ESSENTIAL PRACTICE POINTS AND KEY CLINICAL MESSAGES FROM 2015

Best Practice

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Issue 73 January 2016

2015 in review

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Best Practice

Issue 73 January 2016

Best Practice Journal (BPJ)
ISSN 1177-5645 (Print)
ISSN 2253-1947 (Online)

BPJ is published and owned by bpac[nz] Ltd
Level 8, 10 George Street, Dunedin, New Zealand.

Bpac[nz] Ltd is an independent organisation that promotes health care interventions which meet patients' needs and are evidence based, cost effective and suitable for the New Zealand context.

We develop and distribute evidence based resources which describe, facilitate and help overcome the barriers to best practice.

Bpac[nz] Ltd is currently funded through a contract with PHARMAC.

Bpac[nz] Ltd has six shareholders: Procare Health, South Link Health, General Practice NZ, the University of Otago, Pegasus and The Royal New Zealand College of General Practitioners

Printed in New Zealand on paper sourced from well-managed sustainable forests using mineral oil free, soy-based vegetable inks

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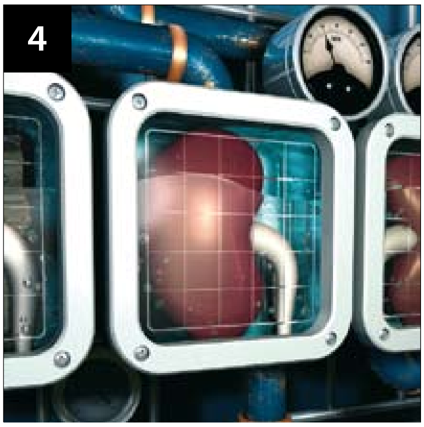

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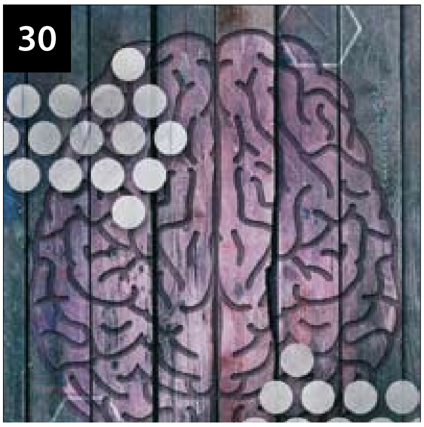

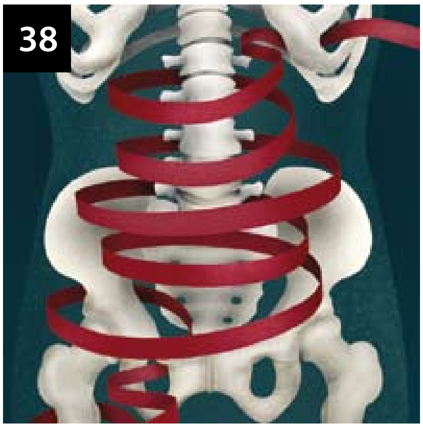

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Welcome to Issue 73 of Best Practice Journal

This edition is a summary of our main articles from 2015. We have highlighted essential practice points and key clinical messages for 21 topics.

The original versions of these articles, published in full, can be found at: **www.bpac.org.nz/BPJ/BPJ.aspx**

bpac[nz]'s 2015 top ten suggestions for primary care:

1. Take responsibility for prescribing antibiotics appropriately
2. Regularly review medicines in patients aged over 70 years
3. Focus on asthma education: assign this task to an "asthma champion" in your practice
4. Identify patients who have been taking oral medicines for diabetes, but have been unable to reach or maintain their target glycaemic level: are they candidates for insulin treatment?
5. Identify patients who have been taking benzodiazepines long-term and work with them to reduce or stop their use
6. Add a serum creatinine and albumin:creatinine ratio (ACR) test to a regular CVD assessment for patients with risk factors for chronic kidney disease
7. Prescribe oral corticosteroids for five days only for patients with moderate or severe COPD exacerbations
8. Prescribe an appropriate quantity of paracetamol tablets instead of just writing "as required" on the prescription
9. Educate parents to use adequate amounts of topical corticosteroids in children with eczema
10. When consulting with a young person, take the opportunity to assess their mental health and wellbeing

The detection and management of **patients with chronic kidney disease** in primary care

Key practice points

- Offer testing for chronic kidney disease (CKD) to patients with risk factors as part of routine CVD risk assessments and diabetes checks, especially Māori and Pacific patients
- A clinical priority is to distinguish patients with progressive CKD from those with age-related declining renal function
- Controlling blood pressure with an angiotensin converting enzyme (ACE) inhibitor or an angiotensin II receptor blocker (ARB) is the cornerstone of CKD management
- Patients with CKD and diabetes require intensive management

Chronic kidney disease (CKD) describes any long-term condition that affects kidney structure and function. Declining kidney function is a natural part of the ageing process and some older patients will have CKD without active or structural kidney disease. The challenge is to distinguish patients with progressively declining renal function due to disease, who require intensive management, from those with age-related declining renal function.[1]

The number of people in New Zealand with CKD is currently unknown; based on international data it is estimated that 7–10% of the population are likely to have CKD. End-stage kidney disease is three to four times more common in Māori and Pacific peoples compared with people of European descent.[2]

It is recommended that primary care clinicians routinely **offer kidney function testing for patients with risk factors for CKD as part of CVD risk assessments and diabetes checks.**[3] Risk factors for CKD include:[3]

- Hypertension
- Proteinuria
- Diabetes
- Age over 60 years
- Body mass index (BMI) > 35
- Family history of CKD
- Māori, Pacific or Indo Asian ethnicity
- Cardiovascular disease resulting in reduced renal perfusion and endothelial dysfunction
- Prostatic syndrome/urologic disease which has the potential to cause obstructive nephropathy

Patients with risk factors for CKD should be assessed at least every one to two years; annual assessment is required for patients with diabetes.[1] Screening for CKD in people without risk factors is not necessary.

Diagnosing chronic kidney disease

Patients with CKD can be identified in primary care by requesting both:[3]

- A serum creatinine, which automatically generates an eGFR from the laboratory
- An albumin:creatine ratio (ACR) test

The presence of persistent albuminuria further categorises the patient's risk. If the patient has microalbuminuria (ACR 2.5 – 25 mg/mmol for males and 3.5 – 35 mg/mmol for females) or macroalbuminuria (ACR > 25 mg/mmol for males and > 35 mg/mmol for females), the ACR test should be repeated one to two times over the next three months to confirm the diagnosis.[1]

Classifying chronic kidney disease

Chronic kidney disease is classified according to Kidney Disease Improving Global Outcomes (KDIGO) criteria which is independent of cause (Table 1).[3] Each stage is characterised by an eGFR range. Patients with an eGFR > 60 mL/min/1.73m^2 are classified with stage 1 or 2 CKD only if they also have documented evidence of kidney disease, e.g. diabetic nephropathy or polycystic kidney disease as shown by imaging or biopsy abnormalities, or persistent proteinuria.[3] Patients with stage 3 CKD may be asymptomatic, or report nocturia, mild malaise or anorexia.[1] The signs and symptoms of stage 4 and 5 CKD include nausea, pruritus, restless legs and dyspnoea.[1]

Table 1: Classification of chronic kidney disease according to KDIGO criteria using estimated Glomerular Filtration Rate (eGFR) mL/min/1.73m^2. [3]

CKD staging	eGFR
1*	≥ 90
2*	60 – 89
3a	49 – 59
3b	30 – 44
4	15 – 29
5	< 15

* In association with documented evidence of kidney disease or persistent proteinuria

Managing patients with chronic kidney disease in primary care

Most patients with stable CKD can be fully managed in primary care.[1] Lifestyle modifications, e.g. increasing exercise and reducing salt intake, can help to reduce the rate of declining renal function. Smoking is an important modifiable risk factor for CKD progression.[4] Reductions in systolic blood pressure can be used as a measure of the benefits of lifestyle modification in patients with CKD.

Blood pressure control is pivotal in chronic kidney disease management

Managing blood pressure is the cornerstone of CKD management both to slow the rate of CKD progression and to reduce the patient's cardiovascular risk. The goal for blood pressure control is to reduce proteinuria by more than 50%.[1]

The target blood pressure for patients with CKD is:[1]

- ≤ 130/80 mmHg for patients with diabetes or proteinuria with an ACR > 30 mg/mmol
- ≤ 140/90 mmHg for most other patients

Angiotensin converting enzyme (ACE) inhibitors are the first-line treatment for controlling blood pressure in patients with CKD.[1] Angiotensin II receptor blockers (ARBs) are an alternative.[1] Many patients will require multiple medicines to achieve blood pressure targets.[1] It is recommended that a calcium channel blocker be added to an ACE inhibitor or ARB as the second stage in managing hypertension in patients with CKD.[5] The combination of ACE inhibitors and ARBs should be avoided when treating patients with CKD in primary care.[1]

Glycaemic control

In patients with CKD and diabetes, glycaemic control is essential to prevent or delay the progression of microvascular complications and to reduce cardiovascular risk.[6] A HbA_{1c} target < 53 mmol/mol is generally appropriate for patients with CKD and diabetes, although in patients at risk of hypoglycaemia a higher target may be more appropriate.[6]

Managing total cardiovascular risk

Patients with stable CKD (stage 3 – 4) have a five-year cardiovascular risk > 15%, which increases to > 20% if diabetes is also present. All patients with CKD need appropriate cardiovascular risk management and it is important that additional medicines, e.g. statins and aspirin, are initiated according to cardiovascular guidelines.

Monitoring patients with established chronic kidney disease

Patients with established CKD should have their eGFR and albuminuria assessed at least annually,[1] and more frequently if they have an increased risk of progressive CKD.

Progressive CKD refers to patients with an eGFR that is declining at a rate > 5 mL/min/year.[3] Patients with progressive CKD have a high risk of experiencing a cardiovascular event, and if they live long enough are likely to require dialysis and/or kidney transplantation. These patients require close supervision, will often need to be intensely managed and may need to be referred to secondary care.[1] Patients with progressive stage 3 – 4 CKD require weekly or fortnightly review of risk factor management until their condition is stable.[3]

Referral to nephrology

The decision to refer a patient with CKD to a nephrologist and/or diabetologist should be made on a case-by-case basis.[1]

All patients with the following factors should be referred to a nephrologist:[3]

- Progressive CKD in patients with an eGFR < 45 mL/min/1.73^2
- Evidence of intrinsic kidney disease, e.g. glomerulonephritis, polycystic kidney disease or interstitial nephritis
- Resistant hypertension and/or significant issues with blood glucose control and/or multiple vascular complications

In younger patients, a lower threshold for referral is usually appropriate.

For further information, see: "The detection and management of patients with chronic kidney disease in primary care", BPJ 66 (Feb, 2015).

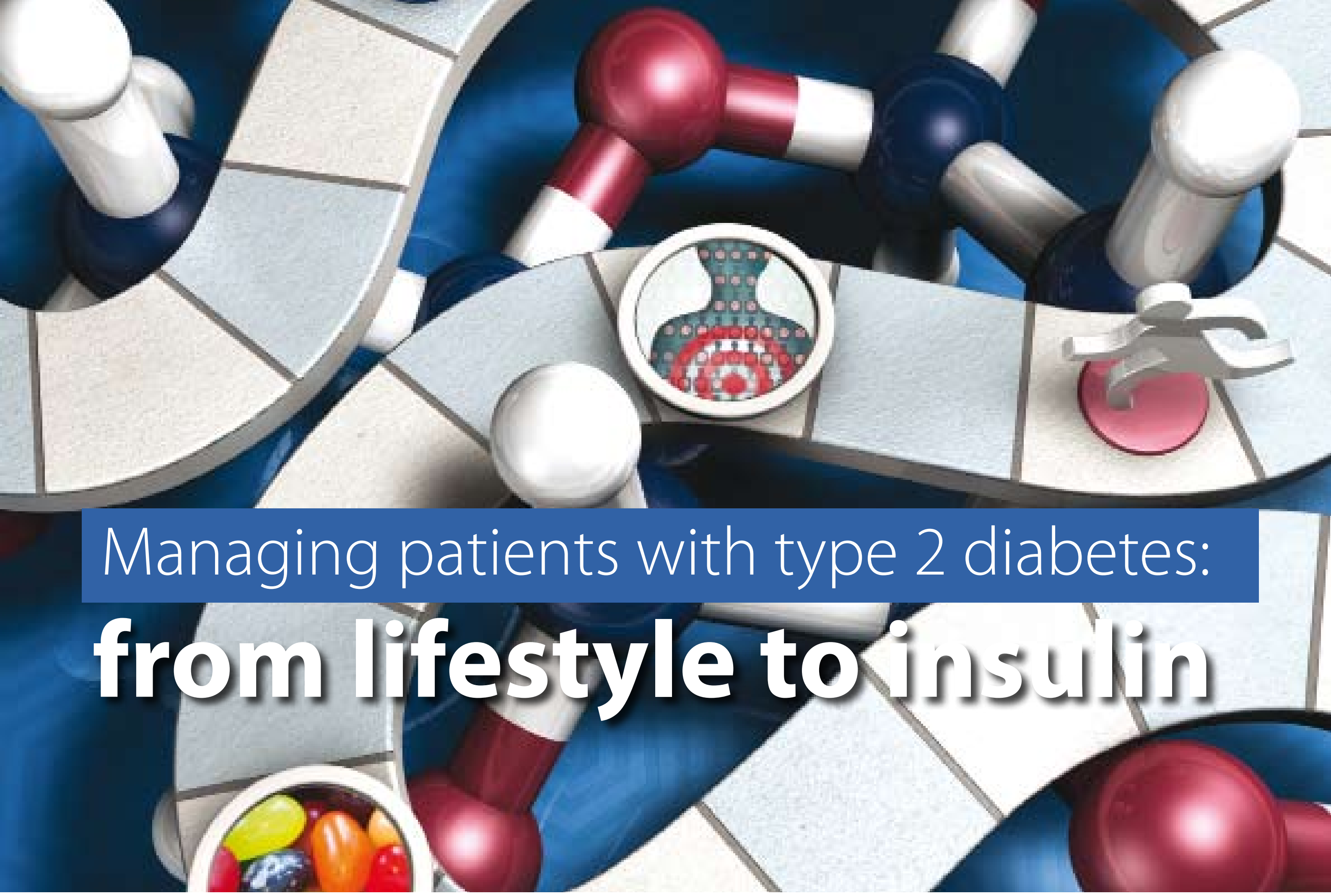
References

1. Kidney Health New Zealand. Chronic kidney disease (CKD): management in General Practice. 2013. Available from: www.kidneys.co.nz/resources/file/ckd_management_in_general_practice._2014_version.pdf (Accessed Dec, 2015).
2. Kenealy T, Elley CR, Collins JF, et al. Increased prevalence of albuminuria among non-European peoples with type 2 diabetes. Nephrol Dial Transplant 2012;27:1840–6. doi:10.1093/ndt/gfr540
3. Managing chronic kidney disease in primary care: a national consensus statement. 2014. Available from: www.kidneys.co.nz/Health-Professionals/CKD-consensus-statement-2015 (Accessed Dec, 2015).
4. Orth SR, Hallan SI. Smoking: a risk factor for progression of chronic kidney disease and for cardiovascular morbidity and mortality in renal patients--absence of evidence or evidence of absence? Clin J Am Soc Nephrol CJASN 2008;3:226–36. doi:10.2215/CJN.03740907
5. National Institute for Health and Clinical Excellence (NICE). Hypertension: clinical management of primary hypertension in adults. 2011. Available from: www.nice.org.uk/guidance/cg127 (Accessed Dec, 2015).
6. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 Clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney Int Suppl 2012;3:5–14. doi:10.1038/kisup.2012.76

CKD SmartPath: decision support module for chronic kidney disease

BPAC Inc in conjunction with the Southern DHB, have created a CKD decision support module for health professionals working in primary care. The module is funded by the Ministry of Health and will be rolled out nationally by region. This tool will automatically classify a patient's CKD as stable or progressive and individual management and referral recommendations will be made based upon information already recorded, e.g. eGFR, including pre-populated electronic referrals, where appropriate.

Further information is available from: **www.bestpractice.net.nz/feat_mod_fullList.php#ckd**



Managing patients with type 2 diabetes: from lifestyle to insulin

Key practice points

- Metformin is the first-line pharmacological treatment for patients with type 2 diabetes and initiation should be strongly considered at diagnosis
- In general, treatment intensification is appropriate for patients whose HbA_{1c} levels do not meet, or closely approach, an agreed target within three months
- Isophane is the fist-line insulin and should be considered for any patients with HbA_{1c} levels persistently above agreed targets (especially HbA_{1c} > 65 mmol/mol)
- Well-controlled blood pressure is associated with substantial reductions in cardiovascular risk in patients with type 2 diabetes, and should be a focus of care

Lifestyle, education and intensifying treatment

A healthy lifestyle is the foundation of treatment for all people with type 2 diabetes. If agreed lifestyle goals are not achieved, discussions should be initiated to help overcome barriers to change, regardless of diabetes duration or type of medicine being taken.

