BEST PRACTICE

34

FEBRUARY 2011

Dyspepsia
Melanoma
Breast cancer screening

bpac nz
better medicine

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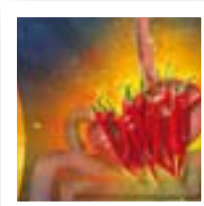

Managing dyspepsia and heartburn in general practice – an update

Dyspepsia is not a diagnosis but rather a description of symptoms that may indicate disease of the upper gastrointestinal tract. However, in the majority of cases there is no clear pathological cause. The initial assessment of a patient with dyspepsia involves ruling out any “alarm features” which may indicate more serious underlying pathology. The presence of heartburn, with or without dyspepsia, is usually associated with gastro-oesophageal reflux disease (GORD). Simple lifestyle modifications may resolve mild symptoms of GORD but acid suppressant treatment, using a step-down approach may be required. In dyspepsia without heartburn that does not require investigation, or if investigations have found no cause, a PPI is considered first-line treatment. If symptoms do not resolve or recur, testing for *H. pylori* may be considered.

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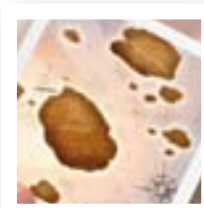

Detecting malignant melanoma

New Zealand has one of the highest rates of melanoma in the world. Melanoma is the most common cancer among New Zealand men aged 25 to 44 years. Primary care plays an important role in early detection. Clinicians should be aware of the clinical signs of melanoma and encourage patients to report any suspicious skin lesions. People who are at increased risk of melanoma, such as those with a large number of moles, atypical moles or a family history of melanoma, should be encouraged to have periodic full-body skin checks. Depending on level of skill and the clinical situation, GPs may consider biopsy, referral or careful follow-up of all suspicious skin lesions. Dermatoscopy, digital photography and mole mapping can be used to aid in detection and surveillance.

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Increasing the uptake of breast screening

Significant progress has been made in increasing the rate of breast cancer screening in New Zealand. However, Māori women still have a higher rate of developing and dying from breast cancer than non-Māori. There are several methods that practices can undertake to increase breast screening rates. Identify eligible women and make sure they are enrolled in the BreastScreen Aotearoa programme. Consider any barriers that may exist and ways to overcome these. Frequently asked questions about breast screening include the role of breast ultrasound and the evidence for screening women aged in their 40s.

Supporting the PHO Performance Programme

PHO
PERFORMANCE PROGRAMME

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ANTIMICROBIALS

the way forward

In 2010 we published the first three articles in our four part series on antimicrobial resistance in New Zealand, from guest contributor Dr Rosemary Ikram. The series concludes in this issue. As part of our ongoing commitment to this important topic we will shortly be distributing an antibiotic prescribing booklet.

The World Health Organisation has identified antimicrobial resistance as one of the three greatest threats to human health, along with food shortages and climate change. Antimicrobial resistance is growing rapidly worldwide, there are very few new antimicrobial medicines in development that offer benefits over existing medicines and increasingly limited treatment options for pathogens such as *Staphylococcus aureus* and *Klebsiella pneumoniae*. There is a very real possibility that we will soon be re-entering an age where common bacterial pathogens are unable to be successfully managed and will pose an increasing threat to human health. In the past few years we have seen antimicrobial resistance spread from hospitals to the community, resulting in the emergence of "super bugs" – multiple drug resistant organisms.

A global commitment from both health professionals and the general public is needed in order to contain, or at least slow, this threat until new medicines can be developed to combat resistance. Interventions include education about basic hygiene measures to prevent infection and the problems posed by antimicrobial resistant bacteria, as well as a clear understanding of appropriate use of antimicrobials.

Previous articles in this series have highlighted the significant problem of antimicrobial resistance in New Zealand and worldwide. Various strategies to promote the rational use of antibiotics in New Zealand have been discussed. In this final article of the series we look at the way forward in the battle against antimicrobial resistance. Lessons learned from international interventions can be combined with local ideas for a co-ordinated national approach to address this evolving issue.

Contributed by **Dr Rosemary Ikram**, Clinical Microbiologist, MedLab South

Raising awareness of antimicrobial resistance: international interventions

"Get Smart" in the USA

"Get Smart" from the Centers for Disease Control and Prevention is an ongoing educational and awareness programme on antimicrobial resistance. The programme includes input from all stakeholders and is aimed at both health professionals and consumers.

