

ACS | ANTITHROMBOTIC MEDICINES | CHILDHOOD ECZEMA | IPIF: A HEALTHY START

# Best Practice

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Issue 67 April 2015

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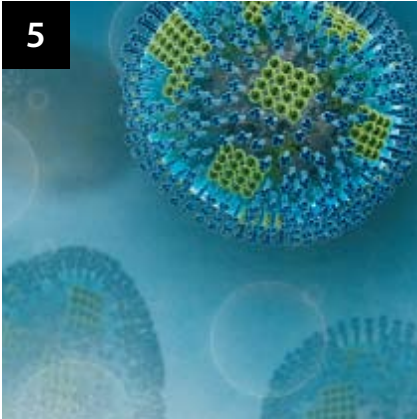
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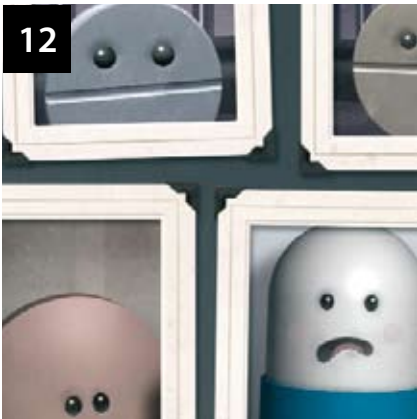
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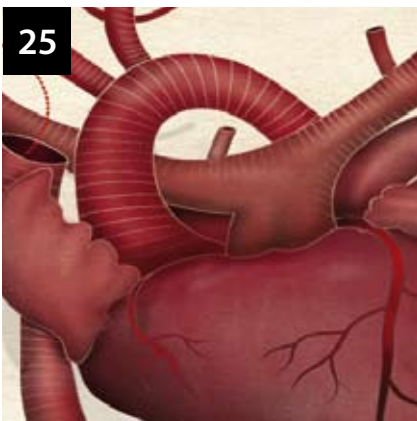
Antithrombotic medicines, such as aspirin and warfarin, have been routinely prescribed in primary care for decades for the prevention or treatment of arterial or venous thrombi. In 2011, we published a consensus statement on the use of antithrombotic medicines in general practice. In the last few years the indications for some oral antithrombotic medicines have expanded, e.g. dabigatran, and access to other medicines has increased, e.g. ticagrelor has been added to the Pharmaceutical Schedule. In this article we examine recent developments in the use of antithrombotic medicines, provide prescribing information for newer medicines commonly used in primary care, and update the evidence available to clinicians who are discussing the benefits and risks of antithrombotic treatment with patients.



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# NICE-bpac<sup>nz</sup> Symposium:

## Guidelines and Pathways – what role do they have in the United Kingdom and New Zealand health sectors?

In April 2014, bpac<sup>nz</sup> entered into an exclusive agreement with the National Institute for Health and Care Excellence (NICE), United Kingdom, to contextualise guidelines for the New Zealand population. As part of this agreement, bpac<sup>nz</sup> will convene expert working groups to review and contextualise recently published NICE guidelines. Once approved by NICE, the resulting guidelines will be made freely available to the New Zealand health sector.

bpac<sup>nz</sup> launched their collaboration with NICE on 4 March, 2015, with a day-long symposium at Te Papa, Wellington. The symposium was attended by over 150 delegates from around the country, from a wide range of disciplines across the health sector. After the symposium was opened by the Hon. Peter Dunne, Associate Minister of Health, ten speakers addressed the audience on the subject of guidelines and pathways, and the roles they play in both the United Kingdom and New Zealand health sectors.

Professor Murray Tilyard, CEO bpac<sup>nz</sup>, began the symposium with an overview of the agreement between bpac<sup>nz</sup> and NICE.

NICE Chairman, Professor David Haslam, then spoke about the genesis and role of NICE in the United Kingdom's National Health Service. As well as detailing the history of NICE, Professor Haslam explored the importance of committee decision-making, and seeking input from patients and service users, as well as clinicians, in the final guidelines. He also spoke about balancing cost effectiveness with clinical effectiveness when collating guidelines for health care with limited resources.

NICE Programme Director, Christine Carson, outlined their guideline development and update process. Ms Carson gave an overview of how NICE puts guidelines together, from the initial commission of the guideline, through consultation and drafting, to the final publication. She also detailed some of the challenges encountered while developing guidelines, such as the problems of addressing co-morbidity in guidelines, time pressure to create the guidelines, and the need to balance the demands of different parts of the health sector, while still ensuring the guidelines are in accordance with the evidence base.


Associate Professor Mark Thomas, Infectious Diseases Physician, University of Auckland, gave a presentation about the challenges that may be faced in contextualising United Kingdom guidelines for New Zealand's unique health environment. For example, the importance of having clinically appropriate guidelines for antibiotic treatment for sore throat, given the context of New Zealand's high incidence of rheumatic fever in certain populations, compared to the United Kingdom where the incidence is very low.

Professor Cindy Farquhar, Professor of Obstetrics and Gynaecology at the University of Auckland, presented a history of guideline production and its reception in New Zealand. She pointed out areas where guidelines can be of use, such as where there is a gap between current practice and evidence-based best practice. She also outlined what constitutes best practice in the development of guidelines – a focus on patient outcomes, adherence to evidence base and flexibility. Professor Farquhar also gave an overview of the work of the New Zealand Guidelines group from 1996 to 2012.

Professor Les Toop, Head of General Practice Department, Christchurch School of Medicine and Chair of Pegasus Health, outlined the benefits and harms of guidelines and pathways in the current clinical environment. He used the unique situation in Canterbury as an example of the increased integration of health and social services that has happened in the last ten to twenty years, and showed how Canterbury HealthPathways, a clinical guidance system, played into that integration.

Other speakers included Professor Tim Stokes from the Department of General Practice, Dunedin School of Medicine, who spoke about the processes of embedding guidelines into health systems; Dr Peter Robinson, Chief Clinical Advisor, ACC, who outlined guidelines versus clinical pathways for the consumer; and Dr Peter Jones, Ministry of Health Chief Advisor, Sector Capability and Implementation, on the role of the Ministry of Health in relation to guidelines and sector performance.

The concluding speaker of the day was Professor Tony Dowell of the Department of Primary Health Care & General Practice, Wellington School of Medicine, who spoke about guidelines in the increasingly common context of patients with multiple morbidities. Professor Dowell showed how clinical complexity, cultural context and organisational restraints may lead to guidelines being ignored by clinicians, and outlined other challenges to guideline implementation.

 Presentation slides from each speaker are available from: [www.bpac.org.nz/downloads/2015-03-04-SymposiumPresentations.pdf](http://www.bpac.org.nz/downloads/2015-03-04-SymposiumPresentations.pdf)

## Guideline contextualisation update

The first two NICE guidelines planned for contextualisation are:

- Urinary incontinence in women
- Respiratory tract infections: antibiotic use

A Guideline Review and Contextualisation Group (GRCG) has been set up for each of the contextualisation processes currently underway, and a review of the appropriateness of their evidence bases for New Zealand has been performed. Both GRCGs will be holding their initial meetings within the next month, and following these meetings the scope of each contextualisation will be confirmed with NICE.

The draft guidelines will be released for consultation and feedback later in 2015, after which both completed guidelines will be published.


The Guideline and Contextualisation Group members are as follows:

### Urinary Incontinence in Women:

Emeritus Professor Don Wilson (Chair), Professor Mark Weatherall, Dr Lynn McBain, Dr Tim Dawson, Sharon Wilson and Lucy Keedle.

### Respiratory Tract Infections:

Associate Professor Mark Thomas (Chair), Dr Emma Best, Professor Bruce Arroll, Dr William Kim and Dr Nigel Thompson.

 For further information or enquiries about the contextualisation of NICE Guidelines, contact Kate Sears: [catherines@bpac.org.nz](mailto:catherines@bpac.org.nz)

# Seasonal influenza vaccines are now available

The Ministry of Health has announced that the first shipments of the two subsidised seasonal influenza vaccines for 2015, Influvac and Fluarix, have been sent to providers who pre-ordered the vaccines.<sup>1</sup> After an initial delay, a continuous supply of the vaccines is expected to be available until the end of the influenza season.

Further updates on the vaccine supply are available from: [www.influenza.org.nz](http://www.influenza.org.nz)

The later than normal arrival of the influenza vaccines will mean that the seasonal influenza programme will only just have started when Immunisation Week begins on April 20, 2015 (see: "Pertussis and influenza vaccination are important themes of Immunisation Week"). The National Influenza Specialist Group (NISG) "Flu Kit" for 2015 is available online and includes information about ordering the vaccine and claiming funding.

For further information, see: [www.influenza.org.nz](http://www.influenza.org.nz)



## Pertussis and influenza vaccination are important themes of Immunisation Week

This year's Immunisation Week aims to raise awareness among parents about the importance of completing the scheduled childhood immunisations, particularly parents of infants aged eight months or younger.<sup>2</sup> Promoting pertussis and influenza vaccination are key messages of Immunisation Week, with the slogans: "Flu can be anywhere" and "Influenza don't get it, don't give it".<sup>2</sup>

On-time administration of pertussis vaccines throughout life to prevent whooping cough is a major theme of Immunisation Week. All infants should receive three doses of the subsidised pertussis vaccine by age six months (DTaP-IPV-HepB/HiB), with booster doses at ages four (DTaP-IPV) and eleven years (Tdap).<sup>3</sup> Pertussis vaccination is also subsidised for women who are pregnant.<sup>3</sup> The Tdap vaccine should be given to pregnant women between 28 to 38 weeks gestation.<sup>3</sup> Immunising adults and older children, that have regular contact with infants, e.g. fathers, siblings, grandparents and other caregivers, can be used to provide a "cocoon of immunity" to help prevent infections until the infant has received all their pertussis vaccinations. One dose of Tdap is sufficient for these people, however, this is usually unsubsidised.<sup>3</sup>

For further information see:

"Pertussis: halting the epidemic by protecting infants", BPJ 51 (Mar, 2013)

"Pertussis immunisation in pregnancy", BPJ 60 (Apr, 2014)

## Two new strains have been included in the 2015 vaccines


The arrival of the 2015 seasonal influenza vaccines was delayed. This was due to a manufacturing reformulation with the introduction of two new influenza strains in this year's vaccines. The aim of reformulating the vaccine was to provide better protection against the circulating influenza strains likely to predominate during the 2015 influenza season, based on knowledge/experience from the 2014/15 Northern Hemisphere season. The components of the 2015 influenza vaccines are:<sup>4</sup>

- A/California/7/2009 (H1N1)-like virus
- A/Switzerland/9715293/2013 (H3N2)-like virus (*new*)
- B/Phuket/3073/2013-like virus (*new*)

The inclusion of the two new strains in the Southern Hemisphere vaccines is intended to avoid the vaccine mismatch problems that were experienced in the 2014/15 Northern Hemisphere influenza season where the influenza A (H3N2) strain predominated. The H3N2 and Phuket strains that have been included in the 2015 Southern Hemisphere influenza vaccines were not present in the 2014/15 Northern Hemisphere's influenza vaccines which resulted in low vaccine efficacy against the circulating H3N2 strain.<sup>5</sup> It is expected that the H3N2 strain will also predominate in New Zealand this winter.<sup>6</sup> The H3N2 strain tends to spread widely and has frequently been associated with severe disease and increased mortality in high-risk groups, particularly in older people.<sup>7</sup>

Along with the two subsidised vaccines (Fluarix and Influx), three other non-subsidised influenza vaccines will be available in New Zealand in 2015.<sup>8</sup> These are the trivalent vaccines Fluvax and Vaxigrip and the quadrivalent vaccine FluQuadri.<sup>8</sup> Fluvax and Vaxigrip both contain the California and Phuket strains along with a South Australian strain which is expected to provide similar protection against H3N2 as the Switzerland strain in the subsidised vaccines. The quadrivalent vaccine contains the same three strains as the subsidised trivalent vaccines along with one additional B influenza virus strain.<sup>8</sup> The availability of the unsubsidised influenza vaccines will vary between locations depending on which vaccines individual providers decide to stock.

Pharmacies and occupational health providers that administer influenza vaccinations are expected to notify the patient's general practice so that their medical records can be updated.

 A list of pharmacies offering influenza vaccination is available from: [www.influenza.org.nz/sites/default/files/Pharmacies%20Vaccinating%202015.pdf](http://www.influenza.org.nz/sites/default/files/Pharmacies%20Vaccinating%202015.pdf)

## Who should receive the influenza vaccine?

All adults and children aged six months and older can be immunised against influenza, although the vaccines are only subsidised for certain groups (see: "The subsidy groups have not changed from 2014", opposite). It is recommended that all people who meet the subsidy criteria are vaccinated. Vaccination should be encouraged in particular for pregnant women, as this provides protection for the woman and her fetus during pregnancy, and then subsequently the newborn child.

Influenza vaccination is also recommended (but not subsidised) for people in close contact with individuals at high risk of complications. This includes healthcare workers and others with regular contact with immunocompromised people, children and elderly people.

**All healthcare providers and non-clinical practice staff should receive the annual influenza immunisation** to help reduce the spread of the virus and protect those people at greater risk of influenza complications. The proportion of DHB employees who received the seasonal influenza vaccine has increased over the past few years, but remains suboptimal (61% in 2014).<sup>9</sup> All DHBs offer free influenza vaccination for their staff. There is no official influenza vaccination rate published for primary care staff, however, it is thought that the rate is higher than the overall DHB figure.

As well as getting vaccinated themselves, healthcare professionals have an important role in promoting the uptake of influenza vaccination, as people may have become complacent about influenza after two relatively mild influenza seasons in New Zealand in 2013 and 2014.<sup>10</sup>

## Who should not receive the influenza vaccination?

**Infants aged under six months should not be vaccinated.**<sup>9</sup> Significant protection for young infants can be achieved by vaccinating the mother during pregnancy. Further protection may also be obtained via "cocooning" i.e. immunising adults and older children who have frequent contact with the infant, e.g. parents, grandparents and siblings.

People with an **acute illness or fever (> 38°C) should not be vaccinated** until they are well.<sup>9</sup>

People with a **latex allergy should receive Influx** and not Fluarix, as the Fluarix needle shield contains natural rubber latex.<sup>9</sup>



Influvac and Fluarix are both produced using hen's eggs and therefore may contain residual amounts of egg proteins. People who have had a **confirmed anaphylactic reaction to egg protein may still be given the vaccine if the benefits outweigh the risks**, however, this should occur under specialist supervision, e.g. allergy specialist or paediatrician.<sup>11</sup> The Australian Society of Clinical Immunology and Allergy (ASCIA) guidelines for influenza vaccination in egg-allergic people report that people who have had **mild reactions or hypersensitivity to egg protein may receive influenza vaccination**.<sup>11</sup> However, these individuals should undergo a 30-minute observation period after the vaccine has been given (the normal recommended observation period is 20 minutes).<sup>11</sup>

### By which route should the vaccines be administered?

Both Fluarix and Influvac can be administered as an intramuscular or subcutaneous injection.<sup>9</sup> The intramuscular route is generally preferred, although subcutaneous injection should be used for people with bleeding disorders, e.g. thrombocytopenia, as bleeding can occur following intramuscular administration.<sup>9</sup>

### How many doses should be administered?

Children aged six months to eight years who have not previously been vaccinated against influenza should receive two doses of the influenza vaccine, administered four weeks apart, as they are more likely to be immunologically naive to influenza.<sup>9</sup> All other people, including children aged six months to eight years who have received an influenza vaccine at any time in the past or anybody aged nine years or older receiving vaccination for the first time, only require a single dose of the vaccine each year.<sup>9</sup>

#### Practice debate

There is growing consensus that the recommended 20 minute observation period may not be necessary for patients who have received three or more previous influenza vaccinations, and have experienced no reaction. The argument for this is that although the antigens may change in the vaccine each year, the other constituents of the vaccine remain the same, and the overall risk of anaphylaxis from influenza vaccine is extremely low.

What is your personal/practice policy or opinion on this?

Comment online at: [www.bpac.org.nz/bpj/2015/april/influenza.aspx](http://www.bpac.org.nz/bpj/2015/april/influenza.aspx)



## The subsidy groups have not changed from 2014


The groups of people who are eligible to receive subsidised influenza vaccination are unchanged from 2014.<sup>12</sup> The eligible groups for 2015 are:<sup>12</sup>

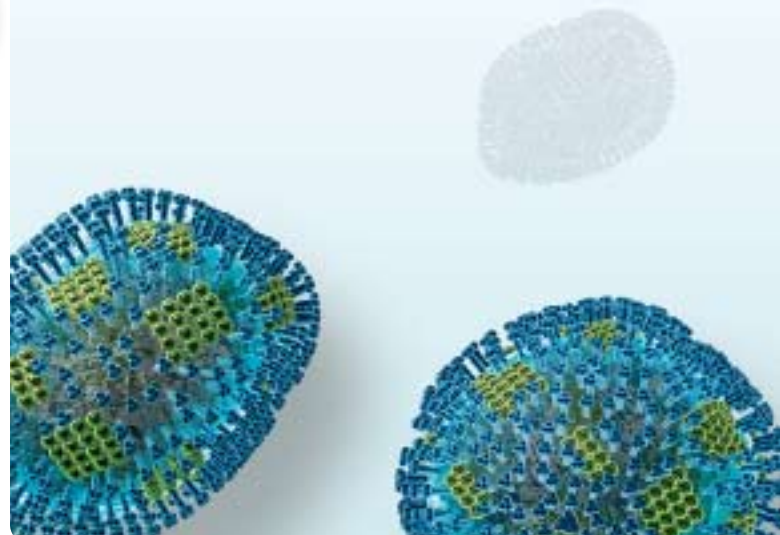
- Women who are pregnant (influenza vaccination can be administered safely during any trimester and during breastfeeding)
- People aged 65 years or older
- People aged six months to 65 years with any medical conditions that place them at an increased risk of influenza complications

Medical conditions that place a person at a high risk, include:

- Coronary disease or chronic kidney disease
- Chronic respiratory conditions, e.g. asthma (if taking regular preventative medicines) or COPD
- Type 1 or 2 diabetes
- Immunosuppressed individuals, e.g. transplant recipients or those with HIV
- Autoimmune disorders, e.g. rheumatoid arthritis
- Cancer or epilepsy

Practices can provide subsidised doses of the influenza vaccine until July 31, 2015, after which time, people will have to pay the full cost of the vaccine and administration.

 The full list of conditions that qualify a patient for subsidised vaccination is available from: [www.influenza.org.nz/eligibility-criteria](http://www.influenza.org.nz/eligibility-criteria)



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## Peer Group Discussions

In this ongoing series, we look back at the key messages and practice points from selected articles in Best Practice Journals. Also included are suggested discussion questions for peer groups, or for personal review.

Available from our website:

[www.bpac.org.nz/PeerGroupDiscussions](http://www.bpac.org.nz/PeerGroupDiscussions)

# Stand up to FALLS

## April was falls month: the Health Quality & Safety Commission's reducing harm from falls campaign

Contributed by the Health Quality & Safety Commission



Falls prevention is everyone's business. A new study shows that the Accident Compensation Corporation (ACC) accepts more than 260 falls-related claims each day from retirement-age New Zealanders.<sup>1</sup> Figures such as this underline why the Health Quality & Safety Commission is revisiting reducing harm from falls as the latest six-month focus of its *Open for better care* national patient safety campaign, in partnership with *First, Do No Harm* in the Northern region.


