitor and beta-blocker, spironolactone may not be required, however, consultation with a cardiologist and referral for echocardiography is recommended. Spironolactone has been shown to reduce both morbidity and mortality in patients with heart failure. Spironolactone should be used with caution in patients with impaired renal function and may cause hyperkalaemia. Renal function and electrolytes should therefore be monitored regularly. Other adverse effects may include gastrointestinal symptoms such as nausea and diarrhoea.[7]

For further information see: "Drug monitoring – Monitoring diuretics in primary care", Best Tests (Mar, 2009).

4. Add ARB, digoxin and anticoagulants as appropriate

If the patient has failed to respond to treatment with maximal doses of all these medicines, an **ARB** may be considered. However, spironolactone would not usually be continued if

Bisoprolol – newly funded beta-blocker

Bisoprolol, a beta-blocker that is a highly selective for beta-1 receptor sites, has been fully subsidised in New Zealand since 1 May, 2012. Tablet strengths are 2.5 mg, 5 mg and 10 mg. An initial starting dose is 1.25 mg, once daily, gradually increasing weekly by 1.25 mg, aiming for a maintenance dose of 10 mg once daily.

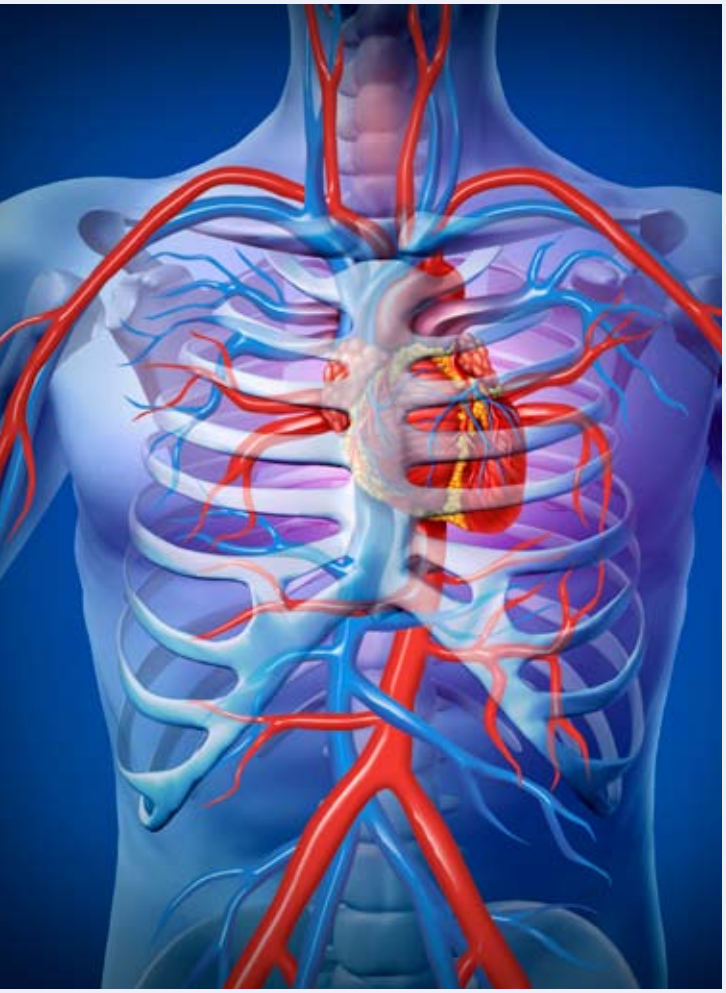
Factors associated with a worsening prognosis

Factors that are independently associated with a worsening prognosis in people with heart failure include:[4, 13, 14]

- Age > 70 years
- Ejection fraction ≤ 30%
- Higher NYHA functional class (see Page 11)
- Anaemia
- Renal impairment
- Hypotension
- Hyponatraemia
- High levels of BNP
- Co-morbidities including IHD, arrhythmias, diabetes, COPD, stroke
- Recurrent hospitalisation

The role of BNP in monitoring treatment for patients with heart failure

A single measurement of BNP can give prognostic information in patients with heart failure – a higher level is associated with a worse prognosis. There is good evidence that many of the medicines used in patients with heart failure lower the concentration of BNP.[12] Serial BNP measurement after initiation of treatment for heart failure may therefore be useful to guide further management, with falling levels an indication of optimal treatment.[12] In a patient whose medical treatment is being adjusted, it is suggested that BNP is requested monthly or two-monthly to monitor progress. Under acute circumstances, BNP may decrease significantly in two – three days, however, research suggests that the most reliable change in the results is seen approximately two weeks after a change in medicine dose and that benefits for the patient are greater if a lower BNP target is sought.[12]



an ARB is added as this combination (ACE inhibitor, ARB and spironolactone) can worsen renal function (Page 6). Discussion with a cardiologist is recommended.

Digoxin can be used to slow the ventricular rate and therefore improve symptoms in patients who have symptomatic heart failure and atrial fibrillation. There is some evidence that digoxin may improve symptoms and reduce the rate of hospitalisation, however, it does not improve mortality.[1]

N.B. All patients with heart failure and atrial fibrillation should be assessed using stroke risk assessment tools, e.g. CHA_2DS_2-VASc to determine their need for anticoagulation.

For further information see: "The use of antithrombotic medicines in general practice", BPJ 39 (Oct, 2011).

Treatment of patients with heart failure with preserved ejection fraction: HF-PEF

The treatment of patients with HF-PEF differs from that of patients with HF-REF, and the evidence for effective treatments to reduce morbidity and mortality in patients with HF-PEF is limited. Patients suspected or known to have HF-PEF should usually be referred to a cardiologist for initial management.

Patients with HR-PEF are usually more "brittle" and require careful control of fluid balance. As in patients with HF-REF, diuretics are used for symptomatic relief of dyspnoea and oedema. A beta-blocker can be used with the aim of prolonging diastole by slowing the heart rate to approximately 70 beats/minute. If blood pressure control is required, an ACE inhibitor can be added. Digoxin can be considered in patients with atrial fibrillation.

There is limited evidence from two small studies suggesting rate-limiting calcium channel blockers, e.g. diltazem, verapamil, can be used as an alternative to a beta-blocker and may improve symptoms and exercise tolerance in patients with HF-PEF. N.B. Rate-limiting calcium channel blockers should not be used in patients with HF-REF because they impair LV function and therefore worsen heart failure.[1]

Non-pharmacological aspects of management of heart failure

Patient education and self-management are important aspects in the management of heart failure. Educate patients to be aware of their symptoms and how to manage them if their condition deteriorates. Many patients will be comfortable with modifying their doses of diuretic. Patients may also be

able to gradually increase the dose of other medicines such as beta-blockers, e.g. by increasing the dose by half a tablet at night and then waiting for a few weeks. A heart failure action plan (e.g. from the Heart Foundation) can assist patients with self-management.

Encourage patients to:

- Weigh themselves daily. It is useful to establish a "dry weight" so that changes in the patient's condition are detected and managed early. If the patient's weight increases rapidly and they become increasingly symptomatic, have a plan in place for the patient to increase their furosemide dose for a few days until the weight decreases again.
- Participate in regular exercise and if appropriate, suggest dietary measures to assist with fat weight loss (as opposed to fluid weight loss)
- Avoid an excessive intake of salt and alcohol
- Monitor their fluid intake – fluid should be restricted to between 1.5 and 2 L/day in patients with moderate or more severe symptoms of fluid overload. There is less evidence that fluid restriction is beneficial in patients with mild symptoms of heart failure.
- Maximise adherence to medicines
- Have an annual influenza vaccination

 A new booklet "Staying well with heart failure" has been developed by the Heart Foundation. It contains information for patients on heart failure (e.g. on symptoms and management), lifestyle modification, daily checks and a heart failure action plan to assist with self-management. The booklet is available from **www.heartfoundation.org.nz** under the Programmes and Resources section.

Device therapy

Device therapy for heart failure includes implantation of a cardioverter defribillator or cardiac resynchronisation therapy (CRT), using devices that provide biventricular pacing or may combine the ability for both pacing and defibrillation.

Device therapy may be considered for some patients with heart failure, e.g. those who remain symptomatic despite optimal use of medicines, those with an ejection fraction that remains low (<35%) or those with left bundle branch block (LBBB) on ECG. Device therapy can improve symptoms, quality of life and ventricular function and reduce the risk of sudden death.[1] Patients with co-morbidities that are likely to reduce their life expectancy (within one year) are generally considered not suitable for device therapy.

