Best Practice

Improving glycaemic control in type 2 diabetes

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Most people with type 2 diabetes require regular and intensive management to achieve individualised HbA_{1c} targets. Inevitable escalation of treatment and the role of insulin should be explained early as this helps patients adjust to the introduction of new medicines and reduces the perception of failure. When considering intensifying treatment, the benefits of improved glycaemic control need to be balanced against the specific risk profile of the medicines selected. Where more established treatments are not tolerated, are inappropriate or ineffective in achieving agreed HbA_{1c} targets, other medicines, e.g. acarbose and pioglitazone, may be considered. Some of these medicines, such as pioglitazone, have recently been associated with safety concerns.

Giant cell arteritis, also referred to as temporal arteritis, is a form of vasculitis which predominantly affects older people. It must be treated urgently, as it is associated with a significant risk of permanent visual loss, stroke, aneurysm and possible death. A low threshold for suspicion and prompt corticosteroid treatment are essential to prevent these complications. However, arriving at a diagnosis of this enigmatic condition can be difficult, as patients can present with non-specific symptoms. Referring the patient for a temporal artery biopsy is a key aspect of confirming the diagnosis, but this must not delay the initiation of corticosteroid treatment if giant cell arteritis is suspected.

Polymyalgia rheumatica is an inflammatory condition that causes a particular pattern of joint pain and stiffness, most commonly in older people. It is a rheumatic disorder closely associated, and often co-existing, with giant cell arteritis. Diagnosis is based on the patient's clinical features, supported by laboratory investigations. Before making a diagnosis, other conditions which can mimic polymyalgia rheumatica should be ruled out, and most importantly, the patient should be assessed for co-existing giant cell arteritis. Treatment of polymyalgia rheumatica, with long-term oral prednisone, can be managed in primary care, but referral to a Rheumatologist may be necessary if the diagnosis is unclear, the response to treatment is poor or multiple relapses of symptoms occur during tapering.

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The cover image is of *Heloderma suspectum* (Gila monster), a lizard native to the southwestern United States and Mexico. The Gila Monster eats less than once a month, and is able to rapidly increase insulin production when required. The first GLP-1 agonist, a novel glucose-lowering medicine, was derived from the salivary excretions of this lizard.

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Is the cupboard bare?
The threat of antimicrobial resistance

Antimicrobial resistance is one of the greatest threats to health that we have faced in recent history. As the rate of resistance grows, fewer antibiotics remain in the arsenal to fight common infectious diseases. These illnesses have the potential to once again become untreatable, as they were in the days before antimicrobial medicines existed. It is estimated that there are currently 630 000 cases of multiple drug resistant tuberculosis worldwide.[1] This accounts for 3.7% of new cases and 20% of previously treated cases of tuberculosis.[1] Resistance varies globally, and in some countries more than 18% of new cases of tuberculosis are now multiple-drug resistant.[1] There is widespread resistance to antimalarial medicines, such as chloroquine and mefloquine, in most countries in which malaria is endemic.[1] Resistance to newer antimalarial medicines (artemisinin-combination treatments) is now emerging in South-East Asia,[1] and it is likely that fully resistant malaria parasites will start to become widespread.

Many multiple drug resistant organisms are found to be clonal, i.e. from the same origin, and are spread widely as people are increasingly mobile. For example, most methicillin-resistant *Staphylococcus aureus* (MRSA) isolates in New Zealand have originated from overseas. There was an epidemic MRSA in New Zealand hospitals in 2000, from a strain imported from the United Kingdom, most likely by both patients and staff. Traditionally, MRSA was mainly associated with hospital-

acquired infections, but it is now increasingly being seen in the community. A recent study in New Zealand found that MRSA is now more commonly associated with infections in the community than in hospitals.[2] Latest ESR surveillance data from 2011 showed that 1020 patients had laboratory confirmed MRSA, of which 44% were from hospital-acquired infections and 56% were from community-acquired infections.[3] There was a 37% increase in MRSA prevalence between 2010 (17.3 people with MRSA per 100 000 population) and 2011 (23.7 per 100 000), which is the largest yearly increase in the last ten years.[3] Prevalence varied by DHB region, and was highest in the Tairawhiti (64.4 per 100 000), Counties Manukau (57.4 per 100 000) and Hawke's Bay (50.1 per 100 000) DHBs. The MRSA prevalence in the Tairawhiti DHB was almost five times higher than in 2010.[3] Community-acquired strains of MRSA have historically been distinct from hospital-acquired strains, however, crossover is now being seen.[3] This shift to a dominance of community MRSA infections follows a similar pattern to that seen in other countries.

There are increasingly limited options for treating MRSA infections. Vancomycin has been the antibiotic of choice for MRSA in a hospital setting, however, this has now resulted in the emergence of vancomycin-resistant enterococci. Multiple drug resistant extended-spectrum beta-lactamase-producing enterobacteriaceae (ESBL-E) are also spreading in both

Why should we care about antimicrobial resistance?

According to the World Health Organisation, antimicrobial resistance poses the following threats:[1]

- Standard antibiotics are often ineffective when used to treat infections caused by resistant bacteria, resulting in prolonged illness and an increased risk of mortality
- Resistance causes the effectiveness of treatment to be reduced, increases the amount of time that a person is infectious and increases the spread of resistant microorganisms to others
- Infections which were previously easily managed may become untreatable and uncontrollable, as seen in the pre-antibiotic era
- The costs of treating resistant infections (to healthcare, individuals and societies) is increased due to the need to use more expensive second-line treatments, longer treatment periods and a greater need for hospital care
- Resistant infections are detrimental to the success of "modern medicine" treatments such as major surgery, chemotherapy and organ transplantation

hospitals and the community, mostly due to quinolone and cephalosporin use, and are increasingly becoming a concern.

We are down to our last line of defence (parenteral ceftriaxone) in the treatment of gonorrhoea, due to increasing resistance to oral ciprofloxacin. Latest surveillance data from ESR show that resistance to fluoroquinolones was at 40.8% in 2011,[4] which means that ciprofloxacin can no longer be considered an appropriate first choice antibiotic for gonorrhoea. There is considerable local variation in resistance rates, with some areas reporting an even higher resistance rate to fluoroquinolones.

As we discard the last of the useful antibiotics, what is left in the cupboard? The Infectious Diseases Society of America (IDSA) has called for a worldwide commitment to develop at least ten new systemic antibiotics by 2020; the 10 × '20 initiative. The IDSA says that pharmaceutical research and development needs to urgently focus on new agents to fight multiple drug resistant Gram-negative bacilli infections (e.g. ESBL-E). However, at this time, many pharmaceutical companies are withdrawing from antibiotic research and development, rather than increasing resources in this area. In the five year period from 1983 – 1987, 16 new systemic antibiotics were approved in the United States, however, this has steadily declined, with only two new antibiotics approved between 2008 and 2012.[5]

Pharmaceutical companies are reluctant to invest in developing antibiotics because it has now become scientifically difficult to develop a new, effective and safe antibiotic, and the cost involved in this development cannot be recouped. Most antibiotics are only used for a short amount of time, and prescribers are encouraged to limit their use of these medicines. This is coupled with the fact that due to the natural process of resistance, a new antibiotic has a relatively short "life-span" before it becomes obsolete in clinical practice. All of these factors deter investment.[6]

There are currently seven parenteral antibiotics active against Gram-negative bacilli in advanced clinical development (Phase 2 or 3) in the United States, but not all will make it through the approval process, and not all in time for the 2020 deadline.[5] In addition, none of these seven medicines are active against all clinically relevant resistant Gram-negative bacilli.[5] Six of the seven antibiotics are being developed for the treatment of complicated urinary tract infection or intra-abdominal infection, and one for acute bacterial skin infection. There are no antibiotics currently in development in the United States for the treatment of community-acquired or hospital-acquired bacterial pneumonia or bloodstream infection, which are considered by the IDSA to be important conditions for which to find new antibacterial treatments.[5]

In Europe, the European Commission has collaborated with the pharmaceutical industry, to help drive the development of new and safer medicines, including antibiotics, and increase the rate in which these medicines are available to patients. The Innovative Medicines Initiative has an ongoing focus on combating antimicrobial resistance, which includes the programme "New Drugs for Bad Bugs". There are currently only a few antibiotics targeting resistant strains of bacteria in an advanced stage of development in Europe.[6]

If waiting for a wave of new antibiotics is not the immediate solution, what can we do? The development of antimicrobial resistance is a natural process of evolution, however, certain behaviours that we are responsible for can accelerate the emergence and spread of resistance.[1] This includes the inappropriate use of antimicrobials in both medicine and veterinary care, and the use of antimicrobials for non-therapeutic purposes, e.g. food and animal feed additives, preservatives and disinfectants, which also results in environmental contamination.[6] The key lies in optimising use of our currently available antimicrobial medicines by preserving them for only when they are absolutely required, prescribing the right antibiotic for the right condition and susceptibility, at the right dose and duration, educating patients to follow instructions for use and improving surveillance and access to resistance data. Adequate infection prevention and control measures underpin all of these interventions.

Work is currently being done in New Zealand to develop a coordinated strategy for addressing antimicrobial resistance at a national level and across all health care sectors. The main players in health care policy and education have expressed a strong willingness to collaborate on this strategy. In the meantime, individual clinicians and healthcare organisations need to make a concerted effort to work towards the common goal of preserving the effectiveness of the antibiotics that we still have.

Watch this space We are currently in the final process of updating our 2011 guide: "Antibiotic choices for common infections". Printed copies of the booklet will be distributed soon, and an interactive version of the guide will also be available on our website: **www.bpac.org.nz**

"Antibiotic resistance as a phenomenon is, in itself, not surprising. Nor is it new. It is, however, newly worrying, because it is accumulating and accelerating, while the world's tools for combating it decrease in power and number."

—**JOSHUA LEDERBERG**, Nobel Prize laureate

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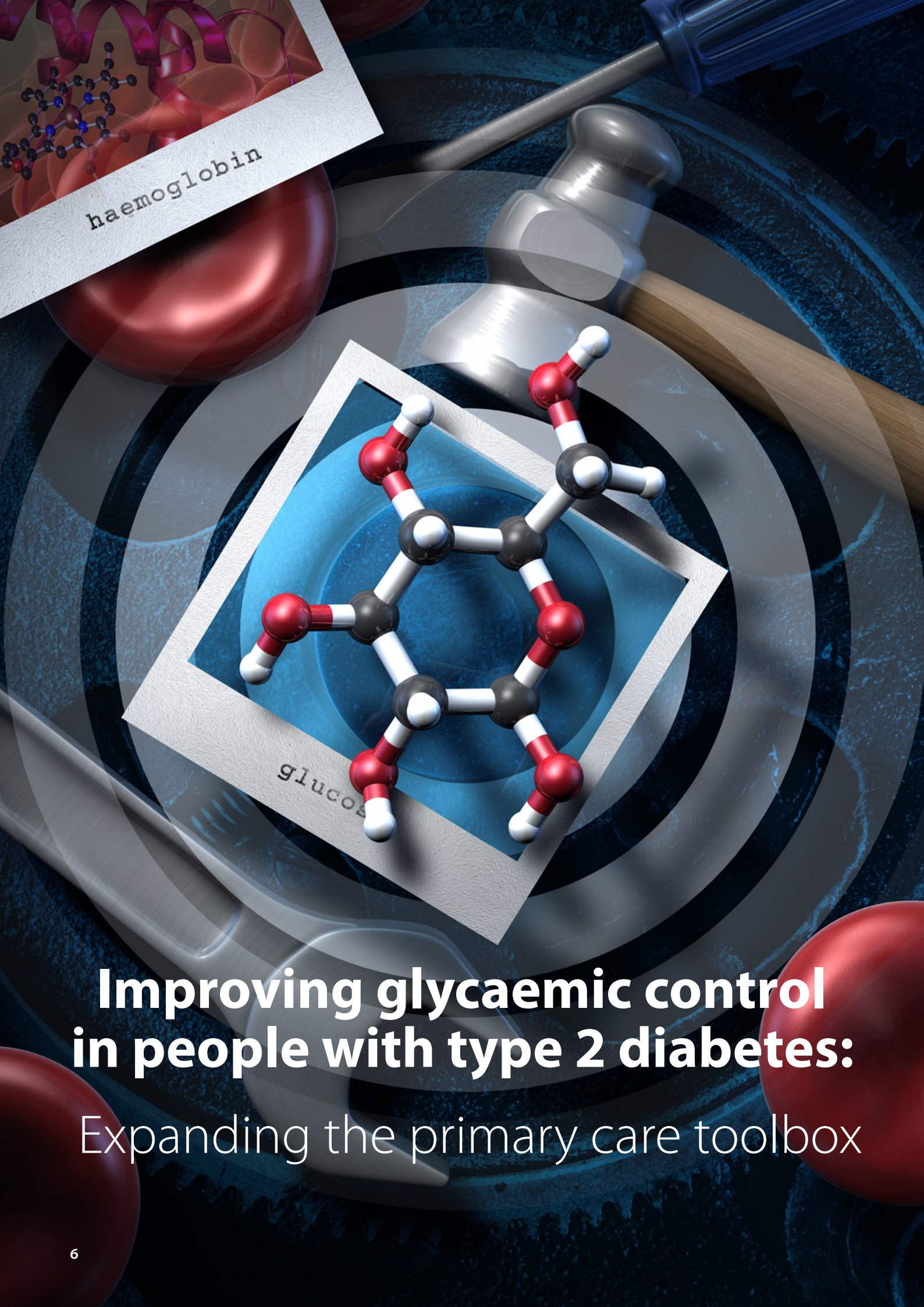
Improving glycaemic control in people with type 2 diabetes:

Expanding the primary care toolbox

Most people with type 2 diabetes require regular and intensive management to achieve individualised HbA$_{1c}$ targets. Patients should be urged to pursue lifestyle interventions, to the best of their ability, to reduce their risk of diabetes-related complications. Type 2 diabetes is a condition of increased insulin resistance and progressive failure of pancreatic beta-cell function. Inevitable escalation of treatment and the role of insulin should be explained early as this helps patients adjust to the introduction of new medicines and reduces the perception of failure. When considering intensifying treatment, the benefits of improved glycaemic control need to be balanced against the specific risk profile of the medicines selected. Where more established treatments are not tolerated, are inappropriate or ineffective in achieving agreed HbA$_{1c}$ targets, other medicines, e.g. acarbose and pioglitazone, may be considered. Some of these medicines, such as pioglitazone, have recently been associated with safety concerns.

Glycaemic control in type 2 diabetes

Widespread obesity, a sedentary lifestyle and an ageing population has resulted in type 2 diabetes being labelled as a global pandemic.[1] Every day in New Zealand 50 people are told by their doctor that they have diabetes.[2] Type 2 diabetes is most prevalent in Pacific males (10.6%) and females (9.9%), Asian males (8.4%), and Māori males (7.9%) and females (6.8%).[3] It has a prevalence of approximately 4 – 5% among European males and females, and Asian females.[3] This "pandemic" is being driven by the high prevalence of intermediate hyperglycaemia, which is estimated to currently affect one-third of Māori and Pacific peoples and one-quarter of New Zealand Europeans aged 45 – 64 years.[4]

Many people with type 2 diabetes will benefit from improved glycaemic control

It is widely accepted that, despite receiving treatment, many people with type 2 diabetes are spending the majority of their life after diagnosis with inadequately controlled blood glucose levels.[5, 6] A recent primary care study of over 26 000 patients diagnosed with type 2 diabetes in the Hamilton region found that approximately 40% of Māori, 30% of people of Asian descent and 20% of New Zealand Europeans had HbA$_{1c}$ levels greater than 64 mmol/mol.[7]

Good glycaemic control in people with type 2 diabetes is known to delay the onset of microvascular complications including renal failure, retinopathy and neuropathy. Good glycaemic control will also have a beneficial effect on macrovascular complications, e.g. coronary artery disease, stroke and peripheral vascular disease, if it is achieved early and maintained.[8]

Type 2 diabetes is a progressive disease which requires lifestyle measures, monitoring and medicines to increase in intensity as pancreatic beta-cell failure progresses. This should be discussed with the patient at an early stage, so that the initiation of additional treatment, including insulin, is not viewed by the patient as being a personal failure. Young people with type 2 diabetes have the most to benefit from intensive management of glycaemic control as they are likely to be exposed to hyperglycaemia for longer due to an increased life expectancy.[9] However, the benefits of the reduced risk of complications need to be balanced against the harms of hypoglycaemia and weight gain associated with more intensive treatment for all patients.