The new focus, which builds on work across the sector and the Commission's ongoing reducing harm from falls programme, began on 1 April, in tandem with April Falls month. April Falls, now in its third year, is an annual Commission-supported promotion for district health boards (DHBs) and other providers,

and is aimed at those working in the health and disability and aged residential care sectors, as well as consumers and their family/whānau.

Sharing the theme "Stand up to Falls", this year's April Falls and the overall campaign focused on emphasising the importance of an integrated whole-of-system approach to falls – incorporating primary care, along with community, aged residential care and hospital settings.

### Why falls and why older people?

Work on the Commission's reducing harm from falls programme began in mid-2012, with the first national April Falls promotion in 2013. This was followed the next month by falls as the inaugural focus of the *Open* campaign. The Commission leads the falls programme, with partners that include ACC and other key stakeholders. Older people are the focus because, although falls occur at all ages, older people are at greater risk and are more susceptible to injury.<sup>2</sup> For an

 For a full version of this article, see: [www.bpac.org.nz/Supplement/2015/April/falls.aspx](http://www.bpac.org.nz/Supplement/2015/April/falls.aspx)

older person, a fall can be life-changing, impacting on their independence and wellbeing, with implications for their family/whānau.

The first priority and focus for the programme was older people in care settings – hospital, aged residential care and receiving care at home. This is because two things can be assumed about care settings: a degree of vulnerability on the part of the older person and the need for a safe care environment. In the case of hospitals, falls are high harm events for patients, consistently representing around half of all serious adverse events reported to the Commission.<sup>3</sup> However, further evidence indicated the volume of falls in the community and the need for a broader approach aimed at helping older people stay independent and keeping them “on their feet”.<sup>4</sup> Consequently, programme activities have grown from the initial emphasis on the hospital setting to also supporting and promoting primary care and community-based efforts for older people – which includes those who are generally healthy and active and those at risk of falling because of frailty or other factors.

## Falls are the most common and costliest cause of injury in older people

Falls are the most common and costliest cause of injury in older people, with around 30 – 60% of people aged 65 and over falling each year and 10 – 20% of those falls resulting in injury such as hip fracture, hospitalisation or death.<sup>6</sup> “Falls can result in fear of falling with subsequent avoidance of physical activity and decline in health, and they are an independent predictor of premature admission to residential aged care, even if there is no injury.”<sup>5</sup>

One estimate of the health service cost of falls is:<sup>4</sup>

- \$600 for a fall with minor injuries
- \$47,000 for a hip fracture with three weeks in hospital
- \$135,000 for a hip fracture with complications and discharge to an aged residential care facility

Of those who have a hip fracture, 27% will die within a year,<sup>7</sup> 10 – 20% will be admitted to residential care,<sup>8</sup> and 50% will require support with daily living or walking.<sup>9</sup>

## Atlas of Healthcare Variation

To coincide with the launch of April Falls and the new campaign focus on falls, the Commission is publishing the findings of a new falls domain in its Atlas of Healthcare Variation – a series of easy-to-use maps, graphs, tables and commentaries to

highlight differences in the provision and use of specific health services and outcomes.<sup>1</sup>

The falls domain shows data relating to falls by people aged 50 years and over, by DHB area. The data is based on people with one or more accepted ACC claim in 2013, as well as on falls-related hospital admissions and hip fracture rates for the same year.

In 2013, there were:<sup>1</sup>

- 92,301 people aged 50–64 years with one or more accepted ACC falls claim
- 44,140 people aged 65–74 years with one or more accepted ACC falls claim
- 33,142 people aged 75–84 years with one or more accepted ACC falls claim
- 20,103 people aged 85 years and over with one or more accepted ACC falls claim.

The figure for people aged 85 years and over represented a quarter of those in that age group and 55 accepted claims a day. People aged 85 years and over were twice as likely to have an accepted claim as those aged 50–64 years, and 15 times more likely to be admitted to hospital as a result. Their average length of stay was 14.3 days. Although those aged 85 years and over make up 5% of the 50-plus age group, they account for nearly half of hip fractures relating to a fall.<sup>1</sup>

## Are falls inevitable?

The Commission – through its falls programme as well as April Falls and the campaign focus on falls – supports and encourages a number of preventive measures that can be integrated into routine health care.

These include:

- Exercise programmes, such as the Otago Exercise Programme, and group exercise classes, such as Tai Chi, which can reduce falls by 30–40% in older people living in the community<sup>10</sup>
- Vitamin D prescribed for those at risk of vitamin D deficiency
- Home safety assessments and modifications where necessary
- Individually targeted multi-factorial interventions

A suite of resources support the programme’s development of the “Ask, assess, act” concept – which poses the question: “Is the older person in your care at risk of falling?” It encourages




early conversations in screening for falls risk, assessing those risk factors, and putting individualised interventions and supports in place as needed. While originally developed with a focus on the hospital environment, the approach and tool is equally relevant across other settings.

### Every older person is different

Underpinning the Commission falls programme are two fundamental principles:

1. The need for individualised care. As British patient safety and falls expert Frances Healey says: *“Every older person is different. Don’t try to answer the question ‘What will stop older people falling?’ and just repeatedly ask ‘What might stop this person falling?’”*<sup>11</sup>
2. The need for an integrated approach – with the aim of getting “the right people, doing the right things, in the right order, at the right time, in the right place, with the right outcome”.<sup>12</sup> That is to say, ensuring services are coordinated around the needs and goals of the older person, their family/whānau and other carers.

### Resources

 For information and resources relating to falls, see: [www.hqsc.govt.nz/our-programmes/reducing-harm-from-falls/](http://www.hqsc.govt.nz/our-programmes/reducing-harm-from-falls/)

For a list of individual resources relating to this document, view this article online at: [www.bpac.org.nz/Supplement/2015/April/falls.aspx](http://www.bpac.org.nz/Supplement/2015/April/falls.aspx)

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An update on

# antithrombotic medicines

What does primary care need to know?

*Antithrombotic medicines, such as aspirin and warfarin, have been routinely prescribed in primary care for decades for the prevention or treatment of arterial or venous thrombi. In 2011, we published a consensus statement on the use of antithrombotic medicines in general practice. In the last few years the indications for some oral antithrombotic medicines have expanded, e.g. dabigatran, and access to other medicines has increased, e.g. ticagrelor has been added to the Pharmaceutical Schedule. In this article we examine recent developments in the use of antithrombotic medicines, provide prescribing information for newer medicines commonly used in primary care, and update the evidence available to clinicians who are discussing the benefits and risks of antithrombotic treatment with patients.*

## **Antithrombotic medicines in New Zealand**

Antithrombotic medicines, i.e. antiplatelets and anticoagulants, have an important role in the prevention and treatment of arterial and venous thrombi. Heparin was first isolated from liver tissue in the 1920s and since then the number of medicines available to prevent excessive thrombosis has increased dramatically. Warfarin, the first oral anticoagulant, was identified in the 1940s as the compound responsible for causing haemorrhage in cattle eating mouldy hay; the research was funded by the Wisconsin Alumni Research Foundation (WARF), hence the name “warfarin”.<sup>1</sup> Although the analgesic and antipyretic properties of aspirin had been known for centuries, in 1950 Dr Lawrence Craven, a general practitioner, first published the idea that aspirin may be protective against coronary thrombosis.<sup>2</sup> Decades later this observation was confirmed by clinical trial.<sup>2</sup> More recently, several novel oral anticoagulants, e.g. dabigatran, and rivaroxaban, have been registered as medicines and guidance on their use continues to expand as more clinical trials are conducted. Refinement of stroke risk assessment tools, e.g. CHADS<sub>2</sub> and CHA<sub>2</sub>DS<sub>2</sub>-VASc, is ongoing and enables the benefits of antithrombotic treatment to be better balanced against their potential adverse effects.

### **Which antithrombotic medicines are currently available for use in primary care?**

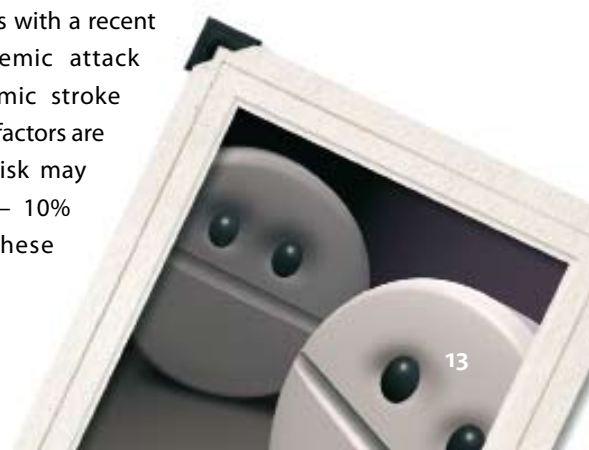
Antithrombotic medicines are widely used by patients in primary care; between July 2013 and June 2014, 110 prescriptions for either warfarin, dabigatran, clopidogrel or dipyridamole were collected from community pharmacies in New Zealand per 1000 registered patients.<sup>3</sup> Tables 1 (Page 20) and 2 (Page 22) show the anticoagulants and oral antiplatelet medicines currently dispensed from community pharmacies in New Zealand, their indications and contraindications.

## **Managing stroke risk in patients with atrial fibrillation**

The diagnosis of atrial fibrillation should be confirmed in primary care with a 12-lead ECG.<sup>6</sup> Atrial fibrillation is the cause of 20 – 25% of all ischaemic strokes and these strokes are often severe and more likely to reoccur.<sup>6</sup> It is therefore important to assess stroke risk in patients with non-valvular atrial fibrillation to determine if they are likely to benefit from anticoagulant treatment.<sup>7</sup> People with non-valvular atrial fibrillation have a four- to five-fold increased risk of ischemic stroke, however, the individual risk can vary by 20-fold depending on the person's age and clinical features.<sup>7</sup> People with valvular heart disease, particularly mitral stenosis, have an even higher annual risk of embolic stroke compared to those with non-valvular atrial fibrillation, therefore adherence to anticoagulant treatment is particularly important.

### **Stroke risk assessment tools**

The CHADS<sub>2</sub> stroke risk assessment tool has been widely tested in patients with non-valvular atrial fibrillation.<sup>7</sup> The CHA<sub>2</sub>DS<sub>2</sub>-VASc (Table 3, over page) adds the categories age, vascular disease and sex to CHADS<sub>2</sub> and is therefore able to more reliably identify patients at very low risk who may not benefit from treatment with an anticoagulant.<sup>6</sup> However, both CHADS<sub>2</sub> and CHA<sub>2</sub>DS<sub>2</sub>-VASc may underestimate the risk of stroke in patients with a recent transient ischaemic attack (TIA) or ischaemic stroke where other risk factors are absent; stroke risk may be closer to 7 – 10% per year in these patients.<sup>8</sup>



## Can antithrombotic medicines be continued during surgical procedures?

Before patients undergo surgery it is important to balance their increased risk of bleeding, if they continue taking an antithrombotic medicine, against their reduced risk of experiencing a thromboembolic event. This is difficult as thromboembolic events are relatively uncommon but highly significant when they do occur, while bleeding may occur more frequently but will often be relatively mild in comparison. The type of procedure that is being planned is an important factor when performing this risk versus benefit analysis.

Patients taking aspirin or warfarin are highly unlikely to increase their risk of clinically significant bleeding if they undergo routine dental procedures.<sup>4</sup> It is also reasonable to continue aspirin or warfarin treatment when patients undergo minor dermatological procedures in primary care; warfarin use is associated with a 1.2% increased risk of bleeding during dermatological procedures.<sup>4</sup> If patients are undergoing more invasive procedures in secondary care, the decision to continue or withdraw antithrombotic treatment will be guided by the clinician performing the procedure.

If an antithrombotic medicine is withdrawn before a surgical procedure, the timing of this withdrawal depends on the half-life of the medicine and the patient's renal clearance. The duration of the antithrombotic effect of aspirin and clopidogrel is reported to be seven days and a single dose of warfarin is reported to have an antithrombotic effect for two to five days.<sup>4</sup> Therefore it is recommended that antiplatelet medicines be stopped seven to ten days before the surgical procedure and warfarin five days before the surgical procedure.<sup>4</sup>


There is less data available on the bleeding risk associated with newer antithrombotic medicines, e.g. dabigatran, if being taken by a patient undergoing a surgical procedure. In patients with a creatinine clearance (CrCl) > 50 mL/min discontinue dabigatran 24 hours before surgery.<sup>5</sup> If there is an increased risk of bleeding or a major surgery is planned dabigatran should be discontinued two days before the procedure.<sup>5</sup> In patients with a CrCl of 30 – 50 mL/min the clearance is likely to be prolonged and dabigatran should be stopped two to four days prior to the procedure.<sup>5</sup>

**Table 3:** CHA<sub>2</sub>DS<sub>2</sub>-VASc ischaemic stroke assessment tool for patients with non-valvular atrial fibrillation<sup>7</sup>

Clinical feature	Score
Congestive heart failure	1
Hypertension	1
<b>Age</b>	
■ 65 – 74 years	1
■ ≥ 75 years	2
Diabetes mellitus	1
Stroke or transient ischaemic attack	2
Vascular disease, e.g. peripheral artery disease, myocardial infarction, aortic plaque	1
Female sex	1
<b>Total out of 9 =</b> <input type="text"/>	

The annual risk of stroke according to CHA<sub>2</sub>DS<sub>2</sub>-VASc score (calculated for a score of up to 6) is:<sup>8</sup>

- Zero points = 0.5%
- One point = 1.5%
- Two points = 2.5%
- Three points = 5%
- Four points = 6%
- Five to six points = 7%

 A number of online tools are available for calculating a patient's CHA<sub>2</sub>DS<sub>2</sub>-VASc score, e.g. <http://clincalc.com/Cardiology/Stroke/CHADSVASC.aspx>

### Previous guidance on the management of stroke risk has changed

Previously, patients with non-valvular atrial fibrillation and a CHA<sub>2</sub>DS<sub>2</sub>-VASc score of zero were offered aspirin in preference to an anticoagulant. However, it is now recommended that these patients should not be treated with either an anticoagulant or an antiplatelet at this time.<sup>6</sup> Aspirin monotherapy should generally not be prescribed for the purpose of stroke prevention in patients with atrial fibrillation.<sup>9</sup>

Currently it is recommended that all patients with atrial fibrillation who have a CHA<sub>2</sub>DS<sub>2</sub>-VASc score ≥ 1 should be considered for anticoagulant treatment and the risks and



benefits discussed with the patient.<sup>10</sup> However, a recent meta-analysis has suggested that the risk of ischaemic stroke in patients with a **CHA<sub>2</sub>DS<sub>2</sub>-VASc score of 1** may have been over-estimated and the routine treatment of these patients with an anticoagulant may not be providing sufficient benefit to justify treatment.<sup>11</sup> Where it is uncertain if a patient will benefit from anticoagulant treatment a discussion with a cardiologist or neurologist may be beneficial. See Page 18 for a discussion on the benefits of warfarin versus dabigatran.

**The evidence:** The average stroke rate in primary prevention trials for untreated patients with non-valvular atrial fibrillation is approximately 4%, and approximately 12% in secondary prevention trials.<sup>12</sup> Warfarin has been used for many years to reduce the stroke risk in these patients. Adjusted-dose treatment with warfarin results in an absolute reduction in all strokes of 2.7% per year (number needed to treat [NNT] for one year to prevent one stroke = 37) for primary prevention, and a 8.4% reduction per year (NNT of 12) in secondary prevention.<sup>12</sup> Treatment with warfarin is associated with a small absolute increase in the risk of intracranial haemorrhage of 0.2% per year.<sup>12</sup>

Anticoagulants are associated with clinically significant reductions in stroke risk in patients with atrial fibrillation compared to aspirin, while the risk of intracranial bleeding associated with both medicines is relatively low.<sup>12</sup> The Birmingham Atrial Fibrillation Treatment of the Aged (BAFTA) study found that in patients aged over 75 years the annual risk of stroke, intracranial haemorrhage and systemic embolus in patients taking warfarin was 1.8%, compared with an annual risk of 3.8% in patients taking aspirin.<sup>13</sup>

### Consider the risk of bleeding before prescribing an anticoagulant

The risk of bleeding should always be considered before discussing anticoagulation treatment with a patient, however, it is important that the bleeding risk is not overstated. Risk factors for bleeding in patients taking anticoagulant treatment include:<sup>10</sup>

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

There are a number of tools available that can be used to assess the bleeding risk of patients with atrial fibrillation. The HAS-BLED tool (Table 4) is relatively simple and its use is recommended in order to identify modifiable risk factors that can be managed in patients undergoing anticoagulation treatment.<sup>6</sup> HAS-BLED may also be useful in balancing the risks versus benefits of anticoagulation treatment in patients with atrial fibrillation who have a CHA<sub>2</sub>DS<sub>2</sub>-VASc score of 1.<sup>6</sup> However, HAS-BLED should not be used to determine whether a patient should be offered anticoagulation treatment as this decision should be based on stroke risk estimation.<sup>6</sup> The BAFTA study found that in patients with a high risk of bleeding who were treated with warfarin the annual risk of intracranial haemorrhage was 0.2%; substantially lower than the annual risk of stroke.<sup>13</sup>

A **HAS-BLED score > 2** is associated with a clinically significant risk of major bleeding,<sup>7</sup> i.e. fatal bleeding, intracranial bleeding, or a significant drop in haemoglobin, and as a patient's score increases there is an increasing need for caution and monitoring when considering the use of anticoagulants.<sup>14</sup>

Percutaneous left atrial appendage occlusion is a recent intervention that is currently only available privately in New Zealand but is likely to be an option in the future for patients in whom anticoagulation is not tolerated or is contraindicated.<sup>9</sup>

**Table 4:** HAS-BLED bleeding risk prediction tool<sup>7</sup>

Risk factor	Score
Hypertension (systolic blood pressure > 160 mmHg)	1
Abnormal renal and liver function	1 point each
Stroke (past history)	1
Bleeding (previous history of bleeding or predisposition to bleeding)	1
Labile INRs (unstable, high or insufficient time with therapeutic range)	1
Elderly (aged over 65 years)	1
Drugs or alcohol (including concomitant use of aspirin, other antiplatelet medicines and NSAIDs)	1 point each
<b>Total out of 9 =</b> <span style="border: 1px solid black; display: inline-block; width: 50px; height: 20px; vertical-align: middle;"></span>	

## Deciding between warfarin or dabigatran to prevent thromboembolism

Once it has been decided that anticoagulant treatment is appropriate, it is necessary for patients and their general practitioners to decide whether warfarin or dabigatran is the preferred treatment option. The decision to initiate other anticoagulants, e.g. rivaroxaban, will be made in secondary care.