Education of the general public has included programmes in daycare, kindergartens, schools, websites, posters, radio and television advertising as well as pamphlets available in primary care practices.

… and "Get Smart" on the Farm

The widespread and indiscriminate use of antibiotics in animals and agriculture can contribute to the problem of antimicrobial resistance. The "Get Smart" programme also incorporated "Get Smart on the Farm", targeting educational and awareness interventions to veterinarians and others involved in the delivery of healthcare to animals.

For further information on the Get Smart programme, visit: **www.cdc.gov/getsmart/antibiotic-use/know-and-do.html**

Antibiotic awareness days

Annual awareness days are regularly held in some countries such as the European Antibiotic Awareness Day from the European Centre for Disease Prevention and Control. This programme includes resources and toolkits for education of the public and prescribers in primary and hospital care.

The important message in such an awareness programme is focused on reducing inappropriate antibiotic use. Typical topics and issues included are:

- Antibiotics are inappropriate for treating viral infections
- Recognition of common viral infections
- Adverse effects of antibiotics on the individual as well as the population problem of antimicrobial resistance

http://ecdc.europa.eu/en/eaad/Pages/Home.aspx

Essential aspects for addressing antimicrobial resistance

Co-ordination is the Key

Educational awareness programmes often involve a number of partners to increase the impact. For example, a promotional activity could include the media, health professional groups and consumer groups. Communication and co-ordination are essential to ensure success.

Antimicrobial resistance survey

In 2010, clinicians were encouraged to respond to a questionnaire to determine important issues in primary care which may cause barriers to implementation of reduced antimicrobial use.

Responses were received from 268 people. The main findings of the questionnaire were:

- More than half of respondents very rarely (49%) or never (9%) used data on local resistance patterns to guide antimicrobial choice
- Almost all respondents are either mostly aware (63%), very aware (18%) or somewhat aware (18%) of the pathogens that antimicrobials are active against
- Most respondents find it difficult about half the time (51%) or rarely (43%) to avoid prescribing antimicrobials for patients with a viral infection
- A back pocket prescription, if appropriate, is used most of the time (35%) or about half of the time (41%)
- However, information pamphlets are used rarely (52%) or never (25%), to help patients understand when antimicrobials are not indicated,
- Most people rated the threat of antimicrobial resistance in New Zealand as very high (15%), high (42%) or moderate (39%)

From interpreting the comments received in the questionnaire, it seems that a large number of practitioners are unaware of local susceptibility patterns because they are not supplied by the laboratory. Many practitioners felt that more education needs to be directed to the general public through a variety of sources such as media and education at all levels. There were also some who felt that more information is required relating to strategies for symptomatic relief in viral infections.

Good information is essential

Surveillance at both national and local levels is important. Most laboratories have the capability for generating susceptibility reports. Central co-ordination of these databases would give information about the type of resistance in different geographical areas, which can be useful with the ease of movement from one area to another. This is often well co-ordinated with hospital transfer but does not occur with patients moving. An example of this is the first isolate of MRSA USA 300 in South Canterbury, which was traced to a patient who had moved from Taranaki in the previous month. The information that the patient had moved should have been provided to the practitioners who would be involved in the patient's care.

Promote infection control

Colonisation and infection prevention strategies need to be highlighted to the general population. Contact spread, either direct or indirect, is the most important means of transmission. Therefore, hand hygiene with either soap and water or alcohol gels is the most effective strategy to prevent transmission. General hygiene, e.g. regular laundering of linen and personal clothing as well as regular cleaning also has a role.