Referral to a cardiologist is recommended for patients with:

- Valvular heart disease
- Heart failure and syncope – insertion of a pacemaker may be required
- Heart failure and LBBB and a wide QRS on ECG associated with dyssynchrony – CRT may be indicated
- A history of cardiac arrest or ventricular tachycardia - defibrillator therapy may be indicated

Implanted cardioverter defibrillators

Implantation of a cardioverter defibrillator may be beneficial for selected patients with heart failure as this can reduce mortality in patients at risk of life-threatening ventricular tachyarrhythmias.

Cardiac resynchronisation therapy

A CRT device or biventricular pacemaker that provides simultaneous pacing of both ventricles may be beneficial for patients who have an ejection fraction <30– 35%, ongoing symptoms despite optimal medical management, LBBB on ECG and a prolonged QRS duration (>150 milliseconds).[1] Some CRT devices also include a defibrillator.

Other surgical treatments

Depending on the underlying cardiac pathology, some patients may benefit from other surgical treatments such as coronary artery bypass grafting, valve replacement or rarely in selected patients with end-stage heart failure, heart transplantation.

Review regularly

All patients with heart failure require regular review. If medicine doses are being gradually increased, monthly review is recommended. For patients who are stable on optimal doses of medicines, six monthly review may be appropriate. If doses of medicine are being decreased, regular monitoring remains important because of the risk that the ejection fraction may reduce again and the patient may redevelop symptoms.

The aim of long-term treatment is for the patient to be no longer taking a diuretic but to be maintained on maximal doses of an ACE inhibitor and a beta-blocker to ensure their ejection fraction remains > 40%.

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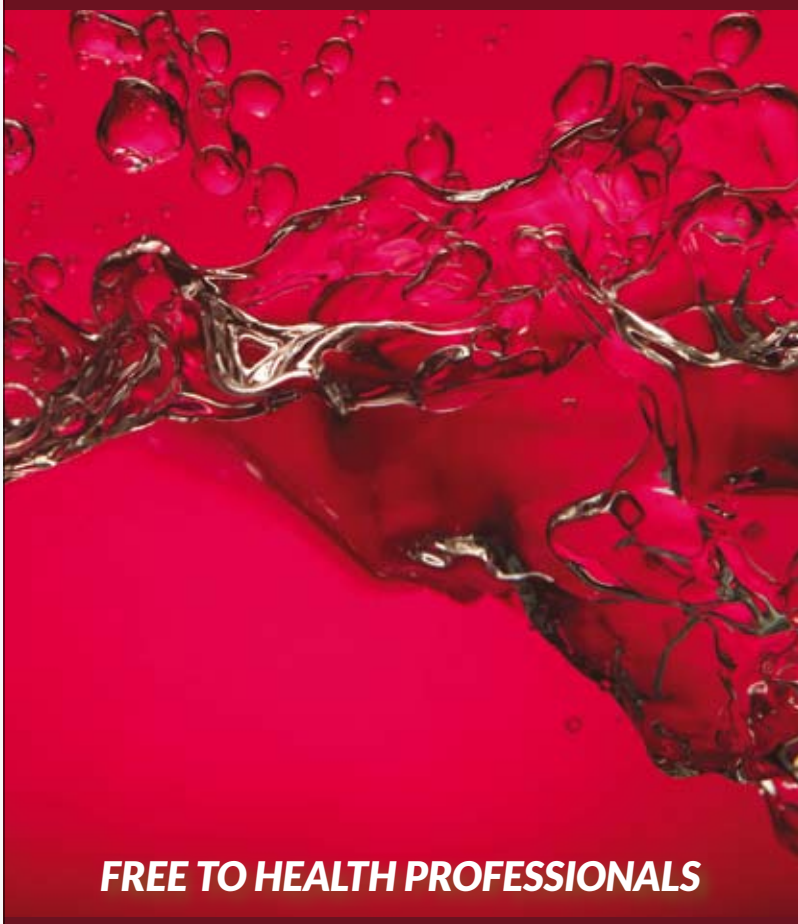

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Dabigatran revisited

Dabigatran has been available for general practitioners to prescribe since July, 2011. Twelve months later, over 14 000 patients were being dispensed this medicine. Dabigatran is indicated for prevention of stroke and systemic embolism in people with non-valvular atrial fibrillation, and for venous thromboembolism prophylaxis after major orthopaedic surgery (specifically hip and knee replacement). There is currently no evidence that it should be used for indications other than these. Non-haemorrhagic gastrointestinal adverse effects (primarily dyspepsia) are the most frequently reported adverse reaction to dabigatran, although bleeding, as with any anticoagulant medicine, remains one of the main risks. There have been no reports of new adverse effects emerging since dabigatran has been used in general practice.

Dabigatran now commonly used in general practice

The oral anticoagulant, dabigatran etexilate, has been available, fully subsidised, on the Pharmaceutical Schedule since July, 2011. Between July 2011 and June 2012, dabigatran was dispensed over 95 000 times to more than 14 000 patients in New Zealand. Usage is continuing to increase with between 8000 and 9000 new dispensings each month.[1]

Dabigatran is available in two formulations – 110 mg and 150 mg. The lower dose (2 x 110 mg/day) is recommended in people aged over 80 years and those with renal impairment (creatinine clearance 30 – 50 mL/min). Figure 1 shows that most people aged over 80 years are being dispensed the 110 mg formulation of dabigatran, however, **just under 10% of people in this age group are receiving a dose that is higher than recommended.**[1]

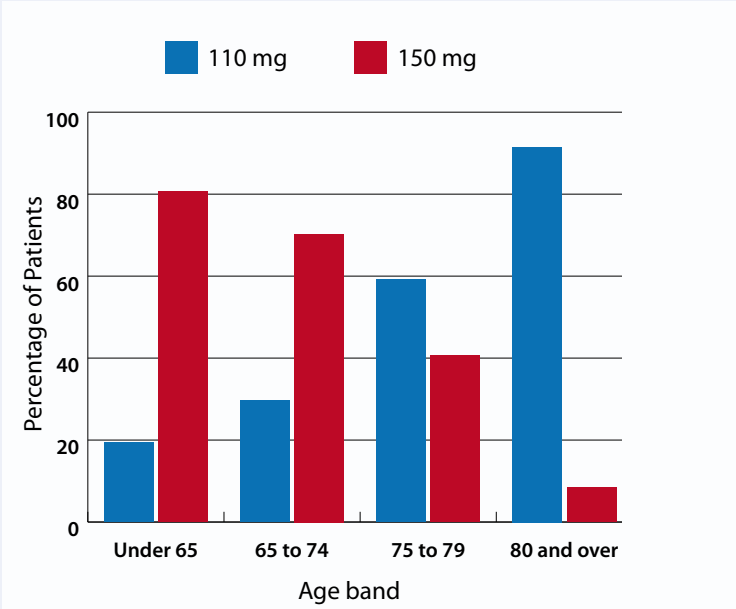

Figure 1: Percentage of patients dispensed dabigatran by age and dose, from July 2011 to June 2012 (Pharmaceutical Warehouse data)[1]

Indications for dabigatran are unchanged

Dabigatran is indicated for prevention of stroke and systemic embolism in people with non-valvular atrial fibrillation, and for venous thromboembolism (VTE) prophylaxis after major orthopaedic surgery (specifically hip and knee replacement).

The specific indication for dabigatran for the prevention of stroke in patients with non-valvular atrial fibrillation requires at least one other risk factor for stroke, e.g. previous transient ischaemic attack or stroke, left ventricular ejection fraction < 40%, symptomatic heart failure, age ≥75 years, age ≥65 years plus diabetes or hypertension or coronary artery disease.[9]

Dabigatran is **NOT** indicated for use in people with valvular heart disease or mechanical heart valves. Dabigatran has not been evaluated in people with bioprosthetic valves and therefore should also **NOT** be used in this situation.[2]

The RE-ALIGN trial – now halted

The RE-ALIGN trial (**R**andomised phase II to **E**valuate the s**A**fety and pharmacokinetics of ora**L** dab**IG**atran etexilate in patients after heart valve replaceme**N**t) began in late 2011 to investigate whether dabigatran could be used as an alternative to warfarin for patients with mechanical heart valves. Participants were randomised to warfarin or dabigatran (150, 200 or 300 mg, twice daily, based on their creatinine clearance) either at the time of their surgery or three months later.