The **advantages** of dabigatran compared to warfarin include:

- Superior ability to prevent stroke when dabigatran 150 mg, is taken twice daily
- Testing of level of anticoagulation and dose adjustments are not currently required, although research into a suitable monitoring test is underway
- Onset of anticoagulation is rapid (two to three hours) compared with 48 – 72 hours with warfarin<sup>15</sup>
- Does not accumulate in the liver and therefore safer than warfarin in patients with hepatic dysfunction<sup>16</sup>
- Fewer interactions with other medicines and foods
- A reduced risk of intracranial haemorrhage when dabigatran 110 mg, is taken twice daily

The **disadvantages** of dabigatran compared with warfarin include:

- An increased incidence of gastrointestinal adverse effects, e.g. dyspepsia
- Twice daily dosing required
- Caution is required in patients with progressive chronic kidney disease (CKD)
- There is no reversal agent to prevent or treat haemorrhage
- A small absolute increase in risk (0.27%) of acute coronary syndrome<sup>17</sup>


Patient preference plays a significant role in determining whether warfarin or dabigatran is the most appropriate treatment choice. Some patients may feel more comfortable initiating treatment with warfarin as it has a long history of being relatively safe when the dose is adjusted appropriately. Patients may also be reassured by the regular INR testing when taking warfarin and the fact that the anticoagulant effects can be reversed with vitamin K. Patients with established cardiovascular disease may also prefer warfarin as the use of dabigatran is associated with a small increase in risk of myocardial infarction or acute coronary syndrome.<sup>17</sup> The increased “health time” that patients taking warfarin have with health professionals due to INR testing may be beneficial,

particularly for patients who live alone. Alternatively, other patients may prefer a newer medicine and the reduced risk of intracranial haemorrhage associated with dabigatran use. Patients and clinicians are likely to find dabigatran more convenient than warfarin because there is no need to perform monitoring to assess anticoagulation.

Some patients may benefit from taking an anticoagulant and an antiplatelet, e.g. patients with atrial fibrillation following an acute coronary syndrome.<sup>18</sup> However, when a patient who is taking an anticoagulant is prescribed an antiplatelet their risk of bleeding is increased by approximately 50%.<sup>18</sup> Therefore a lower dose of dabigatran, i.e. dabigatran 110 mg, twice daily, may be preferable in patients also taking an antiplatelet, due to the decreased risk of major bleeding with the lower dabigatran dose.<sup>18</sup> However, this must also be balanced against the small increased risk of acute coronary syndrome in patients taking dabigatran.

In patients with valvular heart disease and atrial fibrillation warfarin is the preferred anticoagulant; treatment with dabigatran is contraindicated in this situation (see below).

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

 See: “The evidence: Dabigatran vs. warfarin”, Page 18.

### Dabigatran should NOT be prescribed to patients with valvular heart disease

Dabigatran is not indicated for the prevention of thrombosis in patients with mechanical heart valves and should not be prescribed for this indication. There is evidence that patients with mechanical heart valves who take dabigatran are at an increased risk of bleeding or experiencing a thromboembolic event compared to what their risk would have been if they had been prescribed warfarin. Several trials comparing the efficacy and safety of warfarin or dabigatran in patients who had undergone heart valve replacement were stopped early prompting the U.S. Food and Drug Administration (FDA) to release a statement that the use of dabigatran as an anticoagulant is contraindicated in patients with mechanical heart valves.<sup>19</sup>

**The evidence:** Evidence that dabigatran should not be used in patients with mechanical heart valves comes from a study that was stopped early due to an excess of bleeding and thromboembolic events in patients taking dabigatran.<sup>20</sup> Of the 252 patients enrolled in the study who had undergone mitral-

valve replacement, 168 received treatment with dabigatran and 84 received warfarin.<sup>20</sup> Dabigatran dosing was at 150 mg, 220 mg or 300 mg, twice daily, depending on renal function.<sup>21</sup> Ischaemic or unspecified stroke occurred in 5% of patients taking dabigatran but did not occur in any patients taking warfarin, and major bleeding occurred in 4% of patients taking dabigatran and 2% of patients taking warfarin.<sup>20</sup>

### Initiating dabigatran treatment

Dabigatran is rapidly and completely converted to its active metabolite when taken orally. Approximately 80 – 85% of the dose is excreted in the urine therefore dose reduction is appropriate in people with renal impairment.<sup>22</sup> Renal function should be assessed before prescribing dabigatran. In patients with a creatinine clearance less than 30 mL/min dabigatran is contraindicated (see NZF for details).<sup>15</sup> Dosing regimens for the various indications of dabigatran are shown in Table 5, below. Patients aged over 80 years with atrial fibrillation should be prescribed the lower dose of dabigatran 110 mg, twice daily, due to the increased risk of bleeding in this patient group.<sup>15</sup> Regular monitoring of renal function is also recommended for patients taking dabigatran (Table 1, Page 20).

### Ticagrelor is superior to clopidogrel in patients with acute coronary syndromes

It is increasingly likely that patients who have been diagnosed with an acute coronary syndrome will be treated with

ticagrelor, twice daily, in preference to clopidogrel, once daily; both are used in combination with aspirin, i.e. dual antiplatelet treatment. This treatment is particularly beneficial to patients following a coronary stenting procedure as stent thrombosis is often fatal. The choice of anticoagulant is usually made in hospital following diagnosis of an acute coronary syndrome and treatment is then continued in the community for twelve months. In patients who are likely to experience issues with compliance the once daily dosing regimen of clopidogrel may be seen as an advantage over twice daily treatment with ticagrelor.

Ticagrelor is a direct-acting and reversible antagonist of the P2Y<sub>12</sub> receptor found on platelets and causes rapid inhibition of platelet activation and aggregation.<sup>16</sup> Clopidogrel also acts to inhibit platelet aggregation by irreversibly blocking the P2Y<sub>12</sub> receptor; the irreversible inhibition of clopidogrel can be an advantage in patients where treatment compliance is an issue.<sup>16</sup> Unlike clopidogrel, ticagrelor is not a prodrug and therefore does not need to be processed by an enzyme (CYP2C19) to be activated. This explains why ticagrelor is reported to produce faster, greater and more consistent inhibition of platelet reactivity compared with clopidogrel.<sup>26</sup> Evidence supporting the preferential use of ticagrelor over clopidogrel for patients with an acute coronary syndrome with or without a prior history of stroke or TIA is accumulating.<sup>26, 27</sup>

 See: "The evidence: Ticagrelor vs. clopidogrel", Page 19.

**Table 5:** Dosing regimens for indications of dabigatran use in New Zealand<sup>15</sup>

Indication	Dose	Duration
Prophylaxis of stroke and systemic embolism in patients with non-valvular atrial fibrillation	Dabigatran, 150 mg, twice daily OR dabigatran, 110 mg, twice daily in patients aged over 80 years	Ongoing
Treatment of deep vein thrombosis and pulmonary embolism	Dabigatran, 150 mg, twice daily, after at least five days of parenteral anticoagulant treatment	Continued for up to six months
Prophylaxis of venous thromboembolism following major joint surgery	Dabigatran, 110 mg, one to four hours after surgery, then dabigatran 220 mg, once daily	For ten days following knee surgery and 28 – 35 days following hip surgery

 For further information, see: "Dabigatran revisited", BPJ 50 (Feb, 2013).

## The evidence: dabigatran vs. warfarin

The effectiveness and safety of dabigatran in reducing stroke risk in patients with non-valvular atrial fibrillation was largely established by the Randomised Evaluation of Long-Term Anticoagulation therapy (RE-LY) trial. This trial enrolled over 18 000 patients with atrial fibrillation who were treated with either 110 mg dabigatran, twice daily, or 150 mg dabigatran, twice daily, or adjusted-dose warfarin.<sup>21</sup> It was concluded that in patients with atrial fibrillation, 110 mg of dabigatran, twice daily, was associated with rates of stroke and systemic embolism comparable to warfarin treatment, but lower rates of major haemorrhage.<sup>21</sup> Therefore dabigatran 110 mg, twice daily is recommended for patients aged over 80 years in whom a reduced bleeding risk is preferable.<sup>15</sup> Patients treated with dabigatran 150 mg, twice daily, had a lower risk of stroke and thromboembolism compared with warfarin with a comparable risk of major haemorrhage.<sup>21</sup>

After one to three years, almost half of the patients in the RE-LY trial were enrolled in the Long-term Multicenter Extension of Dabigatran Treatment in Patients with Atrial Fibrillation (RELY-ABLE) trial which had a mean follow-up of 4.3 years.<sup>23</sup> The risk of major bleeding and intracranial haemorrhage in patients taking dabigatran was similar to that of the RE-LY trial, although there was no control group of patients taking warfarin enrolled to confirm these findings.<sup>23</sup> The 150 mg, twice daily, dose of dabigatran continued to be associated with an increased rate of major bleeding compared with the 110 mg, twice daily, dose.<sup>23</sup>

A 2013 subgroup analysis of the RE-LY trial has found that the reported benefits of dabigatran in terms of

stroke and systemic embolism prevention compared to warfarin are also seen in patients who are concurrently taking an antiplatelet medicine.<sup>18</sup> The dabigatran 110 mg, twice daily dose was associated with a lower risk of major bleeding than adjusted-dose warfarin; the dabigatran 150 mg, twice daily, dose was associated with the same risk of major bleeding as warfarin.<sup>18</sup> However, the stroke and embolism preventing effects of dabigatran 150 mg, twice daily, did appear to be somewhat reduced by the concurrent use of an antiplatelet.<sup>18</sup>

The available evidence does not, however, completely support dabigatran in preference to warfarin. Recently a different group of investigators performed a retrospective study of patients diagnosed with atrial fibrillation to assess the risk of bleeding in 1302 patients taking dabigatran and 8102 patients taking warfarin.<sup>24</sup> Compared to warfarin, dabigatran treatment (dose not recorded) was found to be associated with an increased risk of major bleeding (regardless of anatomical location) and gastrointestinal bleeding, but a lower risk of intracranial haemorrhage.<sup>24</sup>

A trial of over 2500 patients with acute venous thromboembolism compared dabigatran 150 mg, twice daily, with dose-adjusted warfarin. It was found that dabigatran treatment for patients with venous thromboembolism was associated with significantly fewer clinically relevant bleeds or bleeds of any sort and that dabigatran was associated with a trend towards fewer major bleeds.<sup>25</sup> Contrary to studies in other patient groups the rate of intracranial bleeding was the same in both groups of patients; there were two intracranial bleeds recorded in each group of patients.<sup>25</sup>




## Ticagrelor may be more effective than clopidogrel in Māori or Pacific peoples

Research has identified genetic polymorphisms in the CYP2C19 enzyme that metabolises clopidogrel, which may influence treatment efficacy. Ethnic differences have also been found in the prevalence of these alleles. A study of 312 New Zealand patients with acute coronary syndrome treated with clopidogrel and aspirin found that 47% of Māori and Pacific peoples had a loss-of-function CYP2C19 allele, while 11% had a gain-of-function CYP2C19 allele.<sup>28</sup> In comparison 26% of Europeans with acute coronary syndrome had a loss-of-function allele and 41% had a gain-of-function allele.<sup>28</sup> The authors were also able to correlate the presence of the loss-of-function CYP2C19 allele with increased levels of platelet reactivity on assay from patients taking clopidogrel.<sup>28</sup> High platelet reactivity levels have been associated with poorer outcomes in patients with acute coronary syndromes. The authors of the study concluded that Māori and Pacific peoples should be preferentially treated with ticagrelor over clopidogrel.<sup>28</sup>

Although the clinical implications of the research are not yet fully known, to date no genetic variations in the efficacy of ticagrelor have been reported. Therefore this is a further reason why many cardiologists recommend ticagrelor in preference to clopidogrel for the treatment of patients with an acute coronary syndrome.

### How is ticagrelor initiated?

Treatment with ticagrelor begins with 180 mg as a single dose, then 90 mg, twice daily, for up to 12 months.<sup>15</sup> It should be taken in combination with low-dose aspirin, e.g. 100 mg, daily.<sup>15</sup> The most frequent adverse effect associated with the use of ticagrelor is a transient dyspnoea that does not appear to be caused by bronchospasm. For this reason, ticagrelor should be used cautiously in patients with asthma or COPD.<sup>15</sup> Ticagrelor should be discontinued five days before elective surgery.<sup>15</sup> It is recommended that renal function be tested within one month of initiation of ticagrelor.<sup>15</sup> Patients aged over 75 years, those who have moderate or severe renal impairment, and those taking an angiotensin receptor blocker (ARB) may be more likely to have an increase in creatinine levels.<sup>29</sup> Ticagrelor should be used cautiously in patients with a history of hyperuricaemia or gout. The use of ticagrelor is not recommended in patients with uric acid nephropathy.<sup>29</sup>

 For further information, see: "Ticagrelor – out with the old and in with the new?", *BPJ* 54 (Aug, 2013).


## The evidence: ticagrelor vs. clopidogrel

The Platelet Inhibition and Patient Outcomes (PLATO) trial compared ticagrelor versus clopidogrel for the prevention of cardiovascular events in more than 18 000 patients admitted to hospital with an acute coronary syndrome, with or without ST segment elevation.<sup>26</sup> All patients received aspirin 75 – 100 mg daily, unless they could not tolerate aspirin.<sup>26</sup> Compared with clopidogrel, ticagrelor was found to significantly reduce mortality from vascular causes, myocardial infarction, or stroke, without increasing the overall rate of major bleeding, although, an increase in bleeding not related to coronary-artery bypass grafting was seen in patients taking ticagrelor.<sup>26</sup>


A recent subgroup analysis of 11 080 patients with non-ST segment elevation acute coronary syndrome from the PLATO trial randomised to either ticagrelor or clopidogrel found that ticagrelor significantly reduced the rates of death from vascular causes, myocardial infarction, or stroke without an increase in the rate of overall bleeding.<sup>26</sup> After 12 months, the rates of death from these causes was 9.8% in patients taking ticagrelor and 11.7% in those taking clopidogrel.<sup>26</sup> However, ticagrelor was associated with an increased rate of bleeding not related to surgery, including more instances of fatal intracranial bleeding.<sup>26</sup>

Patients with acute coronary syndrome and a prior history of stroke or TIA have a mortality rate twice that of patients with acute coronary syndrome without a history of stroke or TIA.<sup>27</sup> These patients are also at three times the risk of experiencing a stroke and four times the risk of having an intracranial bleed compared with patients without a history of stroke or TIA.<sup>27</sup> The assessment of the benefits and risks of treatment with an antiplatelet are difficult in this context as many of the factors that indicate high ischaemic risk also suggest an elevated risk of bleeding, e.g. age, hypertension, diabetes.<sup>27</sup> In the PLATO trial, 1152 patients with acute coronary syndrome had a history of stroke or TIA and subgroup analysis found that the benefits of ticagrelor treatment were also applicable in this high-risk patient group.<sup>27</sup> However, this net clinical benefit in patients with a history of cerebrovascular disease has been challenged by some clinicians.<sup>30</sup>

**Table 1:** Anticoagulant medicines currently available from community pharmacies in New Zealand<sup>15</sup>

Anticoagulant	Indications	Contraindications	Comments
<p><b>Warfarin</b> vitamin K antagonist</p>	<p>Prevention of thromboembolism in patients with atrial fibrillation (AF) with at least one risk factor, e.g. previous TIA or stroke, systemic embolism, symptomatic heart failure, age ≥ 75 years, age ≥ 65 years with coronary artery disease, hypertension, or diabetes.</p> <p>Prevention of stroke following myocardial infarction in patients with increased embolic risk.</p> <p>Prevention and treatment of venous thrombosis and pulmonary embolism.</p> <p>Prevention of thromboembolism in patients with prosthetic heart valves.</p>	<p>Haemorrhagic stroke, active bleeding or significant risk of major bleeding.</p> <p>Should not be used during pregnancy or within 48 hours postpartum.</p>	<p>Dose is adjusted according to the patient's INR; the patient should spend more than 65% of the time in the therapeutic range.<sup>6</sup></p> <p>For primary and secondary prevention of stroke the dose is adjusted to achieve an INR of 2–3. In patients with aortic valve prosthesis the target INR is 2.5–3.0, and in patients with mitral valve prosthesis the INR target is 3.0–3.5.</p> <p> For further information, see: "Use of INR for monitoring warfarin treatment", BT (Nov, 2010).</p> <p>Medicines are available to reverse the anticoagulant effect of warfarin, e.g. vitamin K.</p> <p>Fully subsidised without restrictions.</p>
<p><b>Dabigatran</b> direct thrombin inhibitor</p>	<p>The prevention of stroke and systemic embolism in patients with non-valvular AF with at least one risk factor, e.g. previous TIA or stroke, systemic embolism, symptomatic heart failure, age ≥ 75 years, age ≥ 65 years with coronary artery disease, hypertension, or diabetes.</p> <p>Prevention of venous thromboembolism following total hip or knee replacement.</p> <p>Treatment of deep vein thrombosis or pulmonary embolism after at least five days of parenteral anticoagulant treatment (new 2014).</p> <p>Prevention of recurrent deep vein thrombosis or pulmonary embolism (new 2014).</p>	<p>Active bleeding or significant risk of major bleeding.</p> <p>Should not be used as an anticoagulant in patients with prosthetic heart valves.</p> <p>Should not be used in patients with CrCl &lt; 30 mL/min.</p> <p>Concomitant treatment with ketoconazole.<sup>5</sup></p>	<p>Regular monitoring of renal function is required. Test renal function in all patients prior to initiation and preferably three to six monthly (but at least annually) in patients with a CrCl of 30 – 50 mL/min.</p> <p>Test renal function annually in patients aged over 75 years and in all patients where there may be a decline in renal function, e.g. dehydration or diuretic use.<sup>5</sup></p> <p>Currently no reversal medicine is available.</p> <p>Therapeutic testing may be available in the future to improve treatment efficacy, although this would negate one of the benefits of treatment.</p> <p>Fully subsidised without restrictions.</p>

<b>Rivaroxaban</b> inhibitor of factor Xa	<p>The prevention of venous thromboembolism following a total hip or knee replacement.</p> <p>Treatment of deep vein thrombosis.</p> <p>Prevention of recurrent deep-vein thrombosis and pulmonary embolism.</p> <p>Prevention of stroke and systemic embolism in patients with non-valvular AF and at least one risk factor: symptomatic heart failure, hypertension, age <math>\geq</math> 75 years, diabetes, or prior TIA or stroke.</p>	<p>Active bleeding or significant risk of major bleeding, prosthetic heart valve.</p> <p>Hepatic disease associated with coagulopathy.<sup>31</sup></p>	<p>Check renal function before prescribing; doses in patients with renal impairment may need to be reduced (or the medicine avoided) depending on the indication (see NZF for details).</p> <p>Fully subsidised with Special Authority approval for up to five weeks following a hip replacement and up to two weeks following a knee replacement with application from any relevant practitioner.</p>
<b>Apixaban</b> inhibitor of factor Xa	<p>The prevention of venous thromboembolism following hip or knee replacement surgery.</p> <p>The prevention of stroke and systemic embolism in patients with non-valvular AF and at least one risk factor: symptomatic heart failure, hypertension, age <math>\geq</math> 75 years, diabetes, or prior TIA or stroke.</p>	<p>Active bleeding or significant risk of major bleeding.</p>	<p>Check renal function before prescribing; doses in patients with renal impairment may need to be reduced (or the medicine avoided) depending on the indication (see NZF for details).</p> <p>Efficacy not established in patients with prosthetic heart valves.</p> <p>This medicine is approved for use but not currently subsidised.</p>
<b>Enoxaparin</b> low molecular weight heparin - LMWH	<p>The prevention of deep-vein thrombosis in surgical and medical patients.</p> <p>Treatment of deep-vein thrombosis and pulmonary embolism.</p> <p>Treatment of acute coronary syndromes.</p> <p>Prevention of clotting in haemodialysis.</p> <p>Treatment of venous thromboembolism in pregnancy (unapproved indication).</p>	<p>Haemorrhagic disorders, thrombocytopenia, recent cerebral haemorrhage, severe hypertension, peptic ulcer, major trauma or recent surgery to the eye or nervous system, acute bacterial endocarditis, spinal or epidural anaesthesia with treatment doses of unfractionated or LMWH, hypersensitivity to unfractionated or LMWH.</p>	<p>The risk of bleeding may be increased if renal function is impaired; reduce dose if eGFR is <math>&lt;</math> 30 mL/min/1.73m<sup>2</sup>. Monitoring anti-factor Xa may be required in patients with an eGFR <math>&lt;</math> 30 mL/min/1.73m<sup>2</sup> and unfractionated heparin may be preferable.</p> <p>Immune-mediated thrombocytopenia can develop after five to ten days. Platelets should be measured before treatment and monitored if given for longer than four days.</p> <p>Hyperkalaemia can result from inhibition of aldosterone in patients with: diabetes, renal failure, acidosis, or raised plasma potassium.</p>

 For further information on anticoagulants, including initiating warfarin treatment, reversing the effects of anticoagulants, and converting between anticoagulants see: <http://files.www.clotconnect.org/healthcare-professionals/resources-for-health-care-professionals/AnticoagPocketGuide-1.pdf>

N.B. The dosing regimens and indications in the above link are based on current United States guidance and may not always be applicable to the New Zealand context.