Education is a cornerstone of care

Structured diabetes education is recognised in New Zealand as a critical aspect of treatment.[1] The goal is to enable patients to take an active role in their own care.[1] An HbA_{1c} target of 50 – 55 mmol/mol can be explained as the "speed-limit" for patients, i.e. measurements above this level are increasingly unsafe.[2] However, glycaemic targets need to take into account diabetes duration, the presence of co-morbidities, life expectancy, social circumstances and the personal beliefs and priorities of the patient.[3]

Intensifying diabetes treatment with oral medicines

Regular review is essential for improving glycaemic control in all patients with diabetes. Treatment adherence should be assessed in patients who are unable to meet glycaemic targets. In general, intensification is appropriate if the patient's HbA_{1c} levels do not meet, or closely approach, an agreed target within three months.[2, 3]

Metformin is the first-line pharmacological treatment for patients with type 2 diabetes because it is safe, effective, does not cause weight gain and provides patients with additional cardiovascular benefits.[2] There is a low threshold for initiation and metformin should be started at diagnosis, or soon after, for all patients with type 2 diabetes, unless there are contraindications.[3] New Zealand guidelines recommend trialling lifestyle modification for three months in asymptomatic patients before beginning treatment with metformin.[2] In practice, however, treatment with metformin may often be initiated at diagnosis for these patients.

A sulfonylurea can be added to metformin for patients who have not reached an agreed HbA_{1c} target with metformin alone.[2] Caution is required if a sulfonylurea is prescribed to an older patient or a patient with reduced renal function, due to the risk of hypoglycaemia.[4] Weight-gain is a common adverse effect of treatment with sulfonylureas.[4]

Acarbose can be used as a first-line treatment for patients with type 2 diabetes where metformin or a sulfonylurea are contraindicated or not tolerated, or as an adjunctive treatment for patients taking metformin, a sulfonylurea or insulin.[2, 5] Acarbose is not widely used, however, as it is only mildly effective and is associated with significant gastrointestinal adverse effects.[3]

Pioglitazone may be appropriate when treatment with metformin and a sulfonylurea is not tolerated or contraindicated, or if an alternative to insulin is required.[2] Pioglitazone may also be used in combination with metformin and a sulfonylurea, or as an adjunctive treatment with metformin in patients who require escalating doses of insulin.[3] Pioglitazone use can cause significant weight gain and peripheral oedema, and the risk of heart failure is increased.[3] There is also an increased risk of bone fracture, particularly in post-menopausal females taking pioglitazone.[4] Pioglitazone is contraindicated in patients with a history of heart failure, un-investigated macroscopic haematuria or bladder cancer.[4]

Initiating insulin treatment

Insulin has a greater blood glucose lowering ability than any other hypoglycaemic medicine and it is eventually required by many people with type 2 diabetes.[6] However, a reluctance to initiate insulin, by both patients and clinicians, often delays treatment.[6] Initiation of insulin in primary care should be considered for any patients with HbA_{1c} levels persistently greater than their individualised target (especially if HbA_{1c} is > 65 mmol/mol) despite optimal oral treatment,[2] particularly if they have signs such as ketonuria and weight loss.[6]

Isophane is the first-line insulin taken either once daily at night or before breakfast, or twice daily.[2]

The initial insulin dose is a starting point which should be titrated until the agreed glycaemic level is reached or hypoglycaemia limits further increases.

New Zealand guidelines recommend that treatment with a sulfonylurea be withdrawn in patients taking twice daily isophane.[2] However, in practice metformin and sulfonylureas are generally continued throughout treatment with basal insulin. When insulin treatment is intensified to include a short-acting insulin, e.g. with meals, sulfonylureas are withdrawn.

Managing risk factors with regular follow-up

People with type 2 diabetes are three times more likely to die of a cardiovascular event compared with the general population.[7] While good glycaemic control improves microvascular outcomes, e.g. retinopathy, it does not appear to improve cardiovascular outcomes to the same extent.[8] Therefore glycaemic control is part of a wider suite of interventions for patients with type 2 diabetes, including blood pressure control, lipid management and, if appropriate, smoking cessation and antiplatelet treatment.[3]

Pharmacological treatment is recommended for patients with type 2 diabetes with a blood pressure > 130/80 mmHg for three months, despite changes in lifestyle.[2] An ACE inhibitor is the preferred antihypertensive for patients with type 2 diabetes; or an angiotensin II receptor blocker (ARB) if an ACE inhibitor is not tolerated.[2] Systolic blood pressure < 120 mmHg in people with type 2 diabetes is associated with an increased risk of hypotension, syncope and cardiac dysrhythmias.[9]

Measure the albumin:creatinine ratio (ACR) at least annually for people with type 2 diabetes and more frequently for Māori, Pacific and South Asian peoples.[2] Microalbuminuria is the earliest sign of chronic kidney disease (CKD) in people with diabetes and requires prompt treatment.[2]

Consider initiating a statin for patients with a five-year cardiovascular risk of >10%.[10] People with type 2 diabetes often have elevated serum triglycerides, decreased HDL cholesterol levels and normal to elevated LDL cholesterol levels.[8]

Encourage patients with type 2 diabetes to carefully inspect their feet as part of their daily routine or ask a family member to do so. The patient's feet should be clinically assessed at least once a year, or every three months if they are at high risk of foot complications.[2]

Patients with type 2 diabetes require retinal testing at least every two years.[2] Testing is performed more frequently if the patient has been diagnosed with retinopathy.[2]

Be vigilant for mental health problems in patients with type 2 diabetes. Depression is reportedly twice as common, compared with people in the general population.[11] Poor mental health makes it more likely that patients will not adhere to treatment or attend consultations, increasing their risk of diabetes-related complications and reducing quality of life.[11]

For further information, see: "Managing patients with type 2 diabetes: from lifestyle to insulin", BPJ 72 (Dec, 2015).

References

1. Ministry of Health (MoH). Quality standards for diabetes care toolkit. 2014. Available from: www.health.govt.nz/system/files/documents/publications/quality-standards-for-diabetes-care-toolkit-2014-nov14-v2.pdf (Accessed Dec, 2015).
2. New Zealand Guidelines Group. New Zealand Primary Care handbook 2012. 3rd ed. 2012. Available from: www.health.govt.nz/publication/new-zealand-primary-care-handbook-2012 (Accessed Dec, 2015).
3. Inzucchi SE, Bergenstal RM, Buse JB, et al. Management of hyperglycemia in type 2 diabetes, 2015: a patient-centered approach. Update to a position statement of the American Diabetes Association and the European Association for the Study of Diabetes. Diabetes Care 2015;38:140–9. doi: 10.1007/s00125-014-3460-0
4. New Zealand Formulary (NZF). NZF v42. 2015. Available from: www.nzf.org.nz (Accessed Dec, 2015).
5. Mylan New Zealand Ltd. New Zealand data sheet: ACCARB. 2014. Available from: www.medsafe.govt.nz/profs/datasheet/a/accarbtab.pdf (Accessed Dec, 2015).
6. Powers A. Chapter 344: Diabetes mellitus. In: Harrision's principles of internal medicine. McGraw Hill Medical, 2012. 2968–3002.
7. Taylor KS, Heneghan CJ, Farmer AJ, et al. All-cause and cardiovascular mortality in middle-aged people with type 2 diabetes compared with people without diabetes in a large U.K. primary care database. Diabetes Care 2013;36:2366–71. doi: 10.2337/dc12-1513
8. Fox CS, Golden SH, Anderson C, et al. Update on Prevention of Cardiovascular Disease in Adults With Type 2 Diabetes Mellitus in Light of Recent Evidence: A Scientific Statement From the American Heart Association and the American Diabetes Association. Diabetes Care 2015;38:1777–803. doi: 10.2337/dci15-0012
9. ACCORD Study Group, Cushman WC, Evans GW, et al. Effects of intensive blood-pressure control in type 2 diabetes mellitus. N Engl J Med 2010;362:1575–85. doi:10.1056/NEJMoa1001286
10. Cardiovascular disease risk assessment: updated 2013 – New Zealand Primary Care Handbook 2012. 2013. Available from: www.health.govt.nz/system/files/documents/publications/cardiovascular-disease-risk-assessment-updated-2013-dec13.pdf (Accessed Dec, 2015).
11. Ducat L, Philipson LH, Anderson BJ. The Mental Health Comorbidities of Diabetes. JAMA 2014;312:691. doi:10.1001/jama.2014.8040

An update on antithrombotic medicines: What does primary care need to know?

Key practice points

- Patients with atrial fibrillation who have a very low risk of stroke are unlikely to benefit from antithrombotic treatment
- Aspirin monotherapy should not be prescribed solely for stroke prevention; anticoagulation is the preferred treatment
- On balance dabigatran appears at least as effective and may be safer than warfarin for the prevention of ischaemic stroke and systemic embolism
- Dabigatran should NOT be prescribed to patients with valvular heart disease

The number of antithrombotic medicines is increasing, as is the challenge for general practitioners in advising patients about treatment options and managing patients when antithrombotic medicines are initiated in secondary care, e.g. following a percutaneous coronary intervention.

Antithrombotic treatment recommendations for patients with non-valvular atrial fibrillation depend on the patient's risk of ischaemic stroke which can vary by 20-fold depending on their age and clinical features.[1]

Managing stroke risk in patients with non-valvular atrial fibrillation

The individual stroke risk for patients with non-valvular atrial fibrillation needs to be assessed to determine if they are likely to benefit from anticoagulant treatment.[1]

Previous guidance on the management of stroke risk has changed

Previously, all patients with atrial fibrillation were offered antithrombotic treatment and those with a CHA_2DS_2-VASc score of 0 (see: "Atrial fibrillation management tools: CHA_2DS_2-VASc and HAS-BLED") were offered aspirin in preference to an anticoagulant. It is now recommended that these patients **should not** be treated with either an anticoagulant or an antiplatelet at this time.[2] Furthermore, aspirin monotherapy should generally not be prescribed for the purpose of stroke prevention in any patients with atrial fibrillation: anticoagulation is preferred.[3]

Guidance now recommends that anticoagulation be considered for all patients who have a CHA_2DS_2-VASc score ≥ 1.[4] Where it is uncertain if a patient will benefit from anticoagulant treatment discussion with a cardiologist or neurologist may be beneficial.

Always consider the risk of bleeding before discussing anticoagulation treatment with a patient. This risk, however, should not be overstated. Risk factors for bleeding in patients taking anticoagulant treatment include:[4]

- Increasing age
- Uncontrolled hypertension
- History of myocardial infarction, ischaemic heart disease or cerebrovascular disease
- Anaemia
- A history of bleeding
- The use of other medicines that increase bleeding risk, e.g. aspirin or other antiplatelet medicines and non-steroidal anti-inflammatory drugs (NSAIDs)

There are a number of tools available that can be used to assess the risk of bleeding in patients with atrial fibrillation. The HAS-BLED tool is used to identify modifiable risk factors that can be managed in patients undergoing anticoagulation treatment.[2]

Warfarin or dabigatran to prevent thromboembolism?

If anticoagulant treatment is appropriate the decision needs to be made whether warfarin or dabigatran is the preferred treatment option (Table 1). Patient preference plays a significant role in this decision.

On balance the evidence suggests that dabigatran, dosed appropriately, is at least as effective and may be safer than warfarin for the prevention of ischaemic stroke and systemic embolism.

Dabigatran should NOT be prescribed to patients with valvular heart disease: patients with mechanical heart valves who take dabigatran are at an increased risk of bleeding or experiencing a thromboembolic event compared to what their risk would have been if they had been prescribed warfarin.[8]

Atrial fibrillation management tools: CHA_2DS_2-VASc and HAS-BLED

The CHA_2DS_2-VASc stroke risk assessment tool uses risk factors to calculate a score out of nine. This tool is helpful for identifying patients at very low risk of stroke who may not benefit from treatment with an anticoagulant.[2] Figure 1 shows the annual stroke risk for patients with a CHA_2DS_2-VASc score of 0 – 6.

Clinical feature	Points
Congestive heart failure	1
Hypertension	1
Age ▪ 65 – 74 years ▪ ≥ 75 years	 1 or 2
Diabetes mellitus	1
Stroke or transient ischaemic attack	2
Vascular disease, e.g. peripheral artery disease, myocardial infarction, aortic plaque	1
Female sex	1
Total out of 9 =	

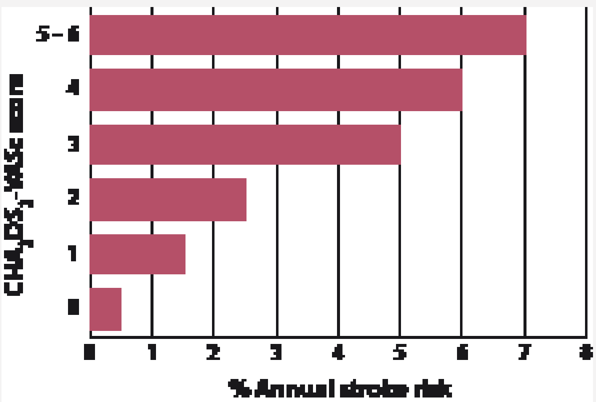


Figure 1: Annual stroke risk for patients with a CHA_2DS_2-VASc of 0 – 6

The HAS-BLED tool is used to identify modifiable risk factors in patients undergoing anticoagulation treatment.[2] HAS-BLED may also be useful in balancing the risks versus benefits of anticoagulation treatment in patients with atrial fibrillation who have a CHA_2DS_2-VASc score of 1.[2] HAS-BLED should not, however, be used to determine whether a patient should be offered anticoagulation treatment as this decision should be based on stroke risk.[2] A HAS-BLED score > 2 is associated with a clinically significant risk of major bleeding.[1]

Risk factor	Score
Hypertension (systolic blood pressure > 160 mmHg)	1
Abnormal renal and liver function	1 point each
Stroke (past history)	1
Bleeding (previous history of bleeding or predisposition to bleeding)	1
Labile INRs (unstable, high or insufficient time with therapeutic range)	1
Elderly (aged over 65 years)	1
Drugs or alcohol (including concomitant use of aspirin, other antiplatelet medicines and NSAIDs)	1 point each
Total out of 9 =	

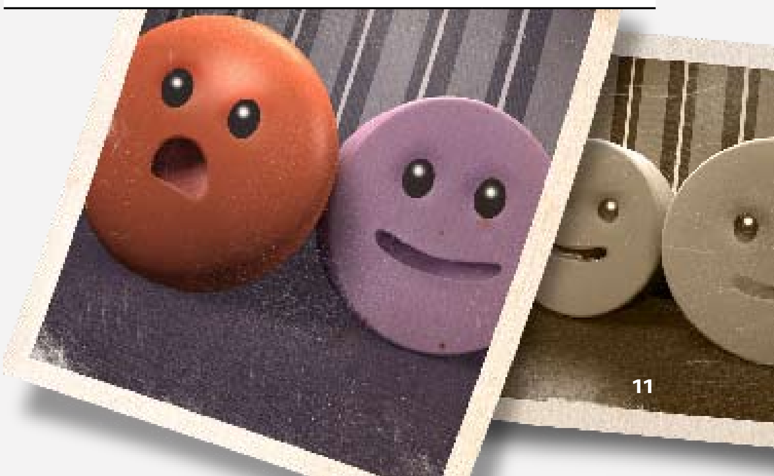


Table 1: The advantages and disadvantages of dabigatran, compared with warfarin, for the treatment of patients with non-valvular atrial fibrillation

The advantages of dabigatran	The disadvantages of dabigatran
■ Superior stroke prevention with dabigatran 150 mg, twice daily ■ Testing and dose adjustments are not currently required ■ Onset of anticoagulation is rapid (two to three hours) compared with 48 – 72 hours with warfarin[5] ■ Does not accumulate in the liver and safer in patients with hepatic dysfunction[6] ■ Fewer interactions with other medicines and foods ■ A reduced risk of intracranial haemorrhage with dabigatran 110 mg, twice daily	■ An increased incidence of gastrointestinal adverse effects, e.g. dyspepsia ■ Twice daily dosing required ■ Caution required in patients with progressive chronic kidney disease (CKD) ■ A small absolute increase in risk (0.27%) of acute coronary syndrome[7]

Ticagrelor is superior to clopidogrel in patients with acute coronary syndromes

It is increasingly likely that patients who have been diagnosed with an acute coronary syndrome will receive long-term treatment with ticagrelor, twice daily, in preference to clopidogrel, once daily; both are used in combination with aspirin, i.e. dual antiplatelet treatment. The choice of anticoagulant is usually made in hospital following diagnosis of an acute coronary syndrome and treatment is then continued in the community for twelve months.