In October, 2012, the immediate post-surgical arm of the trial was stopped. In December, 2012, the manufacturer issued a press release announcing that they had made the voluntary decision to halt the entire trial because the "investigated dosing regimen did not achieve the desired results".[8] Results provided to the FDA by the manufacturer reported higher than expected numbers of thromboembolic events in participants taking dabigatran compared to participants taking warfarin.[2] It has been suggested that this may have been due to the higher thrombotic risk that accompanies the early post-surgical period, however, events also occurred in patients who had valve replacement surgery more than three months previously.[2, 7] Preliminary results from the manufacturer also report that patients taking dabigatran had significantly more events of major bleeding (22.5%) than patients taking warfarin (13.5%).[2]

As a direct result of the problems occurring during this trial, both the Food and Drug Administration (FDA) in the USA and the European Medicines Agency (EMA) have now stated that dabigatran is contraindicated in people with mechanical heart valves.[2]

Thrombosis of mechanical heart valves in patients taking dabigatran

Despite not being indicated for use in patients with mechanical heart valves, New Zealand data from the Centre for Adverse Reactions Monitoring (CARM) show six reports of patients with mechanical values experiencing adverse effects due to the use of dabigatran. Published reports associating dabigatran with valvular thrombosis, leading to valvular dysfunction, in patients with mechanical valves are appearing in the literature.[3–5] In the New Zealand case reports, both patients had mechanical aortic valves and had previously been anticoagulated with warfarin. The patients were compliant with dabigatran treatment, however, they developed thrombosis on the prosthetic valve. One patient also developed multiple embolic cerebral infarctions.[4]

Although evidence from in vitro studies has suggested that dabigatran may prevent thrombosis on mechanical valves, dabigatran has never been indicated for use in this clinical setting.[5, 6] There is speculation that when dabigatran is used in patients with mechanical valves, at doses currently recommended for non-valvular AF, it does not prevent formation of thrombus. A clinical trial that was underway to assess the suitability of dabigatran for people with mechanical heart valves has been halted (December, 2012) due to higher than expected numbers of thromboembolic events (including stroke, valve thrombosis and myocardial infarction) occurring in study participants taking dabigatran (see "RE-ALIGN trial – now halted").[7, 8]

Dabigatran dosing recommendations have not changed

For the prevention of stroke in people with non-valvular atrial fibrillation the recommended dose of dabigatran is:[9, 10]

- 150 mg, twice daily, provided creatinine clearance >30 mL/min
- 110 mg, twice daily, for patients aged ≥80 years

In addition, in patients **aged 75 – 80 years** and patients with **creatinine clearance 30 – 50 mL/min** consider using 110 mg, twice daily, if their risk of bleeding is high and their risk of thrombosis is low.

Stroke and bleeding risk in patients with AF should be assessed using stroke assessment tools, e.g. $CHADS_2$, CHA_2DS_2-VASc and HAS-BLED.

For further information, including the stroke assessment tools, see "The use of antithrombotic medicines in general practice", BPJ 39 (Oct, 2011).

Why calculate creatinine clearance?

Dabigatran is predominantly renally excreted therefore any deterioration in renal function will increase the concentration of dabigatran and increase the risk of adverse effects, primarily bleeding. The Modification of Diet in Renal Disease (MDRD) eGFR calculation reported by laboratories in New Zealand may be inaccurate in older people or people with a BMI < 18.5kg/m^2 or > 30 kg/m^2. When a patient's creatinine level rises above the normal range, alterations to medicine doses may be required. It is recommended that glomerular filtration rate is estimated using the Cockcroft-Gault equation rather than relying on the laboratory supplied MDRD eGFR. Tools for calculating creatinine clearance using the Cockcroft-Gault equation are available online (e.g. **www.mdcalc.com/creatinine-clearance-cockcroft-gault-equation/**) or can be downloaded for use on portable devices such as smart phones or tablet devices.

Dabigatran for VTE prophylaxis after major joint surgery

For the prophylaxis of VTE following major orthopaedic surgery the recommended dose of dabigatran is:[9]

- 220 mg (2 × 110 mg tablets), once daily, for patients with creatinine clearance > 50 mL/min
- 150 mg (2 × 75 mg tablets), once daily, for patients with creatinine clearance 30 – 50 mL/min

N.B. The length of the course varies with the type of surgery – knee replacement surgery ten days, hip replacement surgery 35 days.[9]

Evidence suggests that treatment with oral dabigatran, compared with subcutaneous low molecular weight heparin (LMWH), for the prophylaxis of VTE after knee or hip replacement surgery is well tolerated and associated with high levels of patient and clinician satisfaction.[11–13] The efficacy and safety of dabigatran is comparable to other anticoagulants used for VTE prophylaxis.[12,14] The key advantage of dabigatran in this setting is the use of a fixed dose given by the oral route. One practical advantage of the oral route of administration is that patients do not have to self-administer subcutaneous doses of LMWH after discharge from hospital. Disadvantages include nausea, an inability to tolerate oral medicine in the early postoperative period, increased post-operative wound discharge and limitations in use in patients with spinal anaesthesia.[12]

Should you prescribe warfarin or dabigatran?

Although dabigatran is likely to be more convenient and simpler to use than warfarin, it is not suitable for all people and all situations.

The advantages of dabigatran compared with warfarin include:

- More convenience as frequent INR tests and dose adjustments are not needed
- Effective anticoagulation in patients who have previously been difficult to control on warfarin (as long as poor adherence is not the reason for the unstable INR levels)
- Fewer drug and dietary interactions than warfarin
- Reduction in the risk of intracranial haemorrhage[15]

Some people, however, who were changed from warfarin to dabigatran, have now changed back. Reasons suggested for this include:

- "Missing" the reassurance of knowing that they have effective anticoagulation, i.e. their INR is within the therapeutic range (this applies to both patient and clinician)
- Patients finding the twice daily dosing difficult (and therefore risking ineffective anticoagulation because of the short half-life of the medicine, approximately 12–14 hours in a patient with normal renal function)
- Presence of adverse effects from dabigatran, particularly dyspepsia (there is anecdotal evidence that this may affect up to 30% of patients)
- Deteriorating renal function where eGFR drops close to 30 mL/min

Changing from warfarin to dabigatran requires a different "mindset" with regards to effective dosing and anticoagulation. Both clinicians and patients need to be comfortable with the concept that while taking dabigatran they do not need blood tests to check its effectiveness as an anticoagulant. Ensuring that patients are well informed about dabigatran when it is initiated is likely to assist with adherence. Reminders can be put in place, e.g. a mobile phone alert, to help patients remember the twice daily doses. If a dose is missed, another capsule should be taken as soon as the patient remembers, provided there is more than six hours before the next dose.

How to initiate dabigatran

Prior to initiating dabigatran, all patients should have an assessment of renal function.[9] Dabigatran is contraindicated in people with a calculated creatinine clearance of < 30 mL/min. People with moderate renal impairment (30 – 50 mL/min) are at increased risk of bleeding and dabigatran should be used with caution.

In a patient not previously anticoagulated with warfarin, dabigatran is started at the appropriate dose depending on

An iPhone application is available for use when initiating dabigatran

An application for smart phones has been developed by Dr Paul Harper, Clinical Haematologist, Medlab Central. It is designed to help determine the dose of dabigatran that should be used in patients with non-valvular AF or for orthopaedic prophylaxis. The application gives a recommended dose for each indication based on the patient's age and renal function. It also includes relevant drug information (tablet sizes, pharmacology, storage and advice about taking the medicine), specific dosing instructions and information about adverse effects, interactions and actions to take if a patient is bleeding.

The application "Managing Dabigatran – guidelines for the management of dabigatran" is available for free: Search App Store, keyword: dabigatran.

age and renal function and is continued at the same dose. There is no need for a loading dose to be given.

In a patient already anticoagulated with warfarin, the warfarin should be stopped and the INR monitored. Dabigatran can be started at the appropriate dose for age and renal function when the INR is < 2.0.