**Table 2:** Oral antiplatelet medicines currently available from community pharmacies in New Zealand<sup>15</sup>

Antiplatelet	Indications	Contraindications	Comments
<p><b>Aspirin</b> salicylate non-steroidal anti-inflammatory drug</p>	<p>The prevention of thrombotic cardiovascular and cerebrovascular disease.</p> <p>For use in patients following coronary artery by-pass surgery.</p> <p>For the treatment of acute thrombotic conditions, e.g. acute myocardial infarction and ischaemic stroke.</p>	<p>Previous or active peptic ulcer, haemophilia, severe cardiac failure.</p> <p>A history of hypersensitivity to aspirin or NSAIDs.</p> <p>Not for the treatment of gout.</p>	<p>Guidelines vary for the use of aspirin in primary prevention of cardiovascular disease. Generally, aspirin can be considered for the primary prevention of cardiovascular disease in patients with a five-year cardiovascular risk &gt; 20% and without significant risk factors for bleeding.<sup>32</sup></p> <p>Fully subsidised without restrictions.</p>
<p><b>Clopidogrel</b> thienopyridine antiplatelet</p>	<p>The prevention of vascular ischaemic events in patients with symptomatic atherosclerosis.</p> <p>The prevention of atherothrombotic events in patients with acute coronary syndrome for up to 12 months (with aspirin).</p>	<p>Severe hepatic impairment, active bleeding or significant risk of major bleeding.</p>	<p>Clopidogrel has the benefit over aspirin of not requiring concomitant gastroprotection in patients with previous peptic ulceration, when taken as monotherapy.</p> <p>Following an acute coronary syndrome a flag can be placed in the patient's notes to remind clinicians when the treatment period has finished.</p> <p>Fully subsidised without restrictions.</p>
<p><b>Dipyridamole</b> adenosine reuptake and phosphodiesterase inhibitor</p>	<p>The secondary prevention of ischaemic stroke or TIA.</p> <p>The prevention of thromboembolism in patients with prosthetic heart valves (with aspirin).</p>	<p>Nil</p>	<p>Should be used cautiously in patients with rapidly worsening angina, aortic stenosis, recent MI, left ventricular outflow obstruction, heart failure, hypotension, myasthenia gravis. Migraine may be exacerbated.</p> <p>Fully subsidised without restrictions.</p>
<p><b>Ticagrelor</b> reversible purinoreceptor-P2Y<sub>12</sub> antagonist</p>	<p>The prevention of atherothrombotic events in patients with acute coronary syndrome for up to 12 months (with aspirin)</p>	<p>Active bleeding or significant risk of major bleeding, history of intracranial haemorrhage.</p>	<p>Measure renal function one month after initiation. Should be used with caution in patients with asthma or COPD, or in patients with a history of hyperuricaemia.</p> <p>A flag can be placed in the patient's notes to remind clinicians when the treatment period has finished.</p> <p>Fully subsidised with Special Authority approval following application by any relevant practitioner for patients recently diagnosed with a ST-elevation or non-ST-elevation acute coronary syndrome and in who fibrinolytic treatment has not be given in the last 24 hours (and is not planned to be given).</p>



Antiplatelet	Indications	Contraindications	Comments
<b>Prasugrel</b> thienopyridine antiplatelet	The prevention of atherothrombotic events in patients with acute coronary syndrome who are undergoing percutaneous coronary intervention.	Active bleeding or significant risk of major bleeding, history of TIA or stroke.	<p>Discontinue at least seven days before surgery depending on the clinical circumstance.</p> <p>Fully subsidised with Special Authority approval for patients who have undergone coronary angioplasty in the past four weeks and have a bare metal stent or a drug-eluting stent, and are clopidogrel-allergic i.e. a history of anaphylaxis, urticaria, generalised rash, or unexplained asthma developing shortly after clopidogrel initiation. Subsidy also applies for patients who have had a stent thrombosis while taking clopidogrel.</p>



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

*The majority of patients who present to general practice with chest pain are unlikely to have an acute coronary syndrome. However, all patients who present with current or recent symptoms consistent with a cardiac cause require immediate investigation and treatment. Additional interventions may be appropriate for patients where there will be a significant delay in transport to the nearest Emergency Department.*

### **Managing patients with possible acute coronary syndromes**

Acute coronary syndrome refers to a spectrum of unstable conditions where plaque rupture causes sudden occlusion of the coronary arteries. The spectrum ranges in severity from angina to transmural myocardial infarction. Patients may present to general practice currently experiencing chest pain or they may report recent symptoms, e.g. from the previous evening. In the majority of cases this is unlikely to be caused by an acute coronary syndrome, however, all patients who present with symptoms consistent with a cardiac cause require immediate investigation and treatment. Additional interventions, e.g. intravenous fibrinolysis, may be appropriate depending on the location of the practice, the availability of medicines and transport time to the nearest Emergency Department.

## Checklist: patient presenting with acute chest pain in primary care

1. Perform an ECG in all patients where the possibility of a cardiac cause of chest pain cannot be reasonably excluded
2. If a ST segment abnormality, particularly ST segment elevation, is detected or ECG is inconclusive but suspicion of a cardiac cause remains, refer to hospital immediately and alert the on-call cardiologist or emergency department consultant
3. While awaiting transfer:
  - Monitor blood pressure, heart rate and oxygen saturation
  - Give sublingual glyceryl trinitrate\* and IV morphine (if required) for pain relief
  - Give 300 mg aspirin
  - Give 300 mg clopidogrel if evidence of ischaemia on ECG or elevated troponin levels (see number 4)
  - Only administer oxygen if the patient is breathless, oxygen saturation is <93%, has heart failure or is in cardiogenic shock
4. A blood sample for measuring troponin levels may be considered if time and clinical circumstances permit
5. If transfer will be delayed for more than two hours and patient has ST segment elevation, initiate tenecteplase,\*\* followed by enoxaparin, if available

\* Sublingual GTN should be used with caution in some patients, e.g. those who are cardiovascularly unstable. See NZF for a full list of cautions and contraindications.

\*\* Tenecteplase is usually only available in rural practices.

## Investigate all patients with suspected cardiac chest pain

If a patient with a history of established cardiovascular disease, e.g. previous angina, presents with chest pain, it is likely that their symptoms have a cardiac origin. However, patient history can also suggest other causes for chest pain, such as gastro-oesophageal reflux disease (GORD) or it may be musculoskeletal in origin.

Symptoms suggestive of an acute coronary syndrome include:<sup>1</sup>

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

Additional factors that increase the likelihood of a cardiac cause of chest pain are older age, male sex and a high number of predisposing clinical features, e.g. smoking, diabetes, obesity.<sup>2</sup>

Having a practice protocol that all staff can initiate for patients with suspected cardiac chest pain is likely to streamline management (see: "Have a practice protocol that all staff can initiate", opposite).

**A 12-lead ECG should be performed immediately in all patients** with symptoms suggestive of a recent or current acute coronary syndrome.<sup>2</sup> It is recommended that all general practices have ready access to an ECG machine for this purpose. The finding of a ST segment elevation on an ECG in a patient with a suspected acute coronary syndrome suggests occlusion of an epicardial artery.<sup>3</sup> A ST segment elevation acute coronary syndrome is defined as the presence of one of the following on ECG, in combination with the patient's clinical presentation:<sup>2</sup>

- $\geq 1$  mm ST elevation in at least two adjacent limb leads
- $\geq 2$  mm ST elevation in two contiguous precordial leads
- New onset bundle branch block

If a ST segment elevation is detected, the patient should be immediately referred to hospital, as in these patients, urgent fibrinolytic treatment has been associated with a reduction

in mortality.<sup>2</sup> If the patient's ECG is otherwise abnormal, and suspicion remains of a cardiac cause, then assume that the patient has an acute coronary syndrome and refer them to hospital. If the patient has a previous ECG on record, this is likely to be useful when assessing an atypical result.

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

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

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

Serum troponin levels may be assayed in a community laboratory or a blood sample sent with a patient who is being admitted urgently to hospital. The diagnostic accuracy of troponin testing has improved in recent years, particularly in the first hours following the onset of chest symptoms. A normal serum troponin level two to three hours after symptom onset means there is a low probability of myocardial infarction, although myocardial infarction cannot be completely excluded

until 9 – 12 hours following symptom onset; negative results may need to be repeated.<sup>4</sup> The criteria for myocardial infarction for high-sensitivity troponin T is  $\geq 15$  ng/L, with a rise and/or fall of  $\geq 50\%$  over three to six hours.<sup>5</sup> Differential causes of an elevated serum troponin include: decreased clearance due to renal dysfunction, atrial or ventricular tachycardia, pulmonary emboli with right ventricular infarction, chronic and severe congestive cardiac failure and myocarditis.<sup>5</sup> Creatine kinase muscle brain (CKMB) testing is no longer recommended for the diagnosis of myocardial infarction.<sup>5</sup>

Patients with slight elevations in serum troponin have rates of mortality at one and six months similar to patients who have experienced a major clinical myocardial infarction.<sup>2</sup> However, the presence of a ST segment elevation on ECG is more strongly predictive of an adverse outcome than an elevation in serum troponin.<sup>2</sup>

Full blood count, creatinine and electrolytes, glucose and lipids may also be useful tests and these can be performed on the same blood sample used to measure serum troponin, if time and clinical circumstance permit.<sup>5</sup>

### Treatment for all patients with acute coronary syndromes

All patients with an acute coronary syndrome require immediate referral to an Emergency Department. **Sublingual glyceryl trinitrate** is often used initially for symptom relief in patients with chest pain due to a cardiac cause. It should, however, be used with caution in some patients, e.g. those who are cardiovascularly unstable and those who have recently

## Have a practice protocol that all staff can initiate

If a patient presents to a general practice during an acute coronary syndrome, it may be a non-clinical member of staff who is their first point of contact. It is therefore important that all staff members are aware of the practice protocol for managing patients with unexplained chest pain, and know how to initiate the protocol.

Staff members should know which room in the practice is the most appropriate to locate patients requiring urgent

attention. Ideally this room will have an examination bed or couch with clear access on all sides and an ECG machine on hand, as well as convenient access for ambulance staff and equipment. All staff should be alerted to the location and status of the patient, who should not be left unattended.



used a PDE5-inhibitor such as sildenafil (see NZF for a full list of cautions and contraindications).<sup>6</sup> Blood pressure should be monitored regularly after glyceryl trinitrate has been used because, depending on the site of the suspected coronary event (e.g. inferior, right ventricular), the reduction in preload can result in the patient becoming rapidly hypotensive and intravenous fluids may be required to maintain adequate cardiac output.

Symptom relief with glyceryl trinitrate lasts less than one hour and usually does not provide sufficient pain relief in patients experiencing an active myocardial infarction. An additional analgesic e.g. morphine (see below), may be required.<sup>2,3</sup>

Patients who have known angina will already be familiar with using glyceryl trinitrate for the relief of anginal pain:<sup>2</sup>

1. One to two sprays of glyceryl trinitrate under the tongue at symptom onset
2. A further two doses (of one to two sprays), at five minute intervals, if necessary
3. If symptoms have not resolved five minutes after taking the third dose, i.e. 15 minutes from onset, an ambulance should be called

**Intravenous (IV) morphine** is effective for severe pain in a patient with an acute coronary syndrome.<sup>1,3</sup> For example, give morphine 5–10 mg IV at 1–2 mg/minute, repeat if necessary; morphine 2.5–5 mg for older or frail patients.<sup>6</sup>

**An IV antiemetic**, e.g. metoclopramide 10 mg or cyclizine 25 mg, is usually administered at the same time as, or immediately prior to, IV morphine.<sup>3</sup>

**Dispersible aspirin** 300 mg, should be given to all patients with an acute coronary syndrome, including those already taking aspirin; if enteric coated aspirin is the only formulation available the patient should chew the tablet.<sup>2</sup> Treatment with aspirin 75–150 mg, daily, is then continued indefinitely in all patients unless there are contraindications.<sup>2,3</sup> The immediate and continued use of aspirin in the weeks following an acute coronary syndrome, compared with placebo, approximately halves the rate of further cardiovascular events (absolute risk reduction 5.3%) in patients with unstable angina and reduces this risk by almost one-third (absolute risk reduction 3.8%) in patients with acute myocardial infarction.<sup>2</sup>

**Clopidogrel** 300 mg (75 mg for patients aged over 75 years) given immediately along with aspirin, 300 mg, is recommended

for patients with an acute coronary syndrome who also have evidence of ischaemia on ECG or elevated serum troponin levels.<sup>2,3</sup> Clopidogrel is then continued at a dose of 75 mg, daily (with aspirin), for these patients.<sup>2</sup> N.B. Clopidogrel may not be routinely available in general practices as it is not able to be obtained under a Practitioner's Supply Order.

**Oxygen treatment should not be routinely administered**  
**DO NOT administer oxygen to patients with an ST elevation acute coronary syndrome unless they:**<sup>3</sup>

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

Despite being recommended for many years, there is no evidence from randomised controlled trials supporting the routine use of oxygen in patients with acute myocardial infarction.<sup>2</sup> In patients with a myocardial infarction and an oxygen saturation > 93%, oxygen treatment may actually increase left ventricular afterload due to arterial vasoconstriction.<sup>3</sup>

A Cochrane review of four trials, including 430 patients, found non-significant evidence that compared to breathing air normally, oxygen administration may be harmful to patients with acute myocardial infarction.<sup>7</sup> The same review concluded that the use of oxygen did not appear to reduce pain because it was not associated with a reduction in analgesia used, although, there was a high risk of bias due to the small sample size.<sup>7</sup>

The Air Versus Oxygen In myocardial infarction (AVOID) study enrolled approximately 500 patients with an acute ST elevation myocardial infarction within the preceding 12 hours.<sup>8</sup> Results from AVOID have been presented at a conference, but are yet to be published. It is reported that if patients with symptoms of a ST elevation myocardial infarction, who are not hypoxic, are given oxygen for as little as 15 minutes they are at risk of hyperoxia.<sup>9</sup> This can cause a reduction in coronary blood flow ultimately leading to an increase in the size of the cardiac infarct.<sup>9</sup>

A large scale randomised controlled trial is urgently needed to establish whether oxygen treatment is harmful in patients with an acute coronary syndrome.

**Transfer all relevant information with the patient**

General practitioners can improve the treatment that patients with an acute coronary syndrome receive by ensuring that all

**Table 1:** Major and relative contraindications to fibrinolytic treatment in patients with a ST segment elevation acute coronary syndrome.<sup>3</sup>

Major contraindications to fibrinolytic treatment	Relative contraindications to fibrinolytic treatment
<ul style="list-style-type: none"> <li>■ Severe uncontrolled hypertension, i.e. blood pressure &gt; 180/110 mmHg</li> <li>■ Dementia</li> <li>■ Suspected aortic dissection</li> <li>■ Cerebral aneurysm, arteriovenous malformation or intracranial neoplasm</li> <li>■ Major trauma within six weeks</li> <li>■ Head trauma or brain surgery within six months</li> <li>■ Active bleeding or known bleeding disorder</li> <li>■ Traumatic cardiopulmonary resuscitation within three weeks</li> <li>■ Previous haemorrhagic stroke or stroke of unknown origin</li> <li>■ Ischaemic stroke within one year</li> <li>■ Gastrointestinal bleeding with one year</li> <li>■ Other internal bleeding within six weeks</li> <li>■ Non-compressible vascular punctures within 24 hours, e.g. central venous lines, liver biopsy</li> </ul>	<ul style="list-style-type: none"> <li>■ Treatment with warfarin, dabigatran, rivaroxaban or other anticoagulants</li> <li>■ Previous streptokinase treatment</li> <li>■ Transient ischemic attack (TIA) within the last six months</li> <li>■ An increased tendency to bleed</li> <li>■ Severe kidney impairment, i.e. glomerular filtration rate &lt; 30 mL/min</li> <li>■ Advanced liver disease, e.g. bilirubin level elevated or liver enzymes greater than five times normal</li> <li>■ Internal bleeding within the last six months</li> <li>■ Pregnancy or less than one week postpartum</li> <li>■ Lumbar puncture with the last month</li> <li>■ Acute pancreatitis</li> <li>■ Acute peptic ulceration</li> <li>■ Infective endocarditis</li> <li>■ Intracardiac thrombi</li> <li>■ Active cavitating pulmonary tuberculosis</li> </ul>

relevant information from the patient's record is available to staff as soon as they arrive at hospital. If the patient's ECG shows a ST segment elevation, the on-call cardiologist or emergency department consultant should be alerted to prevent delays in accessing the catheterisation laboratory. Include the following information where possible:

- Time of onset of symptoms and duration
- Previous and current ECGs
- Current blood pressure, heart rate and oxygen saturation levels
- A list of any medicines given acutely, including time and dose
- Co-morbidities
- All medicines currently prescribed as well as any over-the-counter products
- Allergies
- Any relevant person details such as an advanced care plan
- Any relevant family history

### If the patient cannot be transported to hospital immediately

If there will be a significant delay, i.e. more than two hours, in transporting patients with an acute coronary syndrome to hospital then it is appropriate to discuss the patient with an emergency medicine consultant or a cardiologist who may suggest additional interventions, if the required medicines are available. Patients presenting in rural areas are most likely to be considered for these additional treatments.

### Fibrinolysis is recommended in patients with myocardial infarction if there is a transportation delay

The benefit of fibrinolysis for patients with a ST elevation myocardial infarction declines significantly with time from symptom onset. New Zealand guidelines recommend that patients with a ST elevation acute coronary syndrome be considered for pre-hospital fibrinolysis if percutaneous coronary intervention cannot be performed within two hours, in the absence of contraindications (Table 1).<sup>3</sup> Fibrinolytic medicines are not routinely available in general practice, however, tenecteplase (TNK-tissue-type plasminogen

activator) may be available in some rural general practices. A recommended treatment regimen is tenecteplase, IV injection, initiated within six hours of symptom onset, 30 – 50 mg over ten seconds according to body weight:<sup>3,10</sup>

- < 60 kg: 30 mg
- 60 – 69 kg: 35 mg
- 70 – 79 kg: 40 mg
- 80 – 89 kg: 45 mg
- ≥ 90 kg: 50 mg

It is recommended that the generic name “tenecteplase” be used whenever this medicine is administered.<sup>6</sup> Serious errors have occurred when fibrinolytic medicines have been mistakenly given at the wrong dose when the shortened abbreviation tPA has been used; this may refer to tenecteplase or alteplase, which have different dosing regimens.<sup>6</sup> Tenecteplase should not be mixed with solutions containing dextrose and any IV lines should be flushed before and after administration of tenecteplase.<sup>10</sup>

Enoxaparin (Clexane) 30 mg, is then given as an IV bolus, after tenecteplase, in patients aged under 75 years.<sup>3</sup> Fifteen minutes after the IV bolus, enoxaparin is given subcutaneously at 1 mg/kg (up to a maximum of 100 mg) every 12 hours, for at least 48 hours (often continued for several days).<sup>3</sup> Patients aged over 75 years are recommended not to receive the IV bolus of enoxaparin, due to the increased risk of bleeding. Instead, patients aged over 75 years are administered enoxaparin subcutaneously (SC), 0.75 mg/kg (up to a maximum of 75 mg) every 12 hours.<sup>3</sup>

### Medicines frequently initiated following admission to a coronary care unit

Most patients treated for an acute coronary syndrome will be offered dual antiplatelet treatment for one year following discharge to reduce current events, after which point aspirin alone is recommended.<sup>3,5</sup> The majority of these patients will

have undergone a coronary stenting procedure and dual antiplatelet treatment also reduces the likelihood of stent thrombosis.

