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The year that was: Key messages from Best Practice Journal 2013

2013 began with publication of the 50th issue of Best Practice Journal. In this edition we focused on the topic at the heart of primary health care in New Zealand: cardiovascular disease. It is a worrying statistic that cardiovascular disease is the leading cause of mortality in New Zealand, and that significant ethnic disparities exist in the prevalence of disease, access to treatments and overall health outcomes. Other important themes of BPJ in 2013 included promoting the safe use of medicines, profiling new treatment options and raising awareness of antimicrobial resistance. Before we move on to the articles of 2014, it is important to review what we have learnt so far.

Irritable bowel syndrome in adults: Not just a gut feeling

Irritable bowel syndrome (IBS) is a chronic gastrointestinal disorder characterised by recurrent bouts of abdominal discomfort and pain, bloating and a changeable bowel habit. Generally a patient with IBS will have periods of time when they feel well, interspersed with acute bouts of their particular gastrointestinal symptoms. IBS is regarded as the most frequently encountered gastrointestinal diagnosis in primary care. In some patients, IBS can significantly affect quality of life, however, reassurance can be given that IBS itself does not predispose the patient to life-threatening disease.
The management of Parkinson’s disease: Which treatments to start and when?

The treatment of patients with Parkinson’s disease usually involves a multidisciplinary approach to care. The role of the general practice team is to co-ordinate an individualised treatment plan, according to the progression of the patient’s condition. A combination of levodopa with carbidopa or benserazide is generally the first-line pharmacological treatment for functional disability in patients with Parkinson’s disease. A crucial aspect of management is the optimisation of treatment as new symptoms develop.

Managing patients with poor glycaemic control: One size does not fit all

People with type 2 diabetes and poor glycaemic control (HbA1c > 64 mmol/mol) are at increased risk of developing diabetes-related complications and cardiovascular disease. Engaging with these patients and helping them overcome their individual barriers to achieving a healthier life are a priority for primary care.

News Updates

Captopril tablets discontinued: ACE inhibitor alternatives • Removal of Special Authority for combination inhaler Seretide • Rotavirus and varicella vaccines on immunisation schedule from 1 July 2014 • Oral ketoconazole tablets discontinued worldwide

Correspondence

Prescribing salbutamol and oral corticosteroids in a child with wheeze • Are two vaccinators better than one?
The year that was:
Key messages from Best Practice Journal 2013

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The top five themes in Best Practice Journal in 2013 were:

1. Reducing the burden of cardiovascular disease and diabetes
2. Promoting the safe use of medicines
3. Increasing awareness of antimicrobial resistance
4. Profiling new treatments
5. Updating the management of common conditions: Foundation articles

Reducing the burden of cardiovascular disease and diabetes

Strategies for the management of patients with cardiovascular disease (CVD) and diabetes have featured frequently in BPJ over the years. This reflects both the high prevalence of these conditions in New Zealand and the significant role that primary care clinicians have in managing patients with CVD, diabetes and closely related conditions, such as chronic kidney disease and gout.

Cardiovascular disease is the leading cause of mortality in New Zealand. However, disparities exist in both the prevalence of disease and access to treatments. For example, the mortality rate from heart failure for Māori aged over 65 years in New Zealand is approximately double that of non-Māori; the disparity may be even more pronounced in younger age groups (45 – 65 years). Heart failure occurs approximately 10 – 15 years earlier in Māori compared to non-Māori.

The prevalence of type 2 diabetes is two to three times higher in Māori and Pacific peoples compared to European New Zealanders. It is estimated that one-third of Māori and Pacific peoples aged 45 – 64 years have intermediate hyperglycaemia.

With the growing burden of CVD, diabetes, kidney disease and related morbidities in New Zealand, it is imperative that patients at the greatest risk are detected early and receive the most intensive management.
Treating hypertension early to reduce CVD risk

An important article supporting this theme in 2013 was: “Hypertension in adults: the silent killer”, BPJ 54 (Aug, 2013). There is currently a lack of consensus on the ideal management of patients with hypertension, and international guidelines differ in their recommendations. What is agreed is that hypertension is currently under-treated in New Zealand and blood pressure is an important modifiable risk factor for cardiovascular disease.

A recent update to the New Zealand Primary Care Handbook recommends that all patients with significant individual cardiovascular risk factors should have them managed. It specifies that pharmacological treatment be considered for all patients with blood pressure ≥ 170/100 mmHg, irrespective of their calculated CVD risk. However, based on the United Kingdom’s NICE guideline, the European ESH/ESC guidelines and local expert opinion, we recommended that all patients with systolic blood pressure ≥ 160 mmHg should be treated, regardless of their calculated cardiovascular risk.

To diagnose hypertension, blood pressure is best assessed with two measurements, at least two minutes apart. Ideally, measurements should be taken from both arms and repeated if the difference between arms is greater than 20 mmHg. Ambulatory blood pressure testing is the gold standard for confirming a diagnosis of hypertension where availability and cost permit. It should be considered if there are substantial differences between measurements taken in the clinic setting.

Non-fasting lipids now acceptable for CVD risk assessment

The concept of no longer asking patients to fast for a lipid test was raised in a key article from Best Tests Journal in 2013: “Oh and while you are here...’ Fasting may be unnecessary for lipid testing”, Best Tests (Nov, 2013). This article discussed the growing body of evidence and expert opinion suggesting that, in the majority of patients, a fasting lipid test is not necessary for calculating cardiovascular risk or monitoring lipid levels.

In December, 2013, the Ministry of Health released an update to the New Zealand Primary Care Handbook (the national guideline for managing cardiovascular disease and type 2 diabetes). One of the new messages is that a non-fasting test is an appropriate way of measuring lipid levels for the purposes of cardiovascular risk assessment.

The update also contains guidelines on the frequency of lipid monitoring:

- CVD risk > 20%: monitor non-fasting lipids every three to six months until stable, then every one to two years
- CVD risk < 20%: monitor non-fasting lipids at each CVD risk assessment. If lifestyle interventions are implemented to reduce LDL-cholesterol, review non-fasting lipid levels after six to 12 months.

The Handbook offers the following guidelines for initiating pharmacological treatment for lowering CVD risk:

- Healthy lifestyle interventions are appropriate for all patients
- Most patients with a five-year CVD risk < 10% can be managed without pharmacological treatment
- For patients with a five-year CVD risk between 10 – 20%, use a shared decision making approach to initiating lipid-lowering and/or blood pressure lowering medicines
- Most patients with a five-year CVD risk > 20%, and all patients with a history of CVD, are likely to benefit from lipid-lowering, blood pressure lowering and anti-platelet medicines
- All patients with significant individual risk factors should have them managed (irrespective of calculated CVD risk)

Initiating treatment for patients at risk is more important than which antihypertensive treatment regimen is chosen. Hypertension is progressive and patients will usually require several changes in their medicine regimen over time to achieve blood pressure targets and reduce overall cardiovascular risk. In general, patients can be started on an ACE inhibitor or calcium channel blocker, and then these medicines can be combined, followed by the addition of a thiazide diuretic. Beta-blockers may be added to the treatment regimen in patients with co-morbidities such as ischaemic heart disease or atrial fibrillation.

A new management strategy for heart failure

A primary care clinician is likely to have approximately 20 patients with heart failure per 1000 patients – more if the patient population is older. In the foundation articles: "Identifying patients with heart failure in primary care" and "Managing patients with heart failure in primary care", BPJ 50 (Feb, 2013), a standard was outlined for caring for patients with heart failure in the community.

The first article in the series outlined the changes in terminology used for describing and categorising heart failure. This has been driven by evidence from clinical trials which have highlighted the significance of left ventricular ejection fraction. Heart failure should now be differentiated as either heart failure with reduced ejection fraction (H-REF) or with preserved ejection fraction (H-PEF). Making this distinction is important because, as the second article outlined, the underlying cause and the treatment of each type of heart failure differ. The diagnosis and management of heart failure therefore relies on the use of echocardiography, which should ideally be requested for every patient with suspected heart failure.

Focusing on glycaemic control

Every day, approximately 50 people in New Zealand are newly diagnosed with diabetes. Most of these people will require regular and intensive management to maintain their glycaemic levels below their individualised target. In the article: "Improving glycaemic control in people with type 2 diabetes: expanding the primary care toolbox", BPJ 53 (Jun, 2013), the spectrum of diabetes treatments available for managing patients in primary care in New Zealand was outlined. Achieving glycaemic control in patients with type 2 diabetes does not have to be limited to prescribing metformin; add a sulphonylurea, initiate insulin, and if more established treatments are not tolerated or not effective in achieving agreed HbA1c targets, consider whether other medicines such as pioglitazone or acarbose may be appropriate. Lifestyle interventions such as a healthy eating plan, weight loss and increased physical activity are also crucially important in all patients to help to reduce glycaemic levels.

Management of patients with type 2 diabetes is an ongoing and proactive process and patients with the poorest glycaemic control require the most health care resources. Glycaemic control is not a “one size fits all” approach and a treatment plan including appropriate clinical targets should be tailored to each patient, taking into consideration their age, co-morbidities and motivation for treatment. Younger people benefit more from intensive control as they must live with the consequences of diabetes for longer. Older people, who are more vulnerable to hypoglycaemia, may have less stringent HbA1c targets.

See: "Getting to know your patients with diabetes”, Page 40 for discussion on how to effectively engage with patients and understand their motivations and barriers to treatment.
Promoting the safe use of medicines

An underlying theme for all BPJ articles is to provide guidance on the safe use of medicines. A rule that can be applied in most situations is: “Prescribe the lowest effective dose of medicine for the shortest possible time”. Patients treated with any medicine long-term should have their regimen regularly reviewed, with the aim of lowering the dose or ceasing the medicine if it is no longer required or if an alternative medicine would be more appropriate. Exceptions to this would be when treatments need to be escalated to maintain control, such as in the ongoing management of patients with diabetes. Patients should be given information about expected outcomes and potential adverse effects of their medicine(s), and advised to report any symptoms. Laboratory monitoring may also be required.

The safe use of medicines also encompasses safely prescribing medicines and adopting strategies to avoid errors. These strategies include being aware of any contraindications to the use of a medicine and checking for medicine allergies and any previous adverse medicine reactions. When prescribing, use the generic name of the medicine (exceptions include warfarin), avoid the use of abbreviations, include specific instructions for use and an indication for the medicine, check the prescription before signing it and ensure that the patient/caregiver understands how to use the medicine and what it is for.

If a medicine is prescribed for a condition, at a dose range or via a route of administration which it is not indicated for, it is referred to as “off-label” prescribing. An example of this is the use of quetiapine for anxiety, which is not an approved indication. Some medicines may also be prescribed even though they are unapproved, which means that the medicine has not been through the Medsafe regulatory process for approval in New Zealand. An example of an unapproved medicine in New Zealand is benzbromarone (Page 9). An “Upfront” article in BPJ in 2013 provided guidance on the rules and recommendations for prescribing unapproved and “off-label” medicines in New Zealand: “Unapproved medicines and unapproved uses of medicines: Keeping prescribers and patients safe”, BPJ 51 (Mar, 2013).

Consider lower doses of isotretinoin

An important safe prescribing update was reported in the article: “Low dose isotretinoin for acne?”, BPJ 56 (Nov, 2013). Isotretinoin is conventionally prescribed using a cumulative, weight-based dosing regimen of approximately 150 mg/kg over several months. However, this involves patients taking relatively high daily doses of 0.5 – 1 mg/kg, with an increased risk of adverse effects. Recent evidence suggests that isotretinoin prescribed at a lower dose is as effective as higher doses for clearing acne and is less likely to result in adverse effects such as liver abnormalities, photosensitivity and eczema. Treatment is tailored to the individual patient, depending on the severity of their acne and their response to isotretinoin. A suggested regimen is to initiate isotretinoin at a dose of 10 – 20 mg, once daily and to continue until acne lesions have resolved, which generally occurs within three to five months. Treatment, usually at a reduced dose, should be continued for a further two to four months to decrease the risk of relapse and help with resolution of acne scarring.

Prescribing NSAIDs safely

Naproxen or low-dose ibuprofen (up to 1200 mg, daily) are the non-steroidal anti-inflammatory drugs (NSAID) of choice when an NSAID is indicated, as they have a better safety profile than other NSAIDs. This was outlined in the article: “Non-steroidal anti-inflammatory drugs (NSAIDs): Making safer treatment choices”, BPJ 55 (Oct, 2013).

NSAIDs are associated with increased cardiovascular risk (particularly diclofenac), gastrointestinal complications (particularly long-acting formulations) and renal impairment. In general, NSAIDs should be prescribed at the lowest possible dose, for the shortest possible time, and long-acting formulations should be avoided if possible. NSAIDs should always be prescribed with caution as treatment for just a few days, even at recommended doses, can be associated with serious adverse effects in susceptible patients. Older people and people with increased CVD risk, type 2 diabetes or renal impairment are particularly vulnerable to the adverse effects associated with NSAIDs.

Safety snippets

In “Hypomagnesaemia with proton pump inhibitors”, BPJ 52 (Apr, 2013), it was confirmed that there was an association between the use of PPIs and reduced magnesium levels. Most general practices will have large numbers of patients taking PPIs, but it is not necessary for preventative action to be taken for all of these patients. Patients should be informed about the possibility of hypomagnesaemia and asked to report any unexplained symptoms; features of hypomagnesaemia are non-specific and may include muscle cramps, weakness and fatigue. Patients who are concerned can be advised to increase their dietary intake of magnesium-containing foods, e.g. milk, wholegrain cereals, wholemeal bread, green leafy vegetables, lean meats and nuts.
In “Statins and the risk of acute kidney injury”, BPJ 52 (Apr, 2013) recent research showing a dose-dependent association between statin use and acute kidney injury (AKI) was discussed. Prescribers were reassured that, despite this association, the benefits of statins outweigh the modest risk of AKI, and there is insufficient evidence to alter the prescribing of statins in primary care. Increased vigilance is recommended when prescribing higher doses of statins to elderly people with reduced kidney function.

**Increasing awareness of antimicrobial resistance**

Resistance to antimicrobial medicines has become common for most pathogenic microbial species due to the increased use of these medicines in both human and animal health. All antimicrobial use increases resistance, however, inappropriate use increases the speed and spread of this resistance. There are few new antimicrobial medicines currently in development, therefore it is crucial to preserve the use of the medicines that are available.

“Antibiotic stewardship” is a phrase used to describe taking responsibility for the way antimicrobial medicines are used in a population. General practice can take a lead role in ensuring the appropriate use of antibiotics, limiting their unnecessary use and educating patients about the conditions for which antibiotics are, and are not, useful. Improved surveillance of antimicrobial resistance and reporting by local laboratories will further support these aims.

Antimicrobial resistance has been an ongoing theme in BPJ. In 2013, a series of “Upfront” articles set the scene for the increasing concern posed by antimicrobial resistance: “Is the cupboard bare? The threat of antimicrobial resistance”, BPJ 53 (Jun, 2013) and “Antimicrobial resistance in New Zealand: What is my role in primary care?”, BPJ 54 (Aug, 2013). In addition, a revised version of our guide “Antibiotics: Choices for common infections”, Special edition (Jul, 2013), was released. This has been one of our most accessed and requested publications. As resistance rates around New Zealand grow, and new evidence for treating infections emerges, the recommendations for appropriate antibiotics change, and it is therefore important that prescribers keep up to date by using the latest resources and validated advice.