Unlike clopidogrel, ticagrelor is not a prodrug and therefore does not need to be processed by an enzyme (CYP2C19) to be activated. This explains why ticagrelor is reported to produce faster, greater and more consistent inhibition of platelet reactivity compared with clopidogrel.[9] Due to ethnic differences in the prevalence of genetic polymorphisms in the CYP2C19 enzyme that metabolises clopidogrel it has been suggested that Māori and Pacific patients should be preferentially treated with ticagrelor over clopidogrel.[10]

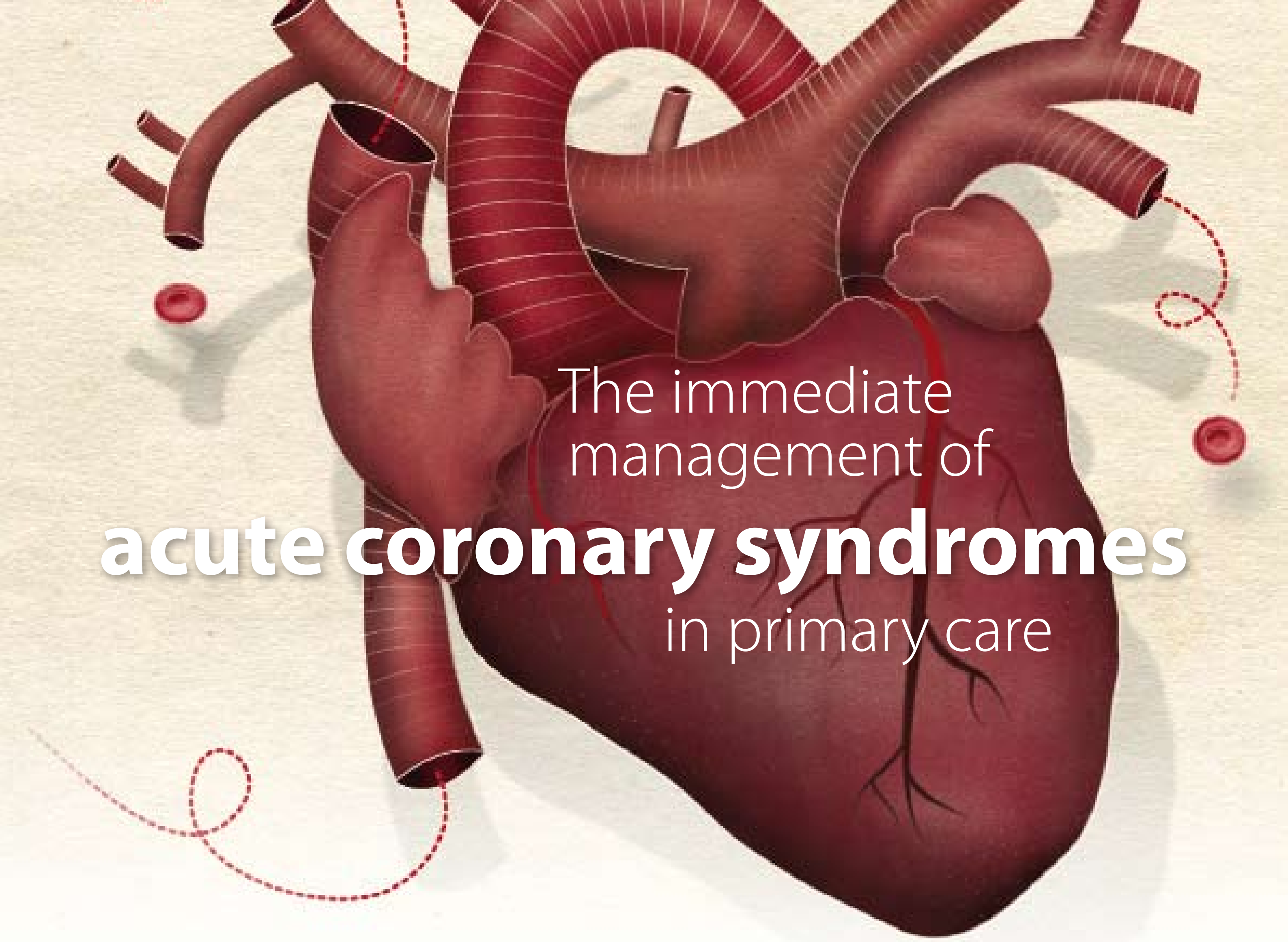
How is ticagrelor initiated ?

Treatment with ticagrelor begins with 180 mg as a loading dose, then 90 mg, twice daily, for up to 12 months.[5] Ticagrelor should be taken in combination with low-dose aspirin.[5] The most frequent adverse effect is a transient dyspnoea that does not appear to be caused by bronchospasm; ticagrelor should be used cautiously in patients with asthma or COPD.[5] Ticagrelor should be discontinued five days before elective surgery.[5] It is recommended that renal function be tested within one month of initiation.[5]

For further information, see: "An update on antithrombotic medicines – What does primary care need to know?" BPJ 67 (Apr, 2015).

References

1. Meschia JF, Bushnell C, Boden-Albala B, et al. Guidelines for the primary prevention of stroke: a statement for healthcare professionals from the American Heart Association/American Stroke Association. Stroke J Cereb Circ 2014;45:3754–832. doi:10.1161/STR.0000000000000004
2. Hobbs FR, Taylor CJ, Jan Geersing G, et al. European Primary Care Cardiovascular Society (EPCCS) consensus guidance on stroke prevention in atrial fibrillation (SPAF) in primary care. Eur J Prev Cardiol 2015;[Epub ahead of print].
3. National Institute for Health Care Excellence (NICE). Atrial fibrillation: the management of atrial fibrillation. 2014. Available from: www.nice.org.uk/guidance/cg180 (Accessed Dec, 2015).
4. Scottish Intercollegiate Guidelines Network (SIGN). Prevention of stroke in patients with atrial fibrillation. Available from: www.sign.ac.uk/pdf/AF_publication.pdf (Accessed Dec, 2015).
5. New Zealand Formulary (NZF). NZF v42. 2015. Available from: www.nzf.org.nz (Accessed Dec, 2015).
6. Weitz J. Antiplatelet, anticoagulant, and fibrinolytic drugs. In: Harrision's principles of internal medicine. McGraw Hill Medical 2012. pp. 988–1004.
7. Uchino K, Hernadez A. Dabigatran association with higher risk of acute coronary events: meta-analysis of noninferiority randomized controlled trials. Arch Intern Med 2012;172:397–402. doi:10.1001/archinternmed.2011.1666
8. U.S. Food and Drug Administration. FDA Drug safety communication: Pradaxa (dabigtran etexilate mesylate) should not be used in patients with mechanical prosthetic heart valves. 2012. Available from: www.fda.gov/Drugs/DrugSafety/ucm332912.htm (Accessed Dec, 2015).
9. Wallentin L, Becker RC, Budaj A, et al. Ticagrelor versus clopidogrel in patients with acute coronary syndromes. N Engl J Med 2009;361:1045–57. doi:10.1056/NEJMoa0904327
10. Larsen P, Johnston L, Holley A, et al. Prevalence and significance of CYP2C19*2 and CYP2C19*17 alleles in a New Zealand acute coronary syndrome population: CYP2C19*2 in acute coronary syndromes. Intern Med J 2015;45:537–45. doi:10.1111/imj.12698



The immediate management of **acute coronary syndromes** in primary care

Key practice points

- Perform an ECG in all patients where the possibility of a cardiac cause of chest pain cannot be reasonably excluded
- Immediate transfer to hospital is recommended for all patients with symptoms suggestive of an acute coronary syndrome, where a cardiac cause cannot be reasonably excluded, regardless of the results of their ECG
- While awaiting transfer:
  - Monitor blood pressure, heart rate and oxygen saturation
  - Give sublingual glyceryl trinitrate and IV morphine (if required) for pain relief
  - Give 300 mg aspirin
  - Only administer oxygen if the patient is breathless, oxygen saturation is <93%, has heart failure or is in cardiogenic shock
- A blood sample for measuring troponin levels may be considered if time and clinical circumstances permit

Acute coronary syndrome refers to an unstable condition with sudden occlusion of the coronary arteries, usually caused by plaque rupture. The spectrum ranges in severity from angina to transmural myocardial infarction. All patients who present with symptoms consistent with a cardiac cause require immediate investigation and treatment, including:[1]

- Chest pain and/or pain in areas such as the upper arms, back or jaw, that lasts longer than 15 minutes
- Chest pain in combination with nausea and vomiting, sweating, breathlessness, dizziness or feeling light-headed
- A sudden deterioration in previously stable angina, with chest pain episodes lasting longer than 15 minutes, recurring frequently, following little or no exertion

A 12-lead ECG should be performed immediately in all patients with symptoms suggestive of a recent or current acute coronary syndrome.[2] Immediate transfer to hospital is recommended where a cardiac cause cannot be reasonably excluded, regardless of the results of the patient's ECG, i.e. a normal ECG does not exclude the possibility of a cardiac cause.

The risk of cardiac arrest is increased during or after an acute coronary event and emergency resuscitation medicines, e.g. injectable adrenaline, and a defibrillator should be close at hand. Monitor and record the patient's blood pressure, heart rate and oxygen saturation levels.

Additional investigations should not delay referral to secondary care. Serum troponin testing may be useful in primary care:

- When investigating patients presenting 24 – 72 hours after a single episode of chest pain, e.g. the "Monday morning" consultation
- As a follow-up investigation of unexplained chest pain when no ECG changes are present
- To investigate atypical symptoms of a possible acute coronary syndrome

Full blood count, creatinine, electrolytes, glucose and lipids may also be useful tests and these can be performed on the same blood sample used to measure serum troponin, if time and clinical circumstances permit.[3]

Treatment for all patients with acute coronary syndromes

Sublingual glyceryl trinitrate (GTN) is used initially for symptom relief in patients with chest pain due to a cardiac cause. Under medical supervision (i.e. while monitoring the patient), the maximum recommended dose of GTN is one to two sprays (or sub-lingual tablets), given at five minute intervals, up to three times. Patients with a previous history of angina may have already taken one or two doses of GTN at home upon onset of symptoms.

GTN is contraindicated in patients with cardiovascular instability or those who have recently used a PDE5-inhibitor, e.g. sildenafil.

For a complete list of contraindications to GTN see: **www.nzf.org.nz/nzf_1324**

An additional analgesic e.g. morphine, may also be necessary and some patients may require an antiemetic.

Dispersible aspirin 300 mg, should be given to all patients with an acute coronary syndrome, including those already taking aspirin; if enteric coated aspirin is the only formulation available the patient should chew the tablet.[2]

DO NOT administer oxygen to patients with an ST elevation acute coronary syndrome unless they:[4]

- Are breathless
- Are hypoxic, i.e. oxygen saturation < 93%
- Have heart failure
- Are in cardiogenic shock

This is a recent change in practice following findings that there was no evidence supporting the routine use of oxygen in patients with acute myocardial infarction.[2] In patients with a myocardial infarction and an oxygen saturation > 93%, oxygen treatment may actually increase left ventricular afterload due to arterial vasoconstriction.[4]

An additional antiplatelet and fibrinolysis may be appropriate if there will be a significant delay, i.e. more than two hours, in triaging and transporting patients with an acute coronary syndrome to hospital. This is most likely to apply in rural settings and discussion with an emergency medicine consultant or a cardiologist is recommended. Recommended medicines may include an antiplatelet (most likely ticagrelor 180 mg or clopidogrel 300 mg [75 mg for patients aged over 75 years]),[5] and pre-hospital fibrinolysis, i.e. intravenous tenecteplase (TNK-tissue-type plasminogen activator) and enoxaparin (Clexane) if a percutaneous coronary intervention cannot be performed within two hours.[4]

For further information, see: "The immediate management of acute coronary syndromes in primary care", BPJ 67 (Apr, 2015).

References

1. National Institute for Health Care Excellence (NICE). Chest pain of recent onset: Assessment and diagnosis of recent onset chest pain or discomfort of suspected cardiac origin. NICE, 2010. Available from: www.nice.org.uk/guidance/cg95/chapter/guidance (Accessed Dec, 2015).
2. Scottish Intercollegiate Guidelines Network (SIGN). Acute coronary syndromes: a national clinical guideline. SIGN, 2013. Available from: www.sign.ac.uk/pdf/sign93.pdf (Accessed Dec, 2015).
3. Non ST-Elevation Acute Coronary Syndrome Guidelines Group and the New Zealand Branch of the Cardiac Society of Australia and New Zealand. New Zealand 2012 guidelines for the management of non ST-elevation acute coronary syndromes. N Z Med J 2012;125:122–47.
4. ST-Elevation Myocardial Infarction Guidelines Group, New Zealand Branch of Cardiac Society of Australia and New Zealand. ST-elevation myocardial infarction: New Zealand Management Guidelines, 2013. N Z Med J 2013;126:127–64.
5. New Zealand Formulary (NZF). NZF v42. 2015. Available from: www.nzf.org.nz (Accessed Dec, 2015).

Age-related macular degeneration: what should a general practitioner know?

Age-related macular degeneration is a progressive condition which results in loss or distortion of the central visual field and is the leading cause of blindness in New Zealand. To reduce the risk of developing age-related macular degeneration, patients can:

- Quit smoking; this is the single biggest step patients can take to reduce their risk
- Consume a diet high in fruit, vegetables and fish
- Avoid UV light

Regular optometrist examinations from the age of 45 years can facilitate **early detection of macular degeneration**, which is usually asymptomatic. If patients are unable to attend an optometrist, visual acuity testing and assessment of retinal changes by direct fundoscopy in general practice can help identify those most in need of further clinical attention.

Patients with early or intermediate macular degeneration can take supplements to **reduce progression of early and intermediate disease**. A major study found that a daily supplement containing the following vitamins and minerals was effective in reducing progression to advanced age-related macular degeneration:[1,2]

- 500 mg vitamin C
- 400 IU vitamin E
- 25 mg zinc
- 2 mg copper
- 10 mg lutein
- 2 mg zeaxanthin

Advanced disease can be classified as "dry" geographic atrophy, or "wet" neovascular age-related macular degeneration. Anti-vascular endothelial growth factor intravitreal injections are **highly effective at reducing vision loss in patients with neovascular age-related macular degeneration**, which accounts for most cases of severe vision loss and blindness. There are currently no pharmacological treatments for patients with geographic atrophy.

Clinicians should assess the psychological wellbeing of patients with age-related macular degeneration as vision loss can often cause depression. Patients with a visual acuity ≤ 6/24 in the better eye with corrective lenses or with serious visual field defects can be referred to the Blind Foundation of New Zealand.

For further information, see: "Age-related macular degeneration", BPJ 70 (Sep, 2015).

References:

1. Age-Related Eye Disease Study Research Group. A randomized, placebo-controlled, clinical trial of high-dose supplementation with vitamins C and E, beta carotene, and zinc for age-related macular degeneration and vision loss: AREDS report no. 8. Arch Ophthalmol 2001;119:1417–36.
2. Age-Related Eye Disease Study 2 Research Group. Lutein + zeaxanthin and omega-3 fatty acids for age-related macular degeneration: the Age-Related Eye Disease Study 2 (AREDS2) randomized clinical trial. JAMA 2013;309:2005–15.

Responsible use of antibiotics in general practice

Key practice points for antimicrobial stewardship in primary care:

- Do not prescribe an antibiotic when it is not required, e.g. for a viral upper respiratory tract infection, sinusitis, self-limiting cases of otitis media and conjunctivitis (which is often viral), boils (unless co-morbidities) and most diarrhoeal illnesses
- Reserve antibiotic treatment for suspected bacterial respiratory tract infections to specific subsets of patients, such as:
  - Those with community acquired pneumonia
  - Where the potential for complications for that person are high
  - If the infection is not resolving within an expected timeframe
- When there is a range of antimicrobials which are indicated for treating a particular infection, choose the option with the narrowest spectrum, e.g. flucloxacillin for *Staphylococcus aureus* or *Streptococcus pyogenes* infection instead of amoxicillin clavulanate or cephalexin; or nitrofurantoin or trimethoprim for first-line treatment of urinary tract infection instead of ciprofloxacin or norfloxacin (unless contraindicated or testing shows infection is due to a resistant organism)
- Prescribe antibiotic treatment for no longer than the recommended duration; avoid prolonged or repeated courses without a strong clinical justification
- Prioritise consideration of antibiotic resistance over palatability and convenience for the patient when deciding which antibiotic to prescribe
- Educate patients: when an antibiotic is not indicated ensure that they understand why an antibiotic is not appropriate. When an antibiotic is prescribed, ensure patients understand what it is being prescribed for, what dose to take, how often and for how long.
- Encourage patients to return any unused antibiotic to the pharmacy and not to use it for a subsequent infection or share it with other family members

People in New Zealand use more antibiotics per head of population, than people in most similar developed countries. Increased antibiotic use exerts a selective pressure for the development of resistance by eliminating antibiotic-susceptible bacteria and leaving antibiotic-resistant bacteria to multiply. The aim of antibiotic stewardship is therefore to limit the use of antibiotics to situations where they are necessary and deliver the most clinical benefit, so that antimicrobial resistance is minimised and the benefits of effective antimicrobials can be sustained.

Implementing antimicrobial stewardship in general practice: from "what's good on paper" to "putting this into practice"

The June, 2015 edition of Best Practice Journal examined a number of different aspects of incorporating antimicrobial stewardship into practice. For example, although antibiotics should not be prescribed for viral upper respiratory tract infections, it is often difficult during an initial consultation to establish whether an infection is viral or bacterial in origin. In order to assist clinicians navigate this dilemma, we examined whether performing C-reactive protein testing can help to differentiate between a viral or bacterial infection, the evidence behind delayed, "back pocket" prescriptions and a debate on prescribing antibiotics for respiratory tract infections including the viewpoints of primary care clinicians in New Zealand.

Key practice points are summarised below for articles covering whether patients may stop a course of antibiotics early if symptoms improve, the usefulness of delayed prescriptions and whether a topical antiseptic could be used in place of a topical antibiotic.

For further information on these articles, and additional information about the use of antibiotics, see: BPJ 68 (Jun, 2015).

Is it okay to stop antibiotics early, e.g. when symptoms resolve?

Traditionally, clinicians and health authorities advocate that patients should complete their full course of antibiotics as prescribed to prevent relapse of infection and the development of antibiotic resistance. Evidence around this advice is beginning to change. The debate around stopping antibiotics, however, is essentially about ensuring that they are commenced appropriately in the first place.