Long-term angiotensin converting enzyme (ACE) inhibitor treatment may be initiated within a few days of admission for an acute coronary syndrome when mortality is highest.<sup>2</sup> An angiotensin II receptor blocker (ARB) is recommended if ACE inhibitors are not tolerated.<sup>5</sup> All patients who are discharged following an acute coronary syndrome complicated by heart failure or pulmonary oedema are likely to be prescribed an ACE inhibitor or ARB, and a beta-blocker and spironolactone.<sup>3</sup> Loop diuretics are also commonly prescribed in this situation.

Beta-blockers, in patients with unstable angina, reduce the likelihood of progression to myocardial infarction by 13%.<sup>2</sup> In patients with ST elevation acute coronary syndromes beta blockade reduces mortality, re-infarction and cardiac arrest.<sup>2</sup> However, the early and aggressive use of beta-blockers in all patients with an ST elevation myocardial infarction is not as widely recommended as it once was.<sup>11</sup> In patients with an acute coronary syndrome, and fast atrial fibrillation or markedly raised blood pressure, beta blockers may be appropriate in an acute setting.

Patients who require anticoagulation to be initiated, e.g. patients who develop atrial fibrillation, may begin treatment with aspirin and clopidogrel or ticagrelor, plus warfarin or dabigatran.<sup>5</sup> However, the patient’s risk of bleeding is relatively high with this treatment combination and ticagrelor or clopidogrel is generally withdrawn at one month and treatment continued with aspirin plus warfarin or dabigatran.

Statin treatment is begun one to five days after the onset of coronary symptoms, which results in an absolute risk reduction of 2.6% in adverse events due to recurrent ischaemia at four months.<sup>2</sup> For example, simvastatin or atorvastatin may be administered within 24 hours of onset of an acute coronary syndrome in patients not already taking a statin.<sup>2,3</sup>





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Treating childhood  
*eczema*  
– a topical solution for a topical problem

*Emollients, topical corticosteroids and avoidance of triggers remain the mainstays of treatment in children with eczema. Under-use of topical treatment continues to be more of a concern than overuse. This highlights the importance of providing comprehensive education to the child's parents or caregivers and overcoming "corticosteroid phobia". Although most children with eczema can be managed with topical treatments in primary care, referral to secondary care may be required in severe cases.*

Eczema, also referred to as atopic eczema or atopic dermatitis, is an itchy inflammatory skin disease most commonly seen in children. It is characterised by pruritis and inflamed, dry, scaling and crusted skin in the acute phase (Figure 1) with lichenification (thickening) and hyperpigmentation of the skin if the condition becomes chronic. Children with eczema will usually experience recurrent flares.

Eczema has been reported to affect approximately 20% of children in New Zealand with disproportionately higher rates among Māori and Pacific children.<sup>1</sup> Over 90% of cases of eczema develop in children before the age of five years and 60% of these cases occur in the first year of life.<sup>2</sup> Although many children experience remission as they grow older, approximately 20 – 40% of those affected in childhood will continue to experience eczema as adults.<sup>1</sup>

The pathogenesis of eczema is complex and it is now thought that skin barrier dysfunction, environmental factors, a genetic predisposition and immune dysfunction all contribute to its development and are closely intertwined.<sup>3</sup> The traditional view, that eczema was primarily an immune-mediated response, has been challenged by recent research that suggests abnormalities

in the skin barrier, including mutations in filaggrin (a structural protein), play a major role in the development of eczema.<sup>4,5</sup>

### **The severity of the child's symptoms should guide treatment**

The diagnosis of eczema in children is usually based on the patient history and clinical signs, e.g. dry, itchy skin and an early age of onset.<sup>2</sup> After a diagnosis of eczema has been made, treatment is tailored to the severity of the child's symptoms (Table 1, over page).

#### **Key management principles for children with eczema**

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



**Figure 1:** Examples of infants with atopic eczema (Images provided by Dermnet NZ)

**Table 1:** Eczema management algorithm (adapted from NICE, 2007)<sup>6,7</sup>

ECZEMA SEVERITY CHARACTERISTICS			
Controlled eczema with no active skin involvement	Mild eczema	Moderate eczema	Severe eczema
Normal skin with no evidence of dryness, redness or itching	Areas of dry skin Infrequent itching (with or without small areas of redness)	Areas of dry skin Frequent itching Redness (with or without excoriation and localised skin thickening)	Widespread areas of dry skin Incessant itching Redness (with or without excoriation, extensive skin thickening, bleeding, oozing, cracking and alteration of skin pigment)
TREATMENT			
Controlled eczema with no active skin involvement	Mild eczema	Moderate eczema	Severe eczema
All: <b>Emollients</b> + parent or caregiver education including advice regarding adherence			
	Mild topical corticosteroids, e.g. hydrocortisone 1%	Moderate topical corticosteroids,* e.g. triamcinolone acetonide, clobetasone butyrate <sup>†</sup>	Potent topical corticosteroids, <sup>‡</sup> e.g. hydrocortisone butyrate 0.1%,** betamethasone valerate (over age one year), mometasone furoate, methylprednisolone aceponate
			Consider referral for systemic and additional treatments

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


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

‡ Avoid use on face, neck, genitals or axillae

\*\* Hydrocortisone butyrate 0.1% (Locoid) is a potent corticosteroid and should not be confused with hydrocortisone 1%, a mild corticosteroid

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

Providing educational materials about eczema to parents or caregivers can help to increase their knowledge about their child's condition, and therefore reinforce effective management and help to promote adherence to topical treatments. Practice nurses are often responsible for this education and ongoing support.

 A leaflet for parents on how to care for the child's eczema is available from: [www.starship.org.nz/media/269759/caring\\_for\\_your\\_child\\_s\\_eczema\\_june\\_2014.pdf](http://www.starship.org.nz/media/269759/caring_for_your_child_s_eczema_june_2014.pdf)

### Recommend daily baths using wash-off emollients

Warm (not hot) baths, once daily, lasting no longer than 10 – 15 minutes are recommended for all children with eczema.<sup>8</sup> Emollients or wash-off emollient products, rather than soaps or detergents, should be used when bathing, and bubble baths avoided. Aqueous cream BP and emulsifying ointment BP (both subsidised) can be used as soap substitutes during bathing.\* These products can also be used as wash-off emollients if the household does not have a bath, applied before the child enters the shower and then washed off.


\* Neither aqueous cream BP nor emulsifying ointment BP should be used as a leave-on emollient as both contain sodium lauryl sulphate and can irritate the skin (see: "Which emollient should be prescribed", Page 36).

 A video on bathing children with eczema is available from: [www.kidshealth.org.nz/eczema-care-bathing](http://www.kidshealth.org.nz/eczema-care-bathing)

### Twice-weekly bleach baths are also recommended

Twice-weekly antiseptic baths with diluted sodium hypochlorite (household bleach) can reduce staphylococcal carriage and improve the child's symptoms.<sup>9</sup> Parents can be advised to add 2 mL of plain bleach (2.2% sodium hypochlorite, e.g. "Budget Household Bleach Regular") per litre of bathwater and bathe the child for 10 – 15 minutes, twice a week. A full-sized bath with a 10 cm depth of water holds approximately 80 litres of water, and will therefore require approximately 160 mL of 2.2% bleach. A baby's bath holds approximately 15 litres of water and will require approximately 30 mL of 2.2% bleach. Parents should be advised that bleach baths are safe when the correct amount of bleach is added to the bath, but to avoid contact between the bath water and the child's eyes. Antiseptic bath oils, e.g. Oilatum Plus or QV Flare up, can be used instead of bleach, but are generally more expensive.

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

 A patient leaflet that provides detailed information on how to prepare a bleach bath is available from: [www.starship.org.nz/media/269481/bleach\\_bath\\_handout.pdf](http://www.starship.org.nz/media/269481/bleach_bath_handout.pdf)

Recent evidence has highlighted the effectiveness of bleach baths in children with eczema, including an improvement in symptoms and reductions in *Staphylococcus aureus* colonisation. A recent study randomised 42 patients aged two to 30 years with moderate-to-severe eczema to either twice-weekly bleach baths (for ten minutes at a time) or normal baths, for two months. Patients in the bleach bath group had significant reductions in the Eczema Area and Severity Index (EASI)\* scores at both one and two months.<sup>9</sup> Reductions in *S. aureus* density were also observed at one and two months.<sup>9</sup> Mild adverse events (burning/stinging) were observed in both treatment groups.<sup>9</sup> A recently completed, but as yet unpublished, small randomised controlled trial in New Zealand found improvements in both the EASI and Scoring Atopic Dermatitis (SCORAD) scores in children with atopic eczema who had dilute bleach added to their bath. Children who did not have bleach added to their bath had very little change in their EASI and SCORAD scores.<sup>10</sup>

\* The EASI score is a tool used mainly in a research setting to measure the extent and severity of a patient's eczema.

### Advise about avoiding triggers/irritants

Avoiding triggers and irritants is beneficial during acute eczema flares as well as for long-term management to avoid the "itch-scratch-itch" cycle. Factors that can exacerbate a child's eczema include soaps, detergents, chemicals, abrasive clothing and temperature extremes.<sup>11</sup>

Useful advice that can be given to parents includes:<sup>11</sup>

- Wash new clothes before use to avoid contact with formaldehyde and other chemicals from the manufacturing process that can irritate the skin
- Use mild detergents labelled for sensitive skin when washing clothes and do a second rinse cycle to remove residual detergent. Avoid the use of fabric softeners.
- Dress children in loose cotton clothing and avoid wool or synthetics next to the skin, i.e. use cotton fabrics as a base layer
- Avoid topical products that contain fragrances, alcohol and other ingredients that can dry the skin, e.g. witch hazel

- Encourage children to rinse in fresh water after swimming in a chlorinated pool and follow with application of an emollient
- Keep children's fingernails trimmed to avoid injury from scratching

Although the influence of airborne allergens, e.g. dust mites, in exacerbating eczema is unclear, some parents may wish to reduce this exposure. This can be achieved by encasing the child's mattress, base and pillows in allergen-barrier bedding covers and washing top bedding in hot water (>55°C), or hot ironing, every two weeks.<sup>12</sup>

### The role of food allergy in eczema is unclear


The role of food allergens in the aetiology of a child's eczema is frequently overestimated, particularly by parents.<sup>13</sup> Food allergy is more likely to be a contributing factor in young infants with severe generalised eczema.<sup>12</sup>

Parents should be advised against putting their child on a very restrictive diet as this is often of limited benefit, and the diet can be expensive to maintain and result in nutritional deficiencies.<sup>12, 14</sup>

Allergy screening with large panels of food allergens is not recommended in children with eczema, as the child is usually atopic and allergy test results can reflect sensitisation to food rather than a clinically relevant allergy.<sup>12, 13</sup> Investigation of potential food allergies in children with eczema is recommended under the following circumstances:<sup>12</sup>

- If there is a history of an immediate allergic reaction following food consumption (this can also occur in a breast fed infant due to maternal ingestion of an allergen)
- If a young child has severe, problematic eczema and is unresponsive to appropriate topical treatment

If food allergy is suspected in a child with eczema, discussion with an immunologist, paediatric dermatologist or paediatrician is recommended, to decide on a course of further investigation, which may include radioallergosorbent test (RAST) or skin prick testing.<sup>12</sup> These tests can be performed in primary care, but results can sometimes be misleading or difficult to interpret.

 For further information, see: "Appropriate use of allergy testing in primary care" (Best Tests, Nov 2011).


## Use emollients frequently and in large quantities

Emollients form the basis of treatment for all children with eczema, as they reduce inflammation and support the natural skin barrier. Increased use of emollients has been shown to improve both the child's and parent's quality of life, reduce the child's eczema symptoms and sleep disturbances and decrease the amount of topical corticosteroids required.<sup>15, 16</sup>

Ideally, emollients should be applied **several times a day** to the entire body and continued even when the child's eczema has cleared.<sup>8</sup> Children should be prescribed **250 – 500 g of emollient per week** to provide sufficient product for moisturising, washing and bathing.<sup>8</sup>

Where possible emollients should be dispensed in a pump container or tube, as emollients prescribed in tubs or jars can become contaminated.<sup>8</sup> If tubs or jars are dispensed, advise carers to scoop the emollient from the tub using a clean spoon or spatula to avoid bacterial contamination.


Children should be encouraged to apply their emollients themselves from a young age, as this helps adherence and self-treatment when they start attending school. School-aged children should ideally keep a supply of emollient at school and be encouraged to use it whenever they feel the urge to scratch.

 **Best practice tip:** when prescribing an emollient it is useful to put the monthly quantity of emollient required on prescription (i.e. 2000 g per month). As most subsidised emollients are "stat" dispensed, the pharmacist is generally obliged to give the entire three months supply at the same time. However, if the prescriber wishes to limit the initial supply this can be achieved by endorsing the prescription with "trial period one month".

### Which emollient should be prescribed?

The best choice of emollient is the one preferred by the child/parent as it is more likely to be used regularly. Emollients have different formulations, including ointments, creams and lotions. The difference is the proportion of oil (lipid) to water in the product. The lipid content is highest in ointments, intermediate in creams and lowest in lotions. As a general rule, the products with the highest lipid content are more effective in treating dry skin, provide better barrier protection and have a longer duration of action,<sup>12</sup> but may be the least convenient due to being the most greasy/sticky on the skin.


The current subsidised emollients include three products that contain cetomacrogol derivatives and are considered as slightly-to-moderately greasy creams. These are Fatty Cream (HealthE) and cetomacrogol cream (PSM) which are available in 500 g tubs, and Sorbolene cream (which contains cetomacrogol + 10% glycerol) which is available in 500 g and 1 kg pump dispensers. Other products are available to purchase if the child or parent prefers another formulation. Aqueous cream BP and emulsifying ointment BP should not be used as leave-on emollients.

 Further information on emollients including subsidy restrictions is available from:  
[www.nzfchildren.org.nz/nzf\\_6237?searchterm=emollients](http://www.nzfchildren.org.nz/nzf_6237?searchterm=emollients)

### Practical tips on emollient use

Some useful advice for parents includes:<sup>8</sup>

- Emollients should be smoothed (not rubbed) onto the child's skin in the direction of hair growth to avoid irritation
- Products in tubs/jars should be discarded after the child has had a skin infection as they may have become contaminated
- Emollients should be continued when topical corticosteroids are being used and can be applied before or after the topical corticosteroid

 A patient video on the use of emollients is available from:  
[www.kidshealth.org.nz/eczema-care-moisturisers](http://www.kidshealth.org.nz/eczema-care-moisturisers)


### Use sufficient amounts of topical corticosteroids once or twice daily for the treatment of flares

Flares are characteristic of eczema, despite efforts to avoid irritants and apply emollients frequently. Topical corticosteroids are effective for treating flares, and, when used correctly, result in minimal adverse effects.<sup>17</sup> As with emollients, underuse of topical corticosteroids is more common than overuse, and discussing the benefits and risks of topical corticosteroid treatment with the family can assist in overcoming "corticosteroid phobia" (see: "Overcoming corticosteroid phobia", Page 39).

 A patient video on use of topical corticosteroids is available from: [www.kidshealth.org.nz/eczema-care-steroids](http://www.kidshealth.org.nz/eczema-care-steroids)

The potency of the corticosteroid prescribed should be matched to the severity of the child's eczema flare (Table 1) and the area of the body affected. It is important that the child's parents are aware of what area of the body the


topical corticosteroid should be applied to, particularly if more than one topical corticosteroid has been prescribed, e.g. hydrocortisone for the face and a more potent corticosteroid for eczema on the body.

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

### Are there any general rules to follow when selecting the appropriate potency?

The potency of the topical corticosteroid should match the severity of the child's symptoms. However, some useful rules of thumb to guide treatment include:

- Low potency corticosteroids (e.g. hydrocortisone cream 1%) should be used as first-line treatment in children of all ages with facial or flexural eczema.<sup>11</sup>
- Moderate potency topical corticosteroids (e.g. triamcinolone acetonide) can be considered as a second-line, short-term (five to seven days) treatment for use on the face in severe cases.<sup>11</sup>
- Infants aged less than one year with eczema on the trunk, legs or arms can usually be managed with a low potency corticosteroid. Pre-school aged children generally require a moderate or potent topical corticosteroid and school-aged children often require a potent topical corticosteroid.<sup>11</sup>
- Potent corticosteroids (e.g. hydrocortisone butyrate 0.1%) should not be prescribed for children aged less than one year and very potent topical corticosteroids, e.g. clobetasol propionate (Dermol), should not be prescribed for children with eczema at any age, without first discussing with a dermatologist.<sup>11</sup>
- In general, short bursts of more potent topical corticosteroids are more effective and have fewer adverse effects than longer term use of lower potency topical corticosteroids
- Mixing a topical corticosteroid with an emollient or another product does not reduce the potency of the topical corticosteroid<sup>8</sup>

 For further information on the topical corticosteroids, see:  
[www.nzfchildren.org.nz/nzf\\_6272](http://www.nzfchildren.org.nz/nzf_6272)

### How often should topical corticosteroids be applied, and for how long?

Topical corticosteroids should be applied no more than twice a day.<sup>8</sup> Once daily application is sufficient in most cases

(preferably after a bath), as applying treatment more frequently has not been shown to result in significantly better results and may adversely affect patient adherence.<sup>17, 18</sup>

Topical corticosteroids should only be applied to areas of active eczema (including broken skin) and usually discontinued when the flare has resolved (see: “Weekend treatment”, opposite).<sup>8</sup> The treatment duration is usually less than two weeks and if the flare does not resolve in this time then the treatment should be reassessed (see below).

**What to consider when treatment is not working**

If there is no improvement in the child’s symptoms after seven to 14 days of treatment, or if topical corticosteroids are required most days, then consider the following:<sup>8</sup>

- Poor adherence to treatment, including missed applications or use of an inadequate amount
- The corticosteroid is not potent enough
- Ongoing exposure to irritants, e.g. soap, sodium lauryl sulphate, or a contact allergen
- Secondary bacterial or viral skin infection
- Incorrect initial diagnosis

**How much topical corticosteroid should be prescribed?**

An **adult fingertip unit (FTU)** should be used as a guide when prescribing topical corticosteroids and when advising parents about appropriate use (Tables 3 and 4). One FTU is the amount of product (approximately 3 cm or 0.5 g) that will cover an adult index finger, from the tip of the finger to the distal interphalangeal joint, from a tube that has a standard 5 mm nozzle (Figure 2).<sup>19</sup> As a general guide, one adult FTU is enough to treat an area of the child’s eczema equal to the surface of two adult hands held side by side with the fingers together.