Improved glycaemic control should always be underpinned by lifestyle measures and every person with type 2 diabetes should have an individualised care plan for lifestyle intervention.[9] Dietary assessment should be undertaken for people with type 2 diabetes. Care plans should be reviewed and when agreed goals are not achieved, discussions should be initiated to overcome barriers to change.

"Exercise is the best medicine". Walking has been shown to increase weight loss, improve glycaemic control and reduce cardiovascular mortality in people with type 2 diabetes. Regular exercise may be more effective than medicines for the treatment of type 2 diabetes in some patients. The number needed to treat (NNT), to prevent one death per year, is reported to be 61 for people with type 2 diabetes who walk at least two hours per week.[10] This compares to a reported NNT of 141 for overweight people with diabetes who are taking metformin.[10]

Setting HbA$_{1c}$ targets

Clinicians in partnership with patients are recommended to set individualised HbA$_{1c}$ targets which take into consideration the potential duration of the patient's exposure to hyperglycaemia.[9] HbA$_{1c}$ levels should be regularly monitored to enable review if targets are not being achieved.

New Zealand guidelines recommend that HbA$_{1c}$ targets be appropriate for, and agreed with, the individual patient. In general, a HbA$_{1c}$ target of 50 – 55 mmol/mol is recommended.[8] In younger patients, who are likely to be exposed to hyperglycaemia for longer, a lower target may be agreed, which should be balanced against the increased risk of hypoglycaemia if sulfonylureas or insulin are prescribed. Patients who have a significant risk of hypoglycaemia or its consequences, e.g. older patients, may have less stringent targets (see: "How low to go?").[9]

Management intensification is the cornerstone of all type 2 diabetes care plans and glycaemic control should be constantly revisited during consultations. Some people with type 2 diabetes may not be aware of the hidden damage that hyperglycaemia can cause, particularly if they feel they are functioning at an acceptable level. Discussing the significance of any laboratory or tests results, e.g. microalbuminuria or retinal imaging, with the patient is one way to reinforce the benefits of tighter glycaemic control.

✎ **Best Practice tip:** The new *Bestpractice* Decision Support diabetes common form standardises retinal images to retinal reports and is useful for illustrating to patients the hidden damage of retinopathy.

Choosing the right tools for the job

Metformin, sulfonylureas and insulin are the front-line medicines in the management of glycaemic control in people with type 2 diabetes. When considering other medicines, e.g. when metformin or sulfonylureas are less well tolerated, contraindicated or not effective, it is important to select the right medicine for the right patient.

How low to go?

"The price of intensive glycaemic control is an increased risk of severe hypoglycaemia." [11]

Trials and systematic reviews have produced conflicting results as to what effect intensive glycaemic control has on all-cause mortality. Intensive glycaemic control in the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial and the Veterans Affairs Diabetes Trial (VADT) was defined as a HbA$_{1c}$ target of ≤ 42 mmol/mol.[9] The Action in Diabetes and Vascular disease (ADVANCE) trial had a target level of 48 mmol/mol, and the United Kingdom Prospective Diabetes Study (UKPDS) achieved a HbA$_{1c}$ level of 53 mmol/mol in the intensively managed arm of its trial.[9]

There was no significant change in cardiovascular or all-cause mortality in the ADVANCE or VDAT trials, although a trend towards increased mortality was seen in the VDAT trial. However, in the intensively managed groups in the ACCORD trial, there were significant increases in both cardiovascular and all-cause mortality resulting in the trial being stopped early. The extent to which this result was influenced by hypoglycaemia, or the use of newer medicines, e.g. dipeptidyl peptidase-4 inhibitors and glucagon-like peptide-1 (GLP-1), is unknown. Rates of hypoglycaemia were three-fold higher in the ACCORD trial.[9]

The United Kingdom Prospective Diabetes Study (UKPDS) ten-year follow-up demonstrated that the relative benefit of having received intensive glycaemic management was maintained despite the mean HbA$_{1c}$ levels of the two treatment groups converging shortly after randomisation had ceased.[9] This has been termed a "legacy effect" of treatment.

These apparently conflicting results suggest that glycaemic control should not be a "one size fits all" approach. Generally, patients in the ACCORD, ADVANCE and VADT studies were older, had a longer history of diabetes at study entry and had a history of cardiovascular disease or multiple cardiovascular risk factors. Younger patients, who were recently diagnosed and had lower cardiovascular risk in the UKPDS study appeared to benefit more from intensive management. Glycaemic control should therefore be appropriate for the individual.

Metformin first-line

Metformin is the first-line medicine for all people with type 2 diabetes.[8] Metformin decreases glucose formation in the liver and increases peripheral utilisation of glucose. It is particularly effective in people with type 2 diabetes who are overweight.[12] Evidence now suggests that initiation of metformin for intermediate hyperglycaemia, or at the time of type 2 diabetes diagnosis, may confer cardiovascular protection beyond that provided by its blood glucose-lowering ability.[13] It is important to start patients on a low dose of metformin to avoid initial gastrointestinal adverse effects and to gradually increase the dose according to response. A typical adult starting dose is 500 mg, once daily – although it is not uncommon to start a patient on half a tablet. Generally, the total daily dose should not exceed 2 g, but in selected patients this may be increased to 3 g per day if tolerated and renal function is not impaired.[14, 15]

Lactic acidosis is a possible rare adverse effect of metformin treatment.[14] It is triggered by tissue hypoxia, which can be a feature of acute renal failure, and acute cardiac or respiratory failure. This is most commonly seen in general practice in association with chronic kidney disease (stage 4 – 5). Temporary cessation of metformin should be considered in situations which may lead to lactic acidosis.[14] Explain to patients that if they develop an illness leading to dehydration they should temporarily cease taking metformin.[14]

Doses should be reduced in patients with eGFR 30 – 60 mL/min/1.73m^2 (maximum 1 g daily).[14] Treatment should not be begun in patients with significant renal impairment (eGFR < 30 mL/min/1.73m^2) without prior discussion with a Nephrologist.[14]

Add sulfonylurea

A sulfonylurea can be added to metformin for people with type 2 diabetes who have not reached their agreed HbA$_{1c}$ target after three months.[8] Sulfonylureas are effective at increasing insulin secretion if the patient has functional pancreatic beta-cells, but this can also cause hypoglycaemia and weight-gain.[14] Due to the risk of hypoglycaemia sulfonylureas should be avoided in patients with severe hepatic or kidney impairment.[14] Sulfonylureas are also contra-indicated in patients with ketoacidosis and should be avoided in patients with acute porphyria.[14] There are currently three fully-subsidised sulfonylureas in New Zealand – glipizide, gliclazide and glibenclamide. Glipizide and gliclazide are shorter-acting and are preferred, with caution, in older patients.[14] Glibenclamide is long-acting and should be avoided in older patients.[14] Table 1 lists recommended doses.

Insulin

Insulin is eventually required for many people with type 2 diabetes and early initiation can be appropriate. Beta-cell function declines linearly and after ten years 50% of people

Table 1: Recommended doses of sulfonylureas[14]

	Adult starting dose	Dose titration	Notes
Glipizide	2.5 – 5 mg daily, with or shortly before breakfast or lunch	Adjust according to response by 2.5 – 5 mg daily, at weekly intervals; usual maintenance dose is 2.5 – 30 mg daily, maximum 40 mg daily; no more than 15 mg in a single dose.	Divided doses are recommended for patients who have high post-prandial blood glucose
Gliclazide	40 mg daily, with breakfast	Adjust according to response, up to 160 mg in a single dose; maximum 320 mg daily	Higher doses should be divided and taken with food
Glibenclamide	2.5 – 5 mg daily, with or immediately after breakfast	Adjust according to response by 2.5 mg daily, every one to two weeks; maximum 10 mg as a single dose; maximum 15 mg daily	Long-acting; not recommended for use in older people

with type 2 diabetes will require insulin.[16] Insulin has a greater blood glucose lowering ability than any other hypoglycaemic medicine, and early initiation may reduce beta-cell damage and is thought to slow disease progression.[17] Early initiation of insulin should be strongly considered for people with type 2 diabetes who have significant hyperglycaemia, e.g. HbA_{1c} > 65 mmol/mol, particularly if there are signs such as ketonuria and weight loss.[8] If there are immediate health concerns, insulin initiation, even if temporary, may be the only treatment option. However, it is important to remember that type 1 diabetes can occur at any age and if there are severe signs, or rapid progression, then testing for autoantibodies may be appropriate. Women with type 2 diabetes who become pregnant almost always require initiation of insulin treatment.[12]

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

Additional treatments require extra considerations

Alternative medicines may need to be considered for select patients where:

- Glycaemic control remains poor following standard treatment
- There is a significant risk of hypoglycaemia, or the patient's circumstances places them at risk if hypoglycaemia does occur, e.g. lives alone
- Standard treatments are either not tolerated or are contraindicated
- Doses of standard treatments cannot be increased

When discussing further treatment options with patients it is important to consider their age, the risk if hypoglycaemia occurs, the potential for weight gain associated with treatment and their preferences regarding the management of adverse effects. Table 2 provides an approximate comparison of the relative efficacy of oral anti-diabetic medicines available in New Zealand.

α-Glucosidase inhibitors

Acarbose is the most widely studied α-glucosidase inhibitor and is the only fully-subsidised medicine in this class available in New Zealand. Acarbose is a safe and mildly effective medicine for improving glycaemic control. It is taken orally and reduces the amount of glucose absorbed in the small intestine by blocking the α-glucosidase enzyme, which breaks down complex carbohydrates into glucose. Acarbose is the most effective oral anti-diabetic medicine available in New Zealand for reducing post-prandial hyperglycaemia, which is thought to be a significant contributor to cardiovascular disease and the microvascular complications of type 2 diabetes.[19] However, it has little effect on fasting glucose levels.

Acarbose can be used as a first-line treatment where metformin or sulfonylurea are contraindicated or not tolerated.[20] When taken as a monotherapy, acarbose does not increase the risk of hypoglycaemia.

Acarbose can also be added to any of the oral anti-diabetic medicines, and insulin, if monotherapy with these medicines fails to achieve HbA_{1c} targets and post-prandial glucose levels continue to be a concern.[19] When used in combination

Table 2: The relative efficacy of anti-diabetic medicines available in New Zealand, adapted from Klam et al (2006)[18]

Medicine	Dose interval	Expected HbA_{1c} reduction (mmol/mol)*
Metformin	One – three times daily	12 – 22
Sulfonylureas	One – three times daily	15 – 20
Acarbose	Three times daily	6 – 11
Pioglitazone	One – two times daily	20 – 21

* The expected reduction is an estimate that excluded the highest and lowest effects reported by studies

with a sulfonylurea or insulin, acarbose may enhance the hypoglycaemic effect of these medicines. If hypoglycaemia occurs in this situation, because of the enzyme-inhibiting action of acarbose, patients should consume glucose, not sucrose which is a complex carbohydrate, e.g. glucose tablets not jellybeans.

How to initiate and monitor acarbose use

Acarbose is available in 50 mg and 100 mg tablets, which should be chewed and swallowed with water immediately before eating, or with the first mouthful of food.[14] Adults begin with 50 mg, three times daily, which is increased to 100 mg, three times daily, after four to eight weeks.[14] The maximum recommended dose is 200 mg, three times daily.[14]

Acarbose adverse effects and contraindications

Flatulence is reported by approximately three-quarters of people taking acarbose. Soft stools and diarrhoea are also common.[19] Abdominal distension, pain and rarely, hepatitis have also been reported.[19]

Acarbose is contraindicated in people who: are pregnant, have hepatic or renal impairment (eGFR < 25 mL/minute/1.73m²), have inflammatory bowel disease or a history of intestinal obstruction or hernia, have had previous abdominal surgery or have a gastrointestinal disorder with malabsorption.[14]

Glitazones (pioglitazone)

The glitazones are oral anti-diabetic medicines which are classified as insulin sensitisers (like metformin) because they increase the body's ability to transport glucose across cell membranes. When used as monotherapy, glitazones do not cause hypoglycaemia.[9] Glitazone use has been associated with heart failure (see "Glitazone use and cardiovascular risk"), bladder cancer and increased risk of bone fractures.

In New Zealand, pioglitazone is the only glitazone approved for use in the treatment of type 2 diabetes. It is available under Special Authority criteria to patients who are already taking maximum doses of metformin or a sulfonylurea, or where one or both medicines are contraindicated or not tolerated, or for patients taking insulin who have not achieved glycaemic control. Rosiglitazone was available in New Zealand, but has now been withdrawn due to concerns about adverse cardiovascular effects (see "Glitazone use and cardiovascular risk").

Pioglitazone may be cautiously considered in select patients

NICE guidance states that pioglitazone may be considered

Glitazone use and cardiovascular risk

In 2010, the United States Food and Drug Administration (FDA) placed restrictions on the prescribing of rosiglitazone following concerns that its use was associated with myocardial ischemia (N.B. the FDA is currently reconsidering this decision).[21] NICE guidelines note a possible increased risk of myocardial ischaemia associated with the use of rosiglitazone, which is further increased with concurrent use of insulin.[22] Rosiglitazone is no longer available in New Zealand.

The extent to which glitazones increase the risk of heart failure is complicated, as many studies reporting on the safety of anti-diabetic medicines are of limited duration and follow-up is often short, or the studies are not designed to assess cardiovascular effects. A meta-analysis of 140 randomised controlled trials found that there was moderately strong evidence to suggest either pioglitzone or rosiglitazone use increased the risk of congestive heart failure in comparison to use of sulfonylureas.[21] However, research on this topic is ongoing.
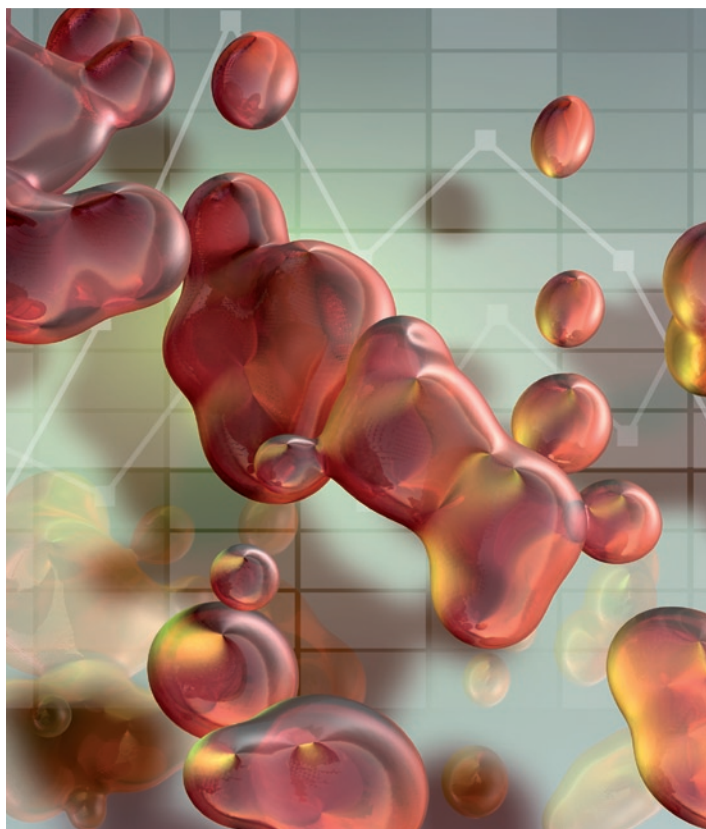
cautiously as:[22]

- A second-line treatment to metformin, instead of a sulfonylurea, if HbA_{1c} is ≥ 50 mmol/mol, or greater than agreed target, and the person is at significant risk of hypoglycaemia or its consequences, e.g. works at heights or lives alone, or sulfonylurea treatment is not tolerated or is contraindicated

- A second-line treatment to first-line sulfonylurea if HbA_{1c} is ≥ 50 mmol/mol, or greater than agreed target, and the patient does not tolerate metformin, or metformin is contraindicated

- A third-line option to add to metformin and sulfonylurea if HbA_{1c} is ≥ 59 mmol/mol or greater than agreed target, and insulin treatment is either inappropriate, or unacceptable

- A combination treatment with insulin if the patient has previously had a therapeutic response to pioglitazone treatment, or the patient is already taking high-dose insulin and their blood glucose is inadequately controlled

How to initiate pioglitazone

Pioglitazone is available in 15 mg, 30 mg and 45 mg tablets. The recommended starting dose for adults is 15 – 30 mg, once daily.[14] The concurrent use of other hypoglycaemic medicines may increase the risk of hypoglycaemia and influence the starting dose, e.g. 15 mg, once daily may be more appropriate for patients taking insulin.[14, 23] The dose may be increased after four weeks to 45 mg, once daily, if greater therapeutic effect is required.[23] If a sulfonylurea or insulin is being taken concurrently then doses of these medicines may need to be reduced.