Antimicrobial stewardship is the buzz word for reducing the inappropriate use of antimicrobials. This needs to occur

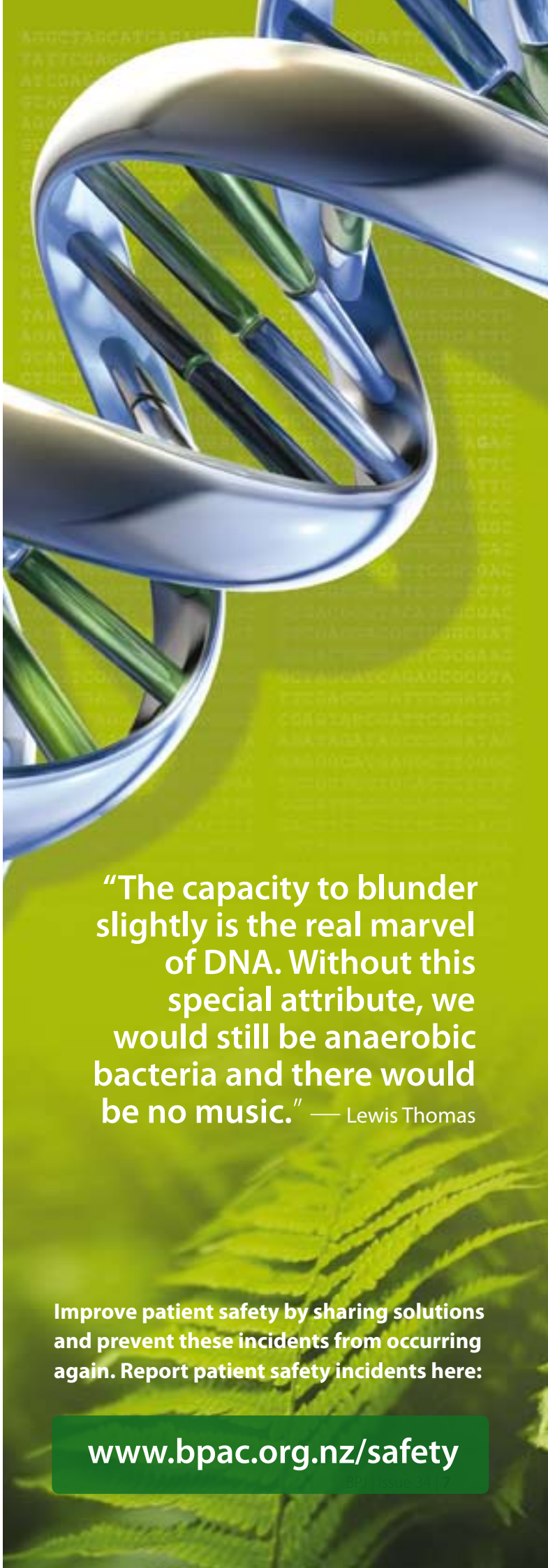
in both hospitals and primary care. Hospitals continue to act as reservoirs, as well as institutions where spread of multiply drug resistant organisms (MDROs) occurs.