How to change a patient from dabigatran back to warfarin

Check the patient's creatinine clearance, unless this has been done within the last few weeks. If the creatinine clearance is > 50 mL/min, warfarin treatment should be started three days before discontinuing dabigatran at a dose similar to the patient's previous dose. If the creatinine clearance is 30 – 50 mL/min, initiate warfarin two days before stopping dabigatran.[9] INR should be checked regularly until stable, when the frequency between tests can be extended.

How to temporarily stop dabigatran for a planned surgical procedure

Patients who have a creatinine clearance > 50 mL/min, should discontinue dabigatran 24 hours before the planned surgical procedure. In patients with a high risk of bleeding or if a major surgical procedure is planned, dabigatran should be discontinued two days before the procedure. Patients with a creatinine clearance of 30 – 50 mL/min should discontinue dabigatran two to four days before the planned procedure, because the clearance of dabigatran is likely to be prolonged.[9]

Renal function must be monitored in people taking dabigatran

In addition to assessing baseline renal function, regular monitoring of renal function is important in the majority of patients taking dabigatran. Renal function should be assessed:[9]

- For all people prior to the initiation of dabigatran
- For people taking dabigatran who have a change in their clinical situation that may be associated with a decline in renal function e.g. dehydration, diuretic usage or hypovolaemia
- At least annually in all people taking dabigatran who are aged over 75 years
- At least annually (but preferably three to six monthly) in all people taking dabigatran who have a creatinine clearance of 30 – 50 mL/min

Laboratory tests are not needed to guide dosing decisions

Unlike warfarin, dabigatran has a wide therapeutic window, predictable pharmacokinetics and pharmacodynamics and a rapid onset of action therefore doses are standardised and monitoring for effectiveness is not required. In addition, there is no readily available, effective laboratory test that can be used to guide the dosage of dabigatran or to assess the effectiveness of the medicine. If bleeding occurs in a patient taking dabigatran, the medicine should be stopped and in some situations (usually in secondary care) laboratory investigation using a combination of tests such as thrombin time, activated partial thromboplastin time, fibrinogen and ecarin clotting time (if available) may assist with management.

No new adverse effects identified to date

In the three months after July, 2011, when dabigatran was included on the Pharmaceutical Schedule, there were multiple reports submitted to CARM (approximately 70–100 per month); however, since December 2011, the number of reports has dropped dramatically.[19] This may in part be explained by a tendency for clinicians not to report on a drug that is no longer "new". An analysis of reports to the end of February 2012 is shown in Table 1.

Table 1: Overview of types of suspected adverse reactions reported[19]

Grouping	**Number of Reports** (n=345)	**% of Total Reports**
Bleeding	139	40.3
GI Symptoms (non-haemorrhagic)	145	42.9
Thromboembolic	14	4.1
Events secondary to inappropriate use	28*	8.1

* includes six reports where dabigatran was used in a patient with a mechanical valve

Non-haemorrhagic gastrointestinal adverse effects (primarily dyspepsia) are the most frequently reported adverse drug reaction, although bleeding, as with any anticoagulant medicine, remains one of the main adverse risks of dabigatran. There were more adverse effects in older people, but this also reflects increased use of dabigatran in older people. This pattern, however, does not apply to patients aged over 80

Is dabigatran RELY-ABLE?

Evidence for the effectiveness and safety of dabigatran as an oral anticoagulant for use in patients with non-valvular AF was based predominantly on the Randomised Evaluation of Long-Term Anticoagulation therapy (RE-LY) trial.[16,17] Multiple studies have been published since, but of key interest is the long-term extension study which has followed patients who participated in the RE-LY study, who have continued with dabigatran treatment. The RELY-ABLE trial was designed to establish the long-term safety of dabigatran in patients with non-valvular AF and also to assess efficacy outcomes.

Preliminarily results from the 5851 patients followed in the RELY-ABLE trial appear to support the findings of the RE-LY trial with a net clinical benefit from both the 110 mg and 150 mg dose.[18] The 150 mg dose continues to be associated with a higher rate of major bleeding than the 110 mg dose.[17]

However, important limitations of this study are that only 32% of patients from RE-LY were included, participation was voluntary and follow-up was stopped when the medicine was stopped. Only 12% of patients from RE-LY were followed for a further 28 months, and they were likely to be slightly younger, more likely to have permanent AF and less likely to have heart failure.[17] Whether these differences between study participants and the other limitations of the RELY-ABLE trial will have any clinical significance in the longer term is not known. Comparisons with warfarin are also not available as patients who had been randomised to warfarin in RE-LY were not included in RELY-ABLE.

years, where the number of reports was higher than would be expected for the usage in this age group.[19] Since the last published Medsafe update in February, 2012, CARM reports that there have not been any newly emerging adverse effects associated with dabigatran.

Minimising adverse effects

The key adverse effects in the CARM reports include bleeding, non-haemorrhagic gastrointestinal effects, thromboembolic events and events secondary to inappropriate use. In general, when initiating dabigatran always consider; the age of the patient, that the indication is appropriate, that the patient's renal function (creatinine clearance) has been checked and that all the patient's medicines have been reviewed.

The **risk of bleeding** can be minimised by ensuring that:

- The dose used is not higher than recommended for the patient's age (particularly in people in the >80 years age group) or renal function
- In patients already anticoagulated with warfarin their INR is < 2.0 prior to the initiation of dabigatran
- Dabigatran is used with caution with medicines that may increase bleeding risk, e.g. aspirin, clopidogrel, dipyridamole and NSAIDs. Ensure also that the patient does not continue taking warfarin.

The **risk of non-haemorrhagic gastrointestinal effects**, primarily dyspepsia, can be minimised by advising patients to take dabigatran with food. If required, a proton pump inhibitor (PPI)* or H2 antagonist can be prescribed, however, patients should be advised that if the dyspepsia persists, they should return for review.

*Although there is evidence from clinical trials that co-administration of a PPI reduces the plasma concentration of dabigatran, it appears that this interaction is not clinically significant.[20]

The **risk of thromboembolic events** can be minimised by ensuring adherence to the twice daily dosing that is required for effective anticoagulation.

The **risk of events secondary to inappropriate use** can be minimised by:

- Not using dabigatran in patients with a creatinine clearance of < 30 mL/min
- Not using dabigatran in patients with mechanical heart valves (including bioprosthetic valves)
- Using lower dose dabigatran (110 mg, twice daily) in older patients and those with moderate renal impairment (30 – 50 mL/min)
- Considering age, renal impairment and bleeding risk when determining the correct dose of dabigatran

Dabigatran has also been associated with a possible increased risk of myocardial infarction (MI).[16] Although researchers continue to debate whether this reflects a true risk of dabigatran use or a protective effect from warfarin, a recent meta-analysis concluded that dabigatran was associated with an estimated 27 – 33% increase in relative risk of MI or acute coronary syndrome, although the absolute risk was small (0.27%).[21]

Other new oral anticoagulants

Dabigatran (an oral direct thrombin inhibitor) is only one of a number of new oral anticoagulant medicines becoming available worldwide. Rivaroxaban and apixaban (both oral, direct factor Xa inhibitors) are being increasingly used internationally for prevention of both stroke and VTE. There is evidence from clinical trials that these medicines may have some advantages and be associated with lower morbidity and mortality than dabigatran, however, further research, in particular head-to-head trials, is required.[22–24] At present, although rivaroxaban is available in New Zealand, it is only subsidised under Special Authority for the prophylaxis of VTE in patients after hip and knee replacement surgery and apixaban is not yet available in New Zealand.