**Figure 2:** Fingertip unit (Image provided by Dermnet NZ)

**Table 3:** Approximate number of adult finger tip units (FTU) of corticosteroid needed per application for children with eczema.<sup>11, 20</sup>

	6 months old	12 months old	5 years old	10 years old
One entire arm and hand	1	1.5	2	2.5
One entire leg and foot	1.5	2	3	4.5
Torso (front)	1.5	2	3	3.5
Back and buttocks	1.5	3	3.5	5

**Table 4:** Approximate weight of product required for a once-daily application of corticosteroid to cover the entire body.<sup>11</sup>

	6 months old	12 months old	5 years old	10 years old
Daily (g)	5	6	10	15
Weekly (g)	35	40	70	100



## Topical corticosteroids can be used as maintenance treatment in children with frequent flares

In most cases, once control of the flare has been achieved, topical corticosteroid treatment can be stopped and emollients continued. However, some children experience frequent flares (two or three per month) and in these cases it may be useful to continue topical corticosteroid treatment between flares.<sup>21</sup> There are two ways to do this – either step down to the lowest potency product that controls symptoms or use the same potency product less frequently, i.e. “weekend treatment”.<sup>21</sup>

**Weekend treatment** can be used to prevent recurrence once control of the initial flare with a topical corticosteroid has been achieved. The topical corticosteroid should be applied once-daily on two consecutive days per week (not necessarily over the weekend, although this is often more convenient).<sup>21</sup> Emollients should be continued every day, including when the corticosteroid is not being applied. This strategy should be reviewed within three to six months to assess effectiveness.<sup>6</sup>

A study that investigated the efficacy of long-term, weekend topical corticosteroid treatment (up to 16 weeks) showed that this treatment reduced the extent and severity of symptoms and reduced the risk of recurrence in children aged four to ten years with a history of severe recurrent eczema.<sup>22</sup>

## Use other pharmacological options as required

Emollients and topical corticosteroids are the evidence-based core treatments for children with eczema, however, other treatment options may be considered in certain circumstances.

## Pimecrolimus can be used as a second-line treatment when topical corticosteroids are contraindicated

Pimecrolimus cream 1% (unsubsidised) is a calcineurin inhibitor that can be used as a second-line treatment for sensitive areas of eczema, e.g. the head, neck and genital area, in children aged three months or older when topical corticosteroids are unable to be used or have been ineffective despite optimal use.<sup>7,8</sup> Treatment should only be applied for short periods – up to three weeks at a time in children aged less than two years and for up to six weeks in children aged two to 18 years.<sup>7</sup>

Pimecrolimus has been shown to be less effective than moderate and potent corticosteroids and has not been compared directly with low potency corticosteroids.<sup>24</sup> A 2011 meta-analysis and systematic review reported that topical

## Overcoming corticosteroid “phobia”: appropriate use does not result in skin atrophy

Parents often underutilise topical corticosteroids due to the fear of adverse effects. Skin thinning is commonly cited as the most concerning adverse effect.<sup>23</sup> However, recent evidence suggests this adverse effect has been over-stated.<sup>17,23</sup>

A 2011 study that investigated the atrophogenic potential of topical corticosteroids in 92 paediatric dermatological patients reported that it was possible to obtain excellent control of symptoms without producing cutaneous atrophy.<sup>23</sup> The children had all received long-term (at least three months) topical corticosteroid treatment.<sup>23</sup> No degree of cutaneous atrophy was observed using a validated five-point dermoscopic scale at any of the 280 body sites measured, even though the children had received treatment for a prolonged period.<sup>23</sup>

An Australasian consensus statement on the adverse effects of topical corticosteroids in paediatric eczema agreed with these findings.<sup>17</sup> The statement reported that what is commonly referred to as skin thinning by parents and non-dermatologists is usually a misinterpretation of active eczema.<sup>17</sup> Other findings from the consensus statement about the use of topical corticosteroids include:<sup>17</sup>

- The fingertip unit should be used as a guide for the amount of corticosteroid to be applied
- Irreversible skin thinning does not occur when topical corticosteroids are used to treat flares and then terminated upon resolution of the flare
- Topical corticosteroids do not result in striae unless used inappropriately, e.g. under occlusion for long periods, or in overdose, and only then at certain body sites, e.g. groin or axillae
- Clinically significant adrenal suppression is very rare with appropriate use
- The hyper- or hypo-pigmentation observed as the child’s eczema clears is caused by the eczema and not the topical corticosteroid

Explaining to parents that topical corticosteroids have an anti-inflammatory effect, and are different to anabolic steroids, can also assist in overcoming any steroid phobia the parents may have.

corticosteroids appeared to be more effective than calcineurin inhibitors for the prevention of flares in people with atopic eczema.<sup>25</sup>

The benefits and risks of treatments should be discussed with parents as pimecrolimus can cause local irritation, most commonly a short-lasting burning sensation.<sup>7</sup> Other adverse effects include irritation, pruritis and erythema at the application site and also skin infections (most commonly folliculitis).<sup>7</sup>

### Antibiotics are required for secondary infection

Children with infected eczema require treatment with an oral antibiotic. The antibiotic regimen should be selected based on local resistance patterns and be active against *S. aureus* and streptococci. Skin swabs can be considered in certain circumstances, e.g. in areas with high prevalence rates of methicillin-resistant *S. aureus* (MRSA) or in children who have failed to respond to the first-line antibiotic treatment.

A first-line recommended treatment regimen is:<sup>26</sup>

- Flucloxacillin 12.5 mg/kg, three times daily, for seven to ten days (maximum 500 mg/dose)


OR

- Cephalexin 12.5 – 25 mg/kg, twice daily, for seven to ten days (maximum 500 mg/dose)

Erythromycin 10 mg/kg/dose, four times daily or 20 mg/kg, twice daily is a second-line alternative.<sup>26</sup>

Flucloxacillin syrup can be unpalatable for some children, therefore those who can swallow capsules should be prescribed these in preference to the syrup. It is not recommended that the syrup is mixed with other liquids prior to administration to help improve the taste, but a sweet drink can be given afterwards. As cephalexin is a broader spectrum antibiotic than flucloxacillin, ideally it should be chosen second-line, however, if compliance with flucloxacillin will be problematic, it is a recommended option.


Prescribing topical antibiotics, e.g. fusidic acid, for children with small localised lesions of infected eczema is now generally not recommended due to the high rates of resistance to fusidic acid in the community. Combination steroid, antibiotic and antifungal creams, e.g. Pimafucort (subsidised), may be appropriate for localised infections in certain circumstances, e.g. children with angular cheilitis.

 A patient handout on infected eczema is available from: [www.starship.org.nz/media/269484/infected\\_eczema\\_handout.pdf](http://www.starship.org.nz/media/269484/infected_eczema_handout.pdf)

### Antihistamines: may aid sleep in children with severe itch

Antihistamines are not routinely recommended for treating children with eczema as they do not generally help with the itch.<sup>8</sup> However, a short (< one month) trial of a non-sedating antihistamine, e.g. cetirizine, can be considered in children with moderate-to-severe eczema or when there is associated urticaria.<sup>8</sup> Non-sedating antihistamines are generally not recommended for use in children aged less than two years, with the exception of cetirizine which can be prescribed to children aged one year or older.<sup>7</sup>

During an eczema flare, itch can become severe and a short course of a sedating antihistamine, e.g. promethazine hydrochloride, can be trialled to aid sleep in children aged over two years.<sup>8</sup> The sedating antihistamine should initially be used at night when the child cannot sleep due to the itch and reduced to “as necessary” when the child’s symptoms have improved. Sedating antihistamines are contraindicated in children aged less than two years for all indications.<sup>7</sup>

 **Best practice tip:** If a child is being prescribed a sedating antihistamine “as required”, ensure that an appropriate volume of medicine is indicated on the prescription.

### Wet wraps: usually now initiated in secondary care

In the past, wet wraps have been recommended to parents as an at-home treatment for children with severe or extensive eczema. However, they are now generally not recommended for use in an outpatient community setting as the benefits of wet wraps over appropriate use of topical corticosteroids has not been proven.<sup>8,27</sup> Wet wraps have a number of drawbacks including systemic absorption of corticosteroids, high cost, necessity for specialised training to apply the wraps effectively and safely, and an increase in cutaneous infections and folliculitis.<sup>12</sup> They are sometimes used in a hospital setting under specialist supervision and require close monitoring if used with topical corticosteroids.

### Oral corticosteroids are generally not recommended

Oral corticosteroids (e.g. prednisolone) are not generally recommended for treating children with eczema as there can be significant rebound flaring of eczema when they are withdrawn.<sup>8</sup>

## Seek specialist advice for children with severe or persistent eczema

The majority of children with eczema can be managed in primary care, although seeking specialist paediatric or dermatological advice should be considered in children with severe or persistent eczema. Referral pathways will vary according to the local services available; contact your DHB. Circumstances where discussion with a specialist is recommended include:<sup>8,11</sup>

- If eczema herpeticum is suspected. Eczema herpeticum is a disseminated viral infection and most cases are due to the *Herpes simplex virus*. It is characterised by rapidly worsening, painful plaques, clustered vesicles or punched out erosions
- If the eczema is severe (or on the face) and the child is not responding to topical corticosteroids. This includes children requiring ongoing daily use of topical steroids to maintain control.
- When phototherapy or systemic treatment, e.g. methotrexate, ciclosporin, is likely to be required
- If a child with bacterially-infected eczema is not responding to appropriate treatment, or has recurrently infected eczema
- Where the eczema is causing the child significant psychological or social problems, e.g. frequent waking at night, school absenteeism
- If the child has suspected immediate food hypersensitivity, poor growth or a severely restricted diet
- Where there is uncertainty over the diagnosis

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## Alternative treatments options are often trialled

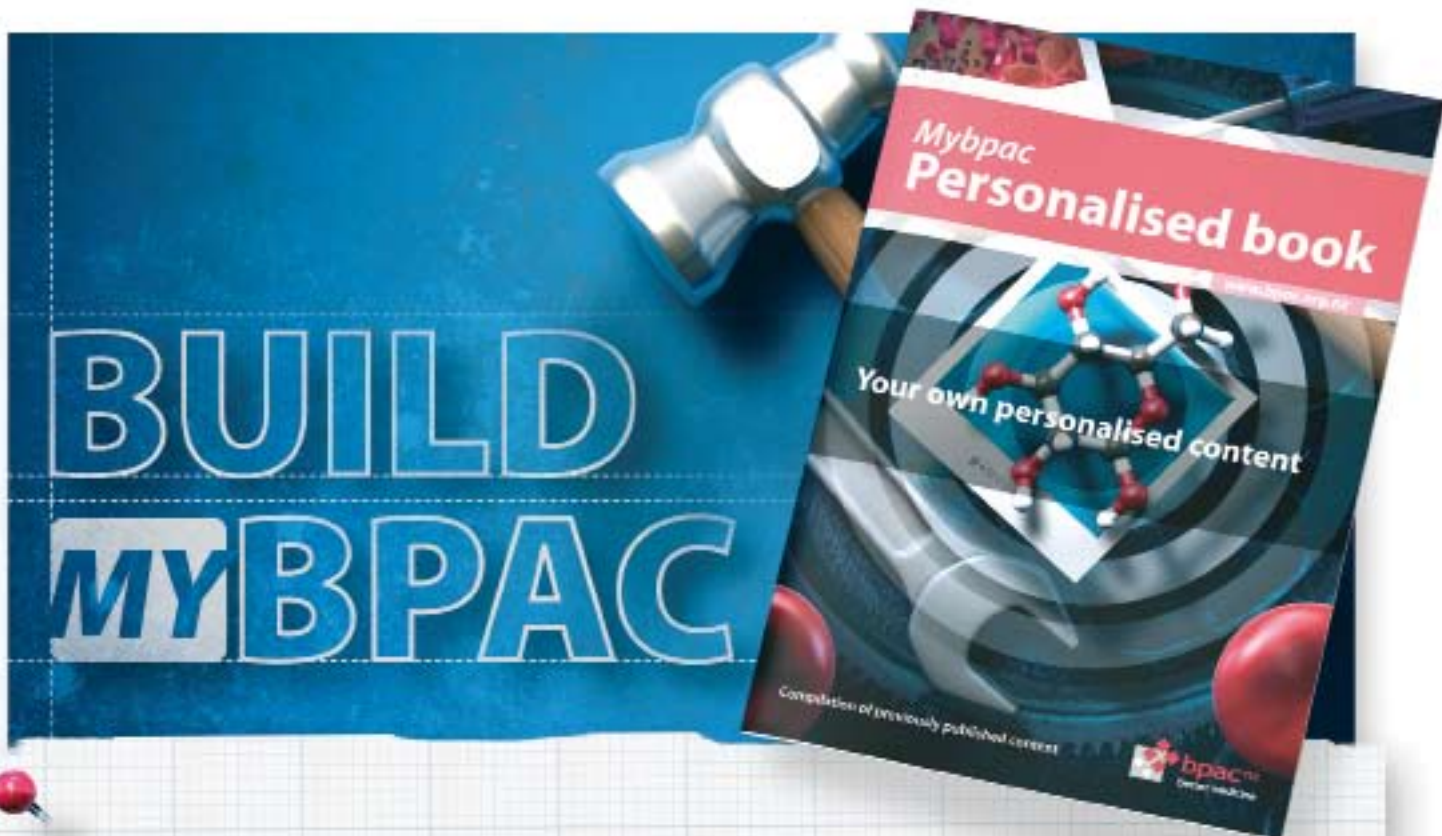
The guidance provided in this article is based on the best published international and local evidence for treating children with eczema in the primary care population in New Zealand. It is acknowledged that there are a number of alternative treatment options available, which, although do not have a solid evidence base to support them, may be considered on an individual basis in children for whom resolution of symptoms has been unable to be achieved with conventional means. These strategies often incorporate different combinations of treatments, other formulations/brands of emollients, the use of vitamins and exploring the avoidance of certain foods.

An open and non-judgemental discussion about strategies the parents may wish to pursue can help to ensure that appropriate treatments are selected that do not adversely affect the child's condition.



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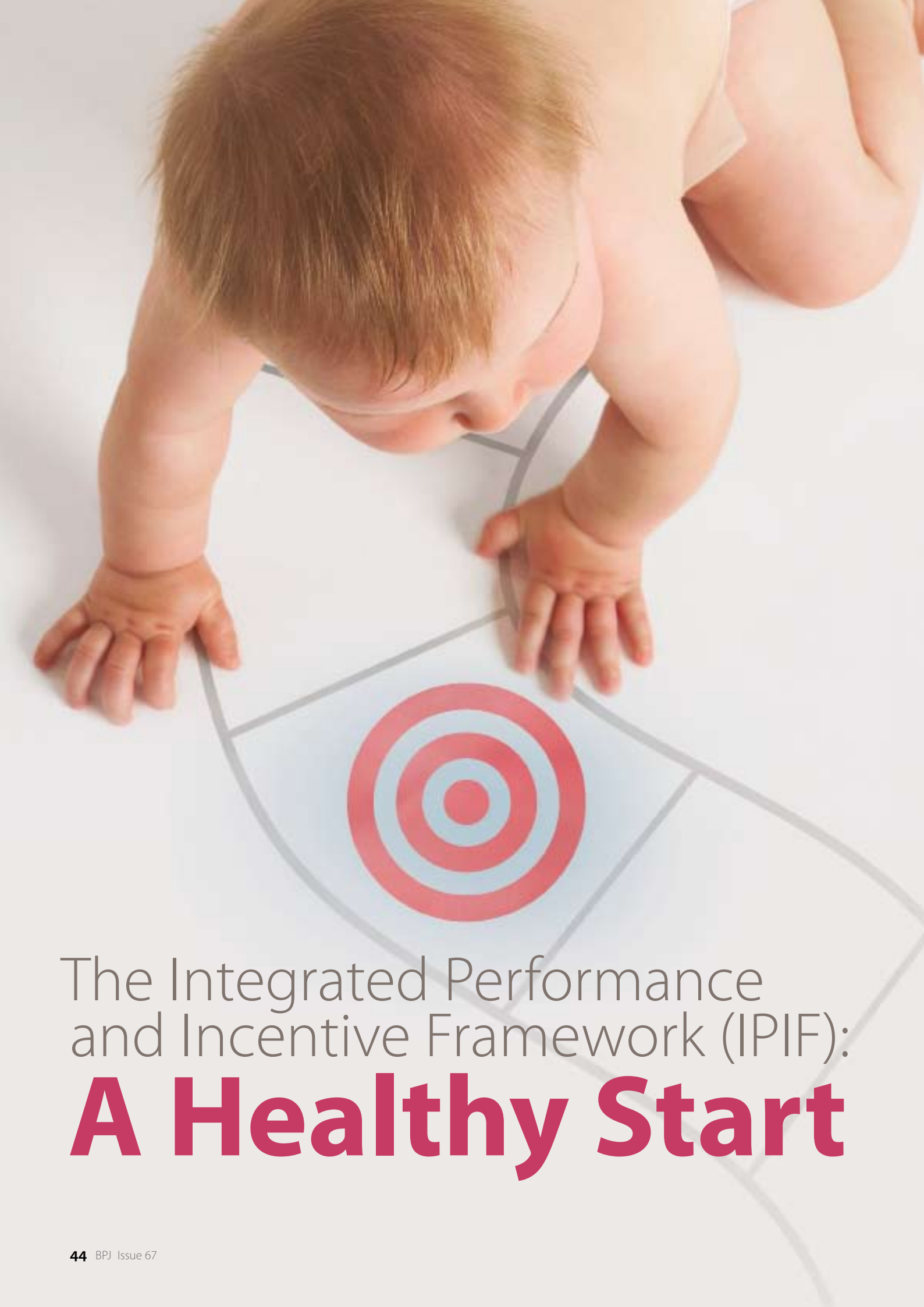
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The Integrated Performance  
and Incentive Framework (IPIF):  
**A Healthy Start**

*IPIF is a quality improvement programme designed to enhance the quality, accessibility, and integration of the New Zealand healthcare system. One of the five high-level system performance measures proposed within IPIF is a “Healthy Start” to life. Providing the best possible start to life for an infant begins with optimising the health of the mother before and during pregnancy. Providing good pre-conception advice, continuity of care during pregnancy, birth and the postnatal period all contribute to giving an infant the optimal chance to thrive.*

The Ministry of Health has introduced IPIF with the aim of setting goals and measures that will, over time, improve all facets of primary and secondary health care in New Zealand. IPIF is an attempt to integrate the whole of the healthcare system and move away from the narrower, purely target-driven PHO Performance Programme (PPP) which ended in June, 2014.

### **It won't happen overnight – but it will happen**

The development and implementation of IPIF will be a gradual process and evolve over a number of years, taking into account the needs and priorities for health and disability services in New Zealand. Phase one (2014/15) of IPIF, which commenced on 1 July 2014, was viewed as a transitional year. The five initial measures that were implemented to provide continuity with, and transition from, the PPP were:

1. More heart and diabetes checks (*target 90%*)
2. Better help for smokers to quit (*target 90%*)
3. Increased immunisation rates at age eight months (*target 95%*)
4. Increased immunisation rates at age two years (*target 95%*)
5. Cervical screening coverage (*target 80%*)

N.B. Not all of these targets will be continued in their present form as the structure of IPIF evolves.