Important updates in the 2013 antibiotic guide included:

- Azithromycin liquid (and tablets) is now available and subsidised for the treatment and prophylaxis of pertussis in children
- Cefaclor was previously a second-line option for many infections, e.g. otitis media, sinusitis, skin infections, however, other options are now favoured as use of cefaclor must be reserved
- New guidance was included for staphylococcal decolonisation in patients with recurrent skin conditions
- Urinary tract infection in males is recommended to be treated for seven days (previously 10 – 14 days)
- The recommended dose of ceftriaxone for treating sexually transmitted infections is 500 mg IM, as a single dose (previously 250 mg)
Profiling new treatments

An important role of BPJ is to provide information and guidance about medicines newly available, or newly subsidised, in New Zealand. In some cases, primary care clinicians may rarely initiate these medicines, but in other cases a newly available or funded medicine may represent a new treatment option for a large number of patients in the practice population who will benefit.

Risedronate provides a new option for bone health

Risedronate is an oral bisphosphonate, indicated for the treatment of osteoporosis and the prevention of glucocorticoid-induced osteoporosis. It became fully subsidised, without restriction, in New Zealand in September, 2013. In the article: “Risedronate now fully subsidised: What is its place in practice?” BPJ 56 (Nov, 2013), it was suggested that risedronate is likely to become the oral medicine of choice for patients with osteoporosis, or at risk of osteoporotic fracture.

Studies to date have shown that risedronate is equally effective as alendronate at reducing fracture risk and both medicines have similar risk profiles. Risedronate has unrestricted subsidy access compared to alendronate, which requires Special Authority approval. Therefore risedronate is the best first-line option for patients who require bisphosphonate treatment. Zoledronic acid is still a recommended treatment option for patients who cannot tolerate or adhere to oral treatment, and who qualify for subsidy.

Etidronate, like risedronate, is fully subsidised without restriction, but it is less potent than other bisphosphonates and less effective in reducing fracture risk. Therefore etidronate is not a recommended first-line treatment option for patients with osteoporosis or at risk of fracture.

Benzbromarone now available in New Zealand

Benzbromarone is a uricosuric medicine which has been used in other countries for the management of patients with gout. This medicine, while not yet approved by Medsafe in New Zealand, was subsidised (with Special Authority criteria) on the Pharmaceutical Schedule in April, 2013, to provide another treatment option to patients who have been unable to achieve target urate levels with other available medicines. While in most cases benzbromarone is likely to be initiated by a Rheumatologist, it is important that primary health care clinicians are aware of this treatment option and can help to manage patients prescribed this medicine. The article: “An update on the management of gout”, BPJ 51 (Mar, 2013), provided guidance about the use of this newly subsidised medicine.

Patients most likely to benefit from benzbromarone include those who have been unable to achieve their target urate level despite optimal use of allopurinol and probenicid, or for whom intolerable adverse effects have occurred with these medicines. Benzbromarone can be used safely for patients with moderate renal impairment and may be more effective than allopurinol in reducing urate levels in this patient group. However, benzbromarone has been associated with liver toxicity, and patients must have regular liver function tests as part of the Special Authority criteria for subsidy of this medicine. Benzbromarone is a CYP2C9 inhibitor so can interact with medicines such as warfarin and aspirin.

Febuxostat is also a newly available treatment option for patients with gout who are unable to achieve target urate levels using more conventional treatment options such as allopurinol. Febuxostat has been approved in New Zealand by Medsafe, but is not currently subsidised. Like benzbromarone, it is safe to use in patients with mild to moderate renal impairment,
but it also associated with hepatotoxicity. Treatment with febuxostat is also not recommended in patients with ischaemic heart disease or congestive heart failure.*

**Ticagrelor provides an alternative to clopidogrel**

Ticagrelor, an oral anti-platelet medicine, was added to the Pharmaceutical Schedule (subsidised with Special Authority criteria) in July, 2013. In the article: “Ticagrelor – out with the old, in with the new?”, BPJ 54 (Aug, 2013), it was explained that ticagrelor, co-administered with aspirin, is an alternative to clopidogrel for the prevention of atherothrombotic events in patients with acute coronary syndromes. Ticagrelor is usually initiated in a hospital setting, however, as treatment is given for at least 12 months, primary care clinicians are likely to be involved in monitoring patients and providing repeat prescriptions.

There is some evidence that patients taking ticagrelor and aspirin may have a lower risk of ischaemic events and death, compared to patients taking clopidogrel and aspirin. Ticagrelor, therefore, is likely to become the preferred antiplatelet medicine in patients with acute coronary syndromes, however, some safety concerns still remain. Ticagrelor is contraindicated in patients with active bleeding or a history of intracranial haemorrhage and should be used with caution in patients with an increased risk of bleeding.

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**Honourable mentions: Foundation articles**

Articles published in BPJ are primarily selected based on their relevance to primary care. We cover a range of topics in each edition, and over the year, in order to provide a variety of information across all aspects of primary care. We have recently widened our focus to include articles which “bridge the gap” and provide useful information for clinicians working in secondary care, as well as “back to basics” articles (or sections within articles) which are useful for students or as a refresher.

As well as articles which supported our main themes, we published many articles in BPJ in 2013 which contributed to broad topics such as pain management, older person’s health, sexual health, dermatology and ophthalmology.

**Highlighting topical treatments for skin cancer**

The detection and treatment of melanoma has been previously covered in BPJ, but in late 2013 an article was published which largely focused on the topical treatments that are available to primary care clinicians for the management of non-melanoma skin cancers: “Managing skin cancer in primary care: A focus on topical treatments”, BPJ 57 (Dec, 2013).

Surgical excision with histology is the first-line treatment for non-melanoma skin cancers such as basal cell carcinoma and squamous cell carcinoma. If the lesion is small, this can be done in primary care, however, referral, according to local guidelines, may be necessary for patients with large lesions.
or lesions with an aggressive growth pattern. If excision is not possible because of the location of the lesion or due to cosmetic considerations, cryotherapy or topical medicines, e.g. imiquimod or fluorouracil creams, may be an appropriate option.

Helping patients overcome urinary incontinence

Patients with urinary incontinence are commonly encountered in primary care, but management extends beyond just treating the symptoms. Often the most significant aspect of incontinence is the impact that it has on the patient’s life, including feelings of shame, depression, social isolation and loss of self-confidence.

The article: “Urinary incontinence in adults”, BPJ 55 (Oct, 2013) covered all facets of management. This includes investigating the underlying cause, implementing lifestyle interventions such as dietary changes and weight loss, referring for physiotherapy, exercise programmes and the learning of behavioural strategies such as bladder training for urgency incontinence. Pharmacological treatments or surgical procedures may be considered if these interventions are unsuccessful. In most patients, incontinence can be substantially improved, even if it cannot be fully cured.

Catching the red eye

When a patient presents to general practice with signs and symptoms of a “red eye”, the most likely diagnosis is conjunctivitis. However, it is important to be vigilant for features that may suggest a more serious cause, which should prompt an urgent referral to an Ophthalmologist.

The article: “Causes, complications and treatment of a red eye”, BPJ 54 (Aug, 2013) explained that there are six main causes of a red eye which can result in visual loss: acute angle closure glaucoma, keratitis, iritis, scleritis, penetrating injury and an acid or alkali burn to the eye. Once the possibility of these conditions has been ruled out, most other minor or superficial causes of a red eye can be managed in general practice. The basic tools that are needed for an eye examination should be available in most general practice clinics; these include a good source of light (usually an ophthalmoscope), a Snellen chart, a pinhole, fluorescein dye and a blue light (usually the cobalt filter on an ophthalmoscope).

The most important points to remember when assessing and treating a red eye are that significant pain is almost always a red flag, and topical antibiotics are only appropriate for bacterial causes of conjunctivitis, but are not necessary in every case.
Getting personal: how to perform a sexual health check-up

The definition of good sexual health is broader than simply being free of disease or dysfunction. As such, a sexual health check should encompass psychosocial aspects of wellbeing and improving sexual health knowledge as well as investigating the likelihood of infection. The article: “A ‘how-to guide’ for a sexual health check-up”, BPJ 52 (Apr, 2013) revised previous information published on this topic and provided an up-to-date foundation article for managing sexual health in primary care.

New information introduced in this article included discussion about how to approach issues such as sexual preference and gender identity and ensuring the safety and health of sex workers. Updates on testing for infections included the introduction of combined NAAT testing for chlamydia and gonorrhoea using a single sample and the advice that self-swabbing is acceptable for an asymptomatic female patient if they decline an examination. Testing recommendations and antibiotic treatments for common sexually transmitted infections, based on updated guidelines from the New Zealand Sexual Health Society were also presented.

Have you signed up yet?

In April 2013, bpac launched a new-look website. Clinicians are encouraged to sign up for a free “My bpac” account in order to personalise the content you see on the website, save favourite articles, access personalised report data (for prescribers) and complete CME quizzes. Over time we will be releasing new interactive features of “My bpac”.

You may actually already have a “My bpac” account; most General Practitioners were signed-up to our old website, and we have carried over these accounts. If you have forgotten your user name and password (and you are a General Practitioner), your user name is most likely your MCNZ number, and you can use the “reset password” option on the website to receive a new password.

To sign up, visit www.bpac.org.nz and click on the “My bpac” tab.
What’s in store for 2014?

In the year ahead we have many more articles planned to support the main themes of BPJ. This includes the article in this edition, “Knowing your patients with diabetes”, Page 40, which follows on from previous articles which have focused on intensifying management of patients with type 2 diabetes. We will also be looking at the role of topical antibiotics in light of increasing antibiotic resistance, continuing our series on seasonal influenza vaccination, examining the upcoming changes to the immunisation schedule, revisiting pain management and covering several topics in gastroenterology. We also await with interest the roll-out and implementation of the new Integrated Performance Incentive Framework, which is to replace the target-focused PHO Performance Programme. We will be publishing a series of articles over the next few months to explain the changes and implications for primary care clinicians.

As always, the bpac™ website is your source for back issues of BPJ and other publications. The website is regularly updated with new publications, important announcements and is also home to your “My bpac” account where you will find your prescribing and laboratory testing reports, CME activities and personalised settings.

To sign up for your free account, visit:

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The Common Form combines features from the Diabetes and CVD modules to produce a streamlined standardised tool that assists in clinical review, disease monitoring and clinical management.

The Common Form module features the matching of retinal screening reports to standardised retinal images. The effects of microvascular complications can be visibly demonstrated to patients to facilitate understanding of their condition and as a method to reinforce good glycaemic control.

More information is available at:

www.bestpractice.net.nz
IRRITABLE BOWEL SYNDROME in adults

Not just a gut feeling
Irritable bowel syndrome (IBS) is a chronic gastrointestinal disorder characterised by recurrent bouts of abdominal discomfort and pain, bloating and a changeable bowel habit. Generally a patient with IBS will have periods of time when they feel well, interspersed with acute bouts of their particular gastrointestinal symptoms. IBS is regarded as the most frequently encountered gastrointestinal diagnosis in primary care. In some patients, IBS can significantly affect quality of life, however, reassurance can be given that IBS itself does not predispose the patient to life-threatening disease. Patients with IBS tend to be high users of health care services and some patients invest a significant amount of time and money on dietary modification and over-the-counter remedies in an attempt to control or relieve their symptoms. Ongoing research is changing the way IBS is viewed and this is providing evidence for new treatment approaches.

What is irritable bowel syndrome?

People with irritable bowel syndrome (IBS) experience recurrent bouts of abdominal discomfort and pain, which may be accompanied by bloating, and a changeable bowel habit. Between bouts of symptoms, people with IBS usually feel well. However, some people may also have non-gastrointestinal symptoms such as fatigue, nausea and backache and feelings of anxiety or depression. IBS can contribute to a reduced quality of life for some people and may affect all aspects of day-to-day life including diet, education, work, travel, personal and social relationships, self-image and psychological well-being. IBS is not, however, associated with structural damage to the bowel, as it is in people with inflammatory bowel disease, and weight loss is usually not a feature of IBS.

People with IBS are more likely to be:
- Female – approximately 70% of people with IBS are female
- Younger than age 50 years
- From a lower socioeconomic group

IBS is the most common gastrointestinal diagnosis in primary care

IBS affects an estimated 10 – 20% of people throughout the western world, although the reported prevalence varies widely due to the use of different diagnostic criteria over time and between populations. There have been no studies in New Zealand which have examined the prevalence of IBS by ethnicity. IBS is reported to be one of the top ten reasons for visiting a General Practitioner, although it is thought that up to 50% of people with symptoms of IBS do not consult their General Practitioner.

Pathophysiology of IBS

The pathophysiology of IBS remains unclear, however, what is known is that it is a complex biopsychosocial illness. Psychological factors (e.g. stress and emotional state), social factors (e.g. upbringing and support systems) and biological factors (e.g. gut motility and visceral sensitivity) interact in a complex way to induce and exacerbate the symptoms of IBS. Although traditionally referred to as a functional bowel disorder because there are no obvious structural or biochemical abnormalities that can explain the symptoms of IBS, ongoing research is changing the way IBS is viewed. A number of mechanisms have been proposed to explain the symptoms experienced by people with IBS. These include food sensitivity, intestinal inflammation, altered gastrointestinal motility, hypersensitivity of the viscera, alterations in microflora, bacterial overgrowth, post-infectious reactivity, dysregulation of immune function, brain-gut interactions and genetic and environmental factors. It is likely that there is a complex interplay between these factors that results in a characteristic array of gastrointestinal symptoms in people with IBS. How this might occur remains a topic of ongoing research (see: "Emerging evidence on the role of gastrointestinal bacteria and the immune system in IBS", over page).
Emerging evidence on the role of gastrointestinal bacteria and the immune system in IBS

Gastrointestinal bacteria have an important role in the normal physiological and immunological function of the gastrointestinal tract. There is a growing body of evidence suggesting that they play a complex role in the pathogenesis of a number of gastrointestinal disorders including IBS, however, it is unclear whether the alterations in bacterial flora are a cause or a consequence of the disorder. There is some evidence that low-grade inflammation and abnormalities of immune function may also have a role in the pathogenesis of IBS.