When prescribing antibiotics, clinicians and patients should agree on clear expectations about:

- Duration of treatment
- Adherence to a regimen
- Whether stopping a course early would be appropriate

Dose and adherence may be more important than duration of antibiotic treatment. Giving the right antibiotic at an adequate dose, along with good patient adherence with the daily regimen, i.e. taking the correct dose at the appropriate intervals, may be more important for treatment success than taking an antibiotic for a long period of time. New treatment guidelines for infections are increasingly recommending shorter courses of antibiotics than were advocated previously.

Shorter courses of antibiotics do not increase bacterial resistance. The association between antibiotic use and resistance is complex. Longer courses of antibiotics, however, have been associated with the greatest risk of antimicrobial resistance at both an individual and community level.[1,2]

There are many situations where a patient could stop taking antibiotics early, and this is not likely to lead to relapse or promote antimicrobial resistance (Table 1). However, the decision to stop an antibiotic should ideally take place only after a follow-up discussion between the treating clinician (or designated clinical staff member, e.g. practice nurse) and the patient, to ensure that clinical features of infection have actually resolved and that there are no misunderstandings about the role of the antibiotic.

Delayed antibiotic prescriptions for respiratory tract infections (RTIs): does the strategy work?

The goals of a delayed antibiotic prescription strategy are to minimise antibiotic use for conditions in which it is suspected that an antibiotic will have little or no benefit, but to do so without increasing symptom duration or rate of serious

Table 1: Factors which can influence the decision to stop antibiotics early

Scenarios where clinicians could consider stopping antibiotics early	Scenarios where antibiotics should be continued for the full course
■ The patient is prescribed empiric antibiotics and subsequently judged unlikely to have a bacterial infection ■ The patient has a self-limiting infection and symptoms resolve, such as patients with: – Moderate pneumonia – Sinusitis – Urinary tract infections – Cellulitis or other skin infections (where an antibiotic is indicated)	■ Infections where eradication of the bacteria is required even if symptoms resolve or are absent, e.g.: – Group A streptococcal (GAS) pharyngitis in patients at risk of rheumatic fever – Asymptomatic bacteriuria during pregnancy – Latent tuberculosis – Patients with severe or complex infections, e.g. osteomyelitis, endocarditis and tuberculosis ■ Patients with severe immune deficiency ■ An antibiotic is prescribed for a clear indication and a minimum duration is supported by evidence-based guidance

For further information, see: "Is it ok to stop antibiotics when symptoms resolve?", BPJ 68 (Jun, 2015)

complications. A number of studies have now evaluated delayed antibiotic strategies, finding that:

- Up to 50% of patients given a delayed prescription for an antibiotic will collect their prescription[3]
- Patients who do not receive an antibiotic for a RTI are just as satisfied as those who do, provided that the reasons for not prescribing an antibiotic are effectively explained[4]
- Patients who take an antibiotic for a RTI are unlikely to have a shorter duration of symptoms, but they may be less likely to experience suppurative complications; however, the development of complications in a patient with an acute RTI, regardless of antibiotic use, is relatively uncommon (approximately 2–3%)[5, 6]

Taking all factors into consideration, evidence suggests that not prescribing the patient an antibiotic initially, explaining why this decision has been made and ensuring that patients understand to contact the practice if symptoms do not resolve and that a prescription will be made available to them if appropriate, is likely to reduce antibiotic use and result in similar clinical outcomes and patient satisfaction than using a delayed prescribing strategy. However, giving the patient a "back pocket" prescription to take with them "just in case", may be considered for some patients.

Delayed prescriptions may be considered for patients who do not need antibiotics at the time of consultation but may need them later and may not be able or likely to return for a follow-up appointment. This strategy leads to far fewer prescriptions being dispensed compared with immediate prescription of antibiotics and only a few more being dispensed than for patients not initially offered a prescription.

Factors that contribute to the decision to offer a delayed prescription for a patient with a RTI include:

- Concerns about the potential for symptoms to worsen significantly in a patient with serious co-morbidities
- Previous history of complications with RTIs
- Socioeconomic factors such as the ability of the patient to return for a consultation if their condition deteriorates

Delayed prescribing can be a good approach for some patients when combined with careful history and examination, reassurance, symptom-control advice and clear instructions on when to fill the prescription. Giving a delayed prescription can have a positive effect on a patient's future expectations for receiving an antibiotic for a RTI, especially if their symptoms resolve without filling the prescription. This may be a good strategy for enabling a patient to become familiar with the idea that they do not always need an antibiotic.

Clinicians should keep in mind that delayed prescription strategies will not suit all patients – some patients will require a face-to-face or telephone follow up.

For further information, see:

"Delayed antibiotic prescriptions for respiratory tract infections: does the strategy work?", BPJ 68 (Jun, 2015).

"Debate: Do you prescribe antibiotics for respiratory tract infections? An everyday conundrum in general practice", BPJ 68 (Jun, 2015).

Should I prescribe a topical antiseptic cream instead of a topical antibiotic for minor skin infections?

There are increasing rates of resistance to fusidic acid in New Zealand. Combined with high rates of resistance to mupiricin in the 1990s and early 2000s, clinicians may wonder whether they can prescribe a topical antiseptic instead of a topical antibiotic.

Most topical antiseptic products are intended for use on intact skin, e.g. for hand hygiene or for skin preparation prior to a surgical procedure, or surface decontamination; their use in these situations is widely accepted. At present, however, **there is a shortage of quality evidence demonstrating any clear benefit for the use of topical antiseptics in minor skin infections**. Therefore, their role remains uncertain. A Cochrane review published in 2012 concluded that there was insufficient evidence to recommend the use of topical antiseptics in the treatment of impetigo; this has also been reiterated in more recent review articles.[7, 8] For children in New Zealand, where antibiotic resistance rates are likely to differ from the countries covered by the Cochrane review, it is not clear whether a topical antiseptic is a feasible alternative to a topical antibiotic for the treatment of minor skin infections such as impetigo.[9]

It is important to keep in mind that **most healthy patients with minor skin infections do not require treatment with a topical antibiotic**. Therefore, the use of topical antibiotics can be reduced by following clinical practice recommendations as opposed to substituting with a topical antiseptic. Recommendations include:

- Skin infections such as furuncles and carbuncles are usually more appropriately managed by incision and drainage
- For children with infected eczema, expert opinion now suggests that topical fusidic acid should no longer be prescribed.[9] The preference is for oral antibiotic treatment, selected based on local resistance patterns, and with appropriate coverage for *Staphylococcus aureus* and *Streptococcus pyogenes* (Group A ß haemolytic streptococcus).

- Fusidic acid may be considered for children with three or less localised areas of impetigo, an oral antibiotic, however, is likely to be more appropriate[10]

Topical antibiotics continue to have a role in patients requiring nasal decolonisation of *S. aureus*, and in these cases substitution with a topical antiseptic is not appropriate. The choice of topical antibiotic should be made according to culture results.[11]

For further information, see: "Should I prescribe a topical antiseptic cream instead of a topical antibiotic for minor skin infections?", BPJ 68 (Jun, 2015).

References:

1. Gilbert GL. Knowing when to stop antibiotic therapy. Med J Aust 2015;202:121–2.
2. Bell BG, Schellevis F, Stobberingh E, et al. A systematic review and meta-analysis of the effects of antibiotic consumption on antibiotic resistance. BMC Infect Dis 2014;14:13. doi:10.1186/1471-2334-14-13
3. Arroll B, Kenealy T, Kerse N. Do delayed prescriptions reduce the use of antibiotics for the common cold? A single-blind controlled trial. J Fam Pract 2002;51:324–8.
4. Spurling GKP, Del Mar CB, Dooley L, et al. Delayed antibiotics for respiratory infections. Cochrane Database Syst Rev 2013;4:CD004417. doi:10.1002/14651858.CD004417.pub4
5. Little P, Moore M, Kelly J, et al. Delayed antibiotic prescribing strategies for respiratory tract infections in primary care: pragmatic, factorial, randomised controlled trial. BMJ 2014;348:g1606. doi:10.1136/bmj.g1606
6. Little P, Stuart B, Hobbs FDR, et al. Antibiotic prescription strategies for acute sore throat: a prospective observational cohort study. Lancet Infect Dis 2014;14:213–9. doi:10.1016/S1473-3099(13)70294-9
7. Koning S, van der Sande R, Verhagen AP, et al. Interventions for impetigo. Cochrane Database Syst Rev 2012;1:CD003261.
8. Hartman-Adams H, Banvard C, Juckett G. Impetigo: Diagnosis and treatment. Am Fam Physician 2014;90:229–35.
9. Williamson DA, Ritchie SR, Best E, et al. A bug in the ointment: topical antimicrobial usage and resistance in New Zealand. N Z Med J 2015;128:103–9.
10. Starship Children's Health. Cellulitis. Starship Clinical Guidelines. 2015. Available from: https://www.starship.org.nz/for-health-professionals/starship-clinical-guidelines/c/cellulitis/ (Accessed Dec, 2015).
11. New Zealand Formulary (NZF). NZF v42. 2015. Available from: www.nzf.org.nz (Accessed Dec, 2015).

Cellulitis: skin deep and spreading across New Zealand

Cellulitis is an acute, spreading infection of the lower dermis and subcutaneous tissue that is frequently caused by *Streptococcus pyogenes* and related streptococci or *Staphylococcus aureus*. Most cases can be diagnosed clinically, without investigation, by the presence of localised pain, swelling, erythema and heat. Furuncles (boils) and carbuncles (multiple-headed lesions) are easily misdiagnosed as cellulitis due to a tender rim of erythema surrounding the central infection. However, this is inflammatory change and not extension of the infection into the surrounding tissue. Patients with these focal staphylococcal infections should not be treated as if they have cellulitis, i.e. antibiotics are not usually required.

Patients with uncomplicated cellulitis can usually be managed in the community; a lower threshold for referral to hospital is appropriate for young children and frail older people or people with bite or puncture wounds.

Red flags for hospital referral include:

- Features of systemic involvement or haemodynamic instability
- Progressing infection despite antibiotic treatment
- Severe pain suggestive of necrotising fasciitis
- Unstable co-morbidities
- Orbital involvement

All patients with cellulitis should rest and elevate any affected limb. Oral flucloxacillin is the first-line treatment for children and adults with mild to moderate cellulitis. Oral erythromycin is a second-line alternative. An increase in erythema and swelling within the first 48 hours of treatment may represent the natural progression of the infection, rather than a failure of treatment. A reduction in pain in the affected skin and an improvement in appetite and energy are clear signs that the infection is being controlled in most patients. Treatment adherence should be assessed in patients who are not responding as well as expected. Intravenous cefazolin with oral probenecid is the recommended community-based treatment for patients who have not responded to oral flucloxacillin or for patients with more widespread cellulitis. Oral co-trimoxazole is the preferred antibiotic for cellulitis caused by MRSA unless susceptibility testing indicates otherwise.

For further information, see: "Cellulitis: skin deep and spreading across New Zealand", BPJ 68 (Jun, 2015).

Treating childhood eczema: a topical solution for a topical problem

Key management principles

1. Provide comprehensive education and support to the child's parents/caregivers
2. Advise frequent use of emollients in adequate quantities
3. Advise use of topical corticosteroids at the appropriate potency for the treatment of flares
4. Seek specialist paediatric or dermatological advice in children with severe or persistent eczema

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Emollients, topical corticosteroids and avoidance of triggers are the mainstays of treatment for children with eczema. Under-use of topical treatment continues to be more of a concern than overuse. This highlights the importance of providing comprehensive education to the child's parents or caregivers and overcoming "corticosteroid phobia".

Eczema affects approximately 20% of children in New Zealand, with disproportionally higher rates among Māori and Pacific children.[1] Over 90% of cases of eczema develop in children before the age of five years and 60% of these cases occur in the first year of life.[2] Although many children experience remission of their eczema as they grow older, approximately 20 – 40% of those affected in childhood will continue to experience eczema as adults.[1]

Provide comprehensive education and support to the child's parents and caregivers

Advise families how to avoid triggers and irritants, such as washing new clothes before use, using mild washing detergents and using cotton fabrics as a base layer rather than wool or synthetics next to the skin.[3, 4] The role of food allergy in eczema is unclear. Food allergy is more likely to be a contributing factor in young infants with severe generalised eczema. Parents should be advised against putting their child on a very restrictive diet as this is often of limited benefit, and the diet can be expensive to maintain and result in nutritional deficiencies.

Warm (not hot) baths, are recommended for all children with eczema.[5] These should be once daily, lasting no longer than 10 – 15 minutes, and use wash-off emollients rather than soaps, detergents or bubble baths.

Twice weekly diluted bleach baths can reduce staphylococcal carriage and improve the child's symptoms: this can be prepared with 2 mL of plain bleach (2.2% sodium hypochlorite) per litre of water. A full-sized bath with a 10 cm depth of water holds approximately 80 litres of water, and will therefore require approximately 160 mL of 2.2% bleach. A baby's bath holds approximately 15 litres of water and will require approximately 30 mL of 2.2% bleach. Avoid contact between the bath water and the child's eyes.

A parent/caregiver information sheet on dilute bleach baths is available from: **www.starship.org.nz/media/269481/bleach_bath_handout.pdf**

For households that do not have a bath aqueous cream BP and emulsifying ointment BP (both subsidised) can also be used as wash-off emollients applied before the child enters the shower.

At the end of bathing, the child should be rinsed off with fresh water and patted dry with a towel, followed by application of emollients and topical corticosteroids.

The severity of the child's symptoms should guide treatment

For all patients, use emollients frequently and in large quantities:[3]

- Apply several times a day and continue even when the child's eczema has cleared
- Children should be prescribed **250 – 500 g of emollient per week** to provide sufficient product for moisturising, washing and bathing

For the treatment of flares, use sufficient amounts of topical corticosteroids, once or twice daily:[3, 4]

- Once daily application is adequate in most cases (preferably after a bath)
- The potency of the corticosteroid prescribed should be matched to the severity of the child's eczema (Figure 1) and the area of the body affected (Figure 2)
- Treatment for flares should be started as soon as signs and symptoms appear and be continued for approximately 48 hours after symptoms subside

Best Practice Tip: Note on the prescription the specific area to which the cream needs to be applied as this will be put on the dispensing label by the pharmacy to prevent confusion

Parents often underutilise topical corticosteroids due to the fear of adverse effects. Clinicians can offer these points of guidance to parents to help overcome "corticosteroid phobia":[6, 7]

- Appropriate use does not result in skin atrophy
- The hyper- or hypo-pigmentation observed as the child's eczema clears is usually caused by the eczema not the corticosteroid; topical corticosteroids cause short-term vasoconstriction which may be mistaken as hypopigmentation
- The fingertip unit, i.e. the amount of product that will cover an adult index finger from the tip of the finger to the distal interphalangeal joint, can be used as a guide for the amount of corticosteroid to be applied (Figure 3). One fingertip unit is enough to treat an area of the child's eczema equal to the surface of two adult hands held side by side with the fingers together.

ECZEMA SEVERITY

Controlled eczema	Mild eczema	Moderate eczema	Severe eczema
Normal skin with no evidence of dryness, redness or itching	Areas of dry skin Infrequent itching (with or without small areas of redness)	Areas of dry skin Frequent itching Redness (with or without excoriation and localised skin thickening)	Widespread areas of dry skin Incessant itching Redness (with or without excoriation, extensive skin thickening, bleeding, oozing, cracking and alteration of skin pigment)
EMOLLIENTS	EMOLLIENTS	EMOLLIENTS	EMOLLIENTS
	TOPICAL CORTICOSTEROIDS	TOPICAL CORTICOSTEROIDS	TOPICAL CORTICOSTEROIDS
	Mild e.g. hydrocortisone 1%	**Moderate*** e.g. triamcinolone acetonide, clobetasone butyrate†	**Potent**‡ e.g. hydrocortisone butyrate 0.1%, betamethasone valerate, mometasone furoate, methylprednisolone aceponate

* Avoid use on face, neck, genitals or axillae for longer than seven to 14 days continuously

† Clobetasol butyrate (Eumovate – partly subsidised) is a moderate potency corticosteroid and should not be confused with clobetasol propionate (Dermol – fully subsidised) which is a very potent corticosteroid

‡ Avoid use on face, neck, genitals or axillae. Avoid use in children aged one year and under unless prescribed under dermatologist supervision

Figure 1: Eczema management algorithm (adapted from NICE, 2007).[3, 9] Note that the choice of topical corticosteroid also varies in relation to the area of body needing treatment and age of the child (see Figure 2).