In 2014, the IPIF Expert Advisory Group (EAG) recommended that the measures, incentives and reporting be organised according to the life stages of Healthy Start, Healthy Child, Healthy Adolescent, Healthy Adult and Healthy Ageing.<sup>1</sup> There is also an intention to introduce a number of measures within IPIF that will address the capacity and capability of the healthcare system to deliver equitable access to services.

The EAG proposed a layered structure of measures, with different approaches to measurement for different purposes and perspectives. At a local level, there will be contributory measures. This will be a selection of measures that are intended

to support clinical governance and service development. Local alliances will have choice over the particular measures which they wish to use, allowing freedom to adopt measures which are most relevant for local challenges. Contributory measures will be chosen on the basis that they reflect activities or outcomes which are relevant to higher level measures of system performance. Contributory measures will be supported by an infrastructure which provides consistent data definitions and information about data collection.

### **What is new in 2015?**

The Deputy Director-General of Sector Capability and Intervention, Ministry of Health, Cathy O'Malley, has confirmed that four new measures will be added to IPIF in July 2015 for the 2015/16 year. These include two Healthy Start measures and one measure each for Healthy Ageing and Capability and Capacity:<sup>2</sup>

- Registration with a lead maternity carer (LMC) within 12 weeks of conception (Healthy Start)
- Enrolment with a PHO within four weeks of birth (Healthy Start)
- Measures to better manage people aged 65 years or older who are prescribed 11 or more medicines (Healthy Ageing)
- Measures to improve the proportion of patients with access to online healthcare, e.g. patient portals (Capability and Capacity)

The aim of the first three measures is to encourage more collaboration between general practitioners and nurses, LMCs, pharmacists and aged-care workers. Discussion on exactly how the new measures will be introduced is planned to take place at a meeting of the PHO Service Agreement Amendment Protocol (PSAAP) group in April, 2015. Discussion will include how the targets are to be applied and what financial incentives may be linked to the measures. Ongoing work continues on other measures to be potentially added to IPIF for 2015/16, including those which will assist service development and quality improvement.

## Healthy Start: three measures will be in place for 2015/16

The aim of the Healthy Start measure is to improve the integration of services, equity and health outcomes for pregnant women and their infants for the first year of life. At this stage, the three Healthy Start measures that will be in place for 2015/16 are:

- Registration with lead maternity carer (LMC) within 12 weeks of conception (new)
- Enrolment within a PHO practice within four weeks of delivery (new)
- Completion of all scheduled immunisations by age eight months (existing)

Other developmental measures being considered within the Healthy Start measure include:

- Smoking cessation advice to pregnant women

- Birth weight in healthy range
- Infants being born at term
- Triple enrolment with a PHO, Well Child/Tamariki Ora and oral health provider
- Infants exclusively breastfed at three months
- Completed all scheduled Well Child/Tamariki Ora contacts at 12 months


Data on these developmental measures will be collected and analysed in 2015/16 and considered for future inclusion in IPIF.

Regardless of the final iteration of the IPIF Healthy Start measures, primary care has a key role in continuing to provide quality healthcare to ensure that women who are pregnant have the best possible chance of giving birth to a healthy infant. Pre-conception care should be considered the starting point for this goal.

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## Part 1: Healthy pregnancy starts with good pre-conception and early pregnancy advice

Education to improve pre-conception health should be viewed as a routine aspect of primary care for all females of reproductive age, with the overall aim of achieving healthy pregnancies and therefore healthy infants. Although some women consult their general practitioner specifically for pre-conception advice, many pregnancies are unplanned, so the integration of pre-conception care opportunistically into general practice consultations can work towards improving future pregnancy outcomes for all women. Specific advice may be required for women with risk factors that can affect pregnancy, e.g. obesity, diabetes, smoking, epilepsy and asthma.

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

### The pre-conception education window: ask women about their pregnancy intent

Women of reproductive age should be asked about their pregnancy intent, as appropriate, e.g. are they trying/intending to become pregnant. If not, what contraceptive measures are they using?

If a woman expresses an intent to become pregnant in the near future, or is at risk of becoming pregnant, there are a number of topics that should be discussed, including advice about smoking cessation, immunisation status, sexual health, healthy diet and BMI, folic acid and iodine supplements, the safety of long-term medicines and avoiding substances that are potentially harmful to a fetus.


### Quitting smoking is one of the most important things a woman can do

All women, regardless of whether or not they wish to become pregnant, should be strongly encouraged to quit smoking. The "Growing up in New Zealand" study reported that 11% of New Zealand mothers who were pregnant during 2009 and 2010 smoked at some stage during pregnancy, with higher rates among Māori (34%) and women from lower socioeconomic areas (17%).<sup>3</sup>

Smoking cessation advice can be particularly effective in women who are pregnant. Women who smoke are more likely to give up during pregnancy than at any other time.<sup>7</sup>




Nicotine replacement therapy (NRT) can be used during pregnancy as the benefits are considered to outweigh the risks.<sup>8</sup> Amitriptyline, bupropion and varenicline should be avoided. Smoking cessation advice should also be given to other household and family/whanau members, as second-hand smoke is harmful to an infant and post-partum smoking relapse is more common for women who live in a household where other people smoke.

 For further information, see: "Encouraging smoke-free pregnancies" BPJ 50 (Feb, 2013).

### Check the safety of long-term medicines


All medicines that a woman is taking should be checked to ensure they are safe and appropriate for use during pregnancy as many medicines can affect pregnancy outcomes. Women should be advised not to automatically stop taking their prescribed medicines when they become pregnant, without a benefit-risk assessment being performed by their healthcare team.

There is an increased risk of teratogenicity and other adverse effects with most anticonvulsant medicines, particularly valproate. Women with epilepsy who are taking anticonvulsant medicines should be discussed with a neurologist or obstetrician (or both), preferably prior to becoming pregnant, so that the most appropriate treatment can be determined and planned for. Women who require antipsychotic medicines should be discussed with their mental health team for appropriate options to use during pregnancy and breastfeeding. SSRIs and benzodiazepines, e.g. to treat depression and anxiety, should generally not be used during pregnancy, unless the potential benefit outweighs the risk. Other management methods may be required, e.g. counselling and cognitive behavioural therapy.

 Refer to the New Zealand Formulary for information on prescribing medicines in pregnancy: [www.nzf.org.nz/nzf\\_151](http://www.nzf.org.nz/nzf_151)

### Ensure vaccinations and cervical screening are up to date

A pre-conception discussion is a chance to assess immunisation status (history of vaccinations and illnesses) and bring all vaccinations up to date. Particular emphasis should be placed on rubella and varicella status prior to pregnancy.

 **Best Practice Tip:** Once pregnancy is confirmed set an electronic reminder task to invite the woman back for pertussis, and seasonal influenza vaccination.


### Contraception: preventing unplanned pregnancies promotes a healthy start

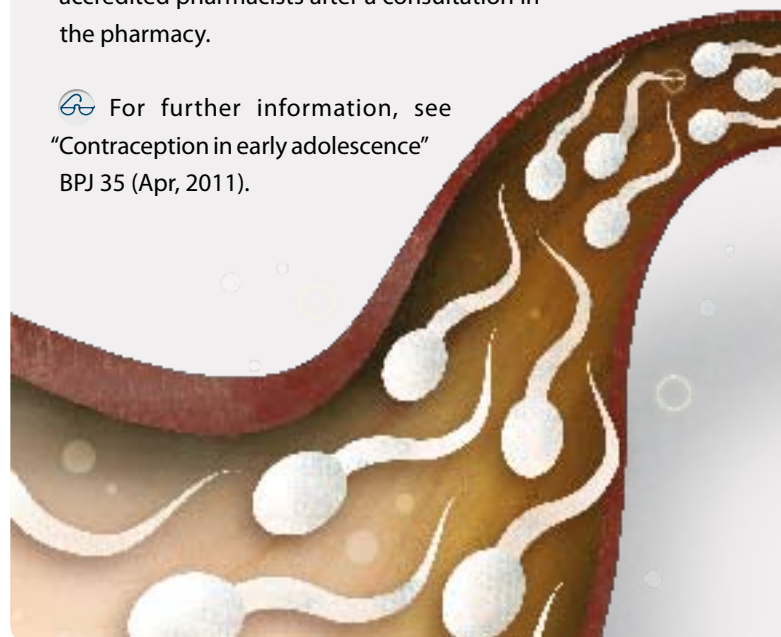
Providing sexual health and contraceptive advice is a key component of pre-conception consultations, as women with unplanned pregnancies are:

- Less likely to take folic acid, iron and vitamin supplements<sup>3</sup>
- More likely to drink and smoke during pregnancy (including before they are aware of being pregnant)<sup>3</sup>
- Less likely to breastfeed and, among those that do, more likely to breastfeed for a shorter time<sup>4</sup>

It has been estimated that approximately 40% of pregnancies in New Zealand are unplanned.<sup>3</sup> New Zealand has the second highest rate of teenage pregnancy in the OECD with approximately 28 births per 1000 females aged 15 – 19 years.<sup>5</sup>

It is recommended that young women who are sexually active are advised to use condoms plus one other form of contraception, e.g. an oral contraceptive. Emergency contraception can be discussed as an option if unprotected intercourse has occurred and the woman does not wish to become pregnant. The emergency contraceptive tablet (fully subsidised) contains 1.5 mg of levonorgestrel and should ideally be taken within 12 hours, and no later than 72 hours, after unprotected intercourse.<sup>6</sup> It may be used 72 – 96 hours after intercourse (unlicensed indication), but efficacy decreases with time.<sup>6</sup> The emergency contraceptive tablet may also be purchased from accredited pharmacists after a consultation in the pharmacy.

 For further information, see "Contraception in early adolescence" BPJ 35 (Apr, 2011).



## Rubella: The MMR vaccine cannot be given to pregnant women

Although rubella is relatively rare in New Zealand, infection during pregnancy can result in serious fetal abnormalities, e.g. congenital rubella syndrome. If there is uncertainty over the woman's rubella status, it is recommended that she is tested for rubella immunoglobulin (IgG) antibodies when pregnancy is planned (not subsidised).<sup>9</sup> Rubella IgG testing is part of routine antenatal care (subsidised) once pregnancy is confirmed.<sup>9</sup>

Two doses of the measles, mumps and rubella (MMR) vaccine (subsidised) should be given to women with no evidence of rubella immunity prior to conception.<sup>9</sup> Pregnancy should be avoided for up to four weeks after vaccination.<sup>9</sup> A woman can be considered to be immune to rubella if she has received two documented doses of MMR, or her immunity has been proven through serological testing as an adult.<sup>9</sup>

The MMR vaccine cannot be given to pregnant women, but can be administered to the mother after delivery and during breast feeding.<sup>9</sup> Pregnant women with low rubella IgG levels (<10 IU/mL) should be advised to avoid situations where contact is more likely (especially in the first trimester), e.g. international travel to countries with endemic disease or known outbreaks of rubella.

## Varicella vaccination is also contraindicated during pregnancy

Contracting varicella during pregnancy poses a risk of congenital varicella syndrome to the fetus, especially in the first 20 weeks.<sup>9</sup> Varicella antibody status should be checked in women who are planning a pregnancy who have no (or uncertain) history of illness, i.e. chicken pox or shingles, or vaccination. Varicella vaccination cannot be given during pregnancy, but can be administered after delivery to non-immune mothers who are breastfeeding. Varicella vaccination is recommended for susceptible women, however, vaccination is usually not subsidised for women planning to become pregnant.<sup>9</sup> Pregnancy should be avoided for four weeks after vaccination.<sup>9</sup>

## Ensure cervical smears are up to date


All women who have ever been sexually active should have a cervical screening test every three years from age 20 – 70 years. A cervical smear is not contraindicated during pregnancy, however, a routine test can usually be delayed until after the pregnancy, taking into account the time since the last test

and if there is a history of abnormal smear results. There is no evidence that performing a cervical smear during pregnancy is harmful to the fetus.<sup>10</sup>

Also check whether the woman has received the human papillomavirus (HPV) vaccine, which was added to the national immunisation schedule in 2008, and is recommended, and subsidised, for women aged 12 – 20 years.<sup>9</sup> There is still benefit in vaccinating young women in this age group who are already sexually active. Women older than 20 years do not routinely require HPV vaccination, however, it may provide some protection for those with risk factors, e.g. multiple partners. It is not recommended that HPV vaccine is given to pregnant women, but there is no evidence that it is harmful to the fetus if inadvertently administered.<sup>11</sup>

## Consider if an STI check is required

Questions about sexual health should be routinely included as part of general history for all sexually-active people seen in primary care. A sexually-transmitted infection (STI) check may be appropriate for some women, e.g. those with a new partner, with multiple partners, or with symptoms suggestive of a STI. Women should be asked about their risk of contracting HIV as HIV testing will be carried out as part of the routine antenatal screening tests unless the woman does not consent.

 For further information, see "A 'how-to guide' for a sexual health check-up" BPJ 52 (Apr, 2013).

## BMI and the benefits of a healthy diet

**The optimal pre-pregnancy body mass index (BMI) is 20 – 25 kg/m<sup>2</sup>.** Women who fall outside this range should be advised that being over- or underweight can affect the chance of becoming pregnant and can result in adverse pregnancy outcomes.<sup>12</sup> It has been reported that overweight and obese women have an increased risk of pre-eclampsia and gestational diabetes, and underweight women have an increased risk of pre-term delivery.<sup>13</sup> Weight loss or gain to attain a healthy pre-pregnancy weight should be recommended as appropriate.

**A healthy and varied diet will meet most nutritional requirements during pregnancy,** along with folic acid and iodine supplementation (see below). N.B. Foods that potentially contain listeria should be avoided during pregnancy, as listeriosis can result in miscarriage, stillbirth or premature birth. Foods that have a higher risk of carrying listeria include cold "deli" meats, raw seafood and soft cheeses made from unpasteurised milk.

## Folic acid, iodine and multivitamins

### Folic acid supplements should be started at least four weeks prior to conception

Folic acid reduces the risk of neural tube defects in the developing fetus. It is recommended that all women planning a pregnancy should start taking at least 400 micrograms of folic acid, daily.<sup>12, 14</sup> Women who have an increased risk of conceiving a child with a neural tube defect require a higher dose of folic acid: 5 mg, daily.<sup>12, 14</sup> Folic acid should ideally be taken for at least four weeks prior to conception and continued for the first 12 weeks of pregnancy.<sup>12, 14</sup>

Women with an increased risk of conceiving a child with a neural defect include those who:<sup>12, 14</sup>


- Are affected by a neural tube defect themselves, or have a family history of neural tube defects (including the partner and the partner's family)
- Have previously had a pregnancy affected by a neural tube defect
- Have a BMI > 30
- Have diabetes mellitus
- Have coeliac disease (or other risk of malabsorption)
- Are taking medicines known to affect folic acid metabolism, e.g. carbamazepine, valproate, clomiphene

Folic acid is available as an 800 microgram tablet or a 5 mg tablet (each taken once daily), subsidised on prescription or purchased over-the-counter from a pharmacy. The Ministry of Health recommends that women should only take folic acid tablets that are registered as medicines and should not rely on dietary supplements.<sup>12</sup> If a woman wishes to take a multivitamin product as her source of folic acid, advise her to check that it is designed for use in pregnancy, that it contains at least 400 micrograms of folic acid and that the other constituents are within recommended levels.

### Iodine supplements should be taken throughout pregnancy and breastfeeding

Iodine is essential for normal growth and brain development in the fetus. It is recommended that pregnant and breastfeeding women take 150 micrograms of supplementary iodine, daily, starting when pregnancy is confirmed and continued until breastfeeding ceases.<sup>12, 14</sup> Potassium iodate (Neuro Tabs) tablets are fully subsidised; each tablet contains 253 micrograms of potassium iodate which is equivalent to 150 micrograms of elemental iodine.<sup>6</sup> It is not necessary to take iodine prior to conception, although it is not harmful to do so as many New Zealanders have low iodine levels.


The recommended daily intake (RDI) of iodine for women during pregnancy is 220 micrograms per day and 270 micrograms in women who are breastfeeding.<sup>12</sup> Therefore, dietary intake of iodine is necessary in addition to an iodine supplement. Foods that contain iodine include cooked seafood (fish, shellfish and seaweed), milk, eggs, iodised salt and bread (iodised since 2009).<sup>12</sup>

 For further information, see: "Snippets: iodine supplements, zoledronic acid & atorvastatin" BPJ 30 (Aug, 2010).

### Iron supplements and multivitamins are not routinely required

Iron supplements are not routinely required during pregnancy if dietary iron intake and iron stores are adequate. The best way to ensure this is to maintain adequate pre-conception iron stores by eating foods high in iron, e.g. lean beef and lamb. Sub-optimal stores are difficult to replenish once a woman has become pregnant.<sup>12</sup> The RDI of iron in pregnant women is 27 mg per day for the duration of pregnancy.<sup>12</sup> If low iron stores or iron deficiency are suspected or confirmed, pregnant women can be prescribed oral iron supplementation. Ferrous fumarate 200 mg tablets (containing 65 mg of elemental iron) and ferrous sulphate 325 mg tablets (105 mg of elemental iron) are subsidised.<sup>6</sup> Iron supplements can cause constipation, therefore women can be advised to include adequate amounts of fluid and fibre in their diet.

**Multivitamin supplements** are not routinely required in pregnancy. If a pregnant woman wishes to take a multivitamin, ensure it contains adequate amounts of folic acid and iodine (if not taking individual supplements) and does not contain excessive amounts of fat soluble vitamins (vitamins A, D, E and K), which can accumulate in the body. Vitamin A-containing supplements, in particular, are not recommended during pregnancy, as excessive consumption of vitamin A has been associated with teratogenicity during the first trimester, e.g. cleft lip and palate, central nervous system abnormalities.<sup>12</sup> The RDI of vitamin A during pregnancy is 800 micrograms of retinol-equivalents (2667 IU) per day.<sup>12</sup> The upper limit of 3000 micrograms of retinol-equivalents (10 000 IU) per day should not be exceeded.<sup>12</sup>

 For further information, see "Nutrition and supplements during pregnancy" BPJ 18 (Dec, 2008).