Evidence has shown that:
- Alterations in the gastrointestinal bacteria affect gastrointestinal function such as changes in intestinal motility and visceral hypersensitivity
- People with IBS appear to have an altered composition of gastrointestinal bacteria, specifically a reduction in diversity of bacterial species and an overabundance of some bacterial species
- Gastrointestinal bacteria responsible for fermentation of poorly absorbed fermentable carbohydrates may be altered in people with IBS resulting in looser stools and increased gas production
- There may be increased permeability of the gut in people with IBS due to alterations in the gastrointestinal bacteria and mucosal inflammation
- Gastrointestinal bacteria may also play a role in gut motility and the perception of pain due to factors such as stimulation of smooth muscle and bile acid malabsorption
- There is a similarity in symptoms between people with small-intestinal bacterial overgrowth and those with IBS
- Some people with IBS have increased levels of activated mast cells, histamine, intestinal epithelial lymphocytes, T cells and pro- and anti-inflammatory cytokines in the gastrointestinal tract

Three key factors are responsible for the majority of symptoms of IBS

The three key factors that appear to most influence the symptoms of patients with IBS are:
- Altered gastrointestinal motility
- Altered sensation within the gastrointestinal tract
- Psychosocial factors, e.g. stress, upbringing, coping strategies

Altered gastrointestinal motility
The traditional understanding of IBS centres around dysfunction of colonic motility with abnormalities that include luminal contractions that are increased in frequency and irregularity, a shorter or prolonged transit time depending on the subtype of IBS and an exaggerated motor response to ingestion of food.

Altered sensation within the gastrointestinal tract
People with IBS tend to experience increased sensations from the gastrointestinal tract in response to stimuli, such as distension. This visceral hypersensitivity occurs when there is selective hypersensitisation of various types of receptors in the gut wall. This has been demonstrated in studies involving balloon distension of the intestine where patients with IBS experience awareness and pain with a smaller balloon volume than patients without IBS.

Psychosocial factors
Psychosocial factors play a significant role in patients with IBS, tending to increase the frequency and severity of symptoms such as abdominal pain and diarrhoea. It also influences the way a patient views their problem, when they decide to present for a consultation and their beliefs and expectations regarding the illness and its treatment.

Making a diagnosis of IBS
IBS is diagnosed clinically from history and examination based on the Rome III diagnostic criteria (see: “Diagnostic criteria for IBS”). These criteria aim to encourage clinicians to make a positive diagnosis based on the patient’s symptoms and to no longer regard IBS as a diagnosis of exclusion. The 2008 NICE guideline also recommends that a diagnosis be made based on the presence of symptoms. A recent study in the UK, however, reports that many clinicians continue to use a diagnostic approach based primarily on the exclusion of sinister symptoms, rather than the presence of characteristic symptoms of IBS, because both clinicians and patients tend to have concerns that the symptoms could indicate a
more “serious” condition, e.g. inflammatory bowel disease or gastrointestinal cancer.3 This represents a valid concern but, in the appropriate clinical context, e.g. a female aged under 50 years, provided red flag indicators are assessed and excluded, a positive clinical diagnosis of IBS can be made without subjecting the patient to multiple unnecessary investigations or health care consultations.

Assess for the presence of symptoms
A diagnosis of IBS should be considered if a patient presents with a history of six months or more of any of the following symptoms:1

- Abdominal pain or discomfort
- Bloating
- Change in bowel habit

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Diagnostic criteria for IBS

The Rome III diagnostic criteria for IBS state that the patient has recurrent abdominal pain or discomfort* for at least three days per month, in the last three months, associated with two or more of the following:13

- An improvement with defaecation
- The onset associated with a change in frequency of stool
- The onset associated with a change in form (appearance) of stool

* “Discomfort” is defined as an uncomfortable sensation not described as pain.

There is debate within the literature regarding the validity of the Rome III criteria for use in primary care with a limited evidence base, and some authors still prefer older criteria such as the Manning criteria.15, 16, 17 The Rome III criteria have also been criticised for not being useful in a practical clinic setting because it is felt that patients who seek medical advice with symptoms of IBS prefer to be investigated, and can become rapidly dissatisfied if this does not occur.18 However, a balance has to be sought between requesting sufficient investigations to check for other conditions, such as inflammatory bowel disease or coeliac disease, and over-investigation.

The Manning criteria, which date from 1978, includes six symptoms that were significantly more common amongst patients and felt to be characteristic of IBS:17, 19

- Looser stools at onset of pain
- More frequent bowel movements at onset of pain
- Pain eased after bowel movement (often)
- Visible distension
- Feeling of incomplete emptying
- Mucus per rectum

The Manning criteria have been criticised for a lack of specificity which led to the development of the Rome criteria.

Abdominal pain – The abdominal pain or discomfort experienced by people with IBS varies widely – not only between individuals but also for each person. Symptoms are often made worse by eating and the patient may already be aware of particular foods that aggravate their symptoms. In females, pain may be worse pre-menstrually.2 Typically with each bout of symptoms, the pain will vary in intensity and site, often being reported anywhere in the abdomen. The location and timing of the pain may help differentiate IBS from other gastrointestinal conditions. Relief of pain or discomfort with defaecation is characteristic of IBS, but is not always reported by patients.
Depending on the clinical context, consider the possibility that similar symptoms could be attributable to another condition such as:

- Coeliac disease
- Inflammatory bowel disease
- Lactose intolerance
- Colorectal cancer
- Small-intestinal bacterial overgrowth, microscopic colitis, diverticulitis and other gastrointestinal conditions
- Gynaecological conditions such as endometriosis, pelvic inflammatory disease, ovarian cancer

**Check for red flags**

The presence of red flag symptoms should raise the possibility of an alternative diagnosis and referral to secondary care is recommended.

Red flags from the history include:

- Unintentional or unexplained weight loss
- Rectal bleeding that is not due to haemorrhoids
- Nocturnal symptoms, e.g. waking from sleep with pain or the need to defaecate
- Onset of symptoms in patients aged greater than 50 years (over 60 years in the NICE guideline)
- A family history of gastrointestinal cancer, inflammatory bowel disease or coeliac disease

**Bloating** – Abdominal bloating is more likely to be described by females with IBS than by males. Patients with IBS often have increased belching and flatus.

**Change in bowel habit** – An altered bowel habit is the most consistent symptom for patients with IBS. The change in bowel habit may include altered stool consistency (either firm or loose), changes in frequency of bowel motions, urgency, straining, incomplete evacuation or faecal incontinence (usually as a result of urgency). Patients may also describe the passage of mucus with bowel motions. Patients often report the need to urgently pass a bowel movement after eating a meal – referred to as an exaggerated gastric-colic reflex. This can occur in response to specific trigger foods but it may be the act of eating itself which initiates the postprandial symptoms. Diarrhoea or constipation may predominate, or the patient may alternate between symptoms.

In addition, patients may have other symptoms including nausea, dyspepsia, early satiety, lethargy, low back ache and bladder symptoms such as frequency and urgency.

IBS tends to be more common in people with a family history of IBS and people with IBS may have other co-morbidities, such as anxiety, depression, fibromyalgia or restless legs. Ask if the patient has had a recent bout of gastroenteritis as this can be a precipitating event, although reported incidence varies widely in the literature – from 5 – 32%. It is estimated that there is a six-fold increase in the risk of developing IBS after a significant episode of gastroenteritis and that this risk remains high for two to three years.
Additional red flags may be detected on clinical assessment or with targeted laboratory testing (see below). These include:
- Abdominal mass
- Rectal mass
- Iron deficiency anaemia
- Raised inflammatory markers

Laboratory investigations
There is no specific diagnostic test for IBS. The following initial tests are usually recommended, primarily to check for the possibility of conditions such as inflammatory bowel disease and coeliac disease:
- Full blood count
- C-reactive protein
- Coeliac antibodies (IgA tissue transglutaminase – IgA TTG)
- Ferritin, liver function tests and renal function may also be considered depending on the clinical situation. Additional investigations are generally only required if the patient presents with atypical or red-flag features. In older patients with a new onset of symptoms, gastrointestinal cancer must be considered as a diagnosis and appropriate investigations and referral arranged depending on the clinical circumstances.
- If the patient has clinical features on history or examination that indicate thyroid dysfunction, consider testing thyroid stimulating hormone. Patients with a shorter duration of symptoms, particularly diarrhoea and risk factors for infectious diarrhoea, e.g. recent overseas travel or immigration, or ingestion of contaminated food or fluid, should be assessed for infectious causes of diarrhoea.

Determine the subtype of IBS
Once a diagnosis is established, patients with IBS can be grouped into three main subtypes based on their predominant bowel symptoms – IBS with diarrhoea (IBS-D), IBS with constipation (IBS-C), and mixed IBS (IBS-M). This approach is useful because it can help guide management of the patient’s symptoms, however, there can be considerable overlap between the subgroups and, for some people, abdominal pain may be the predominant symptom rather than altered stools (Page 24).

IBS-D
IBS with diarrhoea as the predominant symptom is the most common type of subgroup of people with IBS. Patients tend to have frequent loose, often watery stools reflecting a shorter colonic transit time. However, factors such as diet and stress also have a major influence on symptoms and this can result in a pronounced day to day variability of the patient’s bowel habits.

IBS-C
People with IBS who have constipation as their predominant symptom tend to have less frequent, often irregular, firm stools reflecting a prolonged colonic transit time. IBS-C is more often present in females than males.

IBS-M
Patients with IBS who have a mixed picture tend to have alternating episodes of diarrhoea and constipation.

Ferritin, liver function tests and renal function may also be considered depending on the clinical situation. Additional investigations are generally only required if the patient presents with atypical or red-flag features. In older patients with a new onset of symptoms, gastrointestinal cancer must be considered as a diagnosis and appropriate investigations and referral arranged depending on the clinical circumstances.

Ferritin, liver function tests and renal function may also be considered depending on the clinical situation. Additional investigations are generally only required if the patient presents with atypical or red-flag features. In older patients with a new onset of symptoms, gastrointestinal cancer must be considered as a diagnosis and appropriate investigations and referral arranged depending on the clinical circumstances.

For further information on investigating patients with infectious diarrhoea see: “Making sense of testing for enteric pathogens”, Best Tests (Mar, 2008)

Faecal calprotectin, a marker of intestinal inflammation, is not routinely recommended but may have a limited role in selected patients where there is uncertainty about the diagnosis, e.g. younger patients who have presenting symptoms and signs that could indicate inflammatory bowel disease rather than IBS. A negative faecal calprotectin result (the suggested cut off value is 50 micrograms/g) effectively excludes a diagnosis of inflammatory bowel disease. Levels of faecal calprotectin are typically seen to exceed 500 micrograms/g if there is mucosal inflammation, as in the case of patients with inflammatory bowel disease. The faecal calprotectin test is an expensive test and is not universally available. Knowledge and use of this test varies throughout New Zealand.
The concept of a low FODMAP diet

Researchers at Monash University in Australia are regarded as the pioneers of the low FODMAP diet.\textsuperscript{26, 27} The acronym stands for Fermentable, Oligo-saccharides, Disaccharides, Mono-saccharides and Polyols. Their work began with observations of the role of fructose in producing symptoms in patients with IBS. From there, further work resulted in the development of the concept of a low FODMAP diet. It is thought that FODMAPs contribute to the symptoms of IBS by their rapid fermentation and an osmotic effect which results in distension of the lumen of the gut.\textsuperscript{20}

Although there is evidence that individual components of the FODMAP group contribute to IBS symptoms, the new concept was to consider the collective role of these poorly absorbed short-chain carbohydrates and to show the benefits for patients of a diet low in FODMAPs.\textsuperscript{20}

Major dietary FODMAPs include:

- Fructose found in fruits such as apples, pears and mango, honey and high fructose corn syrup. Concentrated sources of fructose, e.g. dried fruit, tomato paste and wine.
- Fructans found in food such as wheat, rye, onions, spring onions, leek, asparagus and artichokes
- Artificial sweeteners such as sorbitol, xylitol, mannitol (found in products such as sugar-free chewing gum, sweets and drinks)

There is increasing evidence that a low FODMAP diet can be of benefit for many patients with IBS, however, it is not a cure-all and as yet, there is little evidence regarding its use in the longer term.

N.B. Some patients may enquire about investigation of fructose malabsorption. This can be measured using a breath hydrogen test after a challenge with fructose, however, this test is not widely available in New Zealand.

Further information on the FODMAP diet is available from: \url{www.med.monash.edu.au}
Management of patients with IBS

IBS can be a difficult condition to manage and there is a potential for frustration and dissatisfaction for both patients and clinicians due to uncertainties surrounding the underlying aetiology of IBS and its diagnosis. It is therefore important to listen to and address any concerns the patient may have. The major concern for most patients is that there is a “serious” organic cause for their symptoms. Ensuring the patient understands IBS and what it may mean for them is likely to be the key to helping the patient self-manage their condition. Aim to provide an explanation of the underlying cause of their symptoms – it may help to draw a parallel with colic in infants and to avoid statements such as “I don’t know what’s wrong...”, “There’s nothing wrong with you...” or “It’s all in your head...” Establishing a positive diagnosis and avoiding unnecessary investigations will help reduce anxiety and reassure the patient. Consider if there are stressors in the patient’s life that may be aggravating symptoms and offer strategies to help the patient manage these.

All patients with IBS are likely to benefit from dietary and lifestyle changes such as increasing exercise and reducing stress and for some, this approach may provide sufficient control over their symptoms. Patients with persistent, often severe, symptoms that have not responded to initial dietary and lifestyle changes can be more challenging to treat.

Dietary modifications can reduce symptoms

The majority of patients with IBS find that certain foods will trigger their symptoms, e.g. a high fat meal may result in abdominal pain followed by diarrhoea that begins relatively soon after eating. Often, patients will have already altered their diet to minimise or exclude foods that trigger their symptoms and some will report benefit from these changes. In the past, however, most guidelines for the management of IBS have not included consistent dietary advice as there has been a lack of evidence that excluding or restricting foods resulted in a significant improvement for patients.

The British Dietetic Association has recently released evidence-based guidelines for the dietary management of IBS in adults. They have produced an algorithm which includes a three-tiered approach to dietary interventions and regular clinical review at each level.

First-line dietary advice

Once a diagnosis of IBS has been established, first-line dietary advice for all patients should be to encourage a diet that is healthy and nutritionally adequate. Assess the patient’s usual eating pattern and dietary choices. Establish if the patient has any known or suspected allergies or intolerances to foods, e.g. to lactose, and how these affect their IBS symptoms. A food and symptoms diary can be a useful tool to establish the frequency and timing of symptoms and whether any patterns are present, e.g. symptoms provoked by meals, exercise, stress or menstrual cycle in females.

General dietary guidance should include advice about:
- Regular meals
- Good eating behaviour such as chewing food thoroughly, taking time over meals, not eating late at night
- Regular adequate fluid intake (aiming for 1.5 – 3.0 L/day), avoiding carbonated beverages, caffeine and alcohol

Common foods that can aggravate symptoms in people with IBS include caffeine, alcohol, fatty food, spicy food, wheat, cheese, milk, pure fruit juices, artificial sweeteners and vegetables that increase flatus, such as cabbage, Brussels sprouts, corn, onion and legumes (e.g. baked beans, lentils, chickpeas).

The patient’s intake of fibre should be assessed. Many patients will have been advised in the past to increase their intake of fibre, particularly insoluble fibre such as wheat bran, however, there is now good evidence that this is unlikely to be beneficial for the majority of patients with IBS, particularly those with IBS-D, and may worsen symptoms. Some patients may therefore need to be advised to reduce their fibre intake.