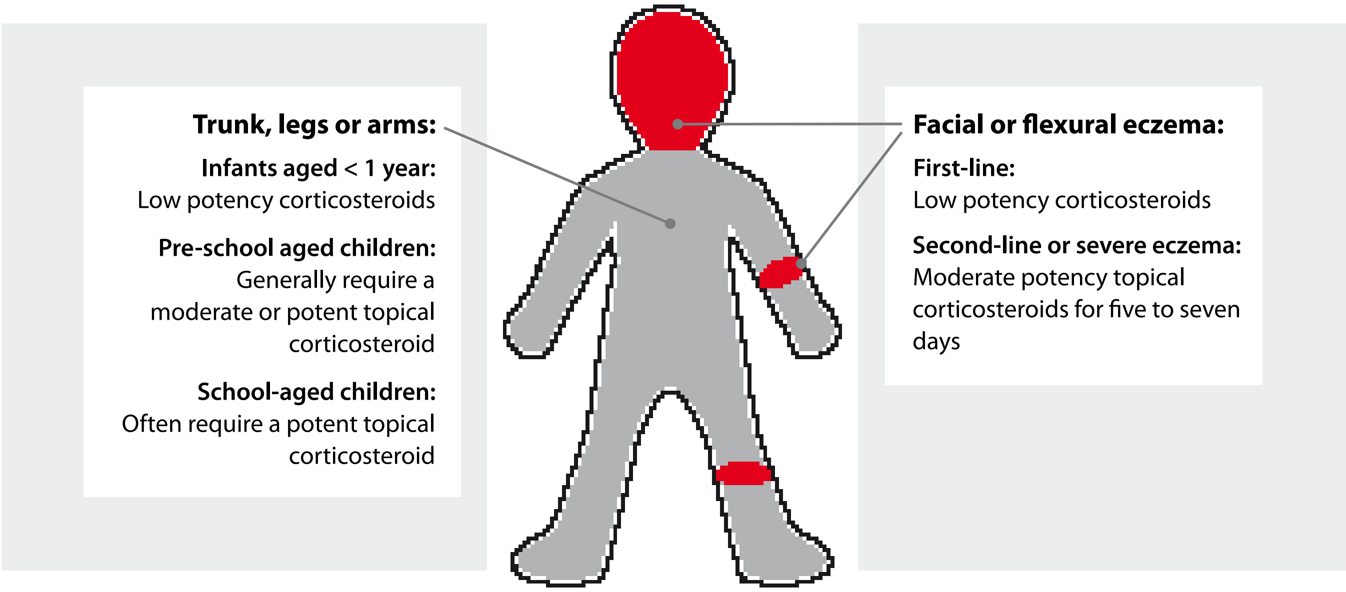


Figure 2: Useful rules of thumb to guide topical corticosteroid prescribing according to the area affected[4]

Pimecrolimus cream 1% (unsubsidised) is a calcineurin inhibitor that can be used in children aged three months or older as a second-line treatment when topical corticosteroids are unable to be used or have been ineffective despite optimal use.[3]

Antibiotics for secondary infection: Prescribing topical antibiotics, e.g. fusidic acid, for children with small localised lesions of infected eczema is now generally not recommended due to the high rates of resistance to fusidic acid in the community. The first-line recommended treatment regimen for children with infected eczema is an oral antibiotic:[8]

- Flucloxacillin 12.5 mg/kg, three times daily, for seven to ten days (maximum 500 mg/dose)
- If compliance with flucloxacillin is a problem, cephalexin 12.5 – 25 mg/kg, twice daily, for seven to ten days (maximum 500 mg/dose) may be used

Seek further advice for children with severe or persistent eczema: Referral pathways will vary according to the local services available; contact your DHB.

Figure 3: Fingertip unit (Image provided by Dermnet NZ)

For further information, see: "Treating childhood eczema – a topical solution for a topical problem", BPJ 67 (Apr, 2015).

References:

1. Clayton T, Asher MI, Crane J, et al. Time trends, ethnicity and risk factors for eczema in New Zealand children: ISAAC Phase Three. Asia Pac Allergy 2013;3:161–78. doi:10.5415/apallergy.2013.3.3.161
2. Starship Children's Health. Child and youth eczema clinical network. Diagnosis and assessment of eczema. 2014. Available from: www.starship.org.nz/for-health-professionals/national-child-and-youth-clinical-networks/child-and-youth-eczema-clinical-network/diagnosis-and-assessment-of-eczema/ (Accessed Dec, 2015).
3. National Institute for Health and Clinical Excellence (NICE). Atopic eczema in under 12s: diagnosis and management. London: NICE 2007. Available from: www.nice.org.uk/guidance/cg57 (Accessed Dec, 2015).
4. Waitemata District Health Board. Eczema in children - a topical issue. 2014. Available from: http://www.saferx.co.nz//full/eczema.pdf (Accessed Dec, 2015).
5. Starship Children's Hospital. Guidelines for the outpatient/primary care management of childhood eczema. 2014. Available from: www.starship.org.nz/for-health-professionals/national-child-and-youth-clinical-networks/eczema/guidelines-for-the-outpatient-primary-care-managment-of-childhood-eczema/ (Accessed Dec, 2015).
6. Mooney E, Rademaker M, Dailey R, et al. Adverse effects of topical corticosteroids in paediatric eczema: Australasian consensus statement. Australas J Dermatol 2015;56:241–51. doi:10.1111/ajd.12313
7. Hong E, Smith S, Fischer G. Evaluation of the atrophogenic potential of topical corticosteroids in pediatric dermatology patients. Pediatr Dermatol 2011;28:393–6. doi:10.1111/j.1525-1470.2011.01445.x
8. Healthpoint Pathways. Guidelines for the assessment and management of recurrent skin infections in children > 3 months - 14 years. Available from: www.healthpointpathways.co.nz/assets/Paediatric%20Skin%20Infections/Guidelines%20for%20the%20assessment%20and%20management%20of%20recurrent%20skin%20infections%20in%20children.pdf (Accessed Dec, 2015).
9. New Zealand Formulary for Children. NZFC. 2015. Available from: www.nzfchildren.org.nz (Accessed Dec, 2015).

When is an allergy to an antibiotic really an allergy?

When a patient has an uncertain history of antibiotic allergy consider the following:

1. Is it more likely that they experienced an allergic reaction, a delayed immune reaction, an adverse effect or an intolerance (Table 1)?
2. Could their symptoms have been caused by another factor, e.g. the illness or another medicine?
3. Have they tolerated the same antibiotic since the initial event?

Antibiotic allergy most commonly occurs in people aged 20 – 49 years. Penicillin is the most frequent antibiotic class allergy, followed by sulfonamides and tetracylines. Parenteral administration of antibiotics is associated with a higher risk of allergic reaction than oral administration. Allergic reactions can occur after a single or multiple exposures, therefore prior tolerance of an antibiotic does not exclude an allergy.

If a patient has a convincing history of an allergic reaction to an antibiotic, there is no need for laboratory investigation; confirmation of the allergy would not change management. Testing for antibiotic allergies is theoretically possible, but it is not available for all antibiotics in New Zealand and the results can be difficult to interpret.

A clinically significant IgE-mediated allergic reaction to an antibiotic, e.g. urticarial rash, is likely, but not inevitable, to reoccur on re-exposure and in some cases this will be more severe, e.g. anaphylaxis. Deliberate re-exposure to the same antibiotic is not recommended unless there are no alternative options and the patient is supervised in hospital. If a patient has a history of intolerance or adverse effects the severity of the previous event and the likely benefit of treatment should be considered before prescribing the antibiotic again. If the patient has a history of a delayed hypersensitivity reaction re-challenge may be possible, depending on the nature of the reaction. People with an allergy to one antibiotic can react to structurally similar antibiotics, e.g. sensitivity to cephalosporins in patients allergic to penicillin, but this is rare.

For further information, see: "When is an allergy to an antibiotic really an allergy", BPJ 68 (Jun, 2015).

Table 1: Typical features of an allergy, delayed immune reaction, adverse effect or intolerance to antibiotics

Allergy	Delayed immune reactions	Adverse effect	Intolerance
An immunological reaction (IgE-mediated) that is usually rapid in onset (e.g. within one to two hours) and may include: ▪ Urticaria ▪ Angioedema ▪ Bronchospasm ▪ Anaphylaxis These reactions usually reoccur with subsequent exposure to the antibiotic and may attenuate over time or persist for a lifetime.	May occur several days after exposure (usually IgG-mediated). More often seen in patients with intercurrent infections, e.g. Epstein-Barr virus. Macular, papular or morbilliform rash are common examples. Usually does not occur upon subsequent exposure to the antibiotic when the patient is well. N.B. rash caused by viral infection can often be mistaken for an allergic reaction to antibiotics	A predictable reaction to an antibiotic, e.g. diarrhoea, nausea and vomiting following treatment with amoxicillin	A sensitivity reaction that does not involve the immune system. Dependent on patient susceptibility and pharmacology of the medicine. May be an exaggerated adverse effect or an adverse effect not normally associated with the antibiotic, e.g. tinnitus following treatment with amoxicillin.

Asthma education in primary care: **A focus on improving outcomes for Māori and Pacific peoples**

Key practice points

- Improving asthma education for Māori and Pacific families helps to reduce health care disparities in New Zealand
- Asthma education should acknowledge and be tailored to existing patient/family knowledge
- Ideally patients with asthma should be followed-up one to three months after starting treatment and every three to 12 months thereafter
- Make sure every patient with asthma has an action plan and that their family knows how to follow it
- Consider nominating an "asthma champion" in your practice to take responsibility for and optimise the care of patients with asthma

There is a gap in asthma care

Asthma is more prevalent and more severe in Māori and Pacific peoples. Māori are almost three times, and Pacific peoples over 3.5 times, more likely to be hospitalised due to asthma than people of other ethnicities in New Zealand.[1]

Part of the reason why Māori and Pacific peoples have a higher asthma burden is under-treatment. Despite having more severe asthma, Māori and Pacific children are less likely to have their treatment escalated.[2] Poor health literacy also contributes to asthma disparities as it is associated with reduced self-efficacy and under utilisation of medicines.[3] The report "He Māramatanga Huangō: asthma health literacy for Māori children in New Zealand" found that caregivers of Māori and Pacific children are often not provided with the information they need to manage asthma effectively.[3] Practices in primary care therefore need to make asthma education a priority.

Making asthma education a priority at your practice

When people with asthma or their families do not understand what good asthma management is they are more likely to accept poor asthma control as normal; health professionals in primary care can change this.

"Hardwire" asthma education into your practice. This involves increasing the patient's or family's knowledge of asthma in a stepwise approach at every point of contact.[3]

Nominate a staff member as "asthma champion" to take responsibility for optimising asthma care in the practice. An asthma champion may be responsible for checking that each patient is receiving regular follow-up as well as identifying those with the greatest need who will benefit the most from more intensive support.

Document asthma education at every stage, including what has not been discussed. This enhances continuity of care and allows other practice staff to easily identify gaps in education that need to be addressed.

Asthma education begins at diagnosis

Avoid "diagnostic limbo" by ensuring clear communication about the patient's symptoms and treatment approach, particularly in young children when a formal diagnosis may not be made for several years.

Assess the patient's/family's knowledge about asthma before providing management advice. This allows for existing information to be acknowledged and reinforced, and gaps in understanding or misconceptions corrected. During discussions health professionals should:

- Use language that is appropriate; adopting terms that the patient or their family has used displays attentiveness and builds a common language
- Explain what will happen next; this avoids confusion and allows patients to plan for and participate in the next stage of asthma management

Discussing asthma treatment

The clinical goals of asthma management are to provide all patients with:[4]

1. Good symptom control without adverse effects
2. Minimal exacerbations and airway limitations

Asthma management is a cycle of ongoing assessment, treatment and review.[4] The patient's personal goals should be addressed whenever asthma management is discussed and included as shared goals of care.[4]

Ideally patients should be followed-up one to three months after starting treatment for asthma and every three to 12 months thereafter.[4] Asthma reviews should be scheduled during periods when the patient's symptoms are well controlled. As part of this process the patient's likelihood of experiencing an exacerbation should be regularly assessed as well as any asthma trigger avoidance strategies that have been put in place. A follow-up should be arranged within one week of a patient experiencing an exacerbation.[4]

Incorrect inhaler technique can contribute to poor asthma control and should be assessed regularly.[4] Spacers are recommended for all patients using pressurised asthma inhalers as they make it easier to use the inhaler and improve medicine delivery.[4]

Explain the "why" as well as the "how". Carers of children with asthma often have a good understanding about how to perform tasks but this does not necessarily equate to an understanding as to why a task is performed.[3] Many families affected by asthma do not realise that people with the condition require preventative treatments even when well.[3]

If forgetfulness is a reason for treatment non-adherence this may be overcome by suggesting patients link administration of preventer medicines with other daily activities or use an electronic reminder.

Provide an action plan for every patient with asthma and ensure the family is able to follow it. Asthma actions plans contain instructions on when and how to make short-term adjustments in treatment in response to worsening symptoms and when to access additional medical care. Action plans are available online that can be customised for individual patients.

A Pictorial Asthma Medication Plan (PAMP) for children translated into Te Reo Māori, Samoan, Tongan and Tuvaluan is available from: **www.pamp.co.nz**

Bestpractice offers a free "Childhood Asthma module" which includes an action plan automatically populated with the patient's details. For further information, see**: www.bestpractice.net.nz**

Asthma action plans for adults are available from: **www.asthmafoundation.org.nz/wp-content/uploads/2012/03/AsthmaSelfManagementPlan08_final.pdf**

For further information, see: "Asthma education in primary care", BPJ 70 (Sep, 2015).

References

1. Barnard L, Baker M, Pierse N, et al. The impact of respiratory disease in New Zealand: 2014 update. 2015. Available from: http://asthmafoundation.org.nz/wp-content/uploads/2012/08/2015-Respiratory-Impact-Report.pdf (Accessed Dec, 2015).
2. Gillies TD, Tomlin AM, Dovey SM, et al. Ethnic disparities in asthma treatment and outcomes in children aged under 15 years in New Zealand: analysis of national databases. Prim Care Respir J 2013;22:312–8. doi:10.4104/pcrj.2013.00068
3. Jones B, Ingham T, Reid S, et al. He Māramatanga Huangō: Asthma Health Literacy for Māori Children in New Zealand. 2015. Available from: http://asthmafoundation.org.nz/wp-content/uploads/2015/07/Asthma-Health-Literacy-Report.pdf (Accessed Dec, 2015).
4. Global Initiative for Asthma (GINA) and Global Initiative for Asthma (GINA). Global strategy for asthma management and prevention. 2015. Available from: www.ginaasthma.org (Accessed Dec, 2015).
5. Gibson PG, Powell H, Coughlan J, et al. Self-management education and regular practitioner review for adults with asthma. Cochrane Database Syst Rev 2003;1:CD001117. doi:10.1002/14651858.CD001117

The optimal management of **patients with COPD**

Key practice points

- In 2015 two medicines were added to the COPD toolkit: indacaterol (fully subsidised) and glycopyrronium (fully subsidised with Special Authority approval)
- Oral corticosteroids are now recommended for only five days for patients with moderate or severe COPD exacerbations; treatment courses of less than two weeks do not need to be tapered
- End-of-life discussions with patients and family/whānau affected by COPD should be initiated early

Chronic obstructive pulmonary disease (COPD) affects one in seven people in New Zealand aged over 40 years.[1] It is largely preventable as more than 85% of cases are caused by smoking.[2]

The burden of COPD among Māori and Pacific peoples represents one of the most significant healthcare disparities in New Zealand. The prevalence of COPD among Māori is more than twice that of non-Māori and the impact of the disease is greater.[3]

Diagnosing COPD

A clinical diagnosis of COPD can be considered in anyone aged over 35 years who has had long-term exposure to cigarette smoke, occupational exposure to dust, fumes or gas and has typical symptoms of COPD, i.e. breathlessness, cough, and/or sputum production.[4]

Spirometry is required to confirm a diagnosis of COPD in patients with symptoms and risk factors.[5] A FEV_1 < 80% predicted and a FEV_1/FVC ratio < 0.7 indicates an airflow limitation.[4] This is not, however, disease specific and it may not be possible to differentiate between conditions such as COPD, chronic bronchitis or asthma using spirometry.[6] Features such as the age of the patient, pattern of symptoms, e.g. constant versus intermittent, and time course of symptoms, e.g. slow progression or spontaneous development, are useful to differentiate between respiratory conditions. Post-bronchodilator spirometry is helpful for differentiating asthma from COPD, but less so if the patient has asthma with fixed airflow limitation.[7]

The results of spirometry are also used to assess the severity of COPD, in combination with the clinical signs and symptoms of hypoxaemia, hypercapnia, pulmonary hypertension, heart failure and polycythaemia.[4]

Screening for COPD with spirometry testing in asymptomatic patients is not recommended as there is no evidence that earlier detection improves outcomes in patients with COPD before they develop significant symptoms.[5]

The management of patients with COPD

The non-pharmacological interventions for patients with COPD are:

- Smoking cessation
- Physical activity

- Pulmonary rehabilitation
- Maintenance of bodyweight in patients with advanced COPD

The pharmacological treatment of COPD is escalated in a stepwise manner according to the severity of the patient's condition in order to:

- Control the patient's symptoms
- Reduce their risk of exacerbations

Step 1: For all patients with COPD prescribe an inhaled short-acting beta2-agonist (SABA, e.g. salbutamol or terbutaline) or a short-acting muscarinic antagonist (SAMA, e.g. ipratropium) for use during periods of acute breathlessness.[4] Patients should be educated in the correct use of inhalers and spacers before treatment is initiated and their technique regularly reviewed, particularly before stepping up treatment. The patient's ability to use an inhaler may dictate the choice of medicine.

Step 2: For patients with COPD and persistent dyspnoea consider the addition of a long-acting beta2-agonist (LABA, e.g. salmeterol, indacaterol or formoterol) or a long-acting muscarinic receptor antagonist (LAMA, e.g. tiotropium* or glycopyrronium*).[4] There is good evidence that both LABA and LAMA can produce day-to-day improvements in lung function, symptom severity and reduce the frequency of exacerbations.[4]

Step 3: For patients with a FEV_1 < 50% of predicted and two or more exacerbations in a 12-month period consider prescribing a fixed-dose inhaled corticosteroid (ICS) in combination with a LABA, e.g. fluticasone + salmeterol or budesonide + formoterol*.[4] If the patient begins combination treatment remember to cease any LABA monotherapy. Patients who continue to experience frequent exacerbations may also benefit from the addition of a LAMA to a combination corticosteroid + LABA inhaler.