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Dabigatran now in blister strips

Dabigatran (Pradaxa) capsules were originally packaged loosely in bottles, but are now available in blister strips. Dabigatran can be put into blister (Medico) packs, however:

- The capsules must remain in their original foil
- When the foil is cut around the capsule, i.e. to fit it into the blister, the seal around the capsule must remain intact
- The size of the capsule and cut foil is quite large so there may not be space for additional tablets/capsules in the blister, which means extra packs for patients and therefore potentially extra cost
- Because of the size of the capsule and cut foil, it needs to go into the largest Medico tray (13 mm) which might not be acceptable to some patients

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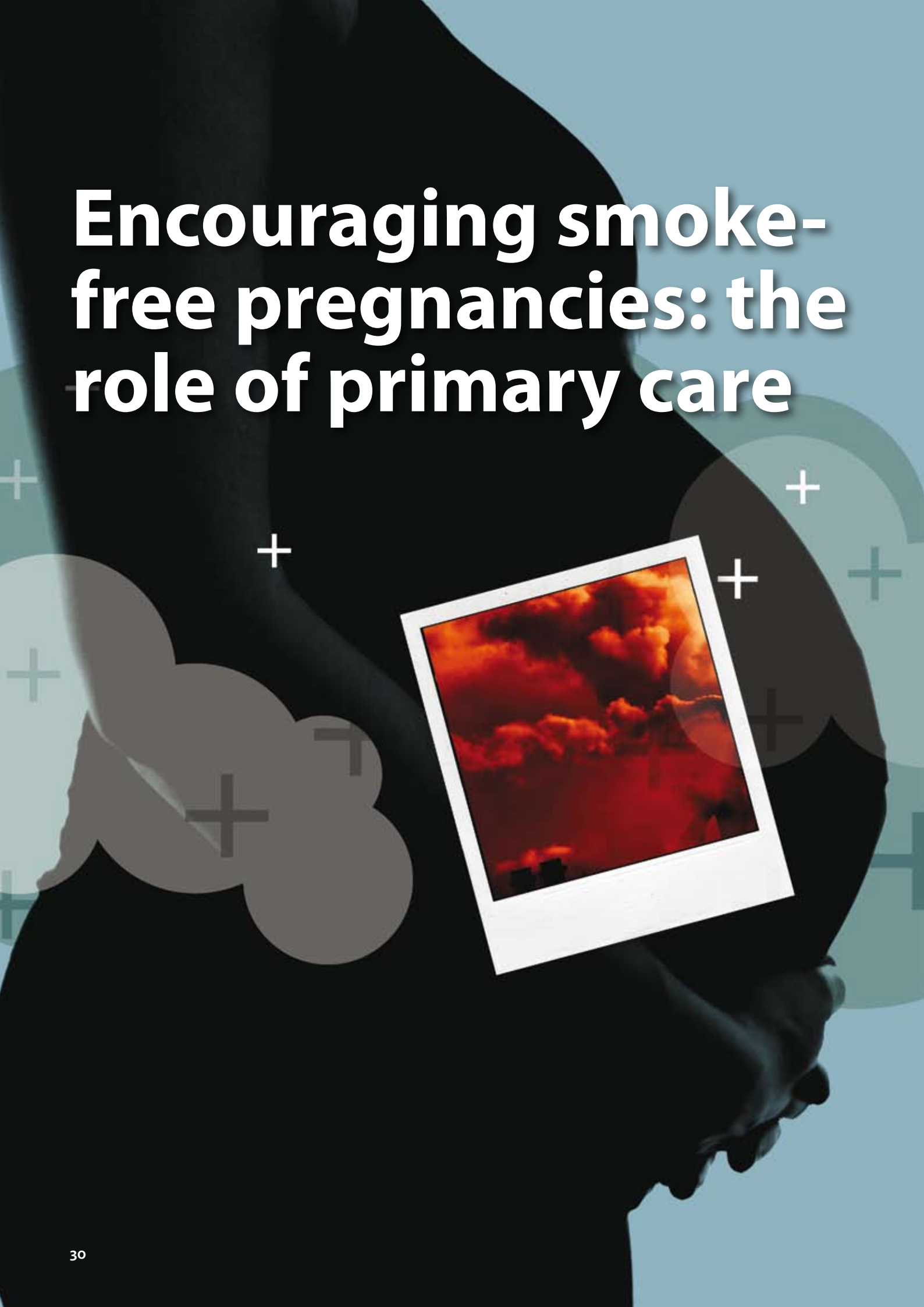
Encouraging smoke-free pregnancies: the role of primary care



One in ten New Zealand women smoke during pregnancy and this figure is significantly higher among Māori and women living in lower socioeconomic areas. Prospective parenthood provides motivation to stop smoking and health professionals can increase smoking cessation rates by offering support at this time. Non-pharmacological interventions are first-line for women who want to stop smoking during pregnancy or while breast feeding, however, nicotine replacement therapy (NRT) is appropriate, following a brief risk-benefit assessment. The post-partum period is characterised by a high level of smoking relapse, especially among women who live in households with other people who smoke. Therefore it is important that smoking cessation advice also includes partners and family/whānau.

Pregnancy provides a golden opportunity to discuss smoking cessation

Maternal smoking is the largest modifiable risk factor affecting fetal and infant health in the developed world.[1] The number of New Zealand women who continue to smoke during pregnancy is a major health concern. The "Growing up in New Zealand" study of over 7000 women who were pregnant during 2009 and 2010 reported that 11% of New Zealand mothers smoked at some stage during pregnancy.[2] This figure was significantly higher among Māori women (34%) and women from lower socioeconomic areas (17%).[2]

Women who smoke are more likely to stop during pregnancy than at any other time in their lives.[3] First time mothers are particularly receptive to cessation advice. A study of over 70 000 women who were pregnant and smoked, found that women who were giving birth for the first time were 2.5 times more likely to stop smoking than women who already had children.[4] Discussions about pregnancy are therefore a crucial opportunity to offer smoking cessation support.[5] When patients present for pre-conception advice or the first antenatal check, smoking status should be confirmed and if appropriate, cessation support offered. Discussions about smoking should, wherever possible, also include family/whānau. Women who are pregnant and living with a person who smokes are four times more likely to resume smoking after giving birth.[6] The goal of smoking cessation treatment is to help families remain smoke-free long-term.

Managing smoking cessation in women who are pregnant

All women who are pregnant should be routinely asked about their smoking status and those who smoke encouraged to use smoking cessation supports, e.g. Quitline and NRT where appropriate. ABC reminds health professionals what to do: Ask

PHO performance goals for smoking cessation

The PHO Performance Programme currently has two smoking related indicators. The "smoking status recorded indicator" aims to capture smoking status for 90% of enrolled patients in New Zealand aged 15 – 74 years. This indicator accounts for 7% of the performance funding; 2% for the total population and 5% for the high need population. During the January 2012 to July 2012 reporting period, 78% of the total population and 77.4% of the high need population within New Zealand had smoking status recorded. Although this continues a strong upward trend for this indicator, this result is below the national target and only three of 35 PHOs met the Programme goal.

The "smoking brief advice and cessation support indicator" aims for 90% of enrolled patients aged 15 – 74 years who smoke and have been seen in General Practice, to be given brief advice and/or cessation support within the last 12 months. This indicator accounts for 13% of the performance funding; 4% for the total population and 9% for the high need population. Brief advice to stop smoking includes any documentation that either a person who currently smokes was advised to stop smoking or that an offer of cessation support was made. Cessation support includes referral to a smoking cessation programme, prescribing NRT or other medicines for the purpose of smoking cessation, or providing behavioural support.

The benefits of stopping smoking during pregnancy

All people who smoke begin to benefit within minutes of stopping. One of the most immediate and measurable changes is a decrease in carbon monoxide levels in the blood, which benefits both the mother and fetus. Stopping smoking also has long-term benefits, including reduced risk of stroke, cancer and coronary heart disease. In women who are pregnant, smoking cessation prevents fetal exposure to over 7000 chemicals contained in cigarette smoke, 69 of which are known to be carcinogenic.[7]

"When you smoke, so does your baby..." When a woman who is pregnant smokes, both carbon monoxide and nicotine accumulate in fetal serum and amniotic fluid at levels higher than those found in maternal serum.[8, 9] Nicotine is also present in the breast milk of mothers who smoke and its metabolites are detectable in the urine of their breast feeding infants.[10]

Carbon monoxide reduces oxygen binding to haemoglobin.[9] Antenatal exposure to nicotine causes increased fetal heart rate and reduced fetal breathing movements.[9] Assessing the long-term effects of antenatal exposure to nicotine is difficult due to a lack of human studies, however, animal studies have shown that nicotine can cause malformation of neural pathways in the developing brain.[10]

The reduced fetal oxygen supply caused by smoking results in intrauterine growth deficiency and infants born to mothers who smoke typically weigh 200 – 300 grams less than infants born to women who do not.[9] Smoking during pregnancy also increases the risk of a pre-term birth between 1.2 – 1.8 times.[9] Ectopic pregnancy, placenta complications, stillbirth, premature rupture of membranes and sudden unexplained death in infancy (SUDI) are also complications that occur more frequently in women who smoke during pregnancy.[9] A significant and dose-dependent increase in the risk of all adverse birth outcomes measured (other than still birth) demonstrates that there is no safe number of cigarettes that can be smoked per day.[11]

Quitting smoking early during pregnancy reduces adverse effects. One study found that there was no significant difference between the birth weights and the rates of pre-term birth in women who stopped smoking before 15 weeks gestation and women who had never smoked.[1] However, women who continued to smoke beyond 15 weeks gestation were at increased risk of having a low birth weight infant and/or a pre-term birth.[1] However, there are still long-term benefits to be gained for mother and fetus by stopping smoking later in pregnancy.