Second-line dietary advice

If the patient has not had an improvement in symptoms with first-line interventions the next steps are recommended.

If constipation is the predominant symptom, an increase in a form of soluble fibre may be beneficial. The patient should be advised this can be achieved by increasing their intake of foods that are high in soluble fibre such as oats, or with a prescription product containing psyllium husk or sterculia. There is some evidence that ground or whole linseeds (also called flax seeds – available from health food stores), which are a source of both soluble and insoluble fibre, may help to relieve symptoms, and their use is recommended in some guidelines.

Consider a trial of a low FODMAP diet which can significantly reduce gastrointestinal symptoms in patients with any of the subtypes of IBS (see: “The concept of a low FODMAP diet”). Patients should be referred to a dietitian to ensure the diet is nutritionally adequate. Many patients will be aware of the low
An elimination diet generally includes a selection of low allergen foods, e.g. Lactobacillus, may improve the overall symptoms, abdominal pain, bloating and distension in patients with IBS but little or no evidence that they will improve other symptoms such as diarrhoea, constipation and flatus.

Third-line dietary advice

If there has been no improvement in symptoms after second-line approaches have been trialled, consider an exclusion diet where one or two foods that appear to aggravate symptoms are excluded for two to four weeks and then re-introduced as a challenge. An elimination diet should only be considered if the patient suspects multiple food intolerances and trials of avoidance of single trigger foods have not been effective.

The advice of a dietitian is required to ensure that the elimination diet is nutritionally adequate. If there has been no improvement in symptoms after two to four weeks of an elimination or exclusion diet then it is usually accepted that those excluded foods are unlikely to be contributing to the patient's symptoms.

Treatment should address the most troublesome symptom

Treatment for IBS is intended to relieve the patients' symptoms rather than to cure them. Treatment is likely to be of most benefit if it is tailored towards the patients' most troublesome symptom, e.g. diarrhoea, constipation or pain. The pattern of symptoms in people with IBS varies widely, however, a combination of medicines may be required to achieve relief. Despite this, the use of multiple medicines for the control of symptoms is often reported as being of insufficient benefit and there is the potential for dissatisfaction with the treatments and for an increase in adverse effects. Medicines that have the potential to target more than one symptom of IBS, such as tricyclic antidepressants, are increasingly recommended. A significant placebo response rate, up to 70%, to all treatments in patients with IBS has been reported.

People with diarrhoea as their predominant symptom

Dietary advice should be given following the three-tiered plan outlined above. Increasing dietary fibre is not recommended because this is likely to worsen symptoms in patients with diarrhoea as their main symptom. A Cochrane review found that the use of bulking agents (a fibre supplement) was not effective in the treatment of patients with IBS, particularly those with diarrhoea-predominant IBS. An increase in fibre not only worsens diarrhoea but is also likely to aggravate abdominal discomfort and bloating.

The combination of a regular daily dose of loperamide and an antispasmodic, such as mebeverine, can help to increase stool firmness, decrease stool frequency and reduce urgency. Loperamide can be used as a regular daily medicine at a fixed daily dose (e.g. 2 mg once or twice a day) rather than the usual dosing regimen for acute self-limiting diarrhoea. Mebeverine (one 135 mg tablet) can be taken three times daily as required, 20 minutes prior to meals which may help postprandial symptoms.

An approach that has been suggested for patients who are fearful of the sudden and urgent need to defaecate that can occur with IBS, is for them to take 2 – 4 mg of loperamide approximately 45 minutes before leaving their house, particularly if access to a toilet is limited such as when shopping or exercising.

There is some evidence that serotonin antagonists (5HT3-receptor antagonists) such as ondansetron may modulate the effect of stressors on gut function and reduce diarrhoea. The dose of ondansetron that is recommended initially is 4 mg, once daily, increasing to a maximum of 8 mg, three times daily, depending on the patient's response. This is, however, an unapproved indication for ondansetron.

People with constipation as their predominant symptom

Some patients in whom constipation is the predominant symptom may find that an increase in either soluble dietary fibre, from foods such as oats or soluble fibre in the form of a bulk-forming laxative such as psyllium husk, and avoiding foods with insoluble fibre, e.g. wheat, bran, brown rice, can help achieve a softer stool and provide relief from constipation. People with IBS-C should avoid eating foods with carbohydrates that are poorly digested in the small intestine (regarded now as FODMAPs) and therefore reach the colon relatively intact to aggravate symptoms.

Laxatives may be required; the dose is usually adjusted by the patient depending on the consistency of the stool. Lactulose should be avoided as it may aggravate bloating. Stimulant laxatives, e.g. bisacodyl, docusate sodium, docusate sodium with sennoside B, should be used intermittently or avoided.
Future directions in the management of IBS

New understanding of the underlying mechanisms that cause the symptoms of IBS has led to increased interest in treatments that target the gastrointestinal flora and the immune system. However, currently there is limited evidence and a lack of consistent guidance on the use of these treatments.11

**Antibiotics** – Due to the increasing evidence that intestinal bacterial may have a role in the pathophysiology of IBS, there has been research into the use of antibiotics (e.g. rifaximin*) to normalise the bacterial flora of the gastrointestinal tract.30 At this stage there is limited evidence regarding their effectiveness and much of the research has been industry sponsored.8

**Anti-inflammatory medicines** – there is currently no evidence to support the use of anti-inflammatory medicines in patients with IBS.11

**Linaclotide** – a synthetic 14-amino acid peptide, has recently been approved for use in Europe and the USA for patients with IBS-C and a clinical trial commenced in New Zealand at the end of 2013. It acts in the gastrointestinal tract to increase colonic transit, to stimulate the secretion of fluid and to reduce abdominal pain.31

**Lupiprostone** – a locally acting chloride channel activator, has approval for use in the USA for treatment of females aged 18 years and over with IBS-C, however, research is ongoing with regards to its effectiveness and safety.32

**Alosetron** – a serotonin antagonist (5-HT3 receptor antagonist), is also available in the USA for the treatment of severe diarrhoea-predominant IBS in female patients only who have not responded to other conventional treatments.30 This medicine has, however, been associated with ischaemic colitis and patient deaths.

* In New Zealand rifaximin is not subsidised and although available, is indicated only to reduce the recurrence of hepatic encephalopathy.22
if possible. The preferred option if a laxative is required is macrogol, an osmotic laxative, however, this is only fully subsidised under Special Authority. The Special Authority criteria are that “the patient has problematic constipation requiring intervention with a per rectal preparation despite an adequate trial of other oral pharmacotherapies including lactulose where lactulose is not contraindicated.” Initial applications are valid for six months with renewals for 12 months, provided that the patient is compliant with treatment and continuing to gain benefit. The recommended dose is one sachet, once daily, dissolved in half a glass (approximately 125 mL) of water, although this can be increased to 2 – 3 sachets daily if required. Some patients may find half a sachet daily sufficient to maintain a soft stool.

**People with pain as their predominant symptom**

Antispasmodic medicines are likely to be effective for the relief of abdominal pain or discomfort. Mebeverine is the recommended first-line antispasmodic medicine (dosed the same as for patients with IBS-D).

Bloating may be relieved or reduced by the use of peppermint oil or tea. Peppermint oil capsules (0.2 mL) are available in New Zealand but are not subsidised. The recommended dose is one to two capsules taken 30 – 60 minutes before meals, three times daily, for up to three months if necessary.

Opioid analgesics should be avoided as they are likely to worsen constipation which may in turn aggravate abdominal pain, however, low dose codeine, used cautiously, can be effective in firming the stool in patients with diarrhoea. “Narcotic bowel syndrome” is a complication of using opioid analgesia in patients with IBS. It is characterised by chronic or frequently recurrent abdominal pain that worsens with escalating or ongoing doses of opioids.

If patients experience nausea as part of their IBS symptoms, domperidone may be effective. Domperidone 10 – 20 mg can be taken up to four times daily if required, 15 – 20 minutes before meals.

There is good evidence that tricyclic antidepressants (TCA) are effective in reducing abdominal pain in patients with IBS and that they can also have a global effect on a variety of other symptoms. The use of a TCA may give relief from abdominal pain by altering visceral sensation and increasing pain thresholds. TCAs may also reduce diarrhoea by slowing colonic transit times and, although recommended doses are low, they may also provide relief from depression if this is present. The main limitation to the use of TCAs is reported to be patient tolerance of the medicines. They should be used with caution in patients who have constipation.

The majority of the research has focused on the use of amitriptyline and imipramine, however, nortriptyline is also thought to be effective and is generally better tolerated by patients. The usual starting dose is 5 – 10 mg of amitriptyline (or nortriptyline) at night with gradual increases in dose as required, e.g. by 10 mg increments every two weeks, to a maximum of 30 mg each night. This is an unapproved indication for the use of TCAs.

There is less evidence that SSRIs are effective in patients with IBS, however, they appear to provide similar benefits to TCAs and can be considered in people who are unable to tolerate these. This is an unapproved indication for the use of SSRIs antidepressants.

**Regular review is required**

Although self-management of IBS should be encouraged, patients should continue to be reviewed medically to assess how they are coping with the condition and to check for the emergence of any red flags or alarm symptoms. The NICE guideline suggests an annual review, although, how often the patient will be seen is likely to be determined by their need for medicines and their response to any interventions. Some patients may improve with dietary and lifestyle changes while others will continue to have lifelong symptoms. Patients who develop any of the red flag or alarm symptoms should be referred for further investigation.

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References


The management of Parkinson’s disease: Which treatments to start and when?
The natural history of Parkinson's disease

Parkinson's disease is a neurodegenerative disorder characterised by the cardinal symptoms of stiffness, resting tremor, slowness (bradykinesia) and reduction of movement (hypokinesia). Often the symptoms are asymmetric and insidious; serious problems may not develop until several years after onset of symptoms.

When patients with Parkinson's disease are examined they generally display:
- Rigidity on passive movement at major joints, e.g. when the patient's arm is moved by the clinician, sometimes with a superimposed ratchet-like sensation known as the “cogwheel” phenomenon
- Resting tremor, most commonly 4 hertz (four cycles per second), typically affecting the upper limbs
- Impairment of dextrous upper limb movements and facial expression due to bradykinesia affecting the small muscle groups of the face and hands, which is usually seen in the early phases of the condition

Bradykinesia in people with Parkinson's disease often causes a deterioration of handwriting in which the script typically slopes upwards and the writing is crabbed and becomes progressively smaller. Gait abnormalities typically manifest later in the course of the disease. However, a lack of spontaneous arm swing when walking is an early sign. Turning en bloc, where the whole body turns when changing direction, and a festinating gait, with small steps and tendency to shuffle as if the patient is chasing their centre of gravity are seen in patients with more advanced disease. Falls, partly due to slow activation of postural reflexes, occur in people with Parkinson's disease.

Non-motor symptoms are very common in patients with Parkinson's disease and may include hypotension, cognitive impairment, disorders of excessive sweating, depression and a reduced sense of smell (hyposmia). In some patients with Parkinson's disease non-motor symptoms can precede the classical motor symptoms by several years (see: “The Braak theory of Parkinson's disease progression”, over page). However, non-motor symptoms are not useful for diagnosing Parkinson's disease as they have limited specificity. Early onset of prominent non-motor symptoms such as orthostatic hypotension and cognitive impairment are also consistent with alternative diagnoses such as multi-system atrophy and Lewy body dementia. Non-motor symptoms in patients with Parkinson's disease can become more troublesome than motor symptoms and their management becomes increasingly important as the condition progresses.

Parkinson's disease pathophysiology

The pathological characteristic of Parkinson's disease is a severe loss of pigmented dopaminergic neurons in the substantia nigra of the midbrain (a brain area involved in movement). These neurons project to the corpus striatum and loss of these projections leads to an overall decrease in cortical motor activity. This process also causes the positive symptoms of Parkinson's disease, such as tremor, by reducing the normal inhibitory neuronal control of movement; known as the release phenomenon.

Loss of dopaminergic neurons in patients with Parkinson's disease is accompanied by the development of intracellular protein aggregates within surviving pigmented neurons, known as Lewy bodies. Lewy bodies in patients with Parkinson's disease are pathologically indistinguishable from Lewy bodies in patients with Lewy body dementia. Long-term
studies have shown that nearly all patients with Parkinson’s disease eventually develop cognitive impairment and it seems likely that Parkinson’s disease and Lewy body dementia represent a similar or overlapping neurodegenerative disorder. However, early cognitive impairment in a patient suggests a diagnosis other than Parkinson’s disease.

As Parkinson’s disease advances, more widespread loss of neurons occurs, which is the likely cause of symptoms that are not controlled by the dopaminergic treatments that are used in the earlier stages of the disease.

Parkinson’s disease itself is not thought to be directly fatal, but falls, fractures and chest infections related to swallowing disorders increase the mortality rate in people with Parkinson’s disease.

The epidemiology and genetics of Parkinson’s disease

Parkinson’s disease affects an estimated 1% of people aged over 65 years. A General Practitioner in New Zealand can expect to have approximately three patients with Parkinson’s disease per 1000 patients, although this will vary depending on practice characteristics. The median age of onset is 60 years and life expectancy is on average 15 years following diagnosis.

The cause of Parkinson’s disease is unknown. Some rare autosomal dominant genes for Parkinson’s disease have been identified, but account for only a few cases. In people diagnosed after age 60 years, there is a negligible increased risk of their children developing the condition, if there is no other family history of Parkinson’s disease. However, in people with Parkinson’s disease, who also have an affected parent or other affected first degree relative, the likelihood of one of the rare genes for Parkinson’s disease being present may be as high as 5%.

Environmental toxins, e.g. industrial waste and pesticides, may be a causative factor in the development of Parkinson’s disease, however, mitochondrial dysfunction, oxidative damage and abnormal protein processing have also been implicated. Non-smokers are twice as likely to develop Parkinson’s disease as people who smoke; it is not known why.

An expert opinion is recommended for diagnosis

Diagnosing patients with Parkinson’s disease is challenging and it is important that all patients suspected of having the condition are examined by an experienced Neurologist or Geriatrician before treatment is initiated. A specialist second
opinion will improve the likelihood of a good outcome and provide reassurance that an alternative diagnosis does not better fit the patient’s presentation.

A response to levodopa is a key criterion for the diagnosis of Parkinson’s disease. Common alternative diagnoses include medicine-induced parkinsonism, essential tremor and multiple cerebral infarctions.

Managing the motor symptoms of Parkinson’s disease

Although there is no cure for Parkinson’s disease, patients can achieve good symptom control during the first few years of treatment, unlike in other neurodegenerative conditions. It is reasonable to expect treatment to provide functional benefit for at least ten years.4

Non-pharmacological treatment

A multidisciplinary approach is usually recommended in the treatment of patients with Parkinson’s disease, although there is a lack of robust evidence to support the usefulness of this approach. Physiotherapists, Occupational Therapists, Speech Therapists and Nurse Specialists may all be involved in the care of a patient with Parkinson’s disease, in addition to a Neurologist or a Geriatrician and a General Practitioner.