Table 1: The stepwise escalation of pharmacological treatment for COPD, based on severity, adapted from Abramson *et al*, 2014[1]

Severity	MILD	MODERATE	SEVERE
	▪ Few symptoms ▪ Breathless on moderate exertion ▪ Recurrent chest infections ▪ Little or no effect on daily activities ▪ FEV_1 ≈ 60–80% predicted	▪ Increasing dyspnoea ▪ Breathless walking on level ground ▪ Increasing limitation of daily activities ▪ Cough and sputum production ▪ Infections requiring corticosteroids ▪ FEV_1 ≈ 40–59% predicted	▪ Dyspnoea on minimal exertion ▪ Daily activities severely restricted ▪ Experiencing regular sputum production ▪ Chronic cough ▪ FEV_1 < 40% predicted
Medicines management	**CHECK DEVICE USAGE TECHNIQUE AND ADHERENCE AT EACH VISIT** – Up to 90% of patients do not use devices correctly		
	FOR ALL PATIENTS: Inhaled short-acting reliever, e.g. salbutamol, terbutaline or ipratropium		
	SYMPTOM RELIEF IF PERSISTENT TROUBLESOME DYSPNOEA: Add a long-acting beta agonist (LABA, e.g. salmeterol, indacaterol or formoterol) OR a long-acting muscarinic antagonist (LAMA, e.g. tiotropium* or glycopyrronium*). **This may also help to prevent exacerbations.** * Special Authority criteria apply; must have tried ipratropium first, see NZF for details		
		EXACERBATION PREVENTION IF TWO OR MORE EXACERBATIONS IN LAST 12 MONTHS AND FEV_1 < 50% PREDICTED: CHANGE TO inhaled corticosteroid (ICS)/LABA combination treatment (fluticasone/salmeterol OR budesonide/formoterol*); ADD a LAMA (e.g. tiotropium* or glycopyrronium*) if the patient continues to experience frequent exacerbations. N.B. When considering the use of inhaled corticosteroids in patients with COPD it is important to consider the risk of adverse effects, particularly pneumonia * Special Authority criteria apply; must have tried ipratropium first, see NZF for details	

Balance the risks versus benefits of ICS treatment. The long-term use of ICS has been shown to reduce the rate of exacerbations and slow the decline in quality of life in people with COPD.[4, 5] However, ICS use can increase the risk of pneumonia and other respiratory conditions in patients with COPD.

The role of ICS in the treatment of COPD will be more closely examined in Best Practice Journal in 2016.

* Subsidised with Special Authority approval

Managing exacerbations

Patients with COPD who have frequent exacerbations are more likely to experience a rapid decline in FEV_1 and are more likely to die of COPD-related complications.[4] Prompt treatment of exacerbations is important; a delay of greater than 24 hours approximately doubles the likelihood of hospital admission.[4] An exacerbation in the previous 12 months is the greatest risk factor for a future exacerbation.[4]

Management of a patient with an acute exacerbation of COPD includes:

- Inhaled bronchodilator (four to eight puffs of 100 microgram salbutamol inhaler), every three to four hours
- Breathing relaxation techniques
- Oral corticosteroids for five days, if moderate to severe exacerbation
- Oral antibiotics for five to ten days if there are signs of chest infection

Oral corticosteroids reduce the severity of COPD exacerbations and improve recovery time for the patient. Prednisone 30 – 50 mg, once daily in the morning, for five days can be prescribed for patients with moderate or severe exacerbations.[4] Prescribing oral corticosteroids for periods of 14 days to reduce the severity of exacerbations is no longer considered necessary.[8] Corticosteroid use does not need to be tapered in patients prescribed treatment courses of less than two weeks.

If patients display signs of chest infection prescribe oral antibiotics for five to ten days. Bacterial infection is thought to be involved in approximately half of exacerbations in patients with COPD.[4] Recommended treatments include: amoxicillin, 500 mg, three times daily or doxycycline, 100 mg, twice daily (other doxycycline regimens may recommend 200 mg, twice daily on day one, followed by 100 mg, once or twice daily).[4] Sputum culture is not routinely required unless the patient is not responding to antibiotic treatment or has had multiple bacterial infections over a period of several months.[4]

Regular follow-up is essential

The lung function of people with COPD can be expected to decline and regular follow-up is important. The patient's response to treatment is used to determine the success of interventions as spirometry may not reliably detect improvements in lung function. When a change is made to the patient's treatment clinically significant changes in symptoms such as dyspnoea can be expected to be detected within six weeks.[4] Changes in the patient's quality of life are best assessed over a longer period of time.[4]

Patients with advanced COPD

Low-dose opioids can relieve dyspnoea by decreasing the patient's respiratory rate without causing hypercapnia or hypoxia.[9] Initially, low doses of morphine can be trialled on an as-required basis for refractory dyspnoea, e.g. 2 mg of an oral solution pre-measured in a syringe or 2.5 mg of an immediate-release tablet (one-quarter of a 10 mg tablet of morphine).

Benzodiazepines can be very effective at reducing the anxiety associated with dyspnoea, although there is no evidence that they relieve breathlessness.[10] Lorazepam 0.5 mg (half of a 1 mg tablet), every four to six hours, as required, is an appropriate starting dose.[10]

Oxygen treatment in a consistently hypoxic patient may reduce polycythaemia, improve sleep quality, prevent cor pulmonale and reduce mortality.[4, 11] Patients with COPD who are stable but have persistent hypoxaemia, i.e. $SpO_2 < 92\%$ on pulse oximetry, should be referred to a respiratory physician to assess their need for long-term oxygen treatment.[4]

Weight loss in people with severe COPD can result in deteriorating lung and heart function.[12] Oral nutritional supplements may be required in patients with advanced disease. Pulmocare is a high-fat, reduced-carbohydrate nutritional supplement subsidised with Special Authority approval to patients with COPD and hypercapnia, i.e. $PCO_2 >$ 55 mmHg.[13]

Judging the right time to initiate end-of-life discussions in patients with COPD can be difficult. Discussions about end-of-life issues should take place early to give patients sufficient time, e.g. 12 months, to plan with their family/whānau how they want their care to be managed. Discussions about end-of-life care are generally less stressful when patients are relatively well. The presence of two or more of the following is an indication that the patient's preferences for end-of-life care should be addressed:

- FEV_1 < 30% of predicted
- Age over 70 years
- Dependence on oxygen treatment
- One or more hospitalisations in the previous year for an exacerbation
- Left heart failure
- Weight loss or cachexia
- Decreased ability to function
- Increasing dependence on family or carer

Further information on end-of-life care is available from: **www.advancecareplanning.org.nz**

For further information, see: "The optimal management of patients with COPD – Part 1: The diagnosis" and "Part 2: Stepwise escalation of treatment", BPJ 66 (Feb, 2015).

References

1. Shirtcliffe P, Weatherall M, Marsh S, et al. COPD prevalence in a random population survey: a matter of definition. Eur Respir J 2007;30:232–9. doi:10.1183/09031936.00157906
2. Town I, Taylor R, Garrett J, et al. The burden of COPD in New Zealand. 2003. Available from: http://asthmafoundation.org.nz/wp-content/uploads/2012/03/burdenCOPD.pdf (Accessed Dec, 2015).
3. The Asthma and Respiratory Foundation of New Zealand. Literature review: Respiratory health for Maori. 2009. Available from: http://asthmafoundation.org.nz/wp-content/uploads/2012/03/Lit_review_maori1.pdf (Accessed Dec, 2015).
4. Abramson M, Frith P, Yang I, et al. COPD-X concise guide for primary care. 2014. Available from: www.copdx.org.au (Accessed Dec, 2015).
5. Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. 2014. Available from: www.goldcopd.com (Accessed Dec, 2015).
6. National Health and Nutrition Examination Survey (NHANES). Respiratory health and spirometry procedures manual. 2008. Available from: www.cdc.gov/nchs/data/nhanes/nhanes_07_08/spirometry.pdf (Accessed Dec, 2015).
7. Global Initiative for Asthma (GINA) and Global Initiative for Chronic Obstructive Pulmonary Disease (GOLD)Global. Diagnosis of diseases of chronic airflow limitation: asthma COPD and asthma-COPD overlap syndrome (ACOS). 2014. Available from: www.ginasthma.org/local/uploads/files/AsthmaCOPDOverlap.pdf (Accessed Dec, 2015).
8. Leuppi JD, Schuetz P, Bingisser R, et al. Short-term vs conventional glucocorticoid therapy in acute exacerbations of chronic obstructive pulmonary disease: the REDUCE randomized clinical trial. JAMA 2013;309:2223–31. doi:10.1001/jama.2013.5023
9. Kamal AH, Maguire JM, Wheeler JL, et al. Dyspnea review for the palliative care professional: treatment goals and therapeutic options. J Palliat Med 2012;15:106–14. doi:10.1089/jpm.2011.0110
10. NHS Lothian. Breathlessness in palliative care. 2010. Available from: www.2010palliativecareguidelines.scot.nhs.uk/documents/breathlessnessfinal.pdf (Accessed Dec, 2015).
11. McDonald CF, Crockett AJ, Young IH. Adult domiciliary oxygen therapy. Position statement of the Thoracic Society of Australia and New Zealand. Med J Aust 2005;182:621–6. doi:10.1111/resp.12678
12. Ferreira IM, Brooks D, White J, et al. Nutritional supplementation for stable chronic obstructive pulmonary disease. Cochrane Database Syst Rev 2012;12:CD000998. doi:10.1002/14651858.CD000998.pub3
13. New Zealand Formulary (NZF). NZF v42. 2015. Available from: www.nzf.org.nz (Accessed Dec, 2015).

Smoking cessation – helping patients stick with it, until they quit

People who want to quit smoking should be offered both behavioural and pharmacological support. Combination nicotine replacement therapy (NRT), e.g. patches *and* gum or lozenges, is recommended as the first-line pharmacological treatment for people who smoke more than ten cigarettes a day or who smoke within an hour of waking. If a person experiences a lapse in their quit attempt, behavioural support and the continued use of NRT decreases the likelihood that they will begin smoking again. Buproprion, nortriptyline and varenicline are additional pharmacological options for smoking cessation. Varenicline is the most effective of these medicines and is approximately as effective as combination NRT. Varenicline is subsidised for patients who have previously tried to quit with other smoking cessation medicines. Before varenicline is initiated prepare patients for the possibility of adverse effects, e.g. nausea, and encourage them to persist with treatment unless these are severe.

For further information, see: "Smoking cessation: helping patients stick with it until they quit", BPJ 71 (Oct, 2015).

Overuse of **benzodiazepines: still an issue?**

Key practice points:

- Non-pharmacological methods, such as cognitive-behavioural approaches are the preferred first-line management of insomnia or anxiety
- If other treatment options have been unsuccessful, benzodiazepines or zopiclone may be considered for short-term use. A treatment plan should cover treatment duration, dose, outcome measures, adverse effects and review dates. This may be written as a contract to help the patient understand the expectations of their treatment and to provide a safeguard for the clinician to avoid escalation of prescribing.
- In elderly patients, lower doses of zopiclone or benzodiazepines should be prescribed, e.g. half the normal adult dose, and benzodiazepines with a long half-life, e.g. diazepam and nitrazepam, should be avoided
- For patients who have been using these medicines long-term, withdrawal should be discussed. A gradual taper improves the success rate of discontinuation and avoids or reduces adverse effects of withdrawal. Patients will require education and follow-up support during this time.

Long-term use of benzodiazepines or zopiclone for insomnia or anxiety is discouraged as these medicines can cause a range of adverse effects, including:

- Vertigo
- Muscle weakness
- Effects on cognition
- Dependency
- Increased risk of falls
- Increased risk of motor vehicle accidents[1]
- Increased risk of dementia and possible increased risk of Alzheimer's disease[2, 3]

Despite these risks, and that zopiclone and benzodiazepines are not first-line treatments for anxiety or insomnia, patients in New Zealand are currently being prescribed large volumes of these medicines. Benzodiazepine and zopiclone use is particularly prevalent in older people: in 2014, one in ten people in New Zealand aged 65-74 years and one in five people aged 85 years and over were dispensed a benzodiazepine or zopiclone.[4]

Prescribing points for benzodiazepines and zopiclone for insomnia or anxiety

Benzodiazepines are indicated for the treatment of insomnia and anxiety, and zopiclone for the treatment of insomnia; however, they are not first-line treatment options for either of these conditions. If patients begin taking a benzodiazepine or zopiclone they may perceive that the rapid symptom relief that is often gained when using these medicines outweighs any adverse effects and risks. Patients may subsequently be less willing to try other treatments, such as psychological interventions or selective serotonin reuptake inhibitors (SSRIs), but these are likely to be safer and more appropriate in the long-term than continued benzodiazepine or zopiclone use.

For the treatment of insomnia:

- Cognitive-behavioural approaches (e.g. discussing ways to improve quality and quantity of sleep - "sleep hygiene") have high levels of efficacy, are supported by a good evidence base and achieve better long-term outcomes than benzodiazepine or zopiclone use[5]
- Benzodiazepines are known to alter sleep architecture with less time spent in slow wave sleep and reduced overall sleep quality compared to the equivalent duration of sleep achieved by cognitive-behavioural approaches[6]

If other interventions have been unsuccessful and a benzodiazepine or zopiclone is being considered, clinicians and patients should be aware that:

- Zopiclone is indicated for the short-term management of insomnia, with the recommended dosing regimen of up to one tablet (7.5 mg) per night, for up to four weeks[7]
- Benzodiazepines should be prescribed at the lowest effective dose for a short duration; no more than four weeks, but preferably five to ten days
- A short-acting benzodiazepine should be chosen, as long-acting benzodiazepines cause greater next day drowsiness and associated adverse effects[5]

For the treatment of anxiety, benzodiazepines:

- Should not be routinely used except as a short-term measure during crises[8]
- Are not recommended for the treatment of stress following a traumatic event[9]
- Are only recommended for short-term use, e.g. two to four weeks

Other treatment options for anxiety include psychological support and counselling, SSRIs, tricyclic antidepressants and buspirone.

In elderly patients:

- Lower doses of benzodiazepines or zopiclone, e.g. half the normal adult dose, are likely to be necessary to minimise adverse effects, due to reduced renal clearance
- Benzodiazepines with a long half-life, e.g. diazepam and nitrazepam, should be avoided due to an increased risk of falls with next-day drowsiness

If benzodiazepines or zopiclone are prescribed**, consider a treatment plan which covers treatment duration, dose parameters, outcome measures, adverse effects and review dates.** This can be written as a contract if necessary, and helps the patient to understand the expectations of their treatment and provides a safeguard for the clinician to avoid escalation of prescribing. The treatment plan can state that regular reviews will take place and that no repeat prescriptions will be made without in-person contact.[10] Patients should be given information about adverse effects, and understand that benzodiazepines or zopiclone are for short-term use only and they should continue with non-pharmacological approaches for managing their insomnia or anxiety.

For further information on the treatment of insomnia, see: **www.bpac.org.nz/BPJ/2008/June/insomnia.aspx**

For further information on the treatment of generalised anxiety disorder in adults, see: **www.bpac.org.nz/BPJ/2009/December/anxiety.aspx**

For further information on the treatment of anxiety disorders in young people, see: **www.bpac.org.nz/BPJ/2015/December/mental-health.aspx**

Withdrawing treatment

Patients who have been using benzodiazepines or zopiclone long-term should be encouraged to stop. Strategies involve attempting to realign the patient's perceptions of risks and benefits, such as:

- Providing information about discontinuing benzodiazepines, e.g.:
  - 'Stopping benzodiazepines and Z-drugs', available from: **http://medical.cdn.patient.co.uk/pdf/4638.pdf**
  - 'Benzodiazepines (tranquillisers and sleeping pills)', available from: **www.reconnexion.org.au/secure/downloadfile.asp?fileid=1015143**
- Regular follow-up letters to patients informing or reminding them of the risks of benzodiazepine use and the benefits of withdrawal
- Fortnightly consultations during withdrawal
- Psychological support: counselling or referral to psychological support services **substantially improves rates of discontinuation** over and above patient education or follow-up approaches

Withdrawal should be "slow but sure". A gradual taper improves the success rate of discontinuation and avoids or reduces effects of withdrawal. Rapid withdrawal of benzodiazepines is associated with an increased risk of seizures, therefore patients should be warned not to stop their medicine abruptly. Patients who have been taking benzodiazepines or zopiclone at high doses (e.g. > 20 mg diazepam per day) or for a long period of time (e.g. more than ten years) are best discussed with an addiction specialist before attempting withdrawal.

For further information, see: "Overuse of benzodiazepines: still an issue?", BPJ 66 (Feb, 2015).