Mothers who stop smoking are more likely to breast feed for periods longer than six months, which has numerous well known short and long-term health benefits for the infant.[5] Health professionals should stress the importance of continuing to breastfeed, regardless of smoking status.[12]

There are also financial benefits to be gained by stopping smoking that may provide additional motivation for young families to remain smoke-free.

about smoking, Briefly advise to quit, and most importantly, offer Cessation support.[12]

All women of a reproductive age should be asked about pregnancy intent or risk. If a woman who smokes is considering, or is at high-risk of becoming pregnant, then the health benefits of smoking cessation should be discussed further and a referral made to a dedicated smoking cessation service. Alcohol, drug use and other risk taking behaviour should be explored, and lifestyle factors, e.g. weight, diet, nutrition and supplement use should be addressed.

For further information see: "Pre-conception care in general practice", BPJ 35 (Apr, 2011).

Ask about and record the smoking history

The smoking habits of a patient are useful for estimating nicotine dependence and identifying individuals who may benefit from extra assistance in their quit attempt. The smoking status of other members of the household is also important, as having a partner who smokes has been said to "almost universally predict" a return to smoking for a pregnant woman attempting to remain smoke-free.[6]

"When was the last time you smoked a cigarette?" Asking about smoking in a non-judgemental way is important as women who are pregnant may under-report smoking. In the mid-1990s, a survey of New Zealand mothers found that nearly one-quarter of women who were smoking while pregnant did not self-report smoking, most likely due to feelings of guilt.[13] A similar result was found in a more recent Scottish study.[14]

"How soon after waking do you usually have your first cigarette?" This is the best question for assessing nicotine dependence.[12] If a person smokes within 30 minutes of waking they have a high degree of nicotine dependence and are more likely to require medical assistance to successfully stop smoking.[12] The number of cigarettes smoked per day can also be used to assess nicotine dependence, however, this provides a less accurate estimate.

Briefly advise to stop smoking

"You've probably already thought about quitting – I'd like to help you do it." This is a positive way to begin a discussion about smoking cessation. The discussion should address the challenge that smoking cessation represents. It should also encourage complete smoking cessation rather than "cutting down". Reducing the number of cigarettes smoked per day typically results in people who smoke taking deeper puffs, holding the puffs for longer and therefore smoking each cigarette more intensively.[12]

Cessation support should be offered to all people who smoke

All women who are pregnant and wish to stop smoking should be referred to a dedicated smoking cessation service. Māori women who want to stop smoking can be referred to a culturally appropriate service (see "Aukati KaiPaipa"). Recent evidence strongly indicates that the offer of smoking cessation support is the most important component of the ABC approach. Furthermore, support should be offered to all smokers without assessing their willingness to stop smoking. A meta-analysis showed that offering cessation support motivated an additional 40 – 60% of people to attempt to stop smoking compared to being advised to stop smoking on medical grounds alone.[15] The authors estimated that if all smokers were given advice to stop smoking, 25% would attempt to stop within six months of a consultation, however, this could be increased to 35% if this advice was followed up with an offer of cessation support.[15] It is important to note that in all trials analysed, offers were made without an assessment of motivation to stop smoking.[15] This and other data suggest that previous recommendations to assess a

Heavy smoking is a risk factor for other risky behaviours

Smoking ten or more cigarettes per day during pregnancy is a marker for additional fetal and maternal risk factors. A Canadian study of almost 250 000 births from 2001 – 2006 found that smoking ten or more cigarettes per day during pregnancy was associated with a 15-fold increase in the risk of drug use. Women who smoked between one and nine cigarettes a day had a ten-fold increased risk.[11] Alcohol use during pregnancy was also five times higher in women who smoked more than ten cigarettes per day.[11]

Aukati KaiPaipa

Aukati KaiPaipa is a free, face-to-face smoking cessation service for Māori delivered from over 30 centres within New Zealand. The programme involves coaches who create a smoking reduction plan prior to an intensive smoke-free intervention with nicotine replacement therapy (NRT). Cessation follow-ups are conducted by phone or in person to prevent relapses.

To find the closest provider go to the Aukati KaiPaipa website: **www.aukatikaipaipa.co.nz/contact-us**

For further information see: "Smoking cessation for Māori", BPJ 22, (Jul, 2009).

Better help for smokers to quit

The Ministry of Health began introducing national health targets in 2007. These targets reflect priority areas of healthcare for the government, and every quarter DHB performance results are published in major metropolitan newspapers. Unlike the PHO Performance Programme, health sector performance is not directly related to funding. In 2012–2013 a new smoking cessation target was released – brief advice and support to stop smoking should be offered to 90% of patients in primary care who smoke, and for 95% of patients who smoke and are seen in public hospitals. Within the target there is an expectation that progress should be made towards providing 90% of pregnant women who smoke with advice and support to stop smoking. This is to be delivered either in General Practice at the time of pregnancy confirmation, or by the LMC.

Further information is available from: **www.health.govt.nz** (key words = smoking health targets)

person's willingness to stop smoking, and to restrict offers of cessation support to those who express a desire to stop is outdated and may even be causing harm.

Support from friends during quit attempts should be encouraged. The regular and positive input of a supporter has been shown to improve eight-month postpartum quit rates.[16]

The Quitline is a smoking cessation support service which can be accessed six days a week on **0800 778 778**. Further information is available from: **www.quit.org.nz**. There are also pregnancy specific smoking cessation services in the Auckland, Mangere, Waitemata, Hastings, Canterbury and Southland regions. A number of services also provide Pacific smoking cessation support. Further information is available from: **www.hiirc.org.nz** (key words = smoking, cessation, providers).

Motivational interviewing is recommended by the American College of Obstetricians and Gynecologists for prompting behaviour change in women who are pregnant and smoke but are resistant to stopping.[17] Motivational interviewing is useful when advice alone is ineffective at reducing risky behaviours because there is a misunderstanding of the connection between the activity and the health risk, or where there is a perceived value or a social connection associated with the behaviour.[18]

The principles that are important when using motivation interviewing as a smoking cessation intervention are:[18]

- Display understanding and avoid arguments by acknowledging how difficult smoking cessation can be
- Highlight discrepancies between goals and behaviour, e.g. smoking is at odds with any expressed desire to do everything possible for the health of an infant
- Accept resistance and provide feedback in situations where the patient may find quitting difficult, e.g. suggesting that the family collectively decide that the home becomes a smoke-free zone
- Support initiative and self-motivation in remaining smoke-free, e.g. reinforcing the collective benefits of being part of a smoke-free family/whānau

The ACOG "Motivational Interviewing: A tool for behaviour change" is available from: **www.acog.org** (Key words = motivational interviewing).

The use of medicines to support quit attempts

Nicotine replacement therapy (NRT) is a useful smoking cessation treatment for all people who want to stop smoking. In pregnant women, smoking cessation without NRT is preferable and women who are "light" smokers may be confident that they can stop without it. However, for women who are pregnant or breast feeding and unable to stop smoking on their own, NRT can be offered after a brief discussion of the risks and the benefits of treatment. The New Zealand smoking cessation guidelines state that the balance of risk versus benefit during pregnancy overwhelmingly supports the use of NRT, compared to the health risks of continued smoking.[12] This is because NRT delivers nicotine at lower levels than smoking, without the additional toxins contained in cigarette smoke. In a large study involving over 1700 pregnant women who used NRT, no significant association was found between NRT use and decreased infant birth weight.[19] Other studies report similar findings.[20]

NRT also reduces cigarette withdrawal symptoms that can cause a smoking relapse. Generally, oral NRT, e.g. gum or lozenges, is recommended for pregnant women in preference to nicotine patches as this provides a lower daily dose of nicotine.[12] If the amount of nicotine delivered by oral NRT is unlikely to be sufficient, the shorter-acting 16-hour patch, removed before sleeping, is considered to be the best option.[12] Women who are pregnant should be advised that if they continue to smoke while using NRT the risk to their foetus may be greater than if either method of nicotine delivery is used alone.