Pioglitazone should only be continued beyond six months in patients who have achieved at least a 5 mmol/mol reduction in HbA_{1c}.[22]

The adverse effects of pioglitazone

Pioglitazone can cause weight gain, fluid retention, peripheral oedema and expansion of plasma volume, which can increase the risk of anaemia and heart failure.[22] Pioglitazone is contraindicated in people with a history of heart failure.[14]

In New Zealand, in 2009, there were five new registrations of bladder cancer per 100 000 people.[24] Bladder cancer risk is increased by 40% in people with type 2 diabetes.[25] One study found that this risk was increased almost two-fold in people with type 2 diabetes who take pioglitazone, with those who use the medicine for longer, or at higher doses, exposed to the greatest risk.[26] Pioglitazone use is contraindicated

in patients with a history of bladder cancer, or in patients with un-investigated haematuria.[27] Assess the risk factors for bladder cancer, e.g. age, smoking history and history of chronic bladder infections, before considering pioglitazone treatment and use with extreme caution in older patients who have an increased risk of bladder cancer, as well as heart failure.[13] Bladder symptoms, in particular haematuria, should be investigated promptly in people taking pioglitazone.

Liver function should be assessed before pioglitazone treatment is begun and then monitored periodically.[14] If patients develop symptoms indicating liver toxicity, e.g. nausea, abdominal pain, dark urine or jaundice, the medicine should be stopped.[14]

The long-term use of glitazones is associated with an increased risk of bone fractures in women.[22] Pioglitazone should not be initiated in people who are at increased risk of bone fracture, e.g. people with oesteoporosis.[22]

Pioglitazone use is also associated with weight gain. The addition of pioglitazone to insulin significantly increases weight gain; 2.3 – 4.9 kg with insulin plus pioglitazone compared to 0.04 – 2.4 kg with insulin alone.[22] Pioglitazone in combination with insulin increases the risk of hypoglycaemia.[22]

Glucose-lowering medicines with novel actions

GLP-1 (glucagon-like peptide 1) agonists, are medicines which mimic endogenous incretins, which are peptides with short half-lives that are secreted from the gut following a meal. The first GLP-1 agonist was derived from extracts of the salivary secretions of the lizard *Heloderma suspectum* (Gila monster) which eats once a month and therefore needs to be able to rapidly increase insulin production as required.[22] Administration of GLP-1 enhances endogenous secretion of insulin following eating and inhibits glucagon secretion.[28] It is also reported to suppress appetite and food intake and is associated with weight loss in overweight or obese people with, or without, type 2 diabetes.[28]

GLP-1 treatment has recently been reported to increase the likelihood of acute pancreatitis approximately two-fold in people with type 2 diabetes compared to a control group matched for age, sex and diabetes related complications.[29] There are also recent concerns that the use of GLP-1 agonists may increase the longer term risk of pancreatic tumours.[30, 31] The American Diabetes Association is now requesting that pharmaceutical companies make patient-level data available for independent review to investigate the link between incretin treatment (including Dipeptidyl peptidase-4, see:

"Anti-diabetic medicines not commonly encountered in New Zealand") and pancreatic abnormalities.[32]

Exenatide (subcutaneous injection) is a GLP-1 agonist approved for use in New Zealand, but not subsidised, as an adjunctive treatment for type 2 diabetes. [14] NICE guidelines recommend that exenatide may be considered as a third-line treatment, in addition to metformin and sulfonylurea, when glycaemic control is inadequate, e.g. ≥ 59 mmol/mol, or as individually agreed, and:[22]

- The patient has a body mass index (BMI) ≥ 35 kg/m^2; or
- The patient has a BMI < 35 kg/m^2 and insulin treatment is inappropriate or the patient is at risk from obesity-related complications

Exenatide is injected twice daily within one hour of the two main meals, at least six hours apart.[14]

Trials have shown exenatide to be effective in reducing HbA$_{1c}$ levels by approximately 10 mmol/mol and to be associated with a reduction in body weight of 1 – 1.5 kg when added to metformin and sulfonylurea treatment.[22] Adverse effects include nausea and occasionally vomiting or diarrhoea when beginning treatment. Exenatide should not be initiated or continued in any patient with a history of pancreatitis.[33]

Surgery is an option if medicines are ineffective

Surgical intervention is an effective option for selected patients who are obese (BMI > 35 kg/m^2), when lifestyle interventions and medicines are ineffective.[34] Gastric bypass surgery and biliopancreatic diversion surgery are reported to have an NNT for diabetes remission at two-year follow-up of 1.3 and 1 respectively.[34] It is unknown for how long people who have had surgery can maintain this level of glycaemic control, and there are preliminary reports that by ten-year follow-up remission rates fall substantially.[34] Further studies are also required to determine the effects of surgery on mortality and long-term morbidity and the extent to which gastric surgery can result in nutritional deficiencies.

Anti-diabetic medicines not commonly encountered in New Zealand

Dipeptidyl peptidase-4 (DPP-4) inhibitors block the enzyme which degrades the incretins. Sitagliptin and saxagliptin are approved in New Zealand, but not subsidised, as oral adjunctive treatments for type 2 diabetes. They may be considered as a second-line treatment to metformin or sulfonylurea, or third-line to metformin plus sulfonylurea.[22] DPP-4 inhibitors are not associated with weight gain and may be considered in preference to pioglitazone where weight gain is a concern, or pioglitazone is contraindicated or does not produce a sufficient response.[22] Unlike exenatide these medicines require only once daily oral dosing. Long-term trials are required to confirm the safety of DPP-4 inhibitors as the DPP-4 enzyme is active against other peptides and, as with GLP-1 agonists, safety in regards to the possible association with pancreatic changes need to be clarified.[30, 31]

The meglitinides are a class of medicine that, like sulfonylureas, increase insulin secretion. They are used if sulfonylureas are not tolerated. There are two anti-diabetic medicines in this class, repaglinide and nateglinide, however, neither are available in New Zealand.

PHO Performance Programme – Diabetes follow-up after detection

Diabetes follow-up after detection is a PHO Performance Indicator that accounts for 9% of performance funding; 6% for the total population and 3% for the high need population.[35] High need populations include Māori and Pacific peoples and people living in NZDep 9 & 10 (most deprived) socioeconomic areas. The target population is all people aged 15 to 79 years who have been identified as having diabetes.[35]

The programme goal is for 90% of individuals identified as having diabetes to have had an annual diabetes review.[35] The target is assessed by counting the number of enrolled people in a PHO with a record of an annual diabetes review (the numerator). This number is then divided by the number of people in the PHO who would be expected to have been diagnosed with diabetes using prevalence estimate data (the denominator).[35]

PHOs that have not achieved the programme goal are expected to make annual increases in the number of people with diabetes who have had an annual review in order to receive funding. In 2011, the diabetes prevalence figures for New Zealand were updated, therefore currently PHO progress data should be treated with caution.[36] Reported performance against this indicator has fallen to 63.8% for the high need population and 62% for the total population. The transition to the Diabetes Care Improvement Package from the "Get checked" programme may explain why there has been a reduction in the reporting of annual diabetic reviews.[36]

Further information regarding the PHO Performance Programme is available from: **www.dhbsharedservices. health.nz/Site/SIG/pho/Default.aspx**

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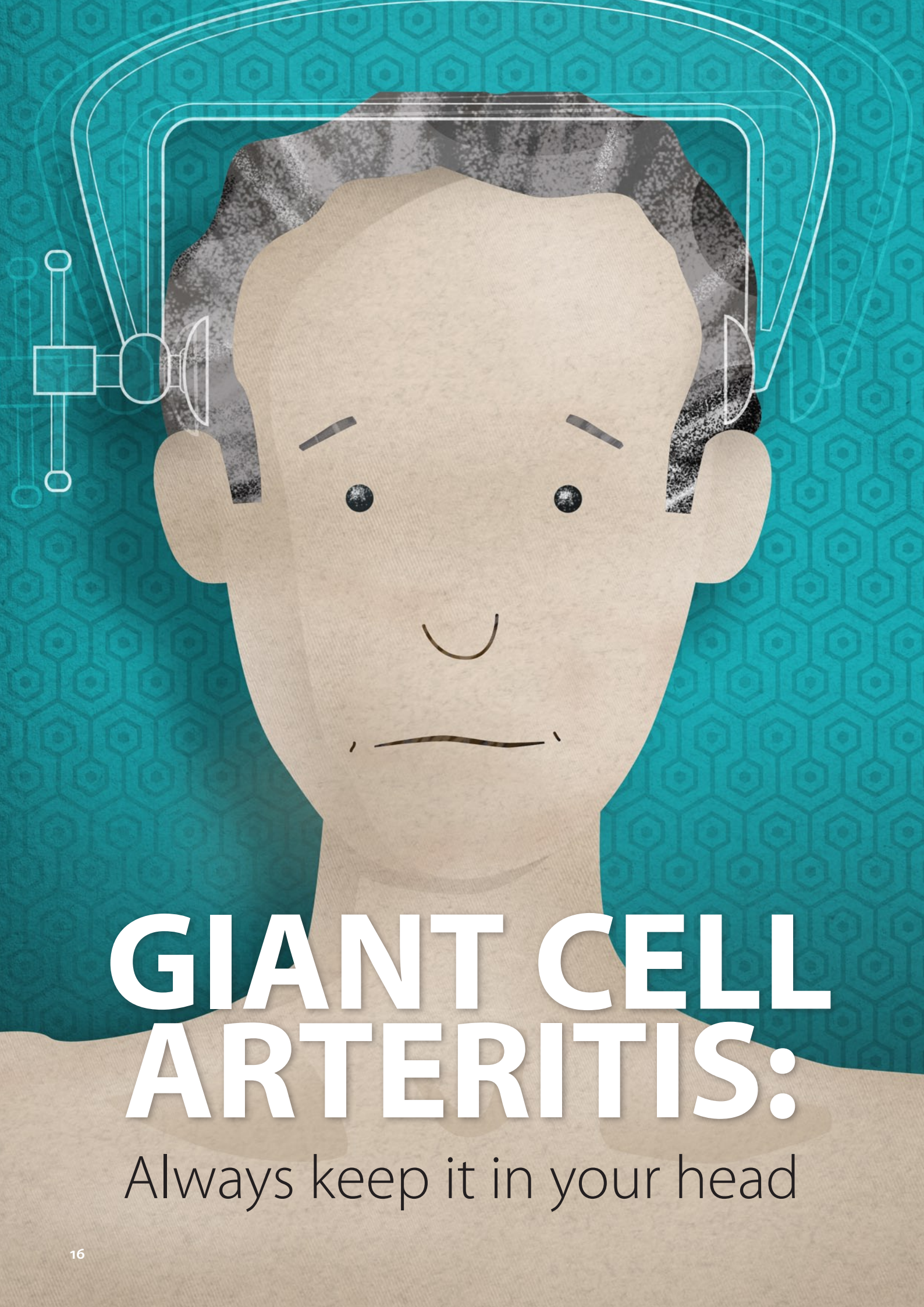
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DECISION SUPPORT FOR HEALTH PROFESSIONALS

GIANT CELL ARTERITIS:

Always keep it in your head

Giant cell arteritis, also referred to as temporal arteritis, is a form of vasculitis which predominantly affects older people. It must be treated urgently, as it is associated with a significant risk of permanent visual loss, stroke, aneurysm and possible death. A low threshold for suspicion and prompt corticosteroid treatment are essential to prevent these complications. However, arriving at a diagnosis of this enigmatic condition can be difficult, as patients can present with non-specific symptoms. Referring the patient for a temporal artery biopsy is a key aspect of confirming the diagnosis, but this must not delay the initiation of corticosteroid treatment if giant cell arteritis is suspected.

A headache not to miss

Giant cell arteritis is an immune-mediated, ischaemic condition caused by inflammation in the wall of medium to large arteries. While it can affect all medium to large arteries in the head, neck and upper torso, the involvement of the temporal artery is usually the only artery in which physical changes are clinically apparent (giving rise to the alternative name of temporal arteritis). It is the most common form of vasculitis in adults.[1]

Giant cell arteritis usually affects people aged over 50 years,[2] and is only rarely seen in younger people. It is most prevalent in Caucasians, particularly of Northern-European (e.g. Scandinavian) descent, and is two to three times more common in females than males.[3] Worldwide, incidence ranges between 10 – 20 cases per 100 000 people aged over 50 years.[3] A New Zealand study found a similar local incidence of 12 cases per year, per 100 000 people aged over 50 years.[4]

Symptoms of giant cell arteritis include headache, scalp tenderness, jaw claudication or other orofacial pain, neck or shoulder pain, visual disturbances and systemic symptoms, such as sweats, fever and anorexia. There may be palpable changes to the temporal artery on examination. An acute phase response is usually seen on laboratory assessment, and a temporal artery biopsy will show inflammation and multinucleated cells with involvement of the internal elastic lamina.

If undetected, giant cell arteritis can result in catastrophic sequelae, such as irreversible visual loss, stroke and aortic aneurysm. Visual loss, due to ischaemic optic neuropathy, is an early manifestation and can be a presenting symptom. This occurs in 20 – 50% of people with giant cell arteritis if they are untreated.[5,6] Large-vessel stenosis, and with it an increased risk of stroke, occurs in 10 – 15% of people.[7,8] Prompt treatment with corticosteroids can markedly reduce these risks. For example, the likelihood of visual loss decreases from 20% to 1% in patients with no preceding visual loss once treatment is initiated.[7] Patients who already have some visual loss at the initial presentation, however, have a poorer prognosis. One-quarter of patients develop further visual deterioration in the same eye, and up to 10% lose vision in the other eye, usually within the first few days, despite treatment.[9]

Giant cell arteritis should be strongly considered in older patients presenting with a new type of headache, jaw pain or visual disturbances (also see: "Making a diagnosis", over page). Whenever there is a reasonable suspicion of the condition, discuss the patient with an Ophthalmologist or Rheumatologist (depending on local guidelines/protocols) to organise referral for a temporal artery biopsy, and initiate same-day treatment with corticosteroids. Where there is a strong clinical suspicion of giant cell arteritis, a delay in treatment will almost always have greater consequences than an unnecessary dose of corticosteroids in someone who is later found to not to have the condition.

The link with polymyalgia rheumatica

Giant cell arteritis is closely associated with polymyalgia rheumatica, although the link between the two conditions is complex and not completely understood.[10] They are considered by some researchers to be different manifestations of the same underlying disease process.[3, 5] Both conditions are likely to be encountered in primary care, but polymyalgia rheumatica is significantly more common. Approximately 40 – 60% of people with giant cell arteritis have concurrent polymyalgia rheumatica.[5] Conversely, 16 – 21% of people with polymyalgia rheumatica will develop giant cell arteritis.[5] Overlapping symptoms and risk factors, and the effect of polymyalgia rheumatica and corticosteroid treatment on inflammatory markers, can make the identification of giant cell arteritis more challenging in a person with polymyalgia rheumatica.

For further information, see "Polymyalgia rheumatica", page 24.

Pathology and aetiology: how does is happen?