Exercise should be encouraged and formal exercise rehabilitation is likely to benefit patients with Parkinson’s disease. Physiotherapists experienced in the treatment of people with Parkinson’s disease may be able to provide specific interventions for overcoming disabilities such as start hesitancy, freezing of gait, festination and falls. The results of clinical trials suggest three broad physical therapy strategies may be useful:9

1. Strategy training, e.g. instruction with reinforcement to use longer stride length
2. Management of musculoskeletal issues, e.g. weakness and loss of range of movement
3. General promotion of physical activity with specific interventions for falls prevention

A systematic review of physiotherapy interventions in patients with Parkinson’s disease found a wide-range of techniques introduced for a period of up to three months improved gait speed and balance as well as improving measures of the impact of Parkinson’s disease, e.g. the Unified Parkinson’s Disease Rating Scale (UPDRS).10 There was no evidence that one particular approach was better than any other, although the quality of the comparisons was poor. A more recent review provides some inconsistent evidence that more intensive and longer duration interventions provide greater benefits.11

Occupational therapy may assist people with Parkinson’s disease to safely maintain activity and employment. Continued activity and employment is likely to improve self-esteem as well as maintaining the patient’s role within their family.12 Patients may also be referred to occupational therapists specially trained in assessing driving performance to determine if they are medically fit to drive (see: “Driving a motor vehicle”, Page 30).

Speech therapy may be appropriate; soft speech (hypophonia) is a particular problem for patients with Parkinson’s disease. Voice training can improve voice quality and audibility.1 Some speech therapists run intensive exercise programmes in which the patient focuses on increasing the volume of their speech. Speech therapists are also able to assess dysphagia in patients with Parkinson’s disease which can affect speech and may also be a contributor to poor dietary intake.

Weight loss may be an issue for some people with Parkinson’s disease, although it is not clear if this is part of the process of Parkinson’s disease, i.e. extra energy expenditure due to tremor or rigidity, altered swallowing, changes to satiety, or due to the appetite reducing affect of dopaminergic treatment. Patients who are underweight may benefit from dietary supplements but there is little evidence of a strong effect. Some patients with Parkinson’s disease experience constipation and dietary changes may alleviate this, although, pharmacological treatments are more likely to be reliable for management. However, be aware that for some patients with Parkinson’s disease the timing and protein content of meals can affect levodopa absorption.

The support and shared experiences of other people of a similar age with the same condition is important. The Parkinson’s New Zealand website provides information on local services and support for people diagnosed with Parkinson’s disease, and their families. The fifth edition of “Parkinson’s: A guide for the newly diagnosed” was published in October, 2013.

Counselling for the patient can assist in the development of self-management techniques for anxiety and depression. Caring for a family member with Parkinson’s disease can place additional strain on relationships. Counselling may help the carer and family with coping strategies. In the final stages of...
Parkinson's disease palliative care and advanced care planning may be beneficial for the patient and their family.

For further information see: “End-of-life care for patients with chronic disease: the need for a paradigm shift”, BPJ 40 (Nov, 2011).

**Pharmacological treatment of motor symptoms**

Motor symptoms in patients with Parkinson's disease typically respond well to medicines that boost dopamine function and this response is part of the diagnostic criteria for Parkinson's disease. When motor symptoms are well controlled this is referred to as the patient's “on” state; conversely periods of poor motor symptom control are referred to as “off” states. There is little evidence that treatment with either levodopa or long-acting dopamine agonists in the early phases of Parkinson's disease results in improved long-term outcomes for the patient. However, levodopa will eventually be used in the treatment of all patients. If a patient does not respond to dopaminergic treatment then alternative diagnoses, e.g. medicine-induced Parkinsonism, essential tremor or multiple cerebral infarctions, should be strongly considered. Motor fluctuations, including dyskinesias, mainly associated with levodopa treatment develop in all patients with Parkinson's disease. These can vary in severity from a “wearing off” phenomenon, where a patient notices an increase in stiffness and slowness after a dose of medication, to very severe fluctuations between rigid-akinetic states and severe episodes of dyskinetic (involuntary) movements (see: “Motor fluctuations and levodopa”, opposite).

**When to start pharmacological treatment?**

Treatment for Parkinson's disease should be considered once the patient reports troubling symptoms. In most cases, a Neurologist or Geriatrician with experience in diagnosing Parkinson's disease will be responsible for initiating treatment. Diagnostic trials of levodopa, e.g. for a patient with functional disabilities and a strong clinical suspicion of Parkinson's disease, should generally not be considered without discussion with a Neurologist or Geriatrician. If there will be a substantial delay in the patient's referral, case-by-case management is required involving initial telephone consultation with a Neurologist or Geriatrician, and consideration of the patient's level of disability, circumstances, e.g. living alone, co-morbidities and individual preference for treatment.

**Driving a motor vehicle**

People with Parkinson's disease may have a reduced ability to drive before a functional disability becomes apparent, due to cognitive impairment or as an adverse effect of dopaminergic treatment, e.g. daytime sleepiness. Limb strength, accuracy of rapid foot movements and joint proprioception should be assessed. If a General Practitioner is uncertain about a patient's ability to drive then referral to an Occupational Therapist trained in driving assessment will be helpful. A Parkinson's disease Nurse Specialist, a Neurologist or Geriatrician may also be consulted before a final decision is made.

Driving should always cease if there is doubt about a person's ability to control a vehicle in an emergency situation. It is reasonable to assume that if a person has trouble walking then they may not be fit to drive.
Levodopa with a dopa-decarboxylase inhibitor is usually first-line

Patients with motor symptoms of Parkinson’s disease will benefit from dopamine treatment. However, dopamine itself does not cross the blood brain barrier easily and causes severe nausea and vomiting when given at doses high enough to have a motor effect. Levodopa, a metabolic precursor to dopamine, is able to cross the blood brain barrier and is therefore used instead. However, levodopa is rapidly metabolised to dopamine by the enzyme decarboxylase which is present in the body’s periphery as well as in the brain. In order to allow sufficient levodopa to reach the brain it must be administered with a peripheral decarboxylase inhibitor. In New Zealand carbidopa or benserazide are commonly used (Table 1, Page 34) and given in fixed combination with levodopa.

In patients aged over 40 years with Parkinson’s disease, combination levodopa medicines are generally the first-line treatment (see “Levodopa treatment should not be delayed in patients aged over 40 years”, over page). These are available in tablets, capsules, immediate release and modified release preparations, and dispersible tablets. Preparations should be swallowed whole, and not halved or broken, unless specified. Dispersible tablets shorten the onset of effect and may be useful for patients with difficulties swallowing or when rapid effect is needed, e.g. in the early morning. Adherence to levo-dopa treatment may be a problem for some patients due to the frequent dosing regimen, e.g. at least three times daily. A Pharmacist may be able to provide further information about which preparation is most suitable.

Over time there is often a need to increase the doses of levodopa or to add dopamine agonists or other medicines that inhibit the metabolism of dopamine. The patient’s treatment should be adjusted according to the level of disability experienced in the performance of everyday activities. The severity of a patient’s dyskinesias will often determine the maximum dose and length of time that levodopa treatment can be tolerated. Modified release levodopa does not reduce motor fluctuations related to the absorption of levodopa but may be useful for patients whose symptom control is insufficient between doses.

In patients aged under 40 years with Parkinson’s disease a dopamine agonist (over page) is generally the first-line treatment, rather than levodopa. This is because in these patients the likelihood of developing motor fluctuations within five years of beginning levodopa treatment is effectively 100%. Levodopa monotherapy is also associated with earlier and more severe motor fluctuations compared with using dopamine agonists for initial treatment.

Motor fluctuations and levodopa

The cause of motor fluctuations in patients with Parkinson’s disease is unknown. In normal physiology, dopamine is stored in pre-synaptic terminals. As people with Parkinson’s disease lose dopaminergic neurons the dopamine storage capacity of the brain is reduced. The length of time that levodopa doses are able to provide benefit then decreases because dopamine in the blood is metabolised more quickly than it is in synaptic terminals.

In patients with more advanced Parkinson’s disease, symptomatic “off” periods can begin when levodopa blood levels drop below therapeutic levels. When this occurs dosing of levodopa needs to be more frequent. However, the adverse effect of more frequent levodopa dosing is the occurrence of peaks of dopamine concentration which cause dyskinesias. Altered dopamine receptor function in the corpus striatum may also cause “supersensitivity” to blood dopamine. Disabling dyskinesias may require a reduction in levodopa dosing and other dopaminergic medicines, e.g. dopamine agonists, may become more useful.
Ergot-derived dopamine agonists, e.g. bromocriptine and pergolide, are generally no longer prescribed for patients with Parkinson’s disease due to the possibility of cardiac valvular fibrosis, pulmonary fibrosis or retroperitoneal fibrosis developing.1 Patients who are still being treated with these medicines should be monitored for dyspnoea, persistent cough, chest pain, cardiac failure, and abdominal pain or tenderness.17 If long-term treatment is expected lung-function tests may be helpful, or consider switching to a non-ergot derived dopamine agonist, i.e. ropinirole or pramipexole.17

A monoamine oxidase type B inhibitor may be appropriate for mild symptoms
Selegiline (Table 1) may be appropriate for patients with Parkinson’s disease who have mild motor symptoms and early treatment with selegiline can delay the need for levodopa treatment.17 Selegiline can be prescribed alone or in combination with a levodopa-dopa-carboxylase inhibitor combination. Selegiline inhibits the catabolism of dopamine and may also be combined with levodopa treatment to reduce

Levodopa treatment should not be delayed in patients aged over 40 years
Patients aged over 40 years should be considered for levodopa treatment as soon as they display significant symptoms.14 Historically there was a concern that early treatment with levodopa resulted in patients developing premature dyskinesias.14 This idea was supported by two observations. Firstly, as many as 90% of patients treated with levodopa for ten years develop dyskinesias.14 Secondly, the younger the age of onset of Parkinson’s disease, the more likely it is that dyskinesia will occur.14 However, the benefit of levodopa treatment is greatest earlier in the course of Parkinson’s disease.14 An Australian study of 149 people with Parkinson’s disease found that at fifteen-year follow-up there was no difference in outcomes for motor complications and mortality for patients whose treatment was initiated with either dopamine agonists or levodopa.15

Conversely, in patients aged under 40 years, treatment with levodopa is delayed and initiated when symptoms become more severe.14
symptoms in patients with advanced Parkinson’s disease. However, in patients who have postural hypotension selegiline together with levodopa should be avoided or used with extreme caution. Currently there are issues surrounding the supply of selegiline and therefore this medicine is unapproved by Medsafe in New Zealand, although this is likely to change in the near future.

Amantadine can be used to treat dyskinesia
Amantadine (Table 1) is a weak dopamine agonist and is a possible treatment option for people with early onset Parkinson’s disease, but should not be considered as a first-line treatment. Amantadine may be used in conjunction with other treatment, usually levodopa, to control dyskinesias once patients have begun to display motor fluctuations. The effect of amantadine is thought to be modest and to last less than eight months. However, a recent trial suggests that amantadine may help control dyskinesias for several years.

Catechol-O-methyltransferase inhibitors may be added later in treatment
When patients with advanced Parkinson’s disease begin to experience “end-of-dose” deterioration that cannot be stabilised by adjusting the regimen of current medicines, catechol-O-methyltransferase (COMT) inhibitors, i.e. entacapone and tolcapone (Table 1), may be used as adjunctive treatment with levodopa and dopa-decarboxylase inhibitors. COMT inhibitors, like dopa-decarboxylase inhibitors, prevent the peripheral conversion of levodopa to dopamine.

Antimuscarinic medicines are less effective than dopaminergic treatments
Antimuscarinic medicines, e.g. benztropine, procyclidine and orphenadrine hydrochloride, reduce medicine-induced Parkinsonian symptoms in patients being treated with antipsychotics, but are generally not used in patients with Parkinson’s disease. However, benztropine may be considered for the treatment of levodopa-resistant tremor in younger patients. Antimuscarinic medicines are poorly tolerated by older patients and are associated with cognitive impairment and sedation. Tardive (slow onset) dyskinesia is not improved by this treatment and may be worsened.

Alternative treatments are not supported by evidence
There is no robust evidence that any herbal medicine or supplement is effective in the treatment of patients with Parkinson’s disease. In particular, vitamin E should not be used as a neuroprotective agent as there is good evidence that it does not slow the progression of Parkinson’s disease.

Managing the non-motor symptoms of Parkinson’s disease
Patients with Parkinson’s disease may display autonomic dysfunction, psychiatric symptoms and cognitive impairment (Table 2, Page 36). These non-motor symptoms are a substantial component of Parkinson’s disease morbidity. Some non-motor symptoms can be associated with the patient’s “off” state and optimisation of dopaminergic treatment may provide symptom relief. Therefore attempting to increase “on” time should be considered first in the management of non-motor symptoms. For example, musculoskeletal and visceral pain, is experienced by over 80% of patients with Parkinson’s disease and can be associated with “off” states.

Treatment of non-motor symptoms may involve additional medicines
Parkinson’s disease involves pathology beyond the nigrostriatal connections of the brain, therefore many of the non-motor symptoms of Parkinson’s disease do not respond to dopaminergic medicines and other treatment options may be necessary. Autonomic dysfunction resulting in orthostatic hypotension, erectile dysfunction, urinary incontinence and constipation is present in most patients with advanced Parkinson’s disease (Table 2). Discussion with other members of the multidisciplinary team is recommended to provide individualised treatment plans.