NRT is fully subsidised at a cost to the patient of $5 for a three-month supply. It can be prescribed by General Practitioners, Nurse Prescribers and Midwives, but is also available from Quitline and Quit Card providers. Some patients with a community services card may receive an additional subsidy. Unsubsidised NRT is also sold over the counter at pharmacies or supermarkets.

Quit cards, which are mainly used by Quit Card providers or Quitline, have been redesigned with a new tick box system to make them easier to fill in. Further information on how to use the new Quit Cards is available from: **www.quit.org.nz/file/quitcards/nrt-assessment-august-2012-online.pdf**

Other smoking cessation medicines are not recommended for use in pregnancy as the potential risk to fetal development is largely unknown and cannot be balanced against the known benefits of smoking cessation. Pregnancy is listed as a precaution for nortriptyline use by New Zealand guidelines.[12] Bupropion has been reported recently by Medsafe (2012)

General Practitioners rarely act as Lead Maternity Carers (LMC)

In New Zealand, 1% of pregnant women have an LMC who is a General Practitioner.[2] The opportunities primary care health professionals, who are not registered as a LMC, have to routinely offer smoking cessation support to pregnant women are therefore often limited to consultations where pregnancy is confirmed and/or the first antenatal screen is performed (this is the only funded primary care consultation for pregnancy). If offers of smoking cessation treatment are not made at these times then opportunities in primary care will be limited to consultations for other reasons.

It is important that the general practice team take every opportunity to provide smoking cessation support and do not assume that this will be done by midwives.

For further information see: "The role of General Practice in the care of pregnant women", BPJ 35 (Apr, 2011).

to potentially increase the risk of congenital cardiovascular malformations and it is recommended that women who are pregnant, or planning to become pregnant, should be informed of this risk before considering treatment.[21] Varenicline is contraindicated in women who are pregnant, according to New Zealand guidelines.[12] A phase 4 clinical trial in the United States is currently enrolling participants to determine whether varenicline use during pregnancy is associated with an increased risk of congenital malformations compared to continued smoking.[22]

For further information see: "Update on smoking cessation", BPJ 33 (Dec, 2010).

Electronic cigarettes (e-cigarettes) are battery powered nicotine delivery devices which resemble cigarettes. Currently there is no evidence to support healthcare workers actively recommending these devices. Further evidence is required to assess their effectiveness as smoking cessation aids.

Follow-up and ongoing support

Between 45% – 75% of women who stop smoking during pregnancy begin smoking again within one year of giving birth.[17] Smoking cessation interventions for pregnant women therefore need to be ongoing and proactive. A follow-up visit can be scheduled for the eighth month of pregnancy at the same time as the quit date is set. This will allow the goals of cessation and strategies for staying smoke-free to be revised. It is particularly important that a follow-up consultation is arranged in primary care, due to the limited contact General Practitioners in New Zealand have with women during the antenatal and postnatal periods. Consultations for the six-week infant immunisation and subsequent immunisation schedule provide additional opportunities for follow-up.

Follow-up consultations should emphasise the ongoing health benefits of staying smoke-free for the mother and the infant, as it reduces the risk of SUDI, bronchitis, asthma and otitis media.[17]

If maternal weight gain is a concern, suggest that the woman focuses on remaining smoke-free and that weight-loss is a secondary goal. Encourage breast feeding, a healthy lifestyle and participation in physical activity which is likely to reinforce the health benefits of remaining smoke-free and to assist in weight reduction.

What to do if the patient begins smoking again?

If a relapse occurs, emphasise that this is a "misstep along a path", and not a failure. Provide a reminder that many people who quit smoking experience relapses.[17] Encourage another attempt and set a new quit date, then support a commitment to not having a single puff from that point on. All smoking related items should be discarded, including lighters and ashtrays. Ask the woman to identify what caused the relapse, to enhance understanding of triggers, and help to implement a plan to avoid it happening again. Smoking cessation support services can provide day-to-day support and help to provide management strategies for the reintroduction of familiar smoking cues such as drinking caffeine and alcohol, and social and occupational situations.[6]

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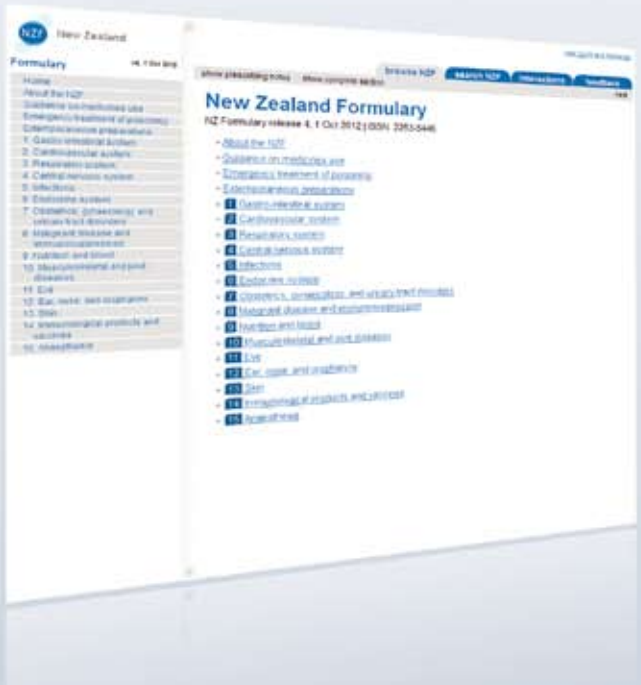

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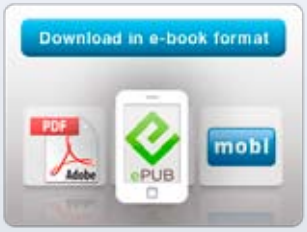

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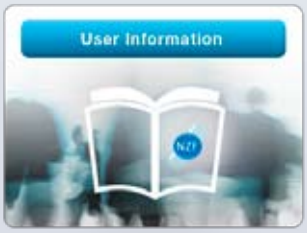

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Catch-up immunisations and funding rules

Dear Editor,
It's good to be reminded that immunisations are not just for kids in Issue 49 of BPJ (Dec, 2012), yet it would be helpful to clarify funding for adult catch ups as even in this journal (Page 7) we are assured that there are funded adult catch-ups yet (on Page 37) you state that adults must pay for catch-ups themselves. My understanding is that funding is available to pay for a primary course of certain vaccines as per page 21 and the back cover of the current Immunisations Handbook.

To be able to fund catch-ups for the over age 18s is reassuring as we know those people who have had a primary course of tetanus have good protection. I never quite understood why the age 45 and 65 tetanus booster vaccine is funded but not the administration, i.e. no fee is claimable for the nurse's time.

Finally I wish it were true that (as per page 37) females age 20 could be caught up for HPV. I think the funding rules are that they must have commenced dose one before their 20th birthday.

***Barbara Warren**, Practice Nurse*
Dunedin

It is correct that certain vaccinations are available, fully funded, for adults who have never had a course of vaccinations, and have not been exposed to the condition being vaccinated against. There are three vaccines in this category that are available to anyone, at any age: Td (tetanus/diphtheria), MMR (measles, mumps and rubella) and IPV (polio). The funding includes the Immunisation Benefit Subsidy to cover the cost of delivery. The funding for the age 45 and 65 year Td booster is different in that, unlike other vaccines, the dose is funded, but the cost of administration (Immunisation Benefit Subsidy) is not. The reason for this is largely historical. So in summary, if the Td is being given as a primary course, not a booster dose, then the Immunisation Benefit Subsidy can be claimed.

Some other vaccinations are funded for adults in certain scenarios, such as people pre- or post splenectomy (HiB, Meningococcal A, C, Y and W135 and pneumococcal polysaccharide vaccines), people who are household or sexual contacts of Hepatitis B carriers and Tdap vaccine for women who are pregnant. In addition, influenza vaccination is funded for people aged over 65 years, women who are pregnant and those with a chronic condition outlined within the New Zealand Immunisation Handbook (although funding rules are subject to change).

Other vaccines that may be useful to adults and should be considered, but are not funded, include varicella for those without a history of chicken pox and pneumococcal vaccines for those with chronic chest conditions.