In people with giant cell arteritis, inflammation, caused by an immune reaction, occurs within the arterial wall. The inflammation is often irregular and is characterised by a granulomatous inflammatory infiltrate with the presence of large, macrophage-induced multinuclear cells - the "giant cells" in giant cell arteritis.[3, 7] This leads to a protective response from the arteries, resulting in myofibroblast proliferation, new vessel formation and thickening of the artery walls, culminating in potential infarction.[3]

The underlying cause of giant cell arteritis is largely unknown, but both genetic and external factors, e.g. infections, are thought to play a role.[3]

Making a diagnosis of giant cell arteritis

Giant cell arteritis is diagnosed by identifying risk factors from the patient's history and red flags from their clinical presentation, followed by laboratory assessment and referral for a biopsy of the temporal artery. Most symptoms in people with giant cell arteritis will develop gradually over one to two months, although rapid onset is possible.

The most significant risk factors for giant cell arteritis are:[2, 7]

- Age > 50 years
- A previous or current diagnosis of polymyalgia rheumatica
- Female gender
- European ethnicity

The patient's description of their symptoms

Specifically enquire about the following symptoms:

- Headache
- Scalp pain or tenderness
- Jaw claudication
- Visual symptoms

Abrupt onset of headache is the most frequent symptom of giant cell arteritis, and will be present in approximately 75% of cases.[2, 11] Any new onset or new type of headache in a person aged over 50 years should be considered a red flag. In giant cell arteritis, the headache is typically unlike a normal headache for the patient, and may be described as "head pain".[10] It is commonly unilateral, with a constant pain that may be severe enough to disturb sleep.[10] It is usually centred over the temporal or occipital area.[12] Occasionally the pain will be bilateral and diffuse.

Scalp pain or discomfort occurs in approximately one-quarter of patients with giant cell arteritis.[5,10] The patient may report pain when brushing their hair or when resting their head on a pillow.

Systemic features, including low-grade fever, anorexia and fatigue, are present in approximately half of patients.[5, 12] Giant cell arteritis may also be associated with weight loss and night sweats, however, these symptoms may also suggest other possible diagnoses, such as a malignancy.[10] In rare instances, systemic symptoms will be the only clinical indication of giant cell arteritis, therefore, the diagnosis of giant cell arteritis should be considered in any patient with systemic symptoms, raised inflammatory markers and no evidence of another cause, such as infection.

Jaw claudication in the muscles of the tongue and jaw, e.g. while chewing, occurs in approximately one-quarter of people with giant cell arteritis.[4, 7] In severe cases, this may lead to numbness or infarction of the scalp or the tongue. It is important to specifically ask patients about jaw claudication, as patients may not connect this with their headache or other symptoms. Pain while chewing and the presence of jaw claudication strongly indicates giant cell arteritis. Distinguishing between jaw pain from other causes (such as temporomandibular joint dysfunction) and true jaw claudication is important – the pain in jaw claudication is a cramping pain occurring after prolonged chewing or talking.

Visual symptoms are less common at initial presentation, but are of critical importance. Symptoms may include transient loss of vision in one eye, blurring and diplopia.[12] Complete loss of vision can also occur.[12]

Limb claudication, particularly in the arms, may also be present, but is a rare finding.[11] It may indicate large-vessel giant cell arteritis (i.e. outside the cranial vessels).[5]

What to include in the examination

The clinical examination should include assessment of:

- Temporal arteries
- Visual acuity
- Pupillary response to light
- Neurological signs
- Peripheral pulses, blood pressure and bruits

Examine the temporal artery and its branches for unusual prominence and erythema.[10] On palpation these vessels may be thickened, hardened, nodular, beaded or have reduced or absent pulses.[12] Tenderness may be present on the scalp or over the vessels. A normal temporal artery, however, does not exclude giant cell arteritis.[12]

An eye exam should be performed, and should include visual acuity (using corrective distance glasses if the patient has them, and excluding any residual refractive error using a pinhole), the pupillary light reflex, visual field testing by finger confrontation and fundoscopy.[12] With optic nerve involvement, the pupillary light reflex may be sluggish or absent, and a swinging light test may indicate a relative afferent pupillary defect (the patient's pupils fail to contract, and therefore appear to dilate, when a light is swung from the unaffected eye to the affected eye).[12] Fundoscopy may reveal swelling or pallor of the optic disc with associated haemorrhage.[5]

A brief, but focused neurological exam should be performed depending on the patients presenting symptoms. Neurological manifestations can occur in one-third of patients with giant cell arteritis, most commonly cranial nerve palsies, peripheral neuropathies and, rarely, strokes in the region of the carotid or vertebrobasilar artery.[5]

Perform auscultation over the carotid, subclavian, axillary or brachial arteries as bruits can be present and may indicate large-vessel involvement. Asymmetry of blood pressure or pulses in the neck and arms may be present, and can indicate large-vessel stenosis.[12] Auscultation over the patient's chest may reveal secondary aortic regurgitation (sometimes audible as a soft, high-pitched diastolic murmur best heard over the upper left sternal edge) from a thoracic aortic aneurysm, which can occur as a late complication in people with giant cell arteritis.[5]

Laboratory investigation

If the patient's risk-factors, symptoms and signs suggest giant cell arteritis the following tests should be urgently requested at the initial presentation:[7]

- C-reactive protein (CRP)
- Erythrocyte sedimentation rate (ESR)
- Full blood count (FBC)
- Liver function tests (LFTs)

While ESR and CRP are no longer routinely requested together for most conditions, either marker (or both) can be raised in giant cell arteritis and given the significant potential for morbidity in people with giant cell arteritis, it is recommended that both are requested in the initial presentation. This is consistant with most guidelines, as combining the two tests

marginally increases the sensitivity and specificity.[5, 12] Any elevation of CRP or ESR is suggestive of giant cell arteritis in a patient with signs and symptoms, although, typically, in acute cases, levels are significantly elevated.[2] A normal CRP or ESR does not exclude giant cell arteritis; up to 20% of people with confirmed giant cell arteritis have only mildly raised inflammatory markers and a small number of patients will have levels within normal ranges on at least one of the tests.[5,10] If both CRP and ESR are normal, the likelihood of giant cell arteritis being present is reduced, but cannot be ruled out.

A full blood count in people with giant cell arteritis will typically indicate anaemia with a mild leukocytosis and an elevated platelet count.[5]

Liver function tests commonly indicate mildly elevated transaminases and alkaline phosphatase.[5]

Creatinine and electrolytes should also be tested (but do not need to be urgent) to provide a base-line for monitoring in people who are likely to be treated with long-term corticosteroids.

Imaging investigation

Imaging tests may be requested in secondary care, after referral, if there is a suspicion of large-vessel involvement. Ultrasound, computed tomography (CT) and magnetic resonance angiography are the most commonly used imaging techniques.

Differential diagnosis

The most important differential diagnoses to consider in patients with symptoms suggestive of giant cell arteritis include:[7, 12]

- Migraine, intracranial haemorrhage and other causes of headache
- Herpes zoster
- Ear, nose and throat conditions, e.g. temporomandibular joint disorder, sinusitis
- Transient ischaemic attack
- Connective tissue diseases
- Cervical spine disease, e.g. spondylosis, radiculopathy causing cervicogenic headaches
- Other causes of acute visual loss, e.g. central retinal artery occlusion, non-arteritic ischaemic optic neuropathy
- Systemic vasculitides, e.g. Takayasu's arteritis (rare)
- Other significant intracranial pathology, e.g. infiltrative retro-orbital or skull lesions

The management of giant cell arteritis

If the findings from the history and examination strongly indicate giant cell arteritis, after considering possible differential diagnoses, urgent treatment and referral should be initiated. The first steps for most patients should be to provide a prescription for corticosteroids and to contact either an Ophthalmologist or Rheumatologist (depending on local referral criteria) to organise a temporal artery biopsy.

Organise a referral for biopsy

Urgent referral, i.e. within one week, to hospital for biopsy and an assessment of vision is required.[12] If the patient has symptoms of ischaemia, such as visual loss or diplopia, with or without jaw claudication, immediate referral is recommended as these features can indicate the rapid development of permanent visual loss.

> The need for biopsy should never delay treatment. A biopsy can usually still be performed and provide accurate results two to six weeks after initiating corticosteroid treatment,[12] although it should ideally be performed within one week.

Give corticosteroids

Most guidelines recommend oral prednisone 40 – 60 mg, once daily, for patients with giant cell arteritis, with the higher dose used in patients with ischaemic symptoms.[2, 12] In practice, as it can be difficult to rule out the presence of ischaemic involvement in primary care, a dose of 60 mg, once daily, should be used in most patients with suspected giant cell arteritis, and if necessary this can be adjusted once the patient has been assessed in secondary care. It is recommended that the prednisone dose is not less than 0.75 mg/kg, therefore a higher dose, e.g. up to 80 mg, may be given to a larger patient.

For patients who already have visual loss symptoms, consult with the Ophthalmologist or Rheumatologist about the possibility of intravenous corticosteroid treatment. Methylprednisolone (e.g. 1 g IV, daily, for three days) may be used in patients with visual loss at presentation or rapidly developing visual symptoms in order to halt their progression, however, evidence that this approach to treatment is more effective is limited.

The first dose of prednisone should be taken as soon as reasonably possible. The response to treatment is usually rapid, with resolution of most symptoms occuring within several days of starting the medicine. Therefore, a lack of response is

a strong indication that the initial diagnosis may have been incorrect.[12]

The initial dose of prednisone should be maintained for four weeks, or longer if symptoms and laboratory abnormalities remain.[12] Given the significant risk of morbidity associated with a relapse of giant cell arteritis, the prednisone tapering regimen must be slow and cautious. Dose reduction intervals can be lengthened, based on the patient's symptoms and history of relapses with previous dose reductions. A treatment duration of at least one to two years, often longer, should be expected.

As a general guide, the British Society for Rheumatology suggests that the daily dose of prednisone is tapered as follows:[2]

- Maintain the inital dose (40 – 60 mg) for at least four weeks, then;
- Reduce by 10 mg, every two weeks, down to 20 mg, then;
- Reduce by 2.5 mg, every two to four weeks, to 10 mg, then;
- Reduce by 1 mg, every four to eight weeks, provided there are no relapses

For further information on tapering long-term corticosteroids and adverse effects, see "Polymyalgia rheumatica", Page 24.

Additional treatment
Aspirin, 100 mg, daily,* should be considered for patients without contraindications as there is some evidence that it decreases the rate of visual loss and other cerebrovascular complications.[2, 12]

Vitamin D supplements and advice to maintain adequate calcium intake should be given to all patients in order to limit the adverse effects of long-term prednisone treatment.[13] Bisphosphonates should be prescribed to all patients with evidence of reduced bone-mineral density.[5]

For further information on the bone sparing treatment in people treated with long-term corticosteroids, see "Polymyalgia rheumatica", Page 24.

A proton pump inhibitor (PPI), such as omeprazole may be considered for people who experience adverse gastrointestinal affects when taking prednisone, particularly when a NSAID is taken concurrently.[13]

* Most guidelines recommend 75 mg daily, however, this dose formulation is not subsidised in New Zealand.

What is a temporal artery biopsy?

A temporal artery biopsy involves removing a small section of the temporal artery. The surgery is performed as a minor procedure with local anaesthesia.

Due to the patchy inflammation that may be present (termed skip lesions), a minimum of 25 mm of the temporal artery is biopsied to reduce false-negative results; a biopsy on the contralateral artery may be considered if the results of the first biopsy are normal in a patient with strongly suspected giant cell arteritis. The biopsy will be negative in up to 10% of people with giant cell arteritis even with these measures, and a negative result should never be considered final if there are signs and symptoms in conjunction with other laboratory findings that continue to suggest the diagnosis.[12]

Follow-up and monitoring

A follow-up consultation should be scheduled to ensure there are no signs or symptoms of relapse of giant cell arteritis, and to monitor the adverse effects of corticosteroid treatment. The first follow-up appointment should be scheduled within a few days of the inital consultation. Further follow-ups should be scheduled one, three and six weeks later.[12] Follow-up appointments should then occur once every three months, for the duration of corticosteroid treatment.[12]

Advise the patient to return if symptoms of giant cell arteritis or corticosteroid-related adverse effects occur between visits.[2]

Each visit should include an assessment for any residual symptoms, a brief physical examination of the patient and consideration given to testing:[2, 7]

- CRP
- FBC
- HbA_{1c} (fasting serum glucose should be used for the first two months of treatment, as the rise in blood glucose levels due to corticosteroid use is too rapid to be accurately measured with HbA_{1c})
- Creatinine and electrolytes (to monitior the potential adverse effects of steroid treatment)

If CRP was normal, and ESR raised, when giant cell arteritis was diagnosed, monitoring ESR instead of CRP may be more appropriate.

Chest x-ray and abdominal ultrasound to assess for thoracic and abdominal aortic aneurysm is recommended annually, and usually for at least ten years.[2] Assessment of bone mineral density (to monitor the adverse effects of corticosteroid treatment) should also be considered,[2] however, regular bone mineral scans may not be available in all areas of New Zealand.

Relapse is common in people with giant cell arteritis

Relapse of symptoms is relatively common in people with giant cell arteritis, particularly once the dose of prednisone is low, e.g. under 15 mg per day. Relapse should be suspected in patients with a return of symptoms, ischaemic complications, unexplained fever or polymyalgic symptoms.[2] Relapse is managed by increasing the dose of prednisone (Table 1).

If patients have three or more relapses or the dose of prednisone is unable to be tapered without complications, discuss with an Ophthalmologist or Rheumatologist. In some cases, adjunctive treatments such as methotrexate may be considered.

For further information on the use of methotrexate, see "Polymyalgia rheumatica", Page 24.

Table 1: The signs of potential relapse of giant cell arteritis and recommended treatment[12]

Signs	Recommended treatment
A giant cell arteritis-suggestive headache	Treat with the previous dose of prednisone, i.e. if the dose is lowered to 10 mg daily, and headaches occur, move dose back to 12.5 mg daily
Jaw claudication, with or without headache	Return to 60 mg daily, and begin taper again
Visual symptoms	Treat with 60 mg prednisone and arrange ophthalmology referral

Prognosis for people with giant cell arteritis

The majority of patients respond rapidly to the initial treatment with prednisone, and visual loss in treated patients (without preceding visual symptoms) is rare, generally under 1%.[2,7] A treatment course of two to three years is often necessary, with some patients requiring low-dose prednisone for several years thereafter.[2] Corticosteroid-related adverse effects are therefore common, occurring in approximately 60% of patients.[7] Major risks include the development of diabetes mellitus and osteoporotic fractures.[2] Patients should be informed of these adverse effects and may need to be advised to make lifestyle changes to lower their risk of these complications.

The mortality rate of people with giant cell arteritis is not significantly different from the general population.[7] However, the risk of aortic aneurysm is reported to be 17 times greater in people who have had giant cell arteritis, when compared to the general population of the same age and sex, even after timely and successful treatment.[7] Annual monitoring with chest x-ray and ultrasound, and the management of modifiable risk factors, such as hypertension, smoking and central obesity, will help to reduce this risk.

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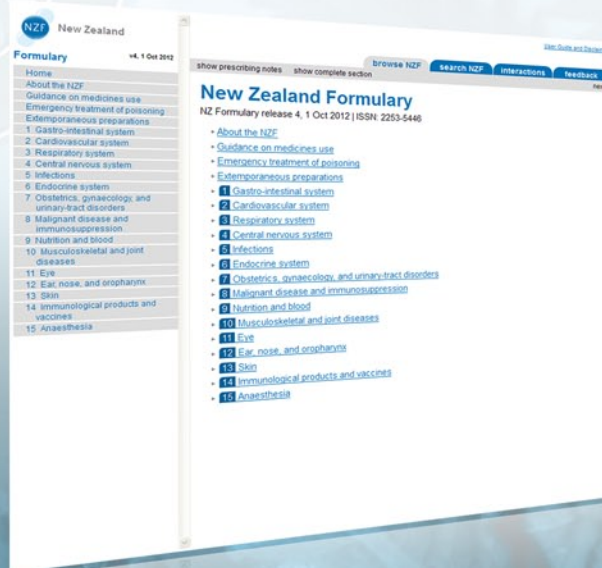
POLYMYALGIA RHEUMATICA:
Look before you leap

Polymyalgia rheumatica is an inflammatory condition that causes a particular pattern of joint pain and stiffness, most commonly in older people. It is a rheumatic disorder closely associated, and often co-existing, with giant cell arteritis. Diagnosis is based on the patient's clinical features, supported by laboratory investigations. Before making a diagnosis, other conditions which can mimic polymyalgia rheumatica should be ruled out, and most importantly, the patient should be assessed for co-existing giant cell arteritis. Treatment of polymyalgia rheumatica, with long-term oral prednisone, can usually be managed in primary care, but referral to a Rheumatologist may be necessary if the diagnosis is unclear, the response to treatment is poor or multiple relapses of symptoms occur during tapering.