References:

1. Brayfield A (ed). Martindale: the complete drug reference. London: Pharmaceutical Press. Available from: http://www.medicinescomplete.com (Accessed Dec, 2015).
2. Wu C-S, Ting T-T, Wang S-C, et al. Effect of benzodiazepine discontinuation on dementia risk. Am J Geriatr Psychiatry 2011;19:151–9. doi:10.1097/JGP.0b013e3181e049ca
3. Billioti de Gage S, Moride Y, Ducruet T, et al. Benzodiazepine use and risk of Alzheimer's disease: case-control study. BMJ 2014;349:g5205. doi:10.1136/bmj.g5205
4. Health Quality & Safety Commission (HQSC). Polypharmacy in older people. HQSC, 2015. Available from: http://www.hqsc.govt.nz/our-programmes/health-quality-evaluation/projects/atlas-of-healthcare-variation/polypharmacy-in-older-people/ (Accessed Dec, 2015).
5. Morin CM, Benca R. Chronic insomnia. Lancet 2012;379:1129–41. doi:10.1016/S0140-6736(11)60750-2
6. Wagner J, Wagner ML. Non-benzodiazepines for the treatment of insomnia. Sleep Med Rev 2000;4:551–81. doi:10.1053/smrv.2000.0126
7. New Zealand Formulary (NZF). NZF v42. 2015. Available from: www.nzf.org.nz (Accessed Dec, 2015).
8. National Institute for Health Care Excellence (NICE). Anxiety disorders. London: NICE, 2014. Available from: https://www.nice.org.uk/guidance/qs53 (Accessed Dec, 2015).
9. World Health Organisation. WHO guidelines on conditions specifically related to stress. WHO, 2013. Available from: http://www.who.int/mental_health/emergencies/stress_guidelines/en/ (Accessed Dec, 2015).
10. The Royal Australian College of General Practitioners (RACGP). Prescribing drugs of dependence in general practice, Part B. Benzodiazepines. Melbourne: RACGP, 2015. Available from: http://www.racgp.org.au/your-practice/guidelines/drugs-of-dependence-b (Accessed Dec, 2015).

Addressing mental health and wellbeing in young people

Two recent articles in the Best Practice Journal covered primary care approaches to young people with mental health issues. This is part of an ongoing series with more to come on this topic in 2016. So far, the articles have introduced current statistics relating to mental health and wellbeing in young people in New Zealand, guidance for identifying those who need assistance and non-pharmacological approaches to frequently encountered mental health problems in young people that can be carried out in primary care.

Key mental health statistics for young people in New Zealand include:[1–3]

- New Zealand has one of the highest rates of youth suicide in the OECD
- 10% of females and 5% of males aged 15 to 24 years report high levels of psychological distress
- In a sample of secondary school students covering 3% of the 2012 New Zealand secondary school roll, 21% of females and 10% of males had seriously thought about suicide in the last 12 months

Risk factors for mental health issues in young people include events early in life, such as childhood trauma, physical or sexual abuse, poverty and social deprivation.[4] In addition, young people of Māori or Pacific ethnicity and those who identify as LGBTI (lesbian, gay, bisexual, transgender or intersex) are at an increased risk of experiencing mental health issues.

Opportunistic screening in primary care is a key strategy to detect young people in need of assistance. A HEADS assessment (also referred to with multiple letters, e.g. HEEADDSSS) is a semi-structured interview covering aspects related to Home, Education and Employment, Eating and Exercise, Activities and peers, Drugs and Alcohol, Depression and suicide, Sexual health and the young person's Safety and Strengths.

Key points for clinicians to consider when conducting a HEADS assessment include:

- Explain the purpose of the assessment so a young person does not wonder why they are being asked questions unrelated to their visit
- Ensure that young people understand that information they provide is confidential
- Begin with topics that a young person is likely to find non-threatening

Depending on the information that is revealed from the HEADS assessment, further exploration of some topics may be warranted, e.g. to examine feelings of depression or suicidal ideation or to assess for alcohol and drug misuse. There are many different screening tools available for use in this situation; it is recommended that clinicians become familiar with a few in particular that they are most comfortable using. Examples include the Patient Health Questionnaire (PHQ-2), Ask Suicide-Screening Questions (ASQ), CRAFFT screening tool, Substances and Choices Scale (SACS) and the bestpractice "Depression in young people" module which incorporates several of these tools.

For further information, see: "Addressing mental health and wellbeing in young people", BPJ 71 (Oct, 2015).

The second article in this series covered non-pharmacological strategies for the treatment of frequently encountered mental health concerns in young people. This includes the initial assessment and management in primary care of young people with depression and anxiety, who are self-harming, have eating disorders, are misusing drugs or alcohol or are subject to bullying and social isolation.

Non-pharmacological strategies for managing young people with mental health conditions in primary care include:

- Building strength and resilience, including simple advice on improving sleep, exercise and diet, all of which can influence a young person's mood and psychological outlook
- Conducting structured problem solving; this incorporates basic principles of cognitive behavioural therapy (CBT) but does not require specialised training to conduct, and is well suited to general practice
- Recommending online CBT resources (e-therapy), such as SPARX or Beating the Blues. E-therapy is most useful for young people with depression and anxiety, but may also be beneficial to teach coping skills to any young person experiencing mental health difficulties

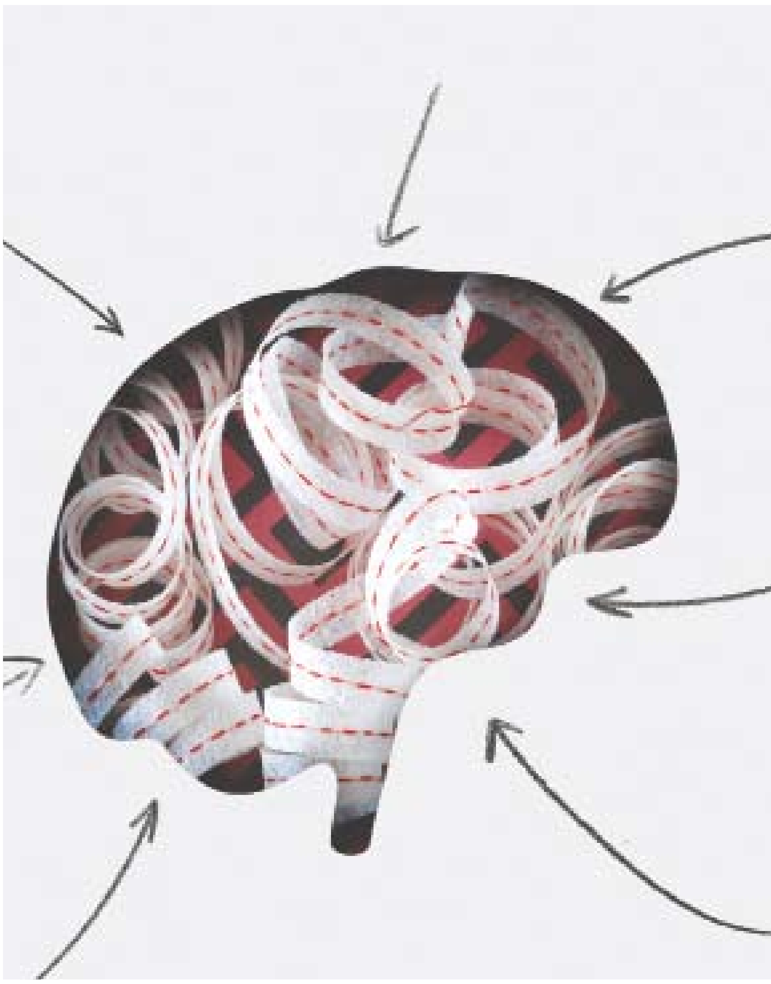
Through the Prime Minister's Youth Mental Health Project, DHB funding of primary mental health services is available for all young people aged 12 – 19 years, including extended general practitioner or practice nurse consultations, brief intervention counselling, group therapy or individual care; contact your local DHB for more information. In some areas, funding may be available from a local PHO or DHB to cover the cost of extended appointments for people aged over 19 years.

For further information, see: "Managing frequently encountered mental health problems in young people: non-pharmacological strategies", BPJ 72 (Dec, 2015).

The final upcoming article in the series will address the role of medicines in the treatment of mental health problems in young people, in particular when, and if, this is appropriate for patients aged under 18 years.

References:

1. Clark T, Fleming T, Bullen P, et al. Youth'12 Overview: The health and wellbeing of New Zealand secondary school students in 2012. Auckland, NZ: The University of Auckland 2013. Available from: www.fmhs.auckland.ac.nz/assets/fmhs/faculty/ahrg/docs/2012-overview.pdf (Accessed Oct, 2015).
2. Patton GC, Coffey C, Cappa C, et al. Health of the world's adolescents: a synthesis of internationally comparable data. Lancet 2012;379:1665–75. doi:10.1016/S0140-6736(12)60203-7
3. Statistics New Zealand. NZ social indicators. Prevalence of psychological distress. 2014. Available from: www.stats.govt.nz/browse_for_stats/snapshots-of-nz/nz-social-indicators/Home/Health/prevalence-psych-distress.aspx (Accessed Oct, 2015).
4. Patel V, Flisher AJ, Hetrick S, et al. Mental health of young people: a global public-health challenge. Lancet 2007;369:1302–13. doi:10.1016/S0140-6736(07)60368-7



Piles of pills:

Prescribing appropriate quantities of medicines

Key strategies for prescribers and pharmacists

Key strategies to reduce medicine wastage and prevent "piles of pills" creating a safety issue in homes include:

- Regular review of a patient's current medicines
- Prescribing a new medicine for a trial period and assessing efficacy and tolerability before continuing
- Prescribing appropriate quantities of "as required" medicines, e.g. analgesics
- Prescribing and dispensing "safety medicines" in smaller than 90-day stat quantities
- Using the Long Term Condition Service offered by pharmacists for support with medicines adherence

Every year in New Zealand, it is estimated that hundreds of thousands of subsidised medicines are dispensed to patients and never used. These medicines often end up accumulating in people's homes. This can cause safety issues such as inappropriate sharing of medicines, accidental or intentional overdose or use of expired medicines which may no longer be effective. If medicines are inappropriately disposed of they can also cause environmental pollution, e.g. if placed in household rubbish or flushed down the toilet.

Medicines are wasted for various reasons, including unintentional oversupply, non-adherence, changes in treatment or dose, allergic reaction or intolerance, resolution of the condition or death of the patient. Many patients collect all medicines prescribed to them including medicine repeats, even if the medicine is no longer needed or wanted.[1]

Whenever medicines are prescribed or dispensed a conversation should take place with the patient about their use of each medicine.

Prescribers:

- Ask what medicines* the patient has at home before prescribing more
- Ask if they are using each medicine they have been prescribed
- Ask if they know what each of their medicines are for
- Ask if they are experiencing any adverse effects or difficulties with taking any of their medicines
- When prescribing "as required" medicines, consider giving these to patients on a separate prescription so that they can collect any other prescription medicines they need and hold onto their separate "as required" prescription for if, or when, it is needed, e.g. as required omeprazole or paracetamol

* Include all options, e.g. pills, inhalers, topical preparations and over-the-counter products

Pharmacists:

- Ask the patient if they require all of the medicines on their prescription before they are dispensed
- Let patients know that they can put items on hold if they are not currently required; any item on the prescription can be held at the pharmacy for up to three months, and dispensed at a later date if needed
- Ask if they have any concerns or questions about the medicines they have been dispensed
- Ask patients to dispose of any unwanted medicines by returning them to the pharmacy

Consider a trial period

The "trial period" dispensing provision of the Pharmaceutical Schedule can be used to allow dispensing of a small portion of the first supply of a new or changed dose of medicine in order to check the acceptability and tolerability of the medicine for the patient. The prescription must be endorsed with the words "Trial period" or "Trial" and the quantity or time for the trial specified, e.g. by writing "trial supply 30 days" on the prescription or by entering the number of days supply in the "Initial Dispensing Period" box in Medtech. A reminder placed in the patient's notes at the start of the trial period can be used to ensure that the outcome of the trial is documented and to check that the patient has correctly understood the reason for the trial and is continuing to take the medicine or has a review in place. If the trial of treatment goes well, the patient can contact their pharmacist so that the remainder of the prescription can be dispensed; this is at no additional cost to the patient provided the medicine is fully subsidised.

Appropriate quantities for "as required" medicines

PHARMAC subsidy regulations require pharmacists to dispense 90-day single "stat" supply for many medicines, even if they are prescribed "as required". This can lead to unnecessarily large quantities of medicines being dispensed. Prescribers can calculate the number of tablets or inhalers needed for a patient on an "as required" basis and specify the quantity to be dispensed.

For example, a prescription for paracetamol to be used occasionally when required, and not continuously, could be:

- Rx Paracetamol 500 mg tablets
- Sig 1 – 2 tablets q4h prn, up to qid
- Mitte 180 tablets

This quantity provides the patient with enough supply to take two tablets, twice daily, for a few days a week, over a three month period.

Consider more frequent dispensings of Safety Medicines, where appropriate

"Safety Medicines" are medicines which carry a risk of harm to the patient when dispensed in large quantities, including tricyclic antidepressants, antipsychotics, benzodiazepines and zopiclone, codeine, buprenorphine with naloxone and Class B controlled drugs. For these medicines the prescriber can determine the dispensing frequency so that a patient receives the same 90-day supply but in smaller quantities dispensed more frequently, at no extra cost to the patient. Clinicians can do this by specifying a maximum quantity of the medicine to be supplied to the patient on each dispensing (e.g. 90 tablets in total, supplied 30 tablets at a time) or time period of supply (e.g. supply tablets for 90 days in total, 30 days at a time). Safety Medicines are identified in the Pharmaceutical Schedule with the words "Safety Medicine" written alongside the medicine's listing.

Consider eligibility for the Long Term Condition (LTC) service

General practitioners, other health professionals, family members or patients themselves can make referrals to the Long Term Condition service which is offered by community pharmacies. The service is delivered by a pharmacist and is designed to help patients to self-manage their medicines regimen and improve their adherence, including assessing factors affecting adherence, determining an appropriate dispensing frequency or increasing a patient's understanding of their medicines and how to use them.

To be eligible for the service:

- The patient must live in the community and have at least one long term condition that requires medicine as part of its management
- The patient must have been referred for assessment by a general practitioner or other allied health service, e.g. district nursing or secondary care, or have concerns about self-managing their condition identified by their family, pharmacist, or the patient themselves
- There must be evidence that the patient has collected less than 80% of their regular medicines over the past six months
  - OR that despite collection there are concerns regarding adherence
  - OR the patient has had a recent review of their medicine use which has identified that support and monitoring is required

For further information, see: "Piles of pills: Prescribing appropriate quantities of medicines", BPJ 69 (Aug, 2015).

Reference:

1. Braund R, Peake B, Shieffelbien L. Disposal practices for unused medications in New Zealand. Environ Int 2009;35:952–5. doi:10.1016/j.envint.2009.04.003

Biosimilars: what does a primary care clinician need to know?

Biosimilars are biological medicines that are developed to be comparable versions of an existing, approved, biological medicine once patent protection on the original has expired. Worldwide, biosimilar medicines are available for the treatment of cancer, diabetes and diseases with an inflammatory or immune component, such as rheumatoid arthritis and inflammatory bowel disease. In New Zealand, two biosimilar medicines are currently approved and subsidised: Zarzio (filgrastim, for neutropenia) and Omnitrope (recombinant human growth hormone); more biosimilars are likely become available as patents expire in the next few years.

Key points for primary care clinicians:

- Biosimilars are not just generic versions of a biological medicine; manufacturing and analysis complexities mean that biosimilars cannot be made, or cannot be demonstrated to be, exactly the same as an existing biological medicine. In comparison, generic medicines can be synthesised to be identical to the original patented pharmaceutical.
- The same degree of clinical benefit is expected to be achieved with a biosimilar as with the original biological medicine
- When a biosimilar medicine is subsidised in New Zealand, whether the original biological medicine will continue to be funded will vary on a case by case basis; the innovator versions of Zarzio and Omnitrope are no longer subsidised
- Decisions regarding switching a patient from a biologic to a biosimilar are likely to be managed in secondary care, but primary care clinicians may help to monitor treatment response and adverse effects
- A patient could have adverse effects, including immune reactions, with a biosimilar that they did not experience while using the original biologic, or vice versa, or from different batches of a biologic or biosimilar medicine
- If a patient develops an adverse reaction after initiating or switching to a biosimilar medicine, the clinician managing the patient's care should be advised and an adverse drug reaction report submitted to the Centre for Adverse Reactions Monitoring (CARM)

For further information, see: "Biosimilars - what does a primary care clinician need to know?", BPJ 71 (Oct, 2015).

Improving the safety of community-based chemotherapy

Traditionally, chemotherapy is carried out in a hospital setting. However, oral chemotherapy is now increasingly being dispensed in the community and taken by patients at home. To improve patient safety and treatment effectiveness, clear, and preferably documented, communication is required between patients, oncologists, general practitioners and pharmacists.

General practitioners can improve the safety of community-based chemotherapy by:

- Discussing the treatment plan with the patient, pharmacist and oncologist
- Being aware of all medicines the patient is taking, including over-the-counter or complementary and alternative medicines and assessing the risk of interactions with the chemotherapy regimen
- Ensuring that the patient has been provided with clear written instructions, including start and stop dates for each chemotherapy cycle
- Providing support to the patient throughout treatment and regularly monitoring them for adverse effects, particularly those requiring immediate referral to secondary care

Pharmacists need to recognise when they receive a prescription for a cytotoxic medicine, and have additional safety procedures in place, e.g. confirming medicines dispensed match those on the treatment protocol, checking any calculations based on the patient's body surface area are correct, checking that quantities for chemotherapy cycles are appropriate, and including the start and stop dates for cycles of treatment on prescription labels. Pharmacists should verify at dispensing that patients understand their treatment protocol.

For further information, see: "Improving the safety of community-based chemotherapy", BPJ 71 (Oct, 2015).