Women have until their 20th birthday to begin the HPV immunisation programme. This means that the first dose must be delivered prior to their twentieth birthday, but subsequent doses may be given beyond this age.

Recommended vaccinations for staff working in primary care

In Table 1 in the article "Recommended vaccinations for staff working in primary care" (BPJ 49; Dec, 2012), some of the table notations were incorrectly labelled. This inadvertently occurred when reproducing the table. The notations have now been corrected in the online version of this article, available from: www.bpac.org.nz

The original table is also available from: **www.immune.org.nz**

ESR and burning feet

Dear Editor,
With regard to your sidebar "burning feet syndrome", within the article "The night time hustle: managing restless legs syndrome in adults", BPJ 49 (Dec, 2012), you mention ESR as an appropriate test for multiple myeloma.

I am curious about this as our regional laboratory, in conjunction with the consultant Haematologists at Palmerston North Hospital, circulated a memo in April, 2010, stating that ESR would not be done for any indication other than Systemic lupus erythematosus, Rheumatoid Arthritis, Kawasaki Disease, Rheumatic Fever and Hodgkin's Lymphoma. They stated that ESR is not an appropriate test in multiple myeloma because of its lack of specificity and quality assurance.

I wonder if this is the case throughout New Zealand, or a local situation?

***Dr. Marion Taylor**, General Practitioner*
Wanganui

In the "burning feet" sidebar of the article you refer to, ESR was suggested as an investigation that may be considered, along with serum protein electrophoresis and serum free light chains or Bence Jones protein in urine to rule out the possibility of multiple myeloma in a patient with burning feet (and other reasons to suspect multiple myeloma as a cause). We agree that ESR alone is not useful for diagnosing multiple myeloma as it lacks specificity - while ESR is usually elevated in people with multiple myeloma when CRP is normal, there are many other potential causes of a very high ESR. This approach to investigating possible multiple myeloma (i.e. ESR + other tests) is recommended in the British guideline for multiple myeloma,[1] and in other literature.[2]

However, after consultation with several laboratories and haematologists it appears that the growing consensus in New Zealand is that measurement of ESR is no longer recommended when investigating possible multiple myeloma. A practical approach, if myeloma is suspected, is to first request serum protein electrophoresis. If an increase in immunoglobulins is found, or the test is normal but clinical suspicion remains, the need for further testing (e.g. serum free light chains or Bence Jones protein) should be discussed with a haematologist or other relevant specialist.

National laboratory testing guidelines are currently in development, and it is likely that serum free light chains will be one of several tests that are recommended for restricted use. We will provide an update on these guidelines when they become available.

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Fasting requirements for blood tests

Dear Editor,
I have been taking fasting bloods from patients for a long time now and have been telling patients that they should fast for twelve hours but that they can have water or black tea or coffee. I thought this was common practice until I received a letter from the laboratory, stating that tea and coffee should not be consumed during the fasting period as caffeine can affect glucose levels.

I would like to know what the research has shown regarding fasting status in lipid and glucose test results (not that a fasting glucose is used very often now). It would be great if everyone in primary health care was treating fasting bloods in the same manner.

***Helen Homan**, Practice Nurse*
Dunedin

Recommendations for the length of a fasting period for glucose and lipid tests vary between laboratories. The accepted minimum fasting time is eight hours,[1] but twelve hours is preferable.

Water may be drunk during the fasting period, but tea and coffee (even without milk) should not be consumed. Caffeine

can temporarily produce a small, but detectable, transient increase in serum glucose levels (approximately 10%).[2] The reason for the increase is not well understood, as overall insulin sensitivity is not affected by caffeine.[2] It is likely that the effect comes from either increased bioavailability of glucose or from a relative effect on insulin secretion. The effect of caffeine on lipid levels is less significant and is unlikely to alter fasting blood test results (unless milk or cream is also added).[3] However, to avoid confusion, it may be best to advise patients not to drink tea or coffee during a fasting period for any fasting blood test.

HbA_{1c} is recommended in preference to fasting glucose for investigating diabetes in most people, as, among other reasons, the requirements of a fasting glucose test are a significant burden to many patients.

There is increasing debate as to whether a non-fasting lipid test is adequate for a cardiovascular risk assessment. Patient compliance is likely to be higher if a lipid test can be performed "now", rather than asking the patient to fast and present at a laboratory in the morning. However, current cardiovascular risk assessment guidelines are based on fasting test results.

We hope to follow this debate and update this issue in the future.

For further information on the use of fasting glucose see: "When to use a fasting glucose to diagnose type II diabetes", Best Tests December (Dec, 2012).

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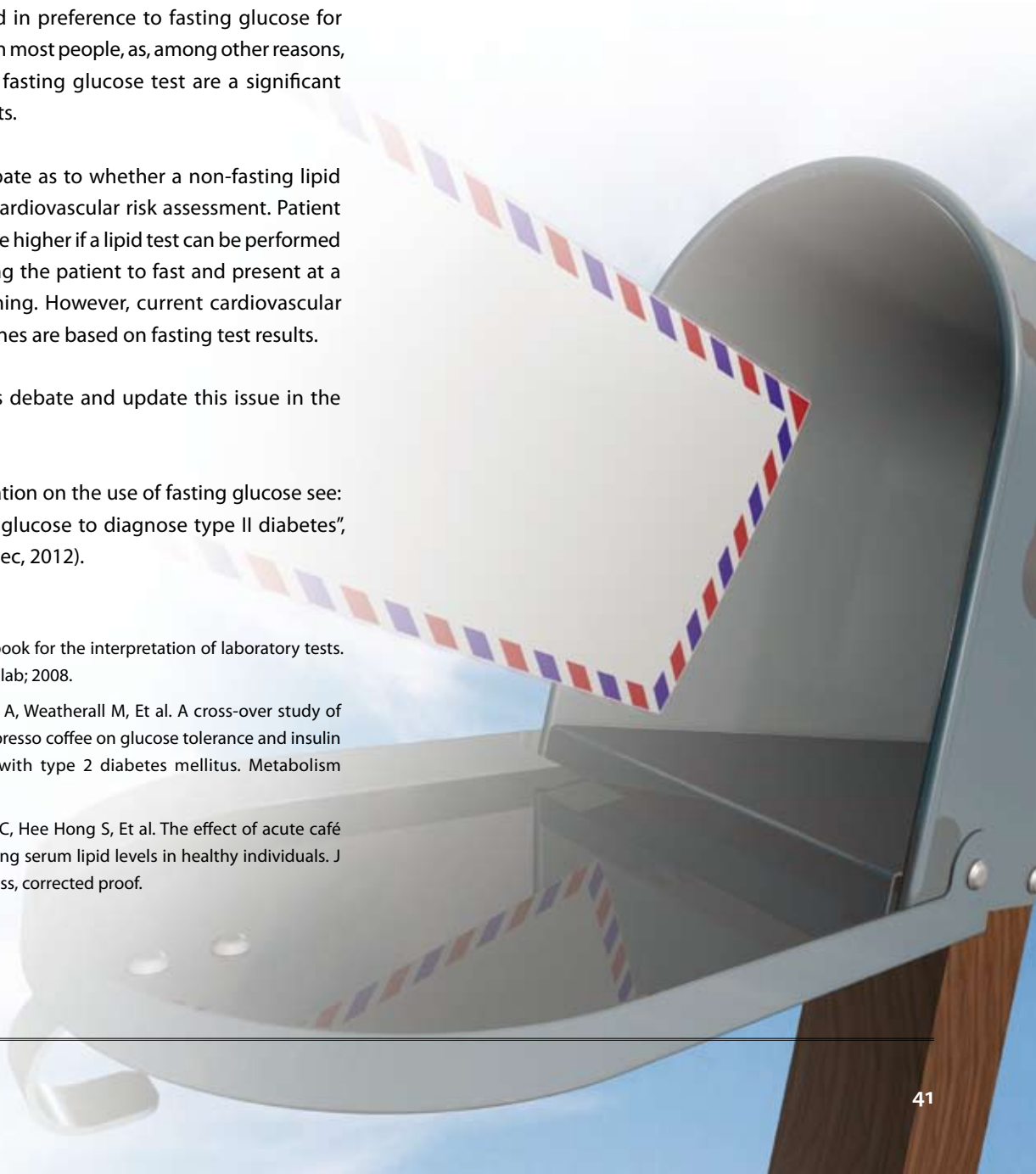

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