What is polymyalgia rheumatica?

Polymyalgia rheumatica is an inflammatory rheumatological syndrome that causes pain and stiffness, most commonly in the neck, shoulders and pelvic girdle. The pain and stiffness is worse in the morning, usually lasts for one hour or more and may be accompanied by systemic features, such as fever, fatigue and anorexia.[1] The onset of symptoms is typically between two weeks and two months.[2]

The incidence of polymyalgia rheumatica increases with age, with an average age of onset of approximately 70 years, and it rarely occurs in people aged under 50 years.[3] The incidence of polymyalgia rheumatica is highest in people of Scandinavian or Northern-European descent, although it does occur in people of other ethnicities.[3] Polymyalgia rheumatica is twice as common in females.[3] In total, the yearly incidence is approximately 50 per 100 000 people aged over 50 years.[4]

It is not known what causes polymyalgia rheumatica. It is closely associated with giant cell arteritis, although it is two to three times more common.[2] Like giant cell arteritis, both genetic and external factors, e.g. infection, are thought to be involved in the development of the condition.[3]

Polymyalgia rheumatica is managed with corticosteroids and significant remission of symptoms can be expected within one week of starting treatment.[5] The prognosis is usually good and complications, such as recurrent relapse of symptoms, are limited.[3]

Never trust a diagnosis of polymyalgia rheumatica

As polymyalgia rheumatica has a non-specific clinical presentation and few significant sequelae, it should be diagnosed with caution. Ruling out other illnesses, such as cancers or insidious-onset rheumatoid arthritis, is more important than immediately treating polymyalgia rheumatica, if it is present. Unlike giant cell arteritis, a delay in treatment will not significantly endanger a patient. Conversely, long-term corticosteroid treatment can have significant adverse effects and a daily treatment course of up to three years will be a burden for many people. In addition, an initial or partial response to corticosteroids may be seen in people with other conditions who present with similar features to polymyalgia rheumatica, such as rheumatoid arthritis, and this may provide false reassurance that the correct diagnosis has been identified. Therefore, even if a patient presents with clinical features typical of polymyalgia rheumatica, and a working diagnosis is made, they should be regularly reviewed and other possible causes always considered, particularly if the patient does not respond to treatment.

Making a diagnosis

The British Society for Rheumatology has developed a set of inclusion and exclusion criteria for diagnosing polymyalgia rheumatica.[6] These criteria were derived by consensus and represent a clinically typical patient with polymyalgia

rheumatica. They are most useful for "ruling in", i.e. a patient who meets the criteria is likely to have polymyalgia rheumatica, rather than "ruling out", as people with polymyalgia rheumatica can present atypically, such as with a shorter duration of symptoms or found to have a normal acute phase response.

The core inclusion criteria are:[6]

- Age > 50 years
- Symptom duration > two weeks
- Bilateral shoulder or pelvic girdle aching, or both
- Morning stiffness duration of > 45 minutes
- Evidence of an acute-phase response, e.g. raised CRP

The core exclusion diagnoses are:[6]

- Infection
- Malignancy
- Giant cell arteritis

Patient presentation, history and examination

Shoulder, neck, hip and pelvic pain

Shoulder pain occurs in 70 – 95% of people with polymyalgia rheumatica.[2] Between 50 – 70% of people report hip and neck pain.[2] Upper arm pain is also common. Pain is usually bilateral and symmetrical, although it may be worse on one side early in the course of the condition.[3] Pain will usually worsen with movement of the affected area. Pain may radiate to the elbows and knees.[3] There may be tenderness on examination, most commonly in the upper arms, neck and shoulders, usually related to synovial or bursal inflammation. Muscle weakness is not a feature of polymyalgia rheumatica, although this may be difficult to assess due to muscle pain.[5]

Stiffness

Marked morning stiffness that persists for at least 45 minutes is typical for people with polymyalgia rheumatica.[6] The patient may describe difficulties with daily activities, such as brushing their hair or getting out of bed. In some patients the stiffness will be so severe that rising from a chair or turning over in bed are difficult. Asking the patient about the severity of stiffness in the morning compared to the evening may be helpful. Stiffness and pain that lessens over the course of the day can be important in differentiating polymyalgia rheumatica from other forms of degenerative arthritis, which usually cause pain or stiffness that is worse with activity and worse later in the day.[1]

Systemic symptoms and signs

Systemic features may be present in approximately one-third of patients and include low grade fever, malaise, anorexia and weight loss.[2] A brief general examination, including assessment of temperature, pulse and blood pressure, is recommended.

Peripheral symptoms

Symptoms, such as pain or stiffness in the joints of the hands and feet, are present in approximately half of people with polymyalgia rheumatica, however, peripheral symptoms are also common in other, similar conditions, such as rheumatoid arthritis and other inflammatory arthritides.[2] A predominance of peripheral symptoms may suggest an alternative diagnosis, such as rheumatoid arthritis.[3] It is important to also examine the hands, feet, knees and elbows for signs of joint inflammation.

> **Giant cell arteritis symptoms**
> Always specifically enquire about symptoms that may suggest giant cell arteritis, such as unilateral temporal headaches, scalp tenderness, jaw claudication or visual symptoms.[3]
>
> For further information, see: "Giant cell arteritis", Page 16.

Differential diagnosis

The differential diagnosis of polymyalgia rheumatica is critically important, particularly for atypical cases, or where inflammatory markers are normal. Incorrectly diagnosing polymyalgia rheumatica and missing a diagnosis such as cancer or an occult infection can have significant consequences. Conversely, a patient with polymyalgia rheumatica who remains untreated in the short term is unlikely to have any significant adverse effects. The aim should be to rigorously exclude all other possibilities rather than quickly diagnosing polymyalgia rheumatica. Atypical clinical features such as age < 60 years, chronic onset (longer than two months), lack of shoulder involvement, muscle weakness, peripheral joint disease, predominance of pain with little or no stiffness, prominent systemic features, a very high or normal CRP (see "Laboratory investigations") or lack of response to a trial dose of prednisone (see "Treatment of polymyalgia rheumatica") should lead to consideration of alternative diagnoses and consultation with a Rheumatologist where necessary.

Conditions that should be considered include:[3, 6]

- Giant cell arteritis
- Malignancy

- Rheumatoid arthritis and other arthritides
- Endocrine and iatrogenic causes of proximal myopathy, e.g. hypothyroidism, Cushing's disease, statin-induced myopathy/myalgia
- Osteoarthritis and other degenerative musculoskeletal conditions, e.g. rotator cuff tendinopathy
- Systemic lupus erythematous or polymyositis
- Fibromyalgia and localised causes of pain
- Occult infection, e.g. sub-acute bacterial endocarditis

Laboratory investigations

If the patient's presentation suggests polymyalgia rheumatica is likely, the following tests should be requested:[4–6]

- C-reactive protein (CRP)
- Full blood count (FBC)
- Liver function tests (LFTs)
- Creatinine and electrolytes – as a baseline prior to initiation of corticosteroid treatment

An elevated CRP level in a patient with symptoms of polymyalgia rheumatica should increase suspicion of the condition.[6] However, a normal acute phase response does not rule out polymyalgia rheumatica. ESR is sometimes recommended in the literature, however, CRP alone is likely to be sufficient to aid the diagnosis of polymyalgia rheumatica in most people. In addition, some laboratories will no longer accept requests for ESR outside of a limited range of conditions. If the initial CRP is normal, and the patient's symptoms strongly suggest polymyalgia rheumatica, it may be appropriate to then request an ESR at follow-up.

Most patients with polymyalgia rheumatica have mild-to-moderate anaemia, and may have elevated white blood cell and platelet levels.[2] Approximately one-third of patients will have mildly abnormal liver function tests, particularly alkaline phosphatase.[2]

Depending on the patients symptoms and signs, additional tests may need to be added to rule out other potential diagnoses, including:[6]

- Thyroid stimulating hormone (TSH)
- Rheumatoid factor and, potentially, anticyclic citrullinated peptide (anti-CCP) antibodies
- Serum protein electrophoresis (consider serum free light chain assay if electrophoresis is negative)
- Creatine kinase
- Antinuclear antibodies

Distinguishing polymyalgia rheumatica from rheumatoid arthritis

Rheumatoid arthritis can be a challenging condition to differentiate from polymyalgia rheumatica, particularly in patients who are subsequently found to have seronegative or late-onset rheumatoid arthritis.[3] Although the initial clinical presentation can be very similar with many overlapping symptoms and signs, the following features may help distinguish between the two conditions:

- Polymyalgia rheumatica is rare in people aged < 50 years, therefore rheumatoid arthritis is a much more likely diagnosis in this age group[5]
- The onset of symptoms tends to be more gradual in people with rheumatoid arthritis
- Typically, symptoms of pain and swelling in the smaller distal joints are more common in people with rheumatoid arthritis, however, approximately half of people with polymyalgia rheumatica will also have involvement of the peripheral joints[3]
- Characteristically the wrist and metacarpophalangeal (MCP) joints are affected in people with rheumatoid arthritis, therefore a patient presenting with myalgia and clinical evidence of symmetric synovitis in the wrists or MCP joints is more likely to have a diagnosis of rheumatoid arthritis than polymyalgia rheumatica[3]
- A family history may increase the individual risk of rheumatoid arthritis, and should be considered[7]

If the clinical diagnosis remains uncertain:

- Rheumatoid factor should be requested, however, a negative test does not rule out the condition as some patients will have seronegative rheumatoid arthritis. If there is still doubt about the diagnosis, anti-CCP antibodies may be useful.[2]
- X-rays of affected joints may show erosive changes consistent with rheumatoid arthritis

A trial of treatment with corticosteroids can be considered in patients who are seronegative for rheumatoid factor and have symptoms and signs that could be indicative of either condition. In a patient with polymyalgia rheumatica there is likely to be a rapid, strong clinical response to low dose prednisone (15 mg). If the patient has rheumatoid arthritis, the response to low dose prednisone is likely to be less pronounced.[3,8] In some patients, clinical features more characteristic of rheumatoid arthritis may evolve during the trial of corticosteroid.

Imaging is not essential for diagnosis

If ultrasound is accessible, assessment of the shoulder and hip joints can be considered.[6] Bursitis and synovitis are common manifestations of polymyalgia rheumatica.[2] Plain x-rays of affected joints will usually be normal and therefore are not required for investigating polymyalgia rheumatica.

Additional investigations such as CT scanning, and MRI imaging may be used in a secondary care setting to help identify bursitis, synovitis or tenosynovitis in the shoulders and hips in atypical cases, and for ruling out other potential diagnoses.

Treatment of polymyalgia rheumatica

Corticosteroids are the first-line treatment for polymyalgia rheumatica. Corticosteroid treatment is predominantly for symptom control, and there is no clear evidence that it will alter the natural history of the condition, which is largely self-limiting.

Once all other differential diagnoses have been considered, the patient should be assessed for response to an initial dose of prednisone, 15 mg, daily.[6] The dose should be taken in the morning, with food.

If the patient reports a significant improvement in their symptoms within one week, this is consistent with polymyalgia rheumatica, and treatment can continue.[6] Alternative diagnoses should be considered if there is a minimal response to corticosteroid treatment.

The patient's acute phase response, measured with CRP, should normalise within four weeks.[6]

The British Society for Rheumatology guidelines suggests the following method for titrating the dose of prednisone in people with polymyalgia rheumatica:[6]

- Initial dose – 15 mg, once daily, for three weeks, followed by;
- 12.5 mg, once daily, for three weeks, followed by;
- 10 mg, once daily, for four to six weeks, followed by;
- A reduction of 1 mg from the daily dose, every four to eight weeks

In practice, Rheumatologists may use a faster tapering regimen to lessen exposure to prednisone, such as reducing the dose every two weeks, down to 10 mg, followed by reductions of 1 mg per month, depending on the patient's symptoms. If the patient is at higher risk of adverse effects from long-term steroid use, e.g. is elderly or has co-morbidities, discuss an appropriate dosing regimen with a Rheumatologist.

If symptoms of polymyalgia rheumatica reoccur during the dose tapering period, return the patient to their previous steroid dose and then re-start the taper again from that point. The low dose "tail" of the taper will need to be very gradual in some people to prevent symptom recurrence. Some patients will require treatment with low-dose corticosteroids for two to three years due to recurrent relapses.

Vitamin D supplements should be prescribed alongside long-term corticosteroid treatment for all people with polymyalgia rheumatica. Adequate dietary calcium, or supplementation if this is not possible, is also necessary.

Bisphosphonates should be considered in patients with a previous history of fragility fractures or reduced bone-mineral density.[6]

A proton pump inhibitor (PPI), such as omeprazole may be considered for people who experience adverse gastrointestinal affects when taking prednisone.[6]

For further information, see "Practical consideration when prescribing long-term corticosteroids".

Follow-up of people with polymyalgia rheumatica

Early follow-up to assess the response to treatment is recommended. A follow-up consultation should be scheduled within a few days after starting corticosteroid treatment, and then further follow up appointments scheduled one, two, three and six weeks later, where possible. Follow-up should then occur once every three months for the duration of corticosteroid treatment.

A history and clinical examination including an assessment for symptoms and signs of giant cell arteritis, such as scalp tenderness, temporal artery tenderness and new-onset or new type of headache, should be included in each follow-up. If symptoms of giant cell arteritis arise, the patient should be presumed to have the condition, and referred to secondary care for temporal artery biopsy.[6] Also assess for symptoms and signs of corticosteroid adverse effects (see: "Practical considerations when prescribing long-term corticosteroids" for further information).

Clinical signs and symptoms are the primary marker for relapse,

with laboratory tests providing supporting information only.[1] CRP, FBC, creatinine, electrolytes and HbA_{1c} tests* (due to the increased risk of diabetes in people taking long-term steroids) are recommended at each follow-up consultation,[6] however, in practice, not all tests would be necessary in each follow up appointment and this is based on clinical judgement.

Relapses of polymyalgia rheumatica symptoms should be treated with a return to the higher, previous dose of prednisone.[6] After two relapses, consideration should be given to a trial of disease-modifying anti-rheumatic drugs (DMARDs), usually methotrexate.[6] This will require consultation with a Rheumatologist, and if a DMARD is prescribed,

regular monitoring is necessary. The dosing and monitoring regimen should be decided upon in consultation with the Rheumatologist. Methotrexate is usually continued until the corticosteroids can be tapered without the recurrence of polymyalgia rheumatica symptoms.[4] Once the steroids have been successfully tapered, methotrexate can usually be tapered over approximately three months.[4]

* A fasting glucose test should be used for monitoring in the first two months of steroid treatment, as serum glucose will rise too rapidly to be accurately captured by HbA_{1c}. After two months, an HbA_{1c} test can be used.

Practical considerations when prescribing long-term corticosteroids

Corticosteroids are associated with significant adverse effects and they must be slowly tapered rather than stopped abruptly. The lowest effective dose should be used, then tapered and stopped as soon as possible.