## Limit alcohol prior to conception and avoid totally during pregnancy

Alcohol consumption should be limited prior to conception and avoided during pregnancy as there are no known safe limits. For non-pregnant females, alcohol intake should be no more than two standard drinks per day and no more than ten drinks per week. High alcohol consumption during pregnancy is associated with fetal alcohol spectrum disorders (FASD) which result in intrauterine and postnatal growth retardation, among other effects.<sup>12</sup> High alcohol consumption also interferes with the absorption and metabolism of micronutrients. Women should avoid drinking alcohol when breastfeeding.<sup>12</sup>

## Limit caffeine intake

It is recommended that women who are pregnant or breastfeeding limit their daily caffeine consumption to approximately 300 mg\*.<sup>12</sup> Energy drinks can contain high levels of caffeine (often in the form of guarana) and should be avoided. High doses of caffeine during pregnancy have been associated with increased risks of congenital abnormalities, miscarriage, low birthweight and withdrawal symptoms in the newborn infant.<sup>12</sup> Caffeine is also transferred into breast milk and high levels can lead to irritability and poor sleeping patterns in the infant.<sup>12</sup> Moderate amounts of caffeine from food and beverages appear to be safe in women who are pregnant or breastfeeding.<sup>12</sup>

\* On average, a long black coffee (160 mL) contains 211 mg of caffeine, a cappuccino (260 mL) contains 105 mg, an instant coffee (250 mL) contains 51 mg, a tea made with a tea bag (250 mL) contains 47 mg, a serve of energy drink (250 mL) contains 80 mg and a chocolate bar (100g) contains 65 mg.<sup>12</sup>



## Pre-conception laboratory investigations

Laboratory investigation as part of pre-conceptual care is dependent on the individual risk factors of the woman. Appropriate testing may include:

- HbA<sub>1c</sub> and lipids if increased BMI
- Chlamydia, gonorrhoea if increased risk of STI
- Rubella antibodies if unknown vaccination history
- Ferritin if risk of iron deficiency
- TSH if suspicion of thyroid dysfunction



## Part 2: Continuity of care and achieving a Healthy Start

Women should ideally be encouraged to attend their general practice to confirm a pregnancy, as this is an opportunity to discuss and assess factors which can influence a healthy pregnancy and a healthy start for the infant. In 2013, 77% of all first antenatal screens were requested by doctors.<sup>15</sup> Approximately 50% of women do not book with a LMC until the end of the first trimester.<sup>15</sup> Women aged < 20 years or ≥ 45 years and Māori women are the most likely groups not to receive any antenatal testing.<sup>15</sup>

A checklist of points to cover at a first pregnancy consultation includes:

- Confirm pregnancy with a dipstick human chorionic gonadotropin (hCG) test (there is no requirement for serum hCG unless the dipstick test is negative, but pregnancy is still suspected)
- Request the first antenatal screen, which includes: blood group and antibodies, full blood count, rubella antibody status, HIV, hepatitis B and syphilis serology (🔗 For further information, see: [www.bpac.org.nz/BT/2011/July/pregnancy.aspx](http://www.bpac.org.nz/BT/2011/July/pregnancy.aspx))
- Discuss screening for Down syndrome and other congenital abnormalities; appropriate testing is dependent on the stage of pregnancy (🔗 For further information, see: [www.nsu.govt.nz/pregnancy-newborn-screening/antenatal-screening-down-syndrome-and-other-conditions](http://www.nsu.govt.nz/pregnancy-newborn-screening/antenatal-screening-down-syndrome-and-other-conditions))
- Assess immune status and potential vaccination needs
- Measure weight and blood pressure
- Advise about lifestyle factors, such as smoking, diet, alcohol intake and exercise
- Enquire about any social aspects that may be relevant to the pregnancy, including occupation
- Prescribe folic acid if it is not already being taken, and iodine
- Check any medicines and long-term conditions that may complicate pregnancy
- Discuss options for choosing a LMC (including whether there is any need for referral to an obstetrician)
- Know what other support services are available for pregnant women, e.g. Māori or Pacific services
- Have a plan in place to ensure the newborn infant is enrolled at the practice in a timely manner

N.B. a “dating scan” is not required in early pregnancy (prior to approximately 11 weeks); dating can be done at the scan for antenatal screening for Down syndrome and other congenital abnormalities, if the woman consents to that screening.

### Helping your patient select a LMC

The Perinatal and Maternal Mortality Review Committee Reports and Health Select Committee’s Inquiry into Improving Health Outcomes and Preventing Child Abuse both recommend early engagement with maternity care, ideally by ten weeks gestation.<sup>16, 17</sup> Registration with a LMC in the first trimester ensures that an appropriately qualified health professional can provide continuity of care, advice and education throughout a woman’s pregnancy, birth and postnatal period, improving health outcomes for both the mother and infant.

#### **The first of the new IPIF measures is for all pregnant women to be enrolled with a LMC within 12 weeks of conception.**

To qualify for subsidised maternity care, pregnant women must register with a LMC. Registration can occur as soon as pregnancy is confirmed until six weeks after delivery. The LMC will oversee the management of the pregnant woman from the time of registration until six weeks after the birth. The general practice team can inform the woman regarding her options for choosing a LMC (and locating/referring if required), including:

- The Find Your Midwife website (run by the New Zealand College of Midwives): [www.findyourmidwife.co.nz](http://www.findyourmidwife.co.nz)
- The Ministry of Health information line 0800 Mum2Be (0800 686 223)
- The local Midwifery Resource Centre (if one is available – check the White and Yellow Pages under Midwifery Resource Centre or Midwives) or maternity services at the local hospital


#### **Māori and Pacific women are less likely to enrol with a LMC in the first trimester**

In 2011, 87% of women who gave birth were registered with a LMC (90% of whom were midwives); the remaining 13% received primary maternity care through DHB services or did not receive care.<sup>18</sup> Of women who registered with a LMC, 62% did so in their first trimester of pregnancy.<sup>18</sup> Pacific and Māori women were less likely to be enrolled with a LMC in their first

trimester (35% and 46% respectively),<sup>18</sup> so should especially be supported by primary care regarding the importance of maternity care during pregnancy, including helping them to find a LMC.


### **Good communication between general practice and the LMC is beneficial for both the mother and infant**

A team approach with good communication between healthcare professionals is likely to result in the best quality of care for the patient and help achieve IPIF targets. The structure of maternity care in New Zealand does, however, make this a challenging area as multiple healthcare professionals are often involved. One of the major aims of IPIF is to improve integration and collaboration, not only between primary and secondary care, but also between primary care providers.

 **Best practice tip:** One method that can encourage collaboration is writing a LMC referral (with the woman's consent). This could be based on a standard template, including the woman's basic health information, e.g. medical history, long-term conditions, medications, and any social aspects relevant to the pregnancy, plus the results of any tests ordered in early pregnancy. It can also include a statement of expectation that the LMC will keep the general practice informed of any relevant information.

### **Ongoing non-pregnancy-related care is still the responsibility of general practice**


General practice remains responsible for managing a woman's non-pregnancy-related healthcare after a LMC has been selected. Asthma is the most common long-term medical condition managed in pregnant women, and when well controlled asthma carries little or no increased risk of adverse fetal or maternal complications. Optimising asthma treatment during pregnancy is important to minimise exacerbations. The management of some other conditions, e.g. pre-existing diabetes, hypertension and epilepsy, requires a collaborative approach with appropriate specialists. For example, it is recommended that a neurologist is involved at an early stage in women with epilepsy (ideally pre-conception) and an obstetrician often has a role in the care of pregnant women with hypertension.


 For further information, see: "Continuing care for pregnant women with asthma" BPJ 35 (Apr, 2011).

### **Pertussis and influenza vaccines are recommended during pregnancy**

Pertussis vaccination is recommended between weeks 28 – 38 of pregnancy and the Tdap vaccination is subsidised during this period.<sup>9</sup> Influenza vaccination is also recommended for

pregnant women and is subsidised for this group during the winter season. The vaccine can be safely administered at any stage of pregnancy.<sup>9</sup>

 For further information, see: "Pertussis immunisation in pregnancy" BPJ 60 (Apr, 2014)

 A patient leaflet on influenza vaccination during pregnancy is available from:  
[www.influenza.org.nz/sites/default/files/2015%20Flu%20Pregnant%20women-midwives%20Brochure%20.pdf](http://www.influenza.org.nz/sites/default/files/2015%20Flu%20Pregnant%20women-midwives%20Brochure%20.pdf)

### **Enrolment with a PHO within four weeks of birth**

In 2012, the Ministry of Health implemented the preliminary newborn enrolment policy (the B code) to facilitate early enrolments in general practice. Prior to the policy, fewer than half of infants were enrolled with a general practice at age 12 weeks; as at 19 August 2013, this number had increased to 70%.<sup>19</sup>

It is important that newborns are enrolled close to birth to ensure that childhood immunisations are given on time and to maximise the child's health as they grow. Furthermore, early enrolment ensures that newborns have access to affordable and essential health care sooner.

**The second of the new IPIF targets is for infants to be enrolled with a PHO within four weeks of birth.** General practices now receive notification about new births from the National Immunisation Register (NIR) via their practice management system (PMS) if the mother has designated the general practitioner as either their infant's preferred general practitioner or Well Child/Tamariki Ora provider (see: "Well Child/Tamariki Ora providers", opposite).

The LMC is responsible for ensuring that the mother/family has been provided with information on the NIR, and has chosen a general practitioner and a Well Child/Tamariki Ora provider for the infant, after they have finished providing maternity care.


All newborns are entered on the NIR, which records the child's name, NHI number and DHB. Parents may choose to "opt off" putting any more of their child's information or details of their immunisations on the NIR. Children are eligible to receive subsidised vaccines even if they have been opted off the NIR.

General practices receive NIR notifications through their provider inbox and these should be ideally actioned within three days of receiving the notification. The "B" code will be


activated once the infant's details have been added into the PMS; the infant does not need to be present for this to occur. When the enrolment form has been signed by the parents the infants code in the PMS is changed to "E".<sup>20</sup>

Once the child has been enrolled, two of the most important things general practice can do to provide quality care in the first year of life are:

1. Promote and support mothers in breast feeding
2. Ensure that infants are fully vaccinated at age appropriate milestones

 Further information on newborn enrolment is available from:

[www.health.govt.nz/publication/newborn-pre-enrolment-toolkit](http://www.health.govt.nz/publication/newborn-pre-enrolment-toolkit)

 **Best practice tip:** To facilitate collaboration between healthcare providers, it is good practice for the LMC to write a "referral letter" back to the woman's general practitioner, outlining any relevant issues that occurred during her maternity care.

## Ensure infants are fully vaccinated at the appropriate age

One of the interim IPIF performance measures for 2014/15, to be continued in 2015/16, is increased immunisation rates at age eight months (target 95%). The latest immunisation coverage rates for full vaccination at age eight months was 94%, for the three-month period ending December 2014.<sup>21</sup>

As per the National Immunisation Schedule, it is recommended that children receive rotavirus vaccine (RotaTeq) along with Infanrix-hexa and the 13-valent pneumococcal vaccine (Prevenar) at age six weeks and three and five months.<sup>9</sup>

Listening to, and acknowledging, any parental concerns about immunisation can help overcome barriers. Providing clear and balanced information regarding the benefits and risks of immunisation and respectfully correcting any misinformation can help build a trusting relationship. Key points to cover with parents that can encourage vaccination include:<sup>22</sup>

### Educate parents about the benefits of vaccination:


- Diseases do not discriminate - vaccination is for all infants
- Vaccination is highly effective and protects infants against severe diseases
- Vaccination protects other family members and the community in general

## Well Child/Tamariki Ora providers

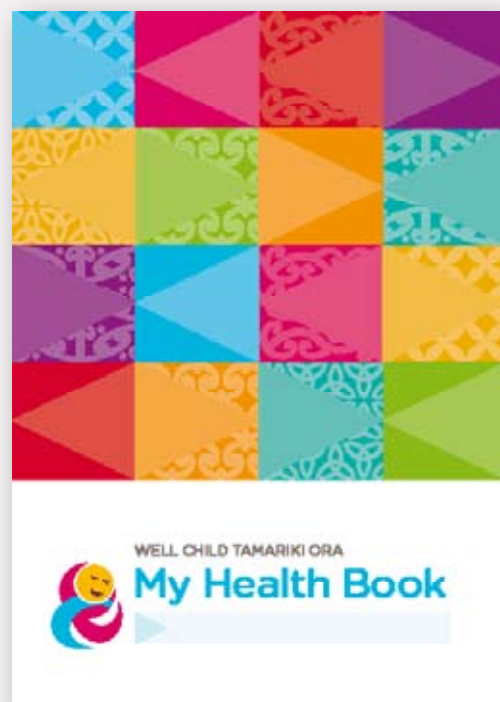
Well Child/Tamariki Ora is a free service that is offered to all New Zealand children from birth to age five years. The first "well baby" checks are performed by the LMC before transfer to the Well Child/Tamariki Ora provider. Thirteen free wellness checks for growth and developmental milestones are available, starting at birth and continued until the "B4 school check" at age four years.

Parents will be issued with a Well Child book for their infant by their Well Child/Tamariki provider and all relevant information should ideally be entered in the book. Accurately filling out the book can also help improve collaboration between healthcare professionals as all parties will have access to the information.

There are a number of Well Child/Tamariki Ora provider options, including Plunket, general practitioners and specialised Māori and Pacific services.

 A list of Well Child/Tamariki Ora programme providers by region is available from:

[www.health.govt.nz/your-health/services-and-support/health-care-services/well-child-tamariki-ora/find-well-child-tamariki-ora-service](http://www.health.govt.nz/your-health/services-and-support/health-care-services/well-child-tamariki-ora/find-well-child-tamariki-ora-service)




### Respectfully correct any misinformation:

- Reassure parents that there is no link between vaccination and autism
- None of the vaccines on the current New Zealand immunisation schedule contain thiomersal (the mercury-containing compound used in some older vaccines)

### Remind parents that each round of vaccinations should be administered at the recommended time:

- Ensure the first appointment at age six weeks is scheduled and reminders are in place for the appointments at age three and five months, and beyond
- Encourage the parents to speak to a practice nurse or their general practitioner when they are considering cancelling a vaccination appointment because the child is unwell (and also inform reception staff of this protocol). In some cases, the infant may still be able to be vaccinated, or they may require an appointment to investigate why they are unwell.

 For further information, see “Immunisation in children by age two years” BPJ 29 (Jul, 2010).

## Breast milk is the preferred food for the infant

The proportion of infants in New Zealand who are exclusively or fully breast fed\* for the first three months of life has remained at approximately 56 – 60% from 2008 – 2013.<sup>23</sup> The corresponding rates at age six months for the same period were 25 – 27%.<sup>23</sup> Improving the rates of breast feeding is one of the measures that may be added as a Healthy Start IPIF component at a later date.




The Ministry of Health and World Health Organisation recommend that infants are exclusively breast fed until they are aged six months.<sup>12</sup> It is recommended that the infant continue to be breast fed, along with the introduction of appropriate complementary foods, until at least age two years.<sup>12</sup>

Improving breast feeding rates presents a challenge as the reasons infants are not being exclusively breast fed are multi-factorial. Measures to improve breast feeding rates need to involve families, communities, and government and non-government groups and agencies. Māori and Pacific women, women from low-income families and young mothers have lower breast feeding rates than other groups.<sup>24</sup>

General practice can help to increase breast feeding rates in a number of ways, such as promoting and educating women about the benefits and techniques of breast feeding and referring them to other providers if further assistance is needed, e.g. to a lactation consultant.

Appropriately managing women with mastitis and cracked nipples can also help with continuation of breast feeding. Both conditions commonly result in discontinuation of breast feeding, often unnecessarily.

 For further information, see “Mastitis and sore nipples while breast feeding” BPJ 18 (Dec, 2008).

\* Exclusively breastfed: The infant has not, to the mother’s knowledge, had any water, formula or other liquid or solid food. Only breastmilk from the breast or expressed breastmilk and prescribed medicines have been given from birth

Fully breastfed: The infant has had only breastmilk with no other liquids or solids except for a minimal amount of water or prescribed medicines in the last 48 hours.

## Where to from here?

The introduction of the first healthy start targets as part of the IPIF programme is a timely reminder for practices to consider how they are working and interacting within a collaborative model in the wider healthcare sector. This may prompt discussion about how the IPIF can be applied within a practice’s own community, and what this may mean for the roles and responsibilities of practice staff. A good starting point is to put plans in place to ensure that infants are enrolled early in the practice, and assigning responsibility for responding to NIR notifications. Consider the practice’s current protocol for reminding and encouraging parents to bring infants for vaccinations, and whether any improvements to this process can be made.



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## Brand changes for cardiovascular medicines: carvedilol, ezetimibe and ezetimibe with simvastatin

Over the next few months there will be changes in the subsidised brand of three cardiovascular medicines. The first medicine to undergo a brand change was carvedilol on 1 April, 2015, which will be followed by ezetimibe and ezetimibe with simvastatin from 1 June, 2015.


The same Special Authority restrictions for access to ezetimibe and ezetimibe with simvastatin will apply after the brand change.

 For further information, see:

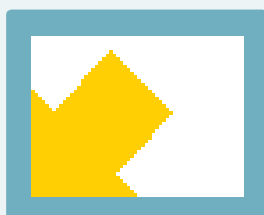
[www.pharmac.health.nz/medicines/my-medicine-has-changed/cardiovascular-medicines/](http://www.pharmac.health.nz/medicines/my-medicine-has-changed/cardiovascular-medicines/)

Patient information can be downloaded and printed from the website or ordered from: [www.pharmaonline.co.nz](http://www.pharmaonline.co.nz)

If you have any enquiries about these changes, please phone 0800 60 00 50 between 9am–5pm, Monday to Friday.

 Special Authority forms are available from:

[www.pharmac.govt.nz/SAForms](http://www.pharmac.govt.nz/SAForms)



## Quality indicators for opioid prescribing

Dear Editor,

Re: "Helping patients cope with chronic non-malignant pain: it's not about opioids", *BPJ* 63 (Sep, 2015).

Thank you for this very useful and comprehensive article. There is now a new tool available in New Zealand, not mentioned in the article, which can be used by individual practitioners or by their services to improve the quality of prescribing for chronic non-malignant pain.

With funding from the Health Quality and Safety Commission, seven suites of indicators were developed in 2012 to facilitate safer prescribing of opioids in this context. The indicators identify appropriate numerators and denominators and list the caveats in indicator implementation and interpretation of the results. The indicators are arranged in suites of related indices and cover important topic areas, aligned to the 10 Universal Precautions outlined in Pages 36 and 37 of the *BPJ* article. The indicators are appropriate for use in an audit cycle with the intention of continuous quality improvement. Any practitioners, specialists or generalists, are able to access these indicators on the HQSC website and use them for quality improvement and to ensure that their patients with chronic pain are offered appropriate and evidence-based advice and support during their convalescence.

The resources are available from: [www.hqsc.govt.nz/our-programmes/health-quality-evaluation/projects/atlas-of-healthcare-variation/opioids](http://www.hqsc.govt.nz/our-programmes/health-quality-evaluation/projects/atlas-of-healthcare-variation/opioids)

*Drs Helen Moriarty and Roshan Perera*  
Wellington

## Early treatment in Parkinson's disease

Dear Editor,

Firstly, I hope your beautifully illustrated Best Practice never totally goes out of print.

To show that the copies are treasured, in [The Year in Review - What did we learn in 2014, BPJ 66, Feb, 2015] it is summarised that Parkinson's disease should be detected and treated early.

Actually the original article in BPJ 58 (Feb, 2014) states that: "There is little evidence that treatment with either levodopa or long-acting dopamine agonists in the early phases of Parkinson's disease results in improved long-term outcomes"

You see - your publications are not in vain!

**Dr John Sarfati, General Practitioner**  
Wellington

Thank you for your comments. You are correct in pointing this out. In patients with Parkinson's disease, symptoms should generally begin to be managed once they become troubling to the patient. Early treatment does not necessarily result in better outcomes, and medicines used to manage Parkinson's disease are associated with adverse effects. Treatments are optimised as new symptoms develop. A combination of levodopa with carbidopa or benserazide is generally first-line treatment for functional disabilities, and then dopamine agonists such as ropinirole or pramipexole may be added to reduce motor symptoms and minimise the adverse effects of levodopa treatment (younger patients may be started on dopamine agonists). Additional pharmacological treatments for non-motor symptoms and other strategies, such as dietary adjustments, physiotherapy and counselling, are all important aspects of management as the patient's condition worsens.

**A special thank you** to all of the readers who expressed their support for retaining a printed version of Best Practice Journal, and also to those who reassured us that they would read our articles online. We really appreciate the feedback, and we will continue to work hard to provide you with the best evidence-based guidance for primary care.

**We value your feedback. Write to us at:**  
Correspondence, PO Box 6032, Dunedin or  
email: [editor@bpac.org.nz](mailto:editor@bpac.org.nz)



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