Guidelines and information

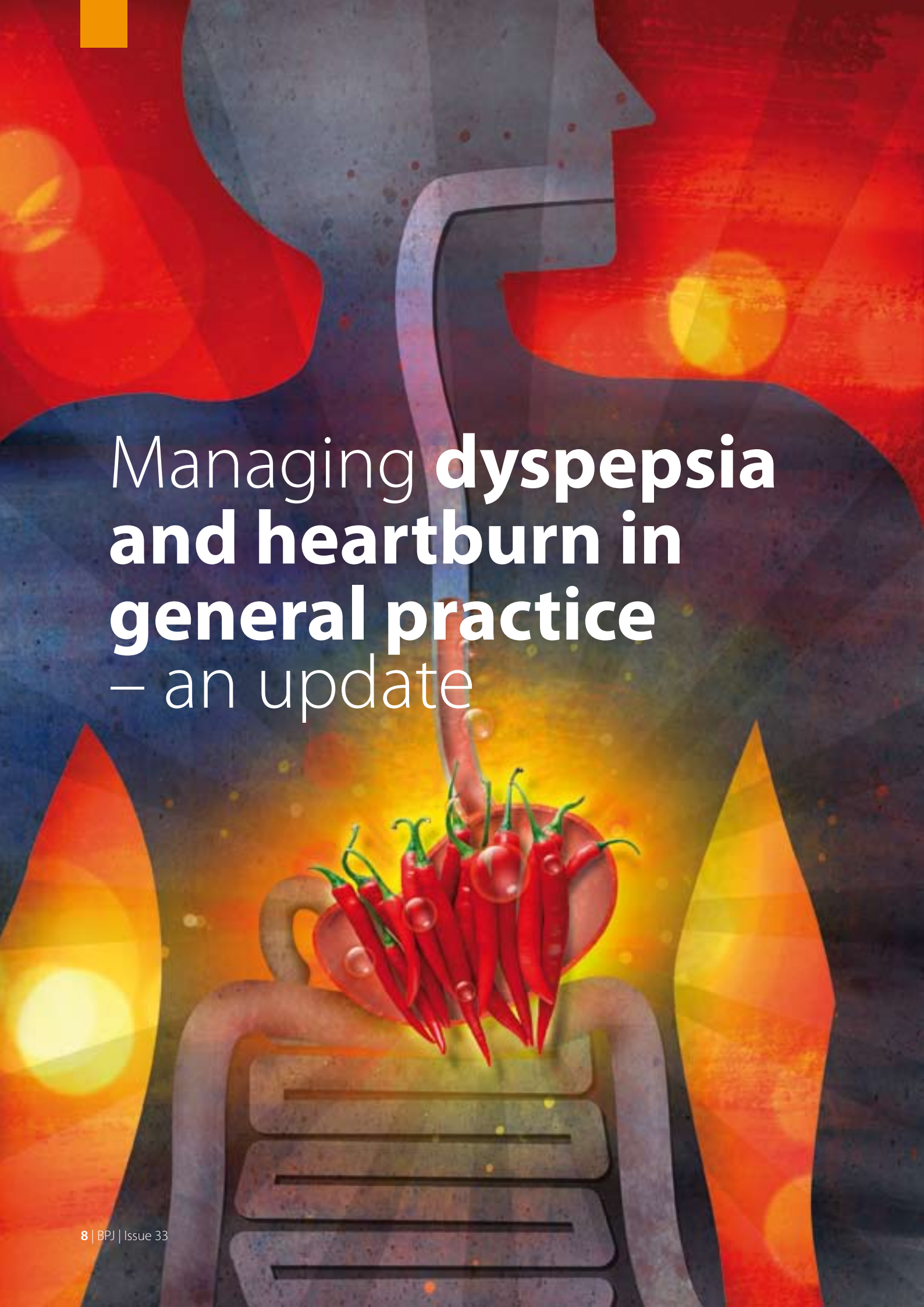
Antibiotic guidelines are important but it is also important to educate about when antibiotics are not required, e.g. viral syndromes where bacterial infection is unlikely. The NICE guideline ("Antibiotic prescribing for respiratory tract infections") is an excellent document which could be adapted for New Zealand and used to formulate "whether to treat guidelines" rather than simply the appropriate antibiotic for a particular condition. With so many issues to remember in the general practice it is important that information is circulated in a practical and relevant form, and updated regularly. To instigate sustained change in the health sector is a major undertaking and it is important to include all stakeholders when implementing these changes.

In summary

Antimicrobial resistance is with us to stay. How much of an issue it becomes in New Zealand is in our hands. We need to direct efforts to combat this serious threat to our healthcare system and this involves all sectors of our community.



Managing **dyspepsia and heartburn in general practice** – an update



In response to many requests, we have updated our 2007 article on managing heartburn, undifferentiated dyspepsia and functional dyspepsia in general practice (BPJ 4, April 2007).