The following practice points should be considered whenever a patient is prescribed corticosteroids long-term:[9]

- The patient's co-morbidities and risk factors for adverse effects should be evaluated and managed where indicated, these include; hypertension, diabetes, peptic ulcer, recent fractures, cataract/glaucoma, chronic infection, dyslipidaemia and concurrent NSAID use
- During the course of treatment, monitor body weight and blood pressure, assess for peripheral oedema and heart failure and test serum lipids, HbA_{1c} (or fasting glucose in the first two months) depending on the individual patient's risk of adverse effects, dose and duration
- If the patient's dose is ≥ 7.5 mg, daily, for more than three months, vitamin D supplementation is necessary, along with adequate dietary calcium
- Bisphosphonates should be prescribed to patients with risk-factors for osteoporosis
- Patients treated with corticosteroids and NSAIDS should be given appropriate gastro-protective medicines, usually a proton pump inhibitor

- Patients taking corticosteroid treatment for longer than one month, who need to undergo surgery, will require perioperative management with adequate glucocorticoid replacement to overcome potential adrenal insufficiency

Tapering the dose

Tapering must be done carefully to avoid relapses of the condition and potential adrenal deficiency resulting from hypothalamic-pituitary-adrenal axis (HPA) suppression. Higher doses of corticosteroid, e.g. 20 mg daily, for more than three weeks, or bedtime dosing increase the likelihood of HPA axis suppression. Higher doses also increase the likelihood of adverse affects. The taper is usually started as soon as symptoms are under control. The dose is reduced by 10% every two to four weeks depending on the severity of symptoms, response to prednisone and the starting dose. The individual condition being treated will alter the length of the taper, e.g. in a person with polymyalgia rheumatica, the course of treatment is usually two to three years, with a gradual taper period. The dose of prednisone should be titrated against the patient's symptoms, not their acute phase response, i.e. the dose may not need to be increased when the CRP rises if the patient remains asymptomatic.

The adverse effects of corticosteroid treatment

Adverse effects of corticosteroids include:[10]

- Skin changes and disorders, e.g. thinning and bruising, striae, acne, alopecia and hirsuitism
- Body composition changes, e.g. weight gain, Cushingoid features
- Ocular disorders, e.g. glaucoma and cataracts
- Cardiovascular disease
- Gastrointestinal disorders, e.g. dyspepsia, oesophagitis, gastritis, ulcers, bleeding
- Osteoporosis
- Central nervous system changes, e.g. mood changes, restlessness, depression, psychosis
- Diabetes
- Renal changes, e.g. hypertension and fluid retention

Older age, higher cumulative doses of corticosteroids and female sex increase the risk of adverse effects occurring.[11]

Preventing the adverse effects of corticosteroids

Vitamin D supplements should be prescribed alongside long-term corticosteroid treatment, in patients taking doses of ≥ 7.5 mg, daily, for more than three months.[9] Colecalciferol* 1.25 mg, once monthly, is recommended for vitamin D supplementation.[10] Patients do not need their vitamin D levels to be tested, but if they have been, and severe deficiency has been detected, a loading dose of one 1.25 mg tablet, daily for ten days is recommended.[10] Calcitriol, 500 – 750 nanograms, daily, can be used instead of colecalciferol for patients with severe renal impairment.[10]

* Recommended International Non-proprietary Names (RINN or INN) spelling

Calcium supplementation is also recommended, but there have been concerns that calcium supplementation may increase cardiovascular risk, particularly in older people.[12, 13] General dietary advice may be more appropriate for most people, and supplementation reserved for people in whom dietary calcium intake alone is insufficient. If calcium supplementation is required, oral calcium carbonate 1.5 g, daily, can be considered.[10]

Ideally a bone-mineral density (BMD) scan of the lumbar spine and hip should be requested for patients when starting long-term corticosteroids, however, this depends on the availability and funding of the local service, e.g. some services require that patients have been taking corticosteroid treatment for three months before a scan is prioritised.[2]

Bisphosphonates should be considered in patients with a previous history of fragility fractures or reduced bone-mineral density.[6] Alendronate or zoledronic acid are recommended for most people who require a bisphosphonate for corticosteroid-related osteoporosis prevention, based on patient preference and the expected length of corticosteroid treatment.

Alendronate, 70 mg, once weekly, should be taken first thing in the morning, on an empty stomach, with a full glass of water to ensure adequate absorption.[10] The patient should then refrain from eating or taking other medicines and remain upright (i.e. sitting or standing) for thirty minutes to minimise the risk of oesophageal irritation or erosion.

Zoledronic acid, 5 mg IV infusion over 15 minutes, once per year is an alternative.[10] The patient should be well hydrated prior to starting the infusion. The patient should have their renal function assessed prior to starting, and be informed that dizziness and influenza-like symptoms are common after infusion.

The Special Authority requirements for the initial application for either alendronate or zoledronic acid require that:

- The patient is receiving systemic glucocorticosteroid treatment (≥ 5 mg per day prednisone equivalent) and has already received or is expected to receive treatment for at least three months, and;
  - The patient has documented BMD ≥ 1.5 standard deviations below the mean normal values in young adults (i.e. T-Score ≤ 1.5), or;
  - The patient has a history of one significant osteoporotic fracture demonstrated radiologically, or;
  - The patient has had a Special Authority approval for alendronic or zoledronic acid* (underlying cause – glucocorticosteroid therapy) or raloxifene

* If either alendronate or zoledronic acid has been approved, and the other bisphosphonate is to be trialled, then the patient is considered to have already meet the requirements for the new medicine.

If a funded bisphosphonate is required, but the patient does not meet the Special Authority requirements of alendronate or zoledronic acid, etidronate disodium may be used, however, etidronate is significantly weaker than either alendronate or zoledronic acid.

Etidronate disodium is prescribed at 400 mg, daily on and empty stomach, for 14 days, repeated every three months.

Risedronate, an alternative to alendronate, is to be listed on the Pharmaceutical Schedule, without restrictions, from 1 September, 2013.

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Smoking prevention and cessation in adolescents:

Changing futures, saving lives
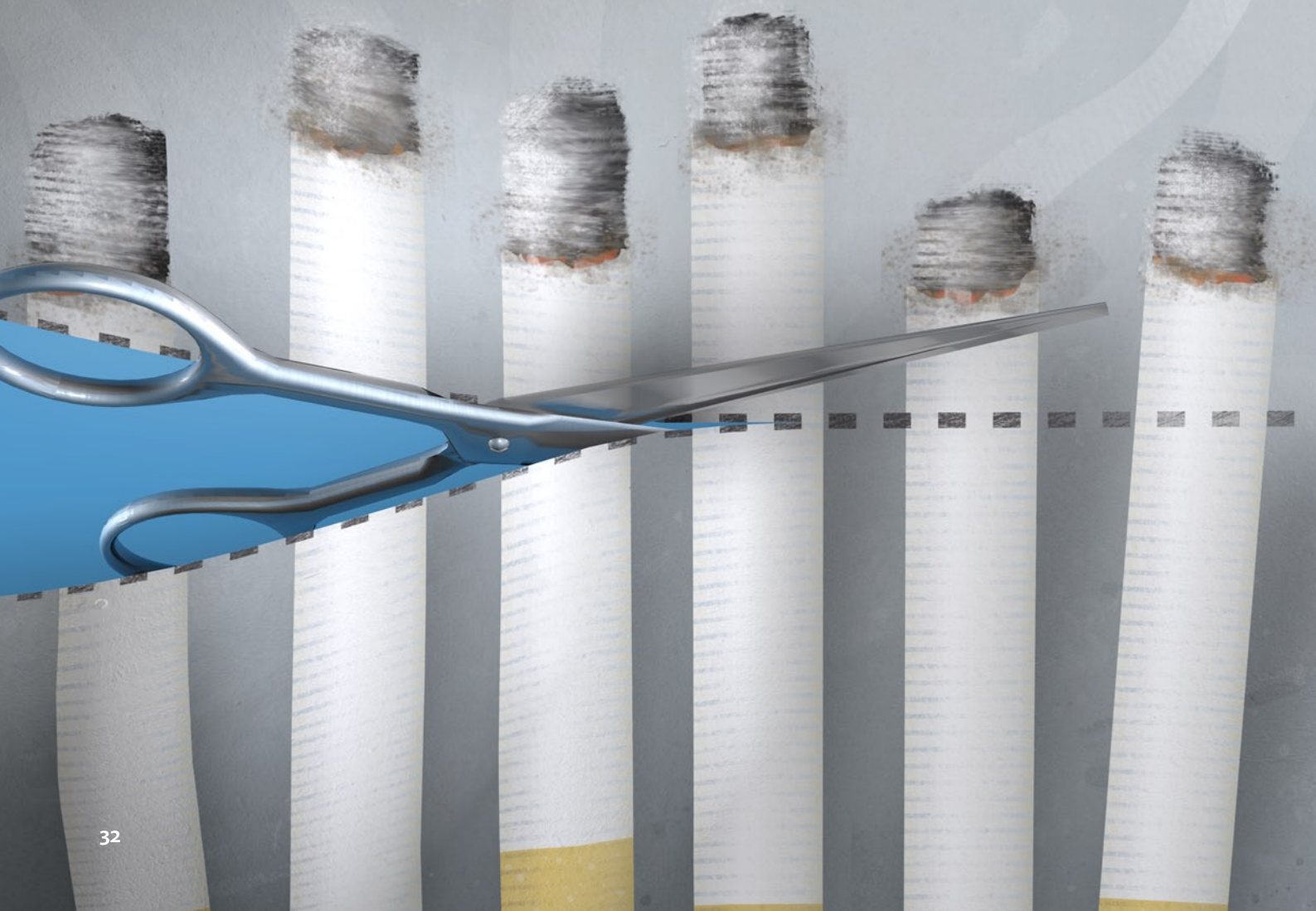
On average, New Zealanders who smoke try their first cigarette between the ages of 11 and 12 years. There are large ethnic disparities in the rate of smoking, with Māori females having the highest rate of smoking among all adolescents. Encouraging smoke-free homes, parental involvement in smoke-free messages and participation in extra-curricular activities, e.g. sport, are important early anti-smoking strategies. Smoking can be a marker for substance misuse and mental health disorders, so adolescents who regularly smoke should have an assessment of their wellbeing using a standardised tool, e.g. HEEADSSS. Where appropriate, adolescents can be referred to a smoking cessation service. Nicotine replacement therapy (NRT) may be considered for some young smokers who are dependent upon nicotine. Other smoking cessation medicines are not recommended for use in people aged under 18 years.

Smoking in New Zealand adolescents

More than 80% of people who smoke are reported to start before age 18 years.[1] Preventing adolescent smoking and supporting cessation attempts are important ways to reduce the rate of smoking in New Zealand. The average age that Māori youth begin smoking is 11.5 years and the average for non-Māori is age 12.7 years.[2] This emphasises the need for early discussion about the dangers of smoking with children and their whānau/families.

The good news is that the rate of daily smoking* among New Zealand adults has decreased by approximately one-third since the mid-1990s.[3] There has also been a large decrease in the rate of daily smoking in adolescents aged 15 – 17 years from 14% in 2006/07 to 6% in 2011/12.[3] However, there is still a lot of work to be done to reach the goal of a smoke-free New Zealand.

Smoking is most prevalent in Māori and Pacific peoples

In New Zealand, rates of current smoking* are unacceptably high, most notably among Māori (41%) and Pacific peoples (26%) compared to Europeans (17%).[3] This disparity is most pronounced in Māori females aged 15 – 19 years, who are over 3.5 times more likely to smoke (47.1%) than non-Māori females (13.1%) in the same age group.[2] In Māori males aged 15 – 19 years, the rate of current smoking is 29.2% compared to 14.4% in non-Māori males.[2]

Socioeconomic deprivation is associated with an increased rate of smoking,[4] however, the increased rates of smoking among Māori and Pacific peoples cannot be solely attributed to differences in socioeconomic status.[5]

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* Daily smoking is defined as at least one cigarette per day. Current smoking is defined as smoking at least one cigarette in the last 30 days and more than 100 cigarettes in a lifetime.

Preventing smoking before it starts

Every consultation with a young person is an opportunity to discuss smoking. Ask about and record smoking status in the patient record, and respond in a positive way each time a patient says that they do not, or no longer smoke. Reinforcing the decision not to smoke as being positive and successful as well as emphasising the negative consequences of the behaviour are key prevention messages. Smoking is known to increase the risk of blood clotting in females taking oral contraceptives, therefore a consultation about contraception is an excellent opportunity to also reinforce an anti-smoking message to young females.[6]

N.B. The tool "Ask about smoking status, give Brief advice and make an offer of help to stop, and provide evidence-based Cessation support (ABC)", is recommended for use in all patients, including adolescents (see: "What to do once an adolescent has started smoking?").[7]

Communicating with adolescents and their whānau

Adolescents are often concerned about confidentiality and issues relating to trust and embarrassment.[8] It is therefore important to stress that the confidentiality of anything the adolescent discloses will be respected. Asking about and acknowledging the cultural background of a patient is important in building a trusting and open relationship and can help to overcome barriers. Communication with adolescents is more successful when it is perceived as being non-judgemental.[9] Patience, good listening skills and asking open ended questions are other qualities that are valued in consultations by adolescents.[9] At the end of a consultation ask the patient about their understanding of what has been discussed – ensure that the messages being communicated are the same messages that have been received. Displaying posters in the practice that target youth issues can enhance the youth-friendliness of a practice.

Deliver a consistent smoke-free message to all whānau/family members. Children from families where the parents have clearly expressed views that smoking is bad are less likely to begin smoking – even when the parents themselves smoke.[10] The Dunedin Longitudinal Study which has followed a cohort born between 1972 – 1973, found that inconsistent parental advice about smoking, i.e. only one parent objected to smoking, resulted in a 50% increased likelihood of smoking in adulthood.[11]

Children with parents who smoke are more likely to be the "early adopters" of smoking in their peer group.[12] Reducing parental smoking therefore may have a wider benefit beyond the family unit by reducing the transmission of smoking through peer groups. This effect is likely to be most pronounced in adolescent females who are more strongly influenced by peers than adolescent males.[13]

Encourage adolescent participation in sport and cultural activity. Research has shown that participation in sport protects adolescents against starting smoking.[14, 15] Extra-curricular activity has additional importance during adolescence when the decision to smoke, or not to smoke, is thought to be an important identity statement. Analysis of group discussions between New Zealand adolescents aged 14 – 15 years found that smoking was generally associated with increased social status, which is consistent with international studies.[16, 17] Non-smokers were generally viewed as being "in the middle" or being "average" and required other strategies, e.g. sport or music, to define their status among their peers.[16]

Increased parental supervision or interaction may decrease smoking. Adolescents who do not receive parental supervision after school are more likely to smoke than those who do. A survey of New Zealand adolescents aged 14 – 15 years from 145 high schools found that higher amounts of parental monitoring outside of school hours had an increasingly protective effect against adolescent smoking.[15] It was also found that adolescents who were the least attached to their parents were more likely to smoke than adolescents with a stronger family attachment, across all ethnicities studied.[15]

What to do once an adolescent has started smoking?

It is recommended that all people who smoke should be advised to stop and be offered cessation assistance in the ABC format each time they visit primary care. This should be delivered regardless of the patient's age, readiness to stop smoking, and how frequently or how long they have been smoking for. Evidence-based support should then be provided to all people who want to stop smoking.[7] It is now recognised that this offer of support is the most important part of the of the ABC approach.[19]

Act early before nicotine dependence develops

The progression from occasional smoker to nicotine dependence generally follows a series of predictable steps during adolescence. In the first months after beginning smoking there is often a naïve self-confidence in the ability to stop.[20] This may be rapidly followed by a desire to quit and a realisation that this is difficult.[20] Over the following two years cravings, withdrawal symptoms and tolerance develop as smoking escalates and confidence in the ability to quit declines.[20] Full nicotine dependence develops, on average, approximately one year later.[20] Adolescents who begin smoking at a young age can therefore become dependent upon nicotine by the age of 14 or 15 years.

Smoking in families is a "vicious cycle"

Adolescent smoking is strongly influenced by exposure to parental smoking, and adult smoking is in turn, correlated with socio-economic disadvantage during childhood.[18] Other factors associated with adult smoking are cognitive ability during childhood, educational achievement, conduct, and again, exposure to parental and peer smoking.[18] Smoking within disadvantaged communities therefore creates a self-perpetuating negative family cycle.

Perform a HEEADSSS assessment

It is recommended that adolescents have a regular assessment of their psychosocial wellbeing using a standardised tool, such as HEEADSSS (Home, Education, Eating, Activities, Drugs, Sexuality, Suicide, Safety).[21] Smoking is a potential marker for other substance misuse, depression and anxiety disorders in adolescents, particularly amongst females.[22] There is evidence that mental health problems during adolescence often precede smoking and that young people with mental health problems start smoking at a younger age.[22]

For further information on performing a HEEADSSS assessment see: "Substance misuse in adolescents" BPJ 42 (Feb, 2012).