Patients with Parkinson’s disease usually experience a gradual worsening of motor and non-motor symptoms. If a patient’s condition suddenly deteriorates then adherence to treatment and other potential causes, e.g. urinary tract infection, should be investigated. If a patient displays unstable non-motor symptoms despite regular treatment then referral to a Neurologist or Geriatrician is recommended.
Table 1: Treatment of motor symptoms associated with Parkinson’s disease\(^\text{17}\)

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Treatment</th>
<th>Adverse effects</th>
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<tbody>
<tr>
<td><strong>Levodopa with a dopa-decarboxylase inhibitor</strong></td>
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<td>Note: The dose of dopa-decarboxylase inhibitor needs to be sufficient to inhibit extracerebral conversion of levodopa to dopamine, e.g. carbidopa 70 to 100 mg daily, which can cause nausea and vomiting due to dopamine stimulation of chemoreceptors. Combination formulations of levodopa with carbidopa or benserazide are designed to provide adequate enzyme inhibition, with minimal extra adverse effects. The relative amount of carbidopa:levodopa is 1:4 or 1:10; for benserazide:levodopa the relative amount in formulations is 1:4.</td>
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<td><strong>Levodopa with carbidopa</strong> i.e. Sinemet (100 mg + 25 mg, 250 mg + 25 mg), Sindopa (100 mg + 25 mg), Sinemet CR modified release (200 mg + 50 mg), Kinson (100 mg + 25 mg, unfunded)</td>
<td>Initiated at 100 mg levodopa (with 25 mg carbidopa), three times daily, e.g. 6 am, 12 pm and 6 pm.(^1) Can be increased by 100 mg, daily, or on alternate days, according to the patient’s response and tolerance, up to 800 mg levodopa (with carbidopa 200 mg, i.e. eight tablets of 100 mg/25 mg each), daily, in divided doses. If higher doses of levodopa are required, and tolerated, a 250 mg levodopa (with carbidopa 25 mg) tablet is used. Levodopa can then be increased by 250 mg, daily or on alternate days, to a maximum of 2 g levodopa (with 200 mg carbidopa, i.e. ten tablets of 200 mg/25 mg each).</td>
<td>Dyskinesias, if severe, may be managed by reducing the levodopa dose and adding a dopamine agonist to “smooth out” motor fluctuations. Both forms of levodopa are contraindicated in patients who have taken a non-selective monoamine oxidase inhibitor (MAOI) within 14 days, or in patients with a history of angle closure glaucoma. When levodopa treatment is initiated, taking the medicine with food may reduce nausea, however, the presence of food and protein in the gut can reduce levodopa absorption. Low protein meals, e.g. fruit and bread, may improve levodopa absorption. Once Parkinson’s disease has advanced, taking medicine 30 minutes before food may further improve absorption and produce a greater therapeutic response. Levodopa may cause dizziness or sudden onset of sleep making driving dangerous. Benign discolouration of urine may occur. Abrupt withdrawal should be avoided due to the risk of neuroleptic malignant syndrome.</td>
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<td><strong>Levodopa with benserazide</strong> i.e. Madopar (50 mg + 12.5 mg, 100 mg + 25 mg, 200 mg + 50 mg), Madopar Rapid dispersible (50 mg + 12.5 mg), Madopar HBS modified release (100 mg + 25 mg)</td>
<td>Initiated at 50 mg levodopa, three to four times daily, with or just after food, or 100 mg, three times daily, in patients with more advanced Parkinson’s disease. Doses of levodopa can be increased by 100 mg (with 25 mg benserazide), daily, once or twice weekly, according to the patient’s response. Older patients may be started on a reduced dose of 50 mg, once or twice daily, increased by 50 mg, daily, once or twice weekly, according to the patient’s response. The usual maintenance dose of levodopa is 400 – 800 mg (with benserazide 100 – 200 mg), daily, in divided doses.</td>
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<td><strong>Dopamine agonists</strong></td>
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<td><strong>Ropinirole</strong></td>
<td>Initiated at 250 micrograms ropinirole, three times daily, with or just after food. Daily doses are increased by 250 micrograms, three times daily, at weekly intervals, up to 3 mg daily. Doses can be further increased according to the patient’s response. Maintenance doses are often 9 – 16 mg, daily, but higher doses to a maximum of 24 mg daily, may be required if ropinirole is taken with levodopa.</td>
<td>Adverse effects include nausea (common) or vomiting, postural hypotension, excessive sleeping, impulse control disorders, cognitive symptoms and hallucinations. Monitor blood pressure when initiating dopamine agonists. This medicine may cause dizziness or sudden onset of sleep making driving dangerous.</td>
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<td><strong>Pramipexole</strong></td>
<td>Initiated at 125 micrograms pramipexole, three times daily, with the dose doubled every five to seven days, if tolerated, to 500 micrograms, three times daily. Doses can be further increased by 250 micrograms, three times daily, at weekly intervals, to a maximum of 1.5 mg, three times daily.</td>
<td>Doses of pramipexole should be reduced in patients with renal impairment (see: NZF for further details). This medicine may cause dizziness or sudden onset of sleep making driving dangerous.</td>
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<tr>
<td>Medicine</td>
<td>Treatment</td>
<td>Adverse effects</td>
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<tr>
<td>Monoamine oxidase type B inhibitors (MAOBI)</td>
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<td><strong>Selegiline</strong> (currently a section 29, unapproved medicine)</td>
<td>Initiated at 5 mg selegiline, in the morning, increasing after two to four weeks, if tolerated, to 10 mg in the morning, or 5 mg in the morning and 5 mg at midday. Selegiline can be used alone or as an adjunct to a levodopa/dopa-decarboxylase inhibitor. When used in combination the dose of levodopa may need to be decreased.</td>
<td>Selegiline is contraindicated in patients with active peptic ulcers, other extrapyramidal disorders, severe psychosis or dementia. Patients may experience gastrointestinal effects, e.g. nausea, constipation, diarrhoea, or cardiovascular adverse effects, e.g. bradycardia, hypo- or hypertension.</td>
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<td>Catechol-O-methyltransferase inhibitors</td>
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<td><strong>Entacapone</strong></td>
<td>Initiated at 200 mg entacapone, taken with each dose of levodopa/dopa-decarboxylase inhibitor, to a maximum of 2 g, daily. Levodopa doses may need to be reduced by 10 – 30% when prescribed with entacapone. Iron or calcium supplements or indigestion remedies should not be taken within two hours of taking entacapone.</td>
<td>Entacapone and tolcapone are contraindicated in patients with phaeochromocytoma, or a history of neuroleptic malignant syndrome or non-traumatic rhabdomyolysis. Tolcapone is also contraindicated in patients with evidence of liver disease, increased liver enzymes or severe dyskinesia. These medicines may cause dizziness or sudden onset of sleep making driving dangerous. Patients should be advised to seek medical attention if they experience symptoms suggestive of liver toxicity, e.g. nausea, abdominal pain and pruritus or rhabdomyolysis, e.g. muscle pain. Benign discoloration of the urine may occur when taking these medicines which may require investigation, e.g. creatine kinase, to differentiate this from more serious adverse effects.</td>
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<tr>
<td><strong>Tolcapone</strong></td>
<td>Initiated at 100 mg tolcapone, three times daily. The first dose is taken at the same time as levodopa, with six hours between doses. The maximum dose of tolcapone is 200 mg, three times daily, which would only be prescribed to patients with severe symptoms.</td>
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<tr>
<td>Dopamine modulating</td>
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<td><strong>Amantadine</strong></td>
<td>Initiated at 100 mg, once daily with food, increased after one week to 100 mg, twice daily, usually in conjunction with another treatment, e.g. levodopa. Some patients may require higher doses, to a maximum of 400 mg, daily. Patients aged over 65 years should be started at 100 mg, daily, adjusted according to the patient’s response.</td>
<td>Amantadine is contraindicated in patients with a history of epilepsy or gastric ulceration or in patients who are pregnant. Amantadine may affect driving and other skilled tasks.</td>
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<td>Symptom</td>
<td>First-line</td>
<td>Additional pharmacological treatment</td>
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<td>First consider optimising dopaminergic treatment and non-pharmacological treatment</td>
<td>Note: treatment options include some “off-label” uses of medicines</td>
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<td><strong>Cardiovascular</strong></td>
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<td>• Postural and postprandial hypotension</td>
<td>Patients can increase fluid and salt intake, eat frequent small meals to reduce postprandial hypotension and wear compression stockings that extend to above the knee. Any antihypertensive medicines should be taken with caution.</td>
<td>Fludrocortisone acetate, 50 micrograms, daily, increasing to 200 micrograms, daily, as needed, may be useful for patients with hypotension following discussion with a hospital specialist.</td>
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<td><strong>Gastrointestinal</strong></td>
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<td>• Drooling (sialorrhoea)</td>
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<td>Dosing can be treated with 1% atropine eye drops, administered sublingually. Radiotherapy may also be useful for some patients.</td>
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<tr>
<td>• Dysphagia</td>
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<td>• Gastroparesis, e.g. nausea, bloating, pain</td>
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<td>Gastroparesis may be alleviated in some patients with domperidone (a dopamine antagonist that does not cross the blood brain barrier), 10 – 20 mg, three to four times daily; maximum 80 mg, daily. For constipation, laxatives can be initiated for patients following dietary advice, e.g. bisacodyl (10 mg – a stimulant), glycerol suppositories (3.6 g – a softener), in the morning, or docusate sodium, 100 – 150 mg, twice daily, or 240 mg at night, up to 480 mg, daily, in divided doses. Docusate sodium with sennoside B is also available but should not be taken for prolonged periods.</td>
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<td>• Constipation</td>
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<td><strong>Pain</strong></td>
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<td>First establish if the pain is present during “on” or “off” states, to decide whether adjusting dopaminergic treatment may provide benefit.</td>
<td>Chronic neuropathic pain can be treated with:</td>
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<td>Musculoskeletal pain can be caused by restricted movement or muscle spasm and patients may experience symptom relief following physiotherapy.</td>
<td>• Nortriptyline or amitriptyline, 10 – 75 mg, once daily</td>
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<td>Peripheral pain can be managed with mild analgesics, e.g. paracetamol, and physiotherapy.</td>
<td>• Carbamazepine, 100 mg, once or twice daily, increased gradually according to response, usually to 200 mg, three or four times daily</td>
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<tr>
<td>Symptom</td>
<td>First-line</td>
<td>Additional pharmacological treatment</td>
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<tr>
<td><strong>Cognitive</strong></td>
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<tr>
<td>Anxiety</td>
<td>Patients who experience “off” state anxiety may benefit from increased dopaminergic treatment.</td>
<td>Tricyclic antidepressants or selective serotonin inhibitors may be appropriate for patients with depression in addition to support and counselling.</td>
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<tr>
<td>Depression</td>
<td>Assess the patient for pain or sleep disturbances which may contribute to depression. Referring patients for counselling is recommended.</td>
<td>Quetiapine may be used with extreme caution, at low doses, in consultation with a Geriatrician or Neurologist to treat patients with psychosis. Other antipsychotics should not be considered for initiation in primary care due to an association with extrapyramidal symptoms. Olanzapine and typical antipsychotics, e.g. haloperidol, can worsen motor symptoms.</td>
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<tr>
<td>Hallucinations</td>
<td>Patients with non-troubling hallucinations do not require treatment, however, if the patient is distressed medicines may need to be adjusted.</td>
<td>Clozapine may be a treatment option that is suggested by a hospital specialist, but this requires weekly full blood count monitoring.</td>
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<tr>
<td>Dementia</td>
<td>Patients with dementia should be evaluated for other causes and consideration given to withdrawing anticholinergic or dopaminergic medicines.</td>
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<td><strong>Genitourinary</strong></td>
<td>Patients can avoid diuretics, e.g. caffeine containing drinks. Before beginning pharmacological treatment a post-void bladder scan will exclude retention as a cause.</td>
<td>Oxybutynin should be used with caution in older patients, but can be initiated at 5 mg, two to three times daily.3</td>
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<tr>
<td>Urgency and frequency</td>
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<td>Tolterodine is available under Special Authority for patients who have an overactive bladder and a documented intolerance of, or are non-responsive to, oxybutynin. Treatment is initiated at 2 mg, twice daily. This can be reduced to 1 mg, twice daily, to reduce adverse effects. Treatment should be reviewed after six months.</td>
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<td>Nocturia</td>
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<td>Nocturia can be treated with desmopressin.</td>
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<td>Incontinence</td>
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<td><strong>Sleep</strong></td>
<td>Fatigue is experienced by one-third of patients with Parkinson’s disease, but is less common in patients taking levodopa compared to dopamine agonists.16 For patients with daytime sleepiness sleep hygiene and other causes of altered sleep patterns should be assessed, e.g. depression, nocturia. A reduction in dopaminergic treatment, if possible, may reduce daytime sleepiness. Amantadine or selegiline for motor symptoms may also benefit patients with fatigue/daytime sleepiness.</td>
<td>Methylphenidate, 10 mg, three times daily, may be useful in treating patient fatigue.20 A benzodiazepine may be effective for patients with REM sleep disorder, e.g. clonazepam, 1 mg, daily.</td>
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<td>REM sleep disorder</td>
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<tr>
<td>Restless legs syndrome</td>
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Treatments for patients with advanced Parkinson’s disease

As patients with Parkinson’s disease develop motor fluctuations and the effectiveness of standard treatments diminishes, more invasive treatments may be recommended by a Neurologist.

Subcutaneous apomorphine, a non-selective dopamine agonist, can be used either intermittently for motor symptom control, or as a continuous subcutaneous infusion.³ Apomorphine has the same potential to cause adverse effects as other dopamine agonists and may cause vomiting, injection site reactions and skin nodules.³

Deep brain stimulation is a reversible surgical procedure in which an area of the brain receives continuous electrical stimulation from an implanted battery, operated with an external controller. This may be appropriate for patients with Parkinson’s disease who have motor fluctuations or tremor that does not respond to medication and for patients with adverse effects to medication.²¹ Complication rates are highly variable and infection is the most frequently reported adverse effect.²¹ It may take three to six months for deep brain stimulation to produce optimal results but tremor and dyskinesias are able to be reduced for five years or longer.²¹

Stereotactic lesion surgery involves ablating an area of the brain in order to control tremor or dyskinesias.

Stem cells taken from human embryonic tissue or transformed from adult tissue may, in the future, be able to replace dopaminergic neurons in patients with Parkinson’s disease. There have been a number of international clinical trials involving foetal cell transplantation, the first of which began in 1987 and so far approximately 400 patients have been involved.²² The results have been variable but some patients continued to experience significant improvements in symptoms several years after treatment. However, there are currently no treatments using stem cells available for patients with Parkinson’s disease in New Zealand.

References

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The bestpractice Decision Support Depression Suite offers a logical and comprehensive resource to ensure effective screening, management and assessment of individuals with depression.

The suite consists of four modules:

- **Depression in Young People**
- **Adult Depression**
- **Ante & Postnatal Depression**
- **Depression in the Elderly**

The entire Depression Suite is available to health professionals at no cost, funded by the Ministry of Health. See [www.bestpractice.net.nz](http://www.bestpractice.net.nz) for information about other nationally funded bestpractice modules.
Getting to know patients with type 2 diabetes and poor glycaemic control: One size does not fit all
Focusing on people with type 2 diabetes most at risk

Poor glycaemic control is relatively common among people with diabetes. A New Zealand review of almost 30,000 patients attending annual diabetes checks found that 29% had HbA1c levels above 64 mmol/mol.\(^1\) There were marked differences between ethnicities; 50% of Pacific peoples, 43% of Māori and 36% of Asian-Indian people had levels above 64 mmol/mol.\(^1\)

The reasons why people with type 2 diabetes have poor glycaemic control, i.e. HbA1c > 64 mmol/mol, are numerous and complex. Health professionals need to effectively engage with patients to understand what these reasons are. A shared decision-making approach to management allows patients and health professionals to form an agreement on diabetes care that may also correct previous clinical assumptions, e.g. concerning treatment adherence, health literacy or motivation. To do this well, primary care teams need to have a good understanding of the patient’s background, beliefs and priorities. For some patients this may even mean accepting that a glycaemic target higher than 64 mmol/mol is appropriate, e.g. for an older patient living alone. This should not be regarded as a failure by the patient or the health professional. However, poor glycaemic control is always a signal for intensification of management and HbA1c is only one measure of cardiovascular risk. For many patients diabetes management will also involve intensive management of other risk factors such as obesity, hypertension, hyperlipidaemia and smoking.

This collaborative approach to diabetes care incorporates many aspects of motivational interviewing and can be combined with this technique. The process of engaging people with type 2 diabetes and assisting them to manage their own health is perhaps the most significant and challenging aspect of their care.