Defining dyspepsia and heartburn

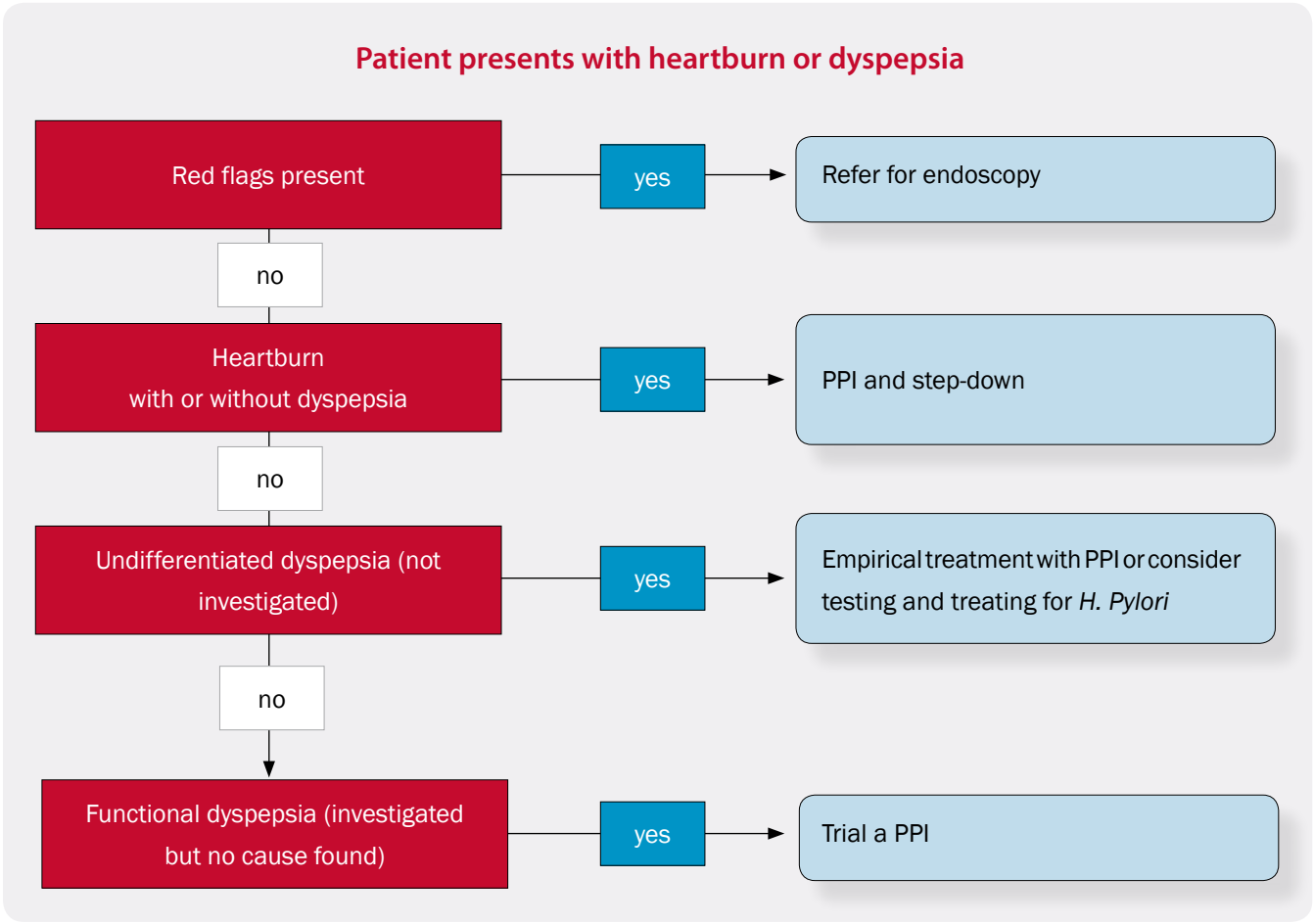
Dyspepsia is not a diagnosis but rather a description of symptoms that may indicate disease of the upper gastrointestinal tract. However, in the majority of cases there is no clear pathological cause and many people manage the symptoms themselves without consulting their GP.

Dyspepsia is pain or discomfort in the upper abdomen which is usually described as a burning sensation, heaviness or an ache. Associated symptoms include a feeling of fullness, early satiety after meals, anorexia, bloating, belching, nausea and vomiting. The symptoms of dyspepsia may be episodic, recurrent or chronic. Symptoms are often associated with eating, but this is not always the case.[1]

Undifferentiated dyspepsia is dyspepsia that has not been investigated. In a person at low risk of underlying pathology (Page 10), symptomatic management is appropriate, without the need for further investigation.

Functional or non-ulcer dyspepsia is dyspepsia, which has been investigated and no underlying pathology found.

Heartburn is described as a burning sensation rising from the epigastrium toward the neck. Heartburn, with or without associated dyspepsia, is most commonly associated with gastro-oesophageal reflux disease (GORD). Heartburn is often included within the description of "dyspepsia".