Deciding which cessation interventions are appropriate

The majority of available evidence on smoking cessation interventions relates to adults, particularly regarding medicines. An estimate of a young person's nicotine dependence can be used to determine which cessation intervention (or combination) is most appropriate. The best question to assess nicotine dependence is: "How soon after waking do you usually have your first cigarette?"[23] If a person smokes within 30 minutes of waking they have a high degree of dependence and are more likely to benefit from medical assistance when attempting to stop smoking.[23] Smoking more than ten cigarettes a day and a history of withdrawal symptoms in previous quit attempts are also markers for nicotine dependence.[24]

Managing cues for smoking
Smoking is often associated with cues, such as drinking caffeine or alcohol, or social situations. Due to the high value adolescents place on their social environment, peer influence is an important cue for smoking. Supporting adolescents to say "no" is an essential part of smoking cessation treatment. This can be done by discussing ways in which the young person can become more confident in managing scenarios where they feel pressured to smoke.[25] To do this, focus on something that is important to the adolescent and incorporate this into a response that they can use to decline smoking, e.g. "The coach says he won't pick smokers in the 1st XV, and rugby is more important to me."

Increasing physical activity can decrease smoking
Physical activity can be an effective smoking cessation intervention for adolescents if smoking has started. A study of over 200 American adolescents aged 14 – 19 years found that students who increased the number of days they performed at least 20 minutes of exercise were significantly more likely to reduce their daily cigarette use.[14] Additionally, physical activity may help in reducing withdrawal symptoms and stress in young people attempting to stop smoking.

Consider referral to a smoking cessation service
Quitline offers a phone-based smoking cessation service which can be accessed six days a week (Monday – Friday 8 am – 9.30 pm, Sunday 10 am – 7.30 pm) on 0800 778 778, by a person of any age. Quitline now accepts electronic referrals via Patient Management Systems with this feature enabled. Quitline also operates a Txt2Quit service which sends tips and cessation support directly to mobile phones. Further information is available from: **www.quit.org.nz**

Aukati KaiPaipa is a free, face-to-face smoking cessation service for Māori of all ages delivered from over 30 centres within New Zealand. The programme involves coaches creating a smoking reduction plan, often involving the support of a school counsellor. Cessation follow-ups are conducted by phone, or in person. To find the nearest provider visit: **www.aukatikaipaipa.co.nz/contact-us**

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

Pacific smoking cessation services for people of all ages, with quit coaches fluent in Pacific languages, are available in the Auckland, Hamilton, Wellington and Christchurch regions. Further information is available from: **www.talapasifika.org.nz**

Social media-based cessation support is available
"Smoking Not Our Future" is a campaign run by the Health Promotion Agency that is aimed at young people. The campaign is delivered via a Facebook page, with educational material and tips for stopping smoking and support from New Zealand celebrities. Further information is available from: **www.facebook.com/notourfuture**

Nicotine replacement therapy (NRT)
New Zealand smoking cessation guidelines state that nicotine replacement therapy (NRT) can be prescribed for young people aged over 12 years who are dependent on nicotine if the health professional believes that it will assist the person to stop smoking.[23] However, NRT alone is not likely to address the reasons why an adolescent has begun, and continues to smoke.[23] There is little evidence that the use of NRT, or other smoking cessation medicines, in adolescents will improve rates of smoking cessation after six months.[25]

Table 1: Guidance on prescribing of fully subsidised nicotine replacement therapy (NRT) for adults,* adapted from McRobbie, 2013[27]

	Patch (24-hour)	Gum	Lozenge
Product information	Three strengths (7 mg, 14 mg and 21 mg)	Two strengths (2 mg and 4 mg)	Two strengths (1 mg and 2 mg)
Instructions for use	Apply to clean, dry and hairless skin. Remove old patch and apply new patch, daily, to a different area of skin; press in place with hand for 10 – 20 seconds. Slight redness under the patch is normal. If sleep disturbance is reported, remove the patch overnight.	Bite to release the peppery taste and then rest between cheek and gums. Chew when taste starts to fade. Discard after approximately 30 minutes.	Suck to release the peppery taste and then rest between check and gum. Suck again when taste starts to fade. Discard after approximately 30 minutes.

Product and dosage	**A guide to product choice:**

A guide to product choice:

- Smoking a cigarette within 30 minutes of waking or smoking ten or more cigarettes per day: recommend 21 mg/24 hour patch and/or gum or lozenge
- Fewer than ten cigarettes per day: recommend gum or lozenge
- Oral product not tolerated: recommend a 14 mg/24 hour patch and review the dose within one week

A guide to dosage:
Use time to first cigarette to guide dose of gum and lozenge.

- If within an hour of waking use 4 mg gum or 2 mg lozenge
- If after an hour of waking use 2 mg gum or 1 mg lozenge

The dose of NRT can be increased if the patient reports significant withdrawal symptoms. All products should be used for eight to 12 weeks. If gum or lozenges are used in combination with nicotine patches, the lowest dose oral medicine should be used and a maximum of twelve pieces or lozenges taken daily.[28]

* Most people who attempt to stop smoking do not use enough NRT. The suggested doses here differ from those listed on the product packaging to account for this. If the patient feels nauseated then the frequency or dose of the product should be reduced.[27]
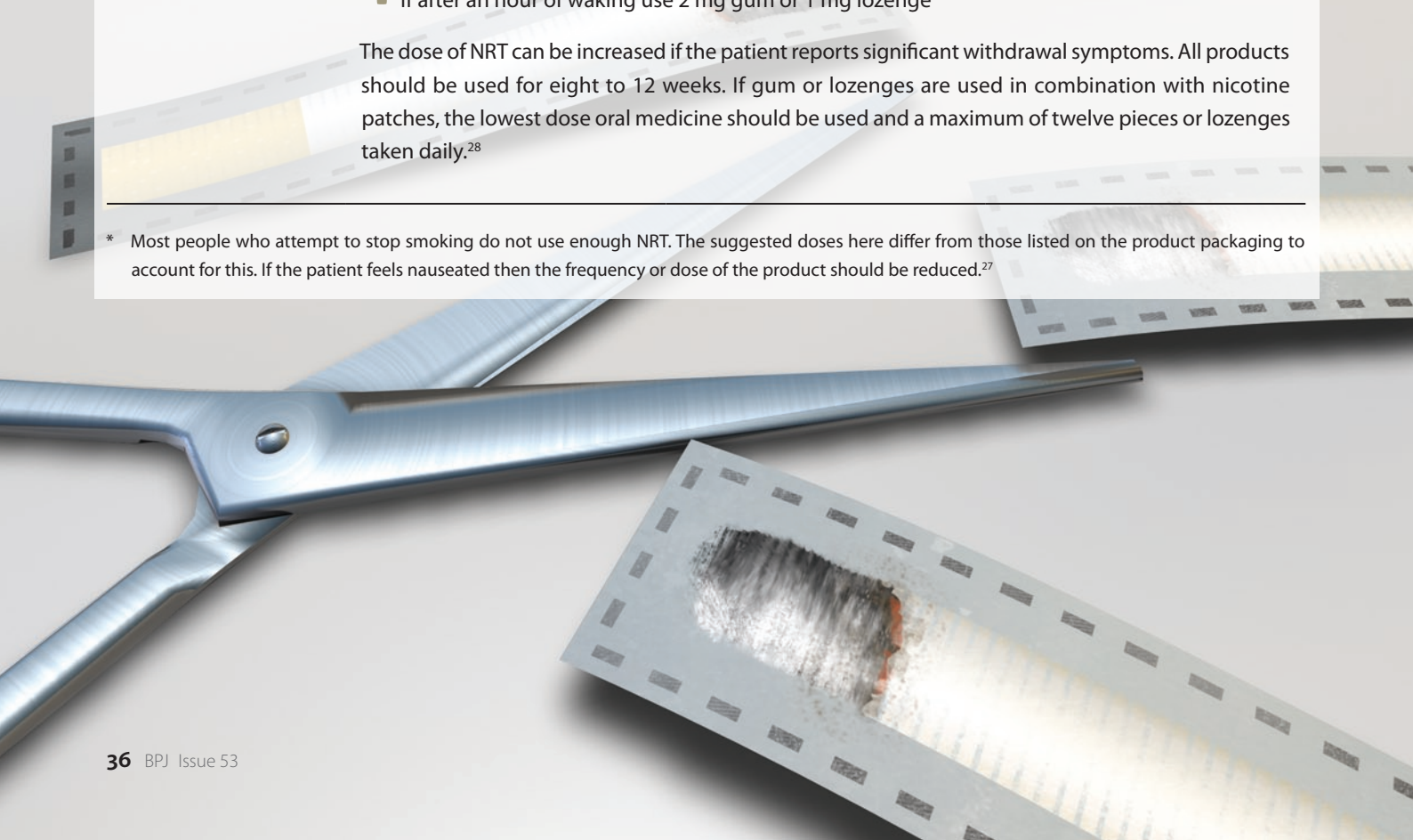
There is no specific guidance for dosing NRT in adolescents therefore adult guidelines are followed (Table 1). Adolescents may experience less severe nicotine withdrawal symptoms than adults (see "Smoking and the adolescent brain"), therefore a shorter course or lower dose of NRT may be appropriate in individual patients. Adolescents who smoke their first cigarette within 30 minutes of waking, or who smoke more than ten cigarettes a day, are more likely to benefit from the use of nicotine patches. Trans-buccal NRT is more appropriate than patches for adolescents who smoke less than ten cigarettes per day. NRT is not appropriate, however, for young people who only smoke in social situations.[23]

There is no evidence of specific safety issues arising from the use of NRT in adolescents and safety concerns should not be a barrier to NRT use.[23, 26]

Other nicotine products which are available but not subsidised include nasal spray (10 mg), inhalation cartridges (10 and 15 mg) and 5 mg, 10 mg and 15 mg per 16 hour patches, which may be appropriate for adolescents who do not want to be exposed to nicotine overnight.[28]

Other medicines are not recommended

The safety of bupropion and nortriptyline as smoking cessation medicines has not been established in people aged under 18 years and New Zealand guidelines list age under 18 years as a precaution for use of both these medicines.[23, 28] A Cochrane review found limited evidence that bupropion by itself was not effective as a smoking cessation medicine in young people.[25] Varenicline use is not recommended in people aged under 18 years.[28]

Smoking and the adolescent brain

The adolescent brain is thought to be more susceptible to nicotine addiction than the adult brain. The proposed mechanism responsible for this is the mesolimbic dopamine system which is involved with learning survival related behaviour through the reward of dopamine release. Nicotine can cause increased dopamine signalling within this pathway by binding to excitatory nicotinic acetylcholine receptors (nAChRs).[29] This causes reinforcement of addictive behaviour in much the same way as learning and memory occurs.[29] The adolescent brain appears to be more sensitive to this excitatory signalling, with many areas displaying transient up-regulation of nAChRs during development and under expression of inhibitory GABAergic receptors.[30, 31] This is consistent with the risk-taking, novelty-seeking and increased social behaviour of adolescence.[30] Adolescents are also reported to experience more positive and less aversive effects than adults during their first experience of smoking.[29] Animal studies show that nicotine exposure is reported to increase intracellular dopamine levels in developing brains compared with adult animals and that developing rat brains are more vulnerable to nicotine addiction.[30]

There is also evidence that adolescents may experience less symptoms following nicotine withdrawal.[31] Several small clinical studies suggest that adolescent withdrawal from nicotine is relatively mild.[32, 33] Animal studies support the idea that adolescents experience less withdrawal due to developmental differences in brain function.[31]

Evidence is also emerging that nicotine dependence (but not the likelihood of starting smoking) is influenced by genetics.[34]
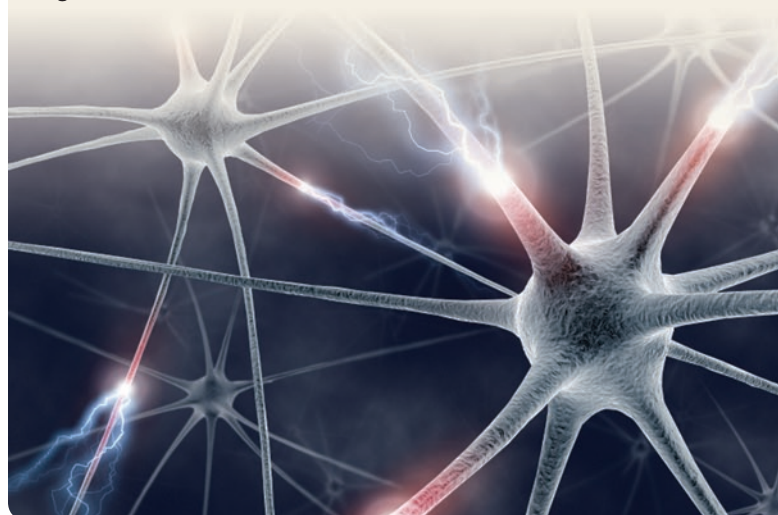
PHO performance targets for smoking cessation

The PHO Performance Programme currently has two funded smoking related indicators. The "smoking status recorded" indicator aims to capture smoking status for 90% of enrolled patients in New Zealand aged 15 – 74 years. This accounts for 7% of the performance funding; 2% for the total population and 5% for the high need population. As of December 2012 82.8% of the high needs population and 82.6% of the total population had their smoking status recorded. This continues a strong upward trend for this indicator with over 80% of PHOs recording an improvement. However, the result is still below the national target of 90%.

The "smoking brief advice and cessation support" indicator aims for 90% of enrolled patients aged 15 – 74 years who smoke and have been seen in General Practice, to be given brief advice and/or cessation support within the last 12 months. This indicator accounts for 13% of the performance funding; 4% for the total population and 9% for the high need population. Brief advice to stop smoking includes any documentation that either; a person who currently smokes was advised to stop smoking, or that an offer of cessation support was made, or that an offer was made but refused by the patient. Recent evidence shows that offers of cessation support are the most effective way to encourage quit attempts.[19] Cessation support includes referral to a smoking cessation provider, e.g. Quitline, Aukati KaiPaipa or Tala Pasifika, prescribing NRT or other medicines for the purpose of smoking cessation, or providing behavioural support either face-to-face or via telephone. As of December 2012, over 60% of PHOs had increased their rates of brief advice and/or cessation support to current smokers. However, additional effort is required before rates of advice and/or support for smoking cessation begin to approach the PHO target.

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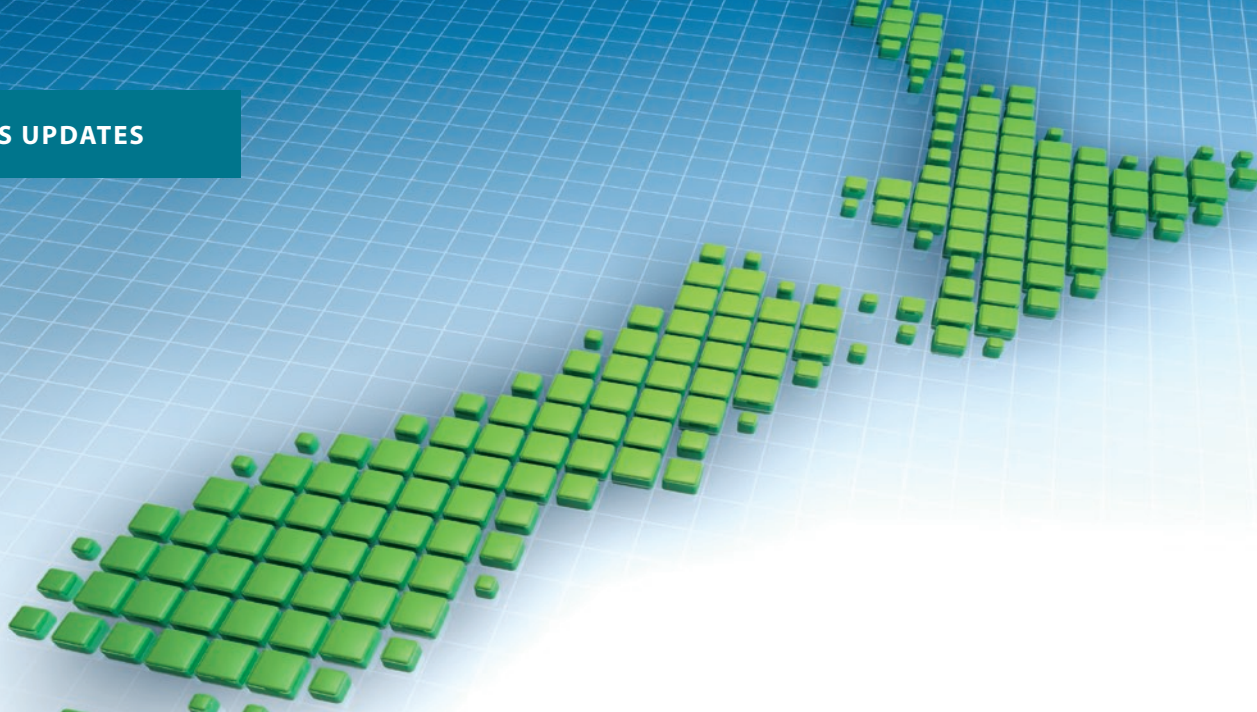
Comparing results between different blood glucose meters

Only the CareSens range of blood glucose meters and testing strips are now fully subsidised, except for two small patient groups via Special Authority (see below). Over 90% of people entitled to a subsidised meter have now picked up a CareSens meter.