Individual, patient-centred management of diabetes

There is increasing evidence that an individual and patient-centred approach to the management of type 2 diabetes is effective.\(^2,3\) In an ethnically diverse United Kingdom population of over 28,000 patients with type 2 diabetes it was found that after being invited to explore reasons for their poor glycaemic control and developing an individualised management plan, 55% of patients with an HbA1c ≥ 86 mmol/mol improved their HbA1c by at least 10 mmol/mol at six month review.\(^4\)

An individual approach to diabetes care is now favoured because guidelines for chronic conditions are generally based on clinical trials of highly selected participants, with many of the “real-world” patients in general practice populations being excluded due to the presence of co-morbidities or other factors. In addition, the results of clinical trials investigating targets for glycaemic control, e.g. UKPDS, ACCORD, ADVANCE and VADT, collectively demonstrate that a hard target-based approach to the management of type 2 diabetes can be harmful to some patients, e.g. older patients with high cardiovascular risk.\(^3\)

Diabetes is more prevalent in Māori, Pacific and Asian-Indian people and people living in low socioeconomic areas. In New Zealand, during 2011/12, the rate of type 2 diabetes for people living in the most deprived areas was 8.6%, compared with 2.7% for people living in the least deprived areas.\(^5\) Approximately 10% of Pacific adults in New Zealand have been diagnosed with diabetes, diabetes rates among Māori (7%) are over twice that of non-Māori and Asian males have a higher rate of diagnosed diabetes (8.4%) compared to other adults.\(^5\) Patients will respond differently to advice from health professionals depending on their age, economic situation, ethnicity and level of health literacy. Management is likely to be more effective when these differences are clearly in mind. Cultural competency, which is essentially
respectful and effective communication, is just as important as clinical and ethical competency in a healthcare interaction. Healthcare professionals must be both understanding and understandable, and this is essential in managing patients with diabetes to achieve successful health outcomes and address disparities.

Understanding patients with poor glycaemic control

Introducing the idea of an optimal target for glycaemic control, i.e. 50 – 55 mmol/mol, as “the speed limit” can help patients to understand that HbA1c levels above this level are increasingly unsafe. However, this target may not be achievable, or even appropriate, for many patients. Glycaemic targets should therefore be mutually agreed on between the patient and clinician, i.e. shared decision-making. This recognises that not all patients have the same values or priorities. For example, a small study of older people with type 2 diabetes found that almost half ranked maintaining independence as their most important outcome, while just over one-quarter ranked staying alive highest.6 Revisiting the patient’s preferences each time their clinical condition changes is also a routine part of diabetes treatment as patient’s priorities may change over time.6

If patients are unable to achieve agreed glycaemic targets, health professionals need to make additional efforts to engage with them. Regular attendance at diabetes reviews is associated with improved glycaemic control. In the United Kingdom, patients who missed more than 30% of diabetes reviews were reported to have an average HbA1c 15 – 16 mmol/mol higher than patients who missed less than 30% of reviews.4

Education is an important aspect of diabetes management. For some patients, e.g. where health literacy is an issue or English is not a first language, it may be necessary to regularly return to basics and explain how they came to be diagnosed with type 2 diabetes, and to revisit general concepts in diabetes education. Patients and their family/whānau are asked to understand and act on lifestyle changes and other interventions on a daily basis, but these can compete with many other aspects of a patient’s life that also require time and energy. Education is an ongoing process that includes refining and reinforcing the patient’s knowledge of their condition. This process is particularly important in communities where understanding and being understood when talking with health professionals is highly valued, e.g. among many Māori and Pacific patients.

Getting the most out of your practice management system

The Practice Management System (PMS) is useful for identifying patients within practice populations who have type 2 diabetes. Some PMS products have a reporting function built-in that allows for the automatic identification of patients with an HbA1c > 64 mmol/mol, e.g. bestpractice Intelligence. Once identified patients can be offered a diabetes review via the normal patient recall process.

For further information, see: “Five tips for getting the most out of your Practice Management System”, BPJ 56 (Nov, 2013).
What does the patient believe about diabetes?

Beliefs that patients hold about diabetes can be broadly divided into five categories:

1. Disease identity, i.e. what type 2 diabetes means to them
2. The cause of type 2 diabetes, e.g. the belief that it is just inherited from parents
3. Timeline, i.e. what is the course of type 2 diabetes and how long will it last
4. The consequences of type 2 diabetes, e.g. the belief that introducing insulin means you are going to die soon
5. Cure/control, i.e. how well the patient will be able to recover from, and control, their diabetes

The strength of a patient’s belief in their ability to influence their own health is a predictor for both adherence to physical activity and life satisfaction. A survey of 82 Tongan and New Zealand European people with type 2 diabetes in the Auckland region found that both groups had similar degrees of understanding about type 2 diabetes. However, compared with the New Zealand European group, Tongan people were more likely to: view type 2 diabetes as a cyclical or acute illness, attribute the disease to external factors (e.g. pollution or God's will), be emotionally distressed by type 2 diabetes and have less confidence in their ability to manage their condition and think anti-diabetic medicines were not necessary.

A patient’s belief about the necessity of taking anti-diabetes medicines can be influenced by factors such as: fear, a fatalistic acceptance of the disease due to a family history, or by a family or whānau’s negative experience with treatment, e.g. gastrointestinal effects experienced after metformin was started at a high dose. It is therefore important to discuss any previous experiences a patient has had with diabetes and its treatment.

What matters to the patient – not what is the matter with the patient

Engaging with patients involves understanding their values and priorities. For example:
- How important is quality of life to them?
- How motivated is the patient to prevent diabetes-related complications?
- What is the patient’s attitude towards insulin and self-injection?
- Is the patient concerned about hypoglycaemia?

This approach emphasises the importance of quality of life and maintenance of function, rather than focusing purely on glycaemic control. This discussion should be repeated each time the patient’s clinical situation changes.

Families/whānau may influence treatment decisions

The degree to which patient decisions are influenced by family members is clinically relevant to diabetes management. Among some families a “collective culture” may exist, where decisions about medical interventions for individuals are decided upon by the whole family. If the patient has the expectation that their family will be involved with treatment decisions then it is appropriate to ask key family members to also attend consultations. Some parents may also place less importance on their own health if they are focused on nurturing and supporting their children. Many of these children and grandchildren are at increased risk of developing diabetes and this can be presented as an opportunity to be a better role model of health behaviours for future generations.

Discussing reasons for poor control

Raising the issue of poor diabetes control often results in feelings of guilt and/or personal failure for patients. This can be overcome by explaining that intensification of type 2 diabetes treatment is usually inevitable due to reduced pancreatic beta-cell function over time.

Barriers to different components of the diabetes management plan should be discussed separately. Problems with concordance with dietary advice and physical exercise are consistently reported by patients and clinicians to be the most significant reason for poor glycaemic control. In general, the longer a patient has had diabetes the more likely they are to eat inappropriately and the less likely they are to exercise.
Depression is twice as prevalent in people with type 2 diabetes compared with the general population and should always be considered in patients who are having problems adhering to a lifestyle regimen. Patients with depression are less likely to adhere to dietary advice and exercise programmes and more likely to have poor glycaemic control and experience diabetes related complications. Depression is also associated with obesity and other psychosocial problems.

Chronic pain is frequently experienced by people with type 2 diabetes; it is reported to be present in up to 60% of older patients with diabetes. Pain should also be considered as a potential reason for non-adherence to lifestyle changes, e.g. pain may reduce a patient’s ability to exercise. The underlying cause of pain may be a co-morbidity, e.g. osteoarthritis or gout, or may be due to diabetes itself, e.g. peripheral neuropathy or peripheral vascular disease.

Concordance with dietary advice
It is important for health professionals to acknowledge that it can be very difficult for patients to accept and implement radical changes in diet, especially if this involves buying and eating foods that are very different from the patient’s usual diet. There may also be cultural reasons why some foods are eaten that are not ideal, e.g. frequent consumption of a traditional food with a high glycaemic index, such as white rice. Factors known to place patients at high-risk for non-concordance with dietary advice include: financial hardship, social pressure to eat, being alone and feeling bored, stress, relationship conflict and social events or holidays. A sudden change in the patient’s HbA1c level may correlate with a change in circumstance that is causing stress or interfering with patterns of behaviour, resulting in inappropriate food choices. Food diaries allow patients to keep track of what foods they are eating and can be used as an educational aid to explain how glycaemic control is linked to food intake.

Other strategies that may assist patients with dietary changes include encouraging them to:

- Be present when food is purchased and prepared to ensure that appropriate choices are made, e.g. choosing foods low in carbohydrates, saturated fat and kilojoules and using healthy cooking methods
- Compare prices at supermarkets and local produce stores so healthy food can be purchased at the least expense
- Use their standing within the family/whānau/community to make healthy food choices more acceptable for everyone

Concordance with exercise advice
Green prescriptions are a health professional’s written advice to be physically active. A two-year study involving over 1000 “less-active” women in New Zealand aged between 40 – 74 years, who were given a green prescription and telephone support, found at 12 and 24 month follow-up there were significant improvements in physical activity. Emphasising the importance to patients of cardiovascular fitness in addition to weight loss can provide added motivation for patients starting exercise programmes. Improving fitness is a marker of positive change and will help the patient maintain motivation if weight loss is occurring slowly. Exercise programmes need to be appropriate for the individual patient and take into account factors such as age, weight, mobility and co-morbidities, e.g. chronic obstructive pulmonary disease. Asking the patient to suggest a level of activity they feel they can commit to on a daily basis is a good starting point. Consider if there are any barriers to exercise that can be overcome, e.g. osteoarthritis may make walking difficult; aqua jogging may be a suitable alternative.

It is useful to be aware of what local activities and organised exercise programmes are available to recommend to patients. Whānau ora collectives are increasingly promoting sport as a medicine and facilitating participation in events such as “Iron Māori”.

Concordance with pharmacological treatment
It is estimated that 75% of patients with a long-term condition requiring medicines are concordant with treatment. However, patients with type 2 diabetes and poor glycaemic control are over three times more likely to be non-concordant with their treatment, than patients with acceptable glycaemic control. A study of patients with type 2 diabetes found that approximately one in seven patients with poor glycaemic control picked up less than 60% of their prescriptions from a community pharmacy. All patients with type 2 diabetes may be referred for a Long Term Conditions (LTC) assessment by a Pharmacist. If eligible, this will involve more regular contact between the patient and the Pharmacist as well as allowing the Pharmacist an opportunity to address barriers.

For further information, see: “New service model for community pharmacy”, BPJ 45 (Aug, 2012).

Collecting medicine from the pharmacy does not mean that it is being taken. Dose omission is the most common form of medicine non-concordance, e.g. patients prescribed metformin three times a day may only take one or two doses, and patients prescribed metformin once daily may miss their dose and take a double dose the next day. Blister packaging
of medicines (or medicine trays), advising patients to take medicines with meals or setting cell phone reminders may help to increase adherence with treatments.

**Education can improve self-management of type 2 diabetes**

A patient’s understanding of diabetes should be constantly revisited. Education can improve treatment adherence and lead to better outcomes. Checking for understanding is an important part of this process as there may be differences between what a health professional believes has been agreed and what a patient has understood.

Patients and their families/whānau need to understand the link between glycaemic control and symptoms. Fatigue and sleepiness is a common symptom of poor glycaemic control; education helps patients recognise this link. If a patient improves their control an increase in energy levels and a sense of wellbeing becomes a “selling point” for adherence to medicine regimens and lifestyle change.

Education should also focus on the action of anti-diabetes medicines and the need for regular dosing. This may also overcome beliefs such as that type 2 diabetes is a short-term condition or that diabetes-related complications are inevitable. Addressing patient concerns will often provide learning opportunities. For example, if a patient taking insulin experiences hypoglycaemia, explaining why it has happened and risk factors, e.g. missing meals, enables patients to recognise symptoms and manage them proactively.

Group-based diabetes education sessions have the advantage of allowing patients with type 2 diabetes to meet each other and discuss management strategies. A meta-analysis of group-based diabetes self-management programmes concluded that this approach resulted in improvements in clinical, lifestyle and psychosocial outcomes. There may also be patients within the practice who are willing to act as a “champion” and be contacted by other patients recently diagnosed with diabetes for peer support.

**Good management improves the “total health” of patients with diabetes**

**Managing patients with co-morbidities**

Managing patients with diabetes involves more than just maintaining glycaemic control. Approximately half of all adults with diabetes have at least one chronic co-morbidity, which can make treatment decisions more complex.

Consider if one condition is clinically dominant as this may help guide treatment decisions. For example, in a patient who has known cardiovascular disease and type 2 diabetes, medicines that reduce blood pressure or hyperlipidaemia are likely to significantly lower cardiovascular risk. However, the same patient may not benefit as much overall from a hard approach to glycaemic control, which increases the risk of hypoglycaemia. In a study of over 11,000 patients aged over 55 years with type 2 diabetes, severe hypoglycaemia was strongly associated with an increased risk of major macrovascular and microvascular events as well as cardiovascular and all-cause mortality. Similar associations were seen between severe hypoglycaemia and an increased risk of respiratory, gastrointestinal and dermatological conditions.

Hypertension should be treated to a target of <130/80 mmHg. Lower blood pressure targets should be approached with caution as a systolic blood pressure of <120 mmHg is associated with a greater frequency of adverse effects in people with type 2 diabetes. Treatment of hypertension should include restrictions to dietary salt intake. Reducing daily salt intake by one teaspoon (5 g) per day is estimated to reduce systolic blood pressure by 5 mmHg and diastolic blood pressure by 3 mmHg.

Dyslipidaemia should be discussed and, where appropriate, statin treatment initiated. The optimal lipid treatment targets for patients with diabetes are:  
- LDL cholesterol < 2.0 mmol/L; this is the primary lipid indicator for management of cardiovascular risk
- HDL cholesterol ≥ 1.0 mmol/L
- Total cholesterol (TC) < 4.0 mmol/L
- TC : HDL ratio < 4.0
- Triglycerides < 1.7 mmol/L

Microalbuminuria (urine albumin:creatinine ratio [ACR] > 2.5 mg/mmol in males or > 3.5 mg/mmol in females) is the earliest sign of diabetic kidney disease and requires prompt treatment.² Māori, Pacific and South Asian people with type 2 diabetes are particularly at risk of kidney disease and require more frequent monitoring.² Treatment with an angiotensin converting enzyme (ACE) inhibitor or an angiotensin II receptor blocker (ARB) is recommended for patients with type 2 diabetes and microalbuminuria regardless of whether hypertension is present.² Patients with diabetes and an ACR ≥ 30 mg/mmol measured on two occasions are classified as having a five-year cardiovascular risk greater than 20% and require intensive management to reduce risk factors.²

Smoking cessation advice and support should be given to all patients with type 2 diabetes who smoke. The ABC tool is recommended: “Ask about smoking status, give Brief advice and make an offer of help to stop, and provide evidence-based Cessation support”¹⁴ For more information see: “Smoking status and cessation support”, BPJ 40 (Nov, 2011).