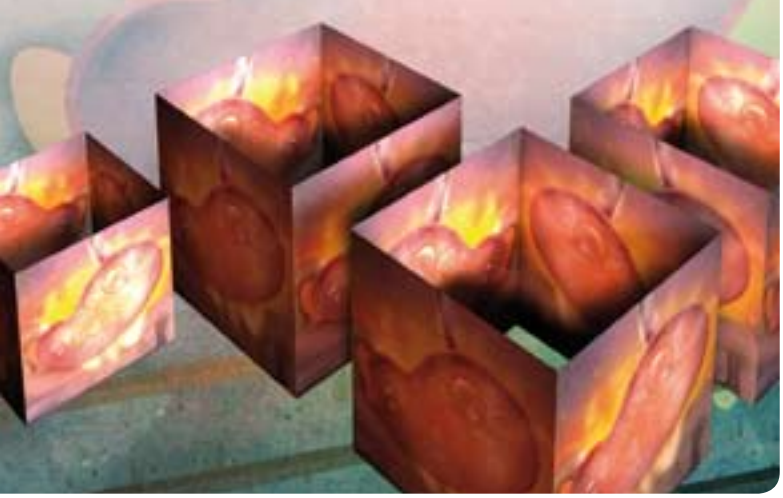


Red flags for people presenting with dyspepsia [1, 3]

The following factors increase the likelihood of significant organic disease:

- Age 50 years or older at first presentation (the incidence of gastric cancer increases with age)
- Age 40 years or older at first presentation for people of Māori, Pacific or Asian descent (gastric cancer tends to occur a decade earlier in these groups)
- Family history of gastric cancer with age of onset < 50 years
- Severe or persistent dyspepsia
- Previous peptic ulcer disease, particularly if complicated
- Ingestion of NSAIDs, including aspirin (check over-the-counter use)*
- Signs and symptoms of chronic gastrointestinal bleeding
- Iron deficiency anaemia
- Difficulty in swallowing
- Persistent or protracted vomiting
- Palpable abdominal mass
- Coughing spells or nocturnal aspiration
- Unexplained weight loss

* If a person taking NSAIDs has no other alarm features and symptoms are mild, initial management is to stop the NSAID and then re-assess symptoms



First check for red flags of significant organic disease

A number of features in the initial history or examination of people with dyspepsia or heartburn increases the likelihood of significant organic disease (see box "Red flags for people presenting with dyspepsia"). The presence of red flags indicates the need for referral for further investigation with endoscopy. If there is evidence of gastrointestinal bleeding or severe dysphagia, referral should be immediate.

Questioning of the patient may also reveal possible causes or precipitating factors for their symptoms including dietary habits (e.g. excessive caffeine or high fat), NSAID or aspirin use, use of other medicines, (e.g. calcium channel blockers, bisphosphonates, oral corticosteroids), past history of peptic ulcer or reflux disease or a family history of gastric cancer. It is also important to consider non-upper gastrointestinal tract causes of the symptoms such as cardiac, pancreatic, hepatobiliary, irritable bowel syndrome and musculoskeletal causes.[2]

N.B. When possible (i.e. with less urgent referral), acid suppressing medicines (H2 antagonists or proton pump inhibitors) should be stopped for at least two weeks prior to endoscopy as they may mask signs of organic disease. Antacids may be continued for symptom control.[3]

Best Practice Tip: Over-the-counter medicines

Treatments for dyspepsia such as antacids, ranitidine and omeprazole are available for purchase over-the-counter (OTC) from pharmacies. Pharmacists should check for alarm features and advise patients to seek medical attention if indicated. Lifestyle advice is also important. GPs should check what OTC medicines a patient has used, as this may give an indication of the severity and duration of the dyspepsia.

Heartburn with or without dyspepsia is usually caused by GORD and step-down PPI treatment is indicated

In the absence of red flags, the presence of heartburn is the single most important feature determining management.

Heartburn, with or without dyspepsia, is usually related to lower oesophageal dysfunction and the presence of GORD. There is some evidence that obesity is a risk factor for the development of GORD.[1] It is important that heartburn is differentiated from other causes of similar symptoms such as cardiac disease.

Simple lifestyle modifications may resolve mild symptoms of GORD, but acid suppressing treatment, using a step-down approach, is required if symptoms persist.

Barrett's oesophagus

Barrett's oesophagus is a complication of chronic GORD. It is a diagnosis made after endoscopy where normal cells lining the oesophagus (columnar epithelium) are found to be replaced by cells that usually line the gastric and intestinal mucosa (squamous epithelium). Patients diagnosed with Barrett's oesophagus are usually treated with long-term, high dose PPIs. They require surveillance with periodic gastroscopy as they are at increased risk of developing adenocarcinoma of the oesophagus even with PPI treatment.