Travel consultation essentials: for departures and arrivals

Travellers requiring medical advice should consult a health professional at least six to eight weeks before departure. The first goal is to establish the traveller's itinerary and determine any risks they are likely to encounter. Remind people that their travel insurance needs to cover pre-existing conditions and any planned activities; supplementary insurance may be required. As a rule, people with unstable medical conditions should not fly and long-term conditions need to be well managed before departure. Travellers taking prescription medicines require sufficient supply to cover the time that they will be away and a letter outlining their current medicines, any allergies and their medical history. Guidance on vaccination, malaria prophylaxis and as-required medicines depends on the region the person will be travelling in, their immunisation status, general health and the length of time until departure. People crossing multiple time zones who are taking medicines dosed at specific times, e.g. insulin or warfarin, may need advice on how to temporarily adjust their regimen.

If a visitor to New Zealand requires a medicine that is unavailable here it may be necessary to research an alternative. A database containing information on medicines used in 185 countries is available from: **www.drugs.com/international.** To ensure continuity of care, give the patient a printed copy of their consultation notes and if appropriate, organise a follow-up consultation. Febrile illness in a patient who has recently visited a country with a high incidence of infectious disease is a potential red-flag: establish the patient's immune status and possible exposure, consider whether precautions should be taken to minimise transmission and have a low threshold for contacting a medical officer of health or infectious diseases specialist.

For further information, see: "Travel consultation essentials: for departures and arrivals", BPJ 72 (Dec, 2015)

Melatonin: is it worth losing any sleep over?

Modified-release melatonin is an unsubsidised medicine that is approved for the treatment of insomnia in adults aged over 55 years; other formulations of melatonin are unapproved. Melatonin is not currently approved for younger patients as the trials that showed modified-release melatonin was moderately effective at treating insomnia only included people aged over 55 years. Prescribers are reminded that non-pharmacological interventions, e.g. improving sleep hygiene, are the first-line treatment for insomnia. Patients taking modified-release melatonin for insomnia should do so one to two hours before bedtime, for up to 13 weeks. There is some evidence that "off-label" use of melatonin may improve sleep quality in shift workers or reduce the severity of jetlag. Melatonin may also be used in specialist situations, such as in people with vision impairments and adolescents or children with neurodevelopmental disorders and sleep disturbances. The effects of long-term melatonin use are unknown due to a lack of studies therefore this should be considered with caution.

For further information, see: "Melatonin: is it worth losing any sleep over", BPJ 69 (Aug, 2015).

Chronic pelvic pain in women

Key practice points:

- Chronic pelvic pain can arise from pathology affecting any of the structures located within the pelvis and lower abdomen, including related structures, or there may be no identifiable cause
- The first goal of treatment is to acknowledge the pain and understand how this affects the woman's life
- Unless a specific cause is found that can be treated, management focuses on strategies for pain modulation, including exercise, diet and sleep
- Analgesia and adjuvant medicines may be considered, such as paracetamol, non-steroidal anti-inflammatory drugs, tricyclic antidepressants and gabapentin
- The overall aim is to provide the woman with support to self-manage and be able to cope with her pain

Chronic pelvic pain is defined as intermittent or constant pain in the lower abdomen or pelvis of at least six months' duration, which does not occur exclusively with menstruation or intercourse. "Chronic pelvic pain syndrome" is the appropriate diagnosis where pain is the dominant feature in the absence of pathology.[1, 2]

For most women with chronic pain, it is of upmost importance for their pain to be validated. In the absence of an identifiable cause, it is essential to educate women that there is no one "magic bullet" that will resolve their pain. It is a journey that both doctor and patient will go on, with the hope of finding strategies to help cope with and minimise the pain over time. Women with chronic pelvic pain report a lower quality of life, with high rates of functional impairment, psychosocial distress and sexual dysfunction, risk being "labelled" as difficult or needy and may struggle to be believed when accessing healthcare services.

Diagnosis and investigation of chronic pelvic pain

Assessment begins with acknowledging the pain and understanding how this affects the woman's life. **A comprehensive history is essential**, covering the characteristics of pain, contributing factors and co-morbidities, which may help identify the underlying cause(s). The history should include questions about the woman's:[3]

- Pain (characteristics, duration, frequency)
- Menstrual cycle
- Bowel and bladder function
- Sexual function (including any history of abuse)
- Level of functioning
- Co-morbidities
- Medicine use including any medicines used to manage the pain

Examine for postural abnormalities, as well as performing abdominal and pelvic examination, including assessment of pelvic floor muscles. Neuropathic testing can be used to identify any altered areas of sensation over the lower abdomen and the perineum, such as allodynia, hyperalgesia or sensory loss. Assessment should exclude any red flags and consider the specific aetiologies of reported symptoms.

Red flags which require referral include:[3]

- Rectal bleeding
- Irregular vaginal bleeding in a woman aged over 40 years
- Post-coital bleeding
- Onset of new bowel symptoms in a woman aged over 50 years
- Excessive or unexplained weight loss
- Onset of pelvic pain in a post-menopausal woman
- Pelvic mass

Laboratory tests may include swabs to rule out sexually transmitted infections, a cervical smear if due or if there is an abnormality on examination, a urine sample to exclude pregnancy or urinary tract infection, and blood tests such as full blood count, creatinine and electrolytes and C-reactive protein. Ultrasound and laparoscopy can help detect pelvic pathology such as uterine leiomyomas, ovarian tumours and some cases of endometriosis, and may be appropriate in some women.

Management of chronic pelvic pain

Unless a specific cause is found that can be treated, management focuses on strategies for pain modulation, including exercise, diet and sleep:

- Exercise produces symptomatic improvements in most patients with chronic pain[4]
- Physiotherapy can be valuable, particularly for women who have hypercontractility of the pelvic floor. Exercises which increase pelvic floor tone should be avoided as these can exacerbate pelvic floor hypercontractility.
- Improving sleep quality with sleep hygiene techniques can decrease chronic pain
- Smoking cessation; smoking is associated with higher levels of physical impairment and increased pain in patients with fibromyalgia and a similar association is likely in patients with any type of chronic pain[5]
- Dietary changes may improve chronic pain symptoms:
  - Increasing intake of fruit and vegetables
  - Bladder irritation can be minimised by reducing the intake of caffeine, citrus fruits, spicy foods, carbonated drinks and alcohol and ensuring adequate hydration[6]

Information on exercises to relax the pelvic floor is available online, e.g. www.pelvicpain.org.au/information/women/yoga-poses-relax-pelvis/

Analgesia and adjuvant medicines may be considered, such as paracetamol, non-steroidal anti-inflammatory drugs (NSAIDs), tricyclic antidepressants (TCAs) and gabapentin. The overall aim is to provide the woman with support to self-manage and be able to cope with her pain.

Prescribing points for the use of analgesics in women with chronic pelvic pain include:[1,7]

- Paracetamol should be used on a regular daily basis rather than "as required", particularly if there is somatic pain
- NSAIDs are widely used for chronic pelvic pain and can be beneficial for some women, particularly if there is an inflammatory component to the pain
- All opioids should be avoided as they can cause a paradoxical increase in sensitivity to pain, as well as the risks of addiction, tolerance and constipation. Benzodiazepines should also be avoided.
- TCAs and gabapentin affect neuropathic or centrally mediated pain, and there is some evidence that these medicines may benefit patients with chronic pelvic pain. TCAs should be trialled for at least six to eight weeks before assessing response as they can take some time to produce benefit.
- Other pharmacological options include clonidine (usually a transdermal patch) as an adjuvant analgesic and botulinum toxin A injections which may reduce spasm of the pelvic floor muscles, particularly if used in combination with pelvic floor physiotherapy

Patient resources

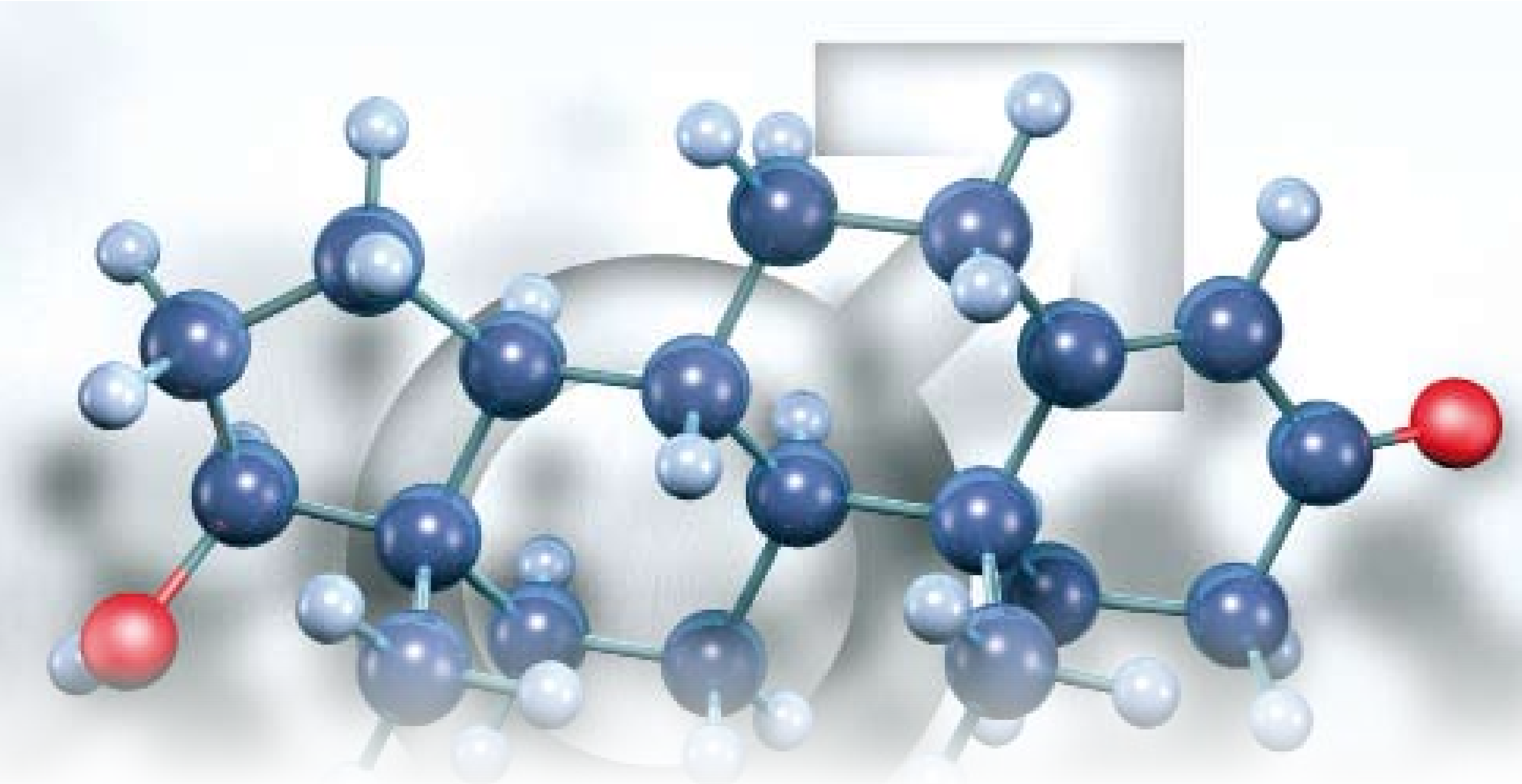
The International Pelvic Pain society produces an educational document for women with chronic pelvic pain, available from: **http://pelvicpain.org/docs/patients/basic-chronic-pelvic-pain.aspx**

The Pelvic Pain Foundation of Australia also has an informative website designed for patients and their families, available from: **www.pelvicpain.org.au**

For further information, see: "Chronic pelvic pain in women", BPJ 70 (Sep, 2015).

References:

1. Engeler D, Barabowski A, Borovicka J, et al. Guidelines on chronic pelvic pain. 2015. Available from: http://uroweb.org/wp-content/uploads/25-Chronic-Pelvic-Pain_LR_full.pdf (Accessed Dec, 2015).
2. International Association for the Study of Pain. Classification of chronic pain, second edition (revised). 2011. Available from: www.iasp-pain.org/PublicationsNews/Content.aspx?ItemNumber=1673&navItemNumber=677 (Accessed Dec, 2015).
3. Royal College of Obstetricians and Gynaecologists (RCOG). The initial management of chronic pelvic pain. RCOG, 2012. Available from: www.rcog.org.uk/en/guidelines-research-services/guidelines/gtg41/ (Accessed Dec, 2015).
4. Ambrose K, Golightly Y. Physical exercise as non-pharmacological treatment of chronic pain: Why and when. Best Pract Res Clin Rheumatol 2015;29:120–30. doi:10.1016/j.berh.2015.04.022
5. Goesling J, Brummett C, Meraj T, et al. Associations between pain, current tobacco smoking, depression, and fibromyalgia status among treatment-seeking chronic pain patients. Pain Med 2015;16:1433–42. doi:10.1111/pme.12747
6. Friedlander J, Shorter B, Moldwin R. Diet and its role in interstitial cystitis/ bladder pain syndrome (IC/BPS) and comorbid conditions. BJU Int 2012;109:1584–91. doi:10.1111/j.1464-410X.2011.10860.x
7. Cheong Y, Smotra G, Williams A. Non-surgical interventions for the management of chronic pelvic pain. Cochrane Database Sys Rev 2014;3:CD008797. doi:10.1002/14651858.CD008797.pub2



Testosterone use in older males

Although testosterone levels in males decline with age, the risks and benefits of testosterone supplementation in this age group are unclear.

Older males may present with signs and symptoms suggestive of hypogonadism; some of these are less specific, such as decreased energy or depressed mood, and others more specific, such as decreased or absent morning or spontaneous erections, reduced libido and erectile dysfunction.[1]

The first step is to consider medical conditions or other factors which could be managed to improve signs and symptoms.

A number of medical conditions can influence the function of the HPG axis and are associated with hypogonadism, including:[2–4]

- Type 2 diabetes
- End-stage renal disease
- Osteoporosis
- Moderate to severe COPD
- Severe obstructive sleep apnoea
- Pituitary tumour
- HIV

- Testicular cancer
- Haemochromatosis
- Chronic inflammatory disease, e.g. arthritis
- Eating disorders (malnutrition)

Lifestyle factors which decrease testosterone levels, include obesity, chronic excess alcohol intake, stress, sleep deprivation, vigorous exercise and illicit drug use.

Medicines that interfere with the HPG axis include opioids, high dose systemic corticosteroids, chemotherapy medicines and phenothiazines.

Biochemical investigation of hypogonadism may be appropriate for patients with symptoms which are adversely affecting their quality of life. The recommended investigation is as follows:[3]

- Request an early morning serum total testosterone level
- If the level is below the reference range, repeat the test as 30% of males with an initially low testosterone level have normal levels on re-testing
- A luteinizing hormone (LH) test can be ordered with the repeat testosterone level to help distinguish between primary and secondary hypogonadism, if the total testosterone level is confirmed as being consistently low
- Measures of sex hormone binding globulin (SHBG) and free testosterone are only necessary if there is reason to suspect that SHBG levels are abnormal, such as patients with marked obesity, thyroid disease or who are taking particular medicines such as anticonvulsants

For males with consistent signs and symptoms and biochemical evidence of hypogonadism, it is recommended that the decision of whether to initiate testosterone is discussed with an endocrinologist; only one formulation of testosterone can be prescribed without endorsement from an endocrinologist. Testosterone replacement is more likely to be worthwhile for those with specific symptoms for which improvements can be evaluated.

Testosterone treatment is contraindicated in males with prostate or breast cancer, primary liver tumours, hypercalcaemia and nephritic syndrome.[1,5] Further investigations which should be conducted before initiation include full blood count, PSA level and digital rectal examination. Testosterone treatment is not recommended in males with a palpable prostate nodule or induration, with PSA level > 4.0 ng/ml (or 3.0 ng/ml if there is a family history of prostate cancer), elevated haematocrit (PCV > 50%), or in patients with severe untreated obstructive sleep apnoea or poorly controlled congestive heart failure.[1]

Prior to the initiation of testosterone, patients should be informed that the benefits and risks of treatment are to some extent both uncertain as detailed data on long-term health outcomes in large randomised controlled trials is currently lacking. In addition, patients should be made aware of the ongoing testing requirements during treatment to assess response and safety (e.g. haematocrit, PSA and testosterone levels).

For further information, see: "Prescribing testosterone in ageing males: why you shouldn't read this article", BPJ 69 (Aug 2015).

"Research Update: Testosterone use and cardiovascular risk in older males", BPJ 70 (Sept 2015).

References:

1. Bhasin S, Cunningham GR, Hayes FJ, et al. Testosterone therapy in men with androgen deficiency syndromes: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab 2010;95:2536–59. doi:10.1210/jc.2009-2354
2. Perry-Keene D. Low testosterone in men. Aust Prescr 2014;37:196–200.
3. SonicEdu, Kyle C (Ed).Sonic Pathology handbook. Available from: www.snp.com.au (Accessed Dec, 2015).
4. Dohle GR, Arver S, Bettocchi C, et al. Guidelines on male hypogonadism. European Association of Urology, 2015. Available from: http://uroweb.org/guideline/male-hypogonadism/ (Accessed Dec, 2015).
5. New Zealand Formulary (NZF). NZF v42. 2015. Available from: www.nzf.org.nz (Accessed Dec, 2015).

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