There have been some reports that people are comparing readings from their previous meter with readings from their CareSens meter, and getting different results. For some, the difference is concerning, and they consider that their old meter has the right reading and their new meter must be wrong. Variances are normal between hand held meters and are to be expected. The international standard for blood glucose meters is that they are accurate to within plus or minus 20% of "what a laboratory test would show". Some people are aware of the 20% variance, but think that this means that there can only be a 20% difference between the readings of two meters, rather than between a meter and a lab test.

The key message for people with diabetes is that directly comparing results between meters is not clinical best practice. It may be useful for a short period of time, while becoming familiar with the new meter, but it is important to reinforce that meter readings from any meter are only indicative. The most meaningful information is to understand the trends, and what the readings mean for them and their diabetes management.

There is support available for people who are having particular difficultly in managing the change to the CareSens meters. For more details, phone PHARMAC on: 0800 66 00 50 or email: **diabetesfeedback@pharmac.govt.nz.**

Changing blood glucose meters is an opportunity to review if self-monitoring is appropriate. Blood glucose meters are routinely used to establish baseline blood glucose levels prior to insulin initiation, to allow for insulin dose adjustment following treatment initiation, and in patients already established on insulin or a sulfonylurea, where there are concerns about hypoglycaemia. Self-monitoring of blood glucose levels may also be useful for checking fasting and post-prandial glucose levels when considering changing medicine regimens, or to optimise glycaemic control prior to conception or during pregnancy. A meter may also be considered for motivated individuals in order to increase their understanding of the effects that certain food types have on post-prandial blood glucose levels.

Special Authority funding is available for patients using:

1. **Insulin pumps** – Patients who were using the Accu-Chek Performa meter with an Accu-Chek Combo insulin pump, before 1 June 2012, will receive continued funding under Special Authority for Accu-Chek testing strips.

2. **Ketone and glucose blood testing meters** – Patients who were using the Freestyle Optium meter for both prescribed blood glucose and ketone testing, before 1 June 2012, will continue to receive Special Authority funding of the Optium blood glucose strips. CareSens testing strips and meters are subsidised for all other patients requiring blood ketone testing.

For further information visit the PHARMAC website: **www.pharmac.health.nz** (Keyword = diabetes).

Beating the Blues: online cognitive behavioural therapy for mild to moderate depression

Beating the Blues® is an evidence-based, online cognitive behavioural therapy (CBT) programme for the treatment of people with mild and moderate depression.

The Ministry of Health has funded the Beating the Blues® E-therapy tool for the assessment and treatment of mild to moderate depression for use in primary care nationwide. Beating the Blues® is offered free of charge to general practices and some non-government organisations involved in primary care services.

The benefits of Beating the Blues® E-therapy tool include:

- Immediate access to CBT for patients with depression and/or anxiety
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- Clinical outcomes achieved similar to those with face-to-face therapy
- Requires minimal clinical input – supports clinical oversight
- Higher patient satisfaction with treatment than with usual care

For assistance on how to register or for further information please contact Andy Whittington of the E-Therapy Project Team; Email: awhittington@medtechglobal.com or visit: **www.beatingtheblues.co.nz**

Sexual health: did we miss the mark?

Dear Editor,

I am a great fan of your publications. I feel there has been a trend, however, toward publishing articles written by specialists, apparently without going through a filter of assessing their relevance to the daily decision making within a true general practice context. Articles authored by General Practitioners with some advice from specialists are more valuable.

As one example, may I refer to the "How-to guide for a sexual health check up", in BPJ 52 (Apr, 2013). The guidance and recommendations in this article are relevant to practice in a sexual health clinic, where there is a high prevalence of STIs in the patients seen, but this article does not address the issues of pre-test probability and judgement around relevance and appropriateness in ordinary general practice consulting. We see some patients for whom these recommendations are appropriate, but frequently make difficult judgements about how far to take sexual health screening, and it would be very helpful if an article such as this helped us with these decisions.

Working through this article, written by sexual health specialists, one reads that "A sexual health check should generally be undertaken … for females attending for routine contraceptive or cervical screening visits." Further on in the article one finds, "Routine examination and testing for females should include …serology for hepatitis B (if not immunised), syphilis and HIV." In mainstream general practice, providing comprehensive care to patients and their families over the years, faced with, for example, a 35 year old woman, well known to us in an apparently stable relationship and with a family, who is seeking a repeat of her contraception, or a 50 year old woman responding to a recall for a now due cervical smear, we need to employ a different set of skills, rather than follow a blanket over inclusive recommendation

which has relevance to a sexual health clinic. We know that with such familiar patients, the probability of an STI being present is low, but not altogether negligible. What questions do we ask the patient and what tests do we offer and with what wording in this context? The suggested lead-in statement, "We ask everyone the same questions, they may seem intrusive but I'm just trying to find out risks and what tests you may need," may not seem appropriate.

Furthermore, if we do obtain a positive chlamydia result in an asymptomatic patient, with a personal profile which suggests a very low pre-test probability, how likely is it that this is a true positive result? This article does not address questions like this.

I wonder whether specialists, when invited to contribute, are aware of the nuances that we encounter on a daily basis? In inviting them to contribute, would it be helpful to provide them with a set of vignette scenarios from general practice which would help keep their idealised articles grounded?

Dr Greg Judkins
General Practitioner and Medical Educator
Auckland

All main articles for Best Practice Journal and Best Tests are authored by our in-house writing team, with assistance and guidance from our clinical team, which consists of four General Practitioners and a Pharmacist. Each article is externally reviewed by a relevant subject specialist (or group), who provides expert comment and correction as required. The articles are also reviewed by our Clinical Advisory Group which is made up of primary and secondary care representatives. We then edit the articles for publication, based on the balance of all of these comments.

The article you refer to ("A how-to guide for a sexual health check up") is considered a foundation article, which is intended to give a general overview of all aspects of a particular condition/disease process. Foundation articles are then followed up by more focused articles on specific aspects of managing a condition. Our foundation guidance is intended to cover "what you should do" to manage a condition, in an evidence-based, New Zealand context. However, we intend for clinicians to interpret the information based on the context of their individual practice, i.e. "what you actually do".

We endeavour to keep our information primary-care and practically based, while incorporating latest evidence and commentary from those who specialise in treating the conditions we write about. Your feedback serves as a useful reminder to us of the importance in getting this balance right.

We have asked Dr Jill McIlraith, an experienced General Practitioner from Dunedin, who teaches sexual health to GP registrars, fellow GPs and undergraduates, to comment further on some of the aspects raised in this letter:

"I feel that the article strikes an excellent balance between the detailed knowledge required for a General Practitioner faced with doing a required sexual health checkup, and that of reminding us all of the basics. I think of it as a resource into which we can dip for information rather than a prescriptive guide that we as General Practitioners should use for each and every patient. It was clear, concise and offered good reminders about the essentials of what is often a difficult area for General Practitioners as well as touching on some of the current issues such as antibiotic resistance.

I disagree with the comment that in mainstream general practice, you would not at least discuss the subject of STIs with each patient when doing smears or renewing contraception. I make opportunities to discuss it with my patients, just as I do the same for smoking cessation. My policy has long been to ask all female patients in general terms whether there "is anything else we need to check for while doing the smear". Some patients then ask "what do I mean?" and I reply that people lead complicated lives and it is my policy to ask everyone for whom I do a smear, whether they have any other concerns that I can help with. In other words, I take on the responsibility of broaching the broader aspects of sexual health. In 23 years of general practice, I have never had a patient indicate they are offended by me asking, and most have appreciated my thoroughness and care - particularly those such as in the correspondents example, i.e. a 50-year-old woman who usually find it very difficult to bring up the topic unless the doctor does so first. They are often the ones who most need us to break the mold and be upfront.

It would be naïve of us General Practitioners to think we know all our patients so well that we don't need to broach such sensitive subjects. It is also worth reminding all our colleagues that the fastest rate of increase of STIs in the western world is

in those aged over 50 years, and that very little sexual health information is targeted to this age group. They are also the least likely to broach the subject with doctor and nurses, least likely to use condoms and most likely to confuse symptoms of STIs with age-related changes and put off talking to medical staff about it.

Regarding positive chlamydia tests, the NAAT tests used now are very sensitive and very specific and it would be very rare to get a false positive. So a positive result is likely to be just that - positive. Any concerns are more likely to surround the discomfort that the clinician may feel in that they now need to discuss how/when/who gave what to whom. It is a similar comment to what we hear from midwives, i.e. that their "nice" patients wouldn't have an STI so why should they offer testing and if it did come back positive it would create difficulties for them in discussing and stress the relationship.

I would highly recommend the article to my general practice colleagues. Each of them can quite easily filter it through their own knowledge and comfort levels to do the best by their patients in an area that a lot of General Practitioners do poorly in."

Dr Jill McIlraith
General Practitioner, GPEP teacher.

Dr Sunita Azariah, is a Sexual Health Physician from Auckland, who provided expert comment on the sexual health article in Best Practice Journal. Dr Azariah offers some further insight:

"I agree that this article is an example of best practice recommendations in an ideal world. I appreciate that General Practitioners have time constraints, as do all practitioners. Sexual health history and assessment and screening of asymptomatic people fits well within the role of an experienced Practice Nurse. With widespread availability of NAAT testing it doesn't need much time to actually test people as they can do self-collected samples.

Different primary care practices will have different risk profiles for their patients. I think the need to establish an environment where people will feel comfortable to talk about their concerns is what is most important, e.g., the gay man who doesn't know how his General Practitioner will react to disclosure of his sexuality. Many primary care practices market themselves as

"Family medicine" so routinely asking people about their sexual health concerns is a way of breaking the ice and making people feel more comfortable to raise issues if they wish. It will also make them aware that they can bring up concerns if their General Practitioner has signalled they are comfortable discussing these issues with them.

I think too, as with any guidance, one has to use common sense as to what you actually do in clinical practice. The point of the sexual history is to check risk factors as many people will not need to have comprehensive STI screening. However, if you don't ask you won't find out relevant information. One can't assume that the "nice married 30 year-old professional woman" is not having concurrent sexual partners or that her husband is not having an affair. People won't get offended if things are discussed in the right way."

Dr Sunita Azariah
Sexual Health Physician,
Auckland Sexual Health Service

Practice report on dabigatran

We received three similar correspondence items in response to our April 2013 practice report on testing renal function in patients receiving dabigatran. The following is an extract from one of these letters; we have removed practice details for confidentiality.

Dear Editor,
I wonder if other practices were as surprised as us by the latest Practice feedback regarding dabigatran. One of its major features was the percentage of patients that had had renal function measured before starting medication, and the national figure was only 32%. In our practice it was 27%. As we had not taken on the task of change management lightly we were rather surprised, and may I say affronted, by this data. We thought we should investigate so that we could learn from the error and folly of our ways and make the necessary changes to our policies.

The results of our investigations (admittedly our sample size is small at 14) show:
- *Two patients were started on dabigatran in hospital and had renal function measured during the admission before dabigatran was started*
- *Most patients were changed over from warfarin after*

informed consent and all but two followed the following procedure: discussion, prescription and explanation; renal function and INR within the following few days and then in communication with the practice when the INR was at a suitable level the patient started dabigatran.
- *Two patients did not have renal function tested within a month of starting dabigatran but had good stable renal function measured within two months*
- *Most of the patients started dabigatran in winter 2011*
- *Our percentage of patients who had had renal function measured within a month before starting dabigatran was therefore actually 86% rather than 27% as appeared on the feedback.*

To us, this raises several questions:
- *What is the relevance of this feedback if the national experience is similar to ours in that most dabigatran was started nearly two years ago*
- *What is the relevance of feedback when the information presented is obviously flawed because of lack of analysis of the raw data*
- *Should we take notice of any feedback that bpac^{nz} presents to us?*

Name withheld

The purpose of the feedback that bpac^{nz} supplies is to facilitate regular audit processes within practices and to stimulate discussion within the primary care team.

Two important factors about practice reports to keep in mind are that:
- Data is presented for all registered patients in a practice, regardless of who prescribed or ordered tests for these patients. In many cases, this includes clinicians outside of the practice and clinicians working outside of primary care.

- Data is extracted from the Ministry of Health Pharmaceutical and Laboratory Claims collections, which encompass prescriptions dispensed from community pharmacies and investigations carried out in community laboratories. This means that medicines given and investigations ordered for patients while in hospital, are not included in the data analysis.

One of the key messages in the dabigatran report was to emphasise the importance of checking renal function prior to starting dabigatran, to ensure that it is prescribed appropriately. In order to investigate this, we identified patients in practices that were prescribed dabigatran, and looked to see if they had a creatinine test within the month prior to their first prescription. In an individual clinical setting, there are many reasons why a test may not fall into this exact time frame, however, for the purposes of putting together a data report, we need to set specific parameters that reflect a "best practice scenario" for all patients.

We reviewed the data from the practice described in the above letter. We found that 15 registered patients had been prescribed dabigatran. Of these patients:

- Four had a creatinine test in the month before their first dabigatran prescription was dispensed (hence the 27% figure reported for this practice)
- Five had a creatinine test one to two days after the prescription was dispensed
- Two had a creatinine test more than one month, but less than three months, before their prescription was dispensed
- Four did not have a creatinine test in the three months before or one month after their prescription was dispensed

In reviewing this practice's data, it is reasonable to say that the patients who had a creatinine test within a day or two of picking up their dabigatran prescription, and the patients who had a creatinine test just over a month prior to starting dabigatran were also managed as recommended. It is possible that some or all of the four patients who did not have a test in a community laboratory, had a test whilst in hospital. Practices could identify this in an audit if they have transcribed this information into the patient record, from the hospital discharge notes.

We acknowledge that our data parameters were strict, and that some leniency on the cut-off dates for testing would have increased the percentages for many practices. However, recommendations are that the results of a creatinine test should be reviewed before prescribing dabigatran, therefore the test needs to take place before the prescription is collected, and a creatinine result should ideally be no more than one

month old, as the clinical situation may have changed, given the older age of the patient population who are usually prescribed dabigatran.

In response to the correspondents additional questions;

Although many patients were changed from warfarin to dabigatran two years ago when dabigatran first became available, new patients are regularly being initiated on dabigatran, and the report serves as a reminder to all practices on important points to take into consideration when prescribing dabigatran.

The data analysis is not flawed, it is just subject to limitations such as the criteria we have set for analysis and the fact that the data captures community dispensing and laboratory testing only.

Practice prescribing and/or laboratory testing data reports are created to help reinforce key messages important to primary care, and we strive to make this useful for practices, and to explain the processes and limitations of each report so it can be interpreted meaningfully. We welcome feedback on our reports so we can perfect these processes.

As a footnote, we have recently distributed a practice report on baseline testing prior to prescribing isotretinoin. We have listened to your feedback and defined a baseline test as one that occurred 12 months before or three weeks after a patient received their first prescription for isotretinoin. Baseline tests should ideally occur within one month, but given the younger patient population that is prescribed this medicine, with generally stable health parameters, a longer time period for a baseline test was used for the purposes of the report.

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