Gout is common in people with type 2 diabetes and should be managed effectively to reduce the risk of cardiovascular disease. An Auckland study of over 18 000 people with type 2 diabetes or impaired glucose tolerance found that 16% of people with type 2 diabetes had gout.¹⁵ The prevalence of gout was higher among Māori (29%) and Pacific peoples (24%) with type 2 diabetes.¹⁵

Intensifying treatment for diabetes
Patients diagnosed with type 2 diabetes are often started on metformin, particularly if they are overweight. The need for additional oral medicines, e.g. a sulfonylurea, should be considered in patients with poor control who are not already taking these medicines.

Insulin initiation should not be delayed in patients with poor glycaemic control as this can result in the development of long-term complications. Ideally, the possibility of insulin initiation will have been discussed with the patient from when they were first diagnosed with diabetes. Treatment intensification should involve revisiting this discussion to explore fears or myths the patient may have and to provide evidence-based advice for the patient about insulin initiation. This may include acknowledging feelings of personal failure, perceptions of a loss of control, concerns about adherence to the insulin regimen, fear of needles or concerns about hypoglycaemia.¹⁶ Explain to the patient that insulin is the most effective glucose-lowering medicine and that over half of patients with type 2 diabetes are reported to eventually require insulin to achieve good glycaemic control.¹⁶ New Zealand guidelines recommend that all patients with type 2 diabetes and poor glycaemic control should strongly consider starting insulin.²

For further information see: “Initiating insulin for people with type 2 diabetes”, BPJ 42 (Feb, 2012).

Regular follow-up
Patients with type 2 diabetes require regular follow-up of all aspects of their care plan as well as regular foot and eye checks.

Foot ulceration in patients with type 2 diabetes can result in amputation. Good glycaemic control and the management of cardiovascular co-morbidities can reduce the peripheral neuropathy and peripheral artery disease that cause foot ulceration. Patients should be encouraged to regularly check their feet, or ask a family member to do so, and should also have their feet checked by a health professional at least once a year and every three months if they have a high risk of developing foot complications.

Risk factors for diabetic foot disease include:²
- Peripheral vascular disease
- Peripheral neuropathy
- Previous amputation or ulceration
- The presence of plantar callus
- Joint deformity
- Visual or mobility problems
Wearing appropriate footwear that does not cause abrasions is important to help prevent diabetic foot disease.

**Patients with type 2 diabetes should undergo retinopathy testing every two years or annually if diabetic retinopathy is present.** Diabetic retinopathy causing vision loss is a common complication of diabetes but patients are often asymptomatic until retinopathy is well progressed.

For further information see: “Diabetes follow-up: what are the PHO Performance Programme indicators and how are they best achieved?”, BPJ 39 (Oct, 2011).

**Referral to a diabetes management programme**

Patients with type 2 diabetes can be referred to a diabetes management programme. Typically, these services involve diabetes nurse specialists, diabetes educators and dieticians with strong local knowledge and skills in working with patients and their families/whānau.

Patients with poor glycaemic control who are at high risk of developing severe and/or additional diabetes-related complications, can also be referred to secondary care diabetes services.

This includes patients with:
- A previous cardiac event, stroke or transient ischemia attack
- eGFR < 45 ml/min/1.73m² and/or ACR > 30 mg/mmol
- Severe retinopathy or moderate maculopathy in either eye
- A previous amputation or ulceration
- Peripheral arterial disease or previous leg vascular disease

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**PHO Performance Programme – Diabetes detection and follow-up indicators active in 2014**

The PHO Performance Programme (PPP) is due to be replaced by the Integrated Performance and Incentive Framework (IPIF) in 2014. However, the PPP indicators “Diabetes detection” and “Diabetes follow-up after detection” currently remain active and funded.

The diabetes detection indicator determines what proportion of the population estimated to have diabetes have been diagnosed. The goal for this indicator is 90%. This indicator accounts for 7.5% of the funding that the PHO receives; 5% for the high needs population and 2.5% for the total population. 

The diabetes follow-up after detection indicator determines what proportion of the population expected to have been diagnosed with diabetes have had an annual review. The goal for this indicator is also 90%. This indicator accounts for 9% of the funding that the PHO receives; 6% for the high needs population and 3% for the total population.
Nurse-led diabetes clinics

The New Zealand Society for the Study of Diabetes (NZSSD) provides diabetes e-learning resources for nurses in primary care, based on the National Diabetes Nursing Knowledge and Skills Framework. This is useful for general practices who want to initiate their own diabetes management programmes.

Nurse-led clinics typically involve a nurse being responsible for maintaining a register of all patients in the practice with diabetes and ensuring that patient recall, monitoring and review is carried out. Many DHBs have dedicated Diabetes Nurse Specialists available to liaise with primary care teams to best meet individual practice needs as well run individual or group-based diabetes education sessions.

For further information visit: www.nzssd.org.nz and www.nzno.org.nz

ACKNOWLEDGEMENT Thank you to Jennifer Somerville, Lead Nurse Specialist – Diabetes, Auckland Diabetes Centre for expert review of this article.

References
Captopril tablets discontinued: ACE inhibitor alternatives

A recall has been issued for stock of the currently funded captopril tablets: 12.5 mg, 25 mg and 50 mg m-Captopril. A continued, long-term supply of captopril tablets has been unable to be secured so captopril tablets will no longer be funded via the Pharmaceutical Schedule. Captopril oral liquid 5 mg/mL will remain fully subsidised for children aged under 12 years.

Nationally, approximately 1300 patients are currently taking captopril, out of a total of 290 000 patients currently taking an ACE inhibitor.

There are few differences in efficacy between ACE inhibitors available for the management of people with hypertension. However, while captopril is typically given in divided doses, most other ACE inhibitors are able to be given as once-daily dosing. An exception to this is quinapril, which is recommended to be given twice daily for strengths of 40 mg and higher.¹

Table 1 (below) suggests equivalent doses of other subsidised ACE inhibitors. These figures are approximate, based on FDA-approved ranges and clinical trials for hypertension treatment. When titrating ACE inhibitors, monitoring renal function and blood pressure is important; check blood pressure one week after switching medicines.

Clinical judgement should be taken into account when transitioning patients taking captopril to another ACE inhibitor, as well as considering individual patient risks. Dosing equivalents may be more complex to estimate for patients taking captopril for conditions such as congestive heart failure and diabetic nephropathy.

References

Table 1: Suggested equivalent doses of ACE inhibitors for treatment of hypertension, adapted from PHARMAC, 2013²

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<th>Current captopril daily dosing</th>
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Removal of Special Authority for combination inhaler Seretide

The combination inhaler Seretide no longer requires Special Authority for subsidy as of 1 January, 2014, improving access for patients who can potentially benefit. Previously, patients were required to be treated with an inhaled corticosteroid (ICS) before Special Authority was approved for Seretide – this requirement still applies to other combination ICS and LABA inhalers. Seretide is a combination of fluticasone and salmeterol, available as a metered dose inhaler (MDI) and Accuhaler in various strengths for asthma and chronic obstructive pulmonary disorder (COPD).

Rotavirus and varicella vaccines on immunisation schedule from 1 July 2014

As of 1 July, 2014, the rotavirus vaccine RotaTeq will be available on the National Immunisation Schedule as an oral suspension, indicated for infants aged 32 weeks and younger. It is given in three doses, with the first dose given between age six to twelve weeks, and the subsequent two doses at least four weeks apart, usually alongside the routine immunisation schedule, and completed by age 32 weeks.1 The vaccine protects against gastroenteritis caused by rotavirus. Infants and young children have the highest risk of contracting rotavirus, which can cause severe diarrhoea and vomiting.

PHARMAC has also announced the addition of the varicella zoster (chicken pox) vaccine (Varilrix) to the Immunisation Schedule, from 1 July, 2014.2 This live vaccine for injection will be funded for people most at-risk of infection, including immunosuppressed children and those in direct contact with these children.

For further information on eligibility for funding of the varicella vaccine, see: www.pharmac.health.nz/news/item/national-immunisation-schedule-changes

Oral ketoconazole tablets discontinued worldwide

Medsafe announced the discontinuation of oral ketoconazole 200 mg tablets (Nizoral) from 1 December, 2013, due to the manufacturer ceasing production.1 Oral ketoconazole is prescribed for fungal infections, but has been discontinued worldwide due to an unsatisfactory adverse reaction profile, including the potential for liver damage. Topical forms of ketoconazole, including shampoos and creams, are not associated with this adverse reaction, and are still available as prescription medicines.

At present, ketoconazole tablets have not been delisted, and can still be prescribed under Section 29 of the Medicines Act 1981. However, Medsafe recommends that prescribers review patients taking oral ketoconazole who require long-term antifungal treatment, and change to an alternative treatment wherever possible.1 Itraconazole is a suitable alternative, however, while the incidence of liver damage is much lower than for oral ketoconazole, other potential risks should be taken into account, including patients at high risk of heart failure, and drug interactions.2, 3 For patients currently taking oral ketoconazole, monitor carefully for symptoms of liver damage, including jaundice, dark urine, anorexia, vomiting and abdominal pain.

References
CORRESPONDENCE

Prescribing salbutamol and oral corticosteroids in a child with wheeze

Dear Editor

I was curious to see the article “Assessing wheeze in pre-school children”, BPJ 56 (Nov, 2013) quoting a maximum dose of salbutamol at 800 micrograms per day for the treatment of acute episodes of wheeze in pre-school children. Hopefully this will be ignored by those at the coalface dealing with a sick child – it would be unfortunate if someone withheld salbutamol based on this guidance. Most guidelines go for up to 6 × 100 micrograms for starters, depending on severity, repeated depending on response. So it is common to exceed the 800 micrograms daily in any child with moderate to severe respiratory distress.

The use of short course oral steroids in the treatment of wheezy episodes (atopic, viral, or more often, not sure) seems to be gaining favour. Some comment on the safety of this would be useful - most folks know long courses of steroids are generally undesirable but how about the safety of using approximately 4 – 6 short (3 – 5 days) courses per year.

General Practitioner

The article “Assessing wheeze in pre-school children”, BPJ 56 (Nov, 2013), covers the management of wheeze in young children without a diagnosis of asthma. The dose of salbutamol in the section “Treating acute episodes of wheeze” was intended to refer to the at-home management of wheeze in a young child with an acute, self-limiting viral illness. In such a child, the maximum recommended daily dose of salbutamol, as suggested in the medicine data sheets, is 200 micrograms, four times daily, i.e. 800 micrograms per day. The dosing advice for salbutamol was not meant to refer to the management of an emergency situation in a child with...
asthma requiring hospitalisation. In retrospect, our use of the term “acute episode of wheeze” in the title of this section was ambiguous, and the intention of the section should have been explicitly stated.

The correspondent is correct that in a severe or life-threatening acute episode of breathlessness in a child with asthma, the dose of salbutamol given can be significantly higher than 800 micrograms. In this scenario the adverse effects of insufficient treatment will almost always outweigh any adverse effects of high-doses of salbutamol. The New Zealand Formulary for Children states the recommended initial acute treatment in a child with a moderate, severe or life-threatening asthma attack is salbutamol, six puffs from a 100 microgram inhaler via a spacer. Each puff should be inhaled separately, and five breaths taken between each puff. This regimen should then be repeated every ten to twenty minutes for one to two hours, with the frequency reduced to hourly if the child’s symptoms improve. Oxygen, corticosteroids (usually oral, but in life-threatening situations IV can also be used) and potentially ipratropium are also recommended where available. Referral to hospital should be considered depending on the child’s response to salbutamol.

As stated in the article, evidence of the efficacy of oral corticosteroids for the treatment of wheeze in children aged under five years is conflicting. This is likely to be a reflection of the many potential causes of wheeze in pre-school children. There is evidence that children with episodic viral wheeze will not respond to corticosteroids (both inhaled and systemic) as well as children with atopic wheeze but as discussed in the article, it is difficult to make this distinction in pre-school children.

Short courses (i.e. up to five days) of low-dose oral corticosteroids do not appear to be associated with adrenal or immune suppression, bone mineral density loss or reduced height growth. However, there has been only limited investigation of repeated short courses of corticosteroids in children. The few available studies indicate that most adverse biochemical changes, such as reductions in bone-forming proteins, following a single short course of oral steroids in a child return to baseline levels within one month. Adverse effects may be more likely to occur if increasing numbers of courses are given, but it is difficult to say how often is “too often”. Giving four to six short courses (as the correspondent queried) of corticosteroid to a child in one year, while not ideal, does not appear to be associated with significant long-term adverse effects.

So what is the role of oral corticosteroids in young children with wheeze? Oral corticosteroids are recommended in a child who requires hospitalisation for wheeze or breathlessness, however, if the child does not require hospitalisation, the decision to prescribe oral corticosteroids should be based on the clinician’s judgement. If a child has an acute episode of wheeze that cannot be controlled with salbutamol, oral corticosteroids will produce a more rapid clinical response than an inhaled corticosteroid. If the child is presenting frequently with acute episodes of wheeze requiring oral corticosteroids, however, other management options, such as regular inhaled corticosteroid (ICS) use, should be considered. An additional option, as outlined in the article, is the use of montelukast which is now funded under Special Authority criteria for the prevention and management of exacerbations of wheeze in pre-school children, either alone or in combination with an ICS.

References

Are two vaccinators better than one?

Dear Editor

We have recently been informed that it is not best practice to have two vaccinators administering multiple vaccinations at the same time for child immunisations by our local immunisation co-ordinator. Many nurses have been doing this for years and it is what the majority of parents ask for. Would someone be able to advise what is current best practice please - is there any documentation to support this?

Many thanks,

Practice Nurse
Northland

When a child requires two or more immunisations in the same consultation, one method is for two clinicians to simultaneously administer the vaccines. This method reduces the length of time that a child has to be restrained, and is thought to decrease overall pain and the anxiety of anticipating the next injection. The technique should be explained to the parent or caregiver and consent must be gained by both vaccinators. Simultaneous administration of vaccines is regarded as safe, however, there is insufficient evidence to recommend it as “best practice”.

Simultaneous administration of vaccines by two vaccinators is not covered within the New Zealand Immunisation Handbook, which sets out the requirements for vaccine administration in primary care in New Zealand. The 2013 Australian Immunisation Handbook and the 2012 United States CDC Vaccine Administration Guidelines do, however, cover simultaneous administration of vaccines. Both state that, at present, there is insufficient evidence to recommend for or against having two vaccine providers administer two vaccines at the same time, rather than one after the other.

Three studies were identified that cover simultaneous administration of vaccines. None of the studies were able to reliably demonstrate a difference in pain response in a child when simultaneous administration and sequential administration were compared. One study noted that parents preferred simultaneous administration.

We asked Dr Helen Petousis-Harris, Director of Immunisation Research and Vaccinology, Immunisation Advisory Centre, to comment on the practice of simultaneous administration of vaccines. Dr Petousis-Harris said: “I have never come across any evidence for the practice. Certainly it is resource intensive which perhaps is why it has not been investigated. It could certainly not be recommended as best practice although there is no evidence against doing it either.”

References

We value your feedback. Write to us at: Correspondence, PO Box 6032, Dunedin or email: editor@bpac.org.nz