Lifestyle modifications for managing GORD

Offer simple lifestyle advice including; healthy eating, weight reduction, smoking cessation and limiting alcohol intake.

Patients can be advised to avoid or minimise factors that seem to worsen their symptoms, such as bending over, eating shortly before going to bed and ingesting specific foods and beverages like alcohol, chocolate, spicy food and food with a high fat content. Some people may find that slightly raising the height of the head of the bed, while sleeping, may lessen symptoms.

Step-down acid suppressing treatment for managing GORD

The following step-down treatment regimen is appropriate for most patients. Patients should spend four to eight weeks at each step:[3]

Step One: Begin with a full dose PPI, e.g. omeprazole 20 mg daily

Step Two: Halve the dose of the PPI

Step Three: Change to a H2-antagonist, e.g. ranitidine 150 – 300 mg, twice daily

Step Four: Change to antacids or alginates as required

If there is no response to the full dose PPI after eight weeks, the dose can be doubled, e.g. to omeprazole 40 mg daily, and the response reviewed after six months. If response to treatment is still inadequate or if symptoms recur within one month of stopping, referral for endoscopy should be considered.[3] Although GORD is the most likely diagnosis in patients with predominant heartburn and reflux symptoms, these symptoms do not preclude the possibility of peptic ulcer disease, especially in patients who are infected with *Helicobacter pylori*.[4]

Best Practice Tip: It is generally recommended that PPIs (particularly omeprazole) are taken in the morning, 30 minutes before food, for optimal acid suppression. There is a theoretical basis for this but for many people, the timing in association with food is not important. However, when assessing response to a PPI or before considering a dose increase, it is worthwhile checking to see if the medicine is being taken as recommended.

Dyspepsia and heartburn in pregnancy

The most common cause of dyspepsia and heartburn in pregnancy is GORD.[1] Dyspepsia does not usually cause complications in pregnancy and is likely to resolve after the woman has given birth. Assessment to exclude a more serious cause includes enquiring about alarm features and a past history of GORD or peptic ulcer disease. Lifestyle, eating habits and current use of over-the-counter medicines such as antacids should also be checked.

Lifestyle advice is the usual first-line management, especially in the first trimester. If lifestyle advice does not adequately control symptoms, antacids or alginates can be tried if symptoms are relatively mild. Alginates, e.g. gaviscon, are particularly useful if heartburn symptoms are predominant. If symptoms are more severe, or persist despite treatment with an antacid or alginate, consider prescribing an acid-suppressing medicine such as ranitidine or omeprazole. Both of these medicines are considered to be relatively safe in pregnancy but omeprazole is more effective and a recent study has shown no association with major birth defects when administered in early (first trimester) pregnancy.[8] As with any medicine used in pregnancy, especially in the first trimester, treatment should be with the minimum effective dose for the shortest possible time.

Dyspepsia without heartburn

Who gets dyspepsia?

Dyspepsia can occur at any age but in older people it is more likely to be associated with organic diseases such as peptic ulcer disease or gastric cancer. NSAIDs, including aspirin, are a major cause of dyspepsia and peptic ulcers and these medicines are more frequently prescribed in people over 65, who in turn are more susceptible to complications.

There are no accurate figures linking the prevalence of dyspepsia with ethnicity in New Zealand. However, *H. pylori* infection which is associated with peptic ulceration is more common among Māori and Pacific peoples.

Initial management of undifferentiated dyspepsia without heartburn

In dyspepsia without heartburn that has not been investigated (undifferentiated dyspepsia), first rule out the possibility of serious disease, based on the presence of red flags. Review lifestyle factors and use of medicines that may be exacerbating symptoms. Patients can then be managed by either empiric treatment (usually with a PPI) or testing for *H.pylori*.

For most people, empiric treatment is appropriate. A suggested approach is as follows:[1]

- An antacid (or alginate) can be used for immediate relief of symptoms
- Prescribe a full dose PPI, e.g. omeprazole 20 mg, for one month
- If there is no response to the PPI, test and treat for *H.pylori*
- If there is no response to a PPI or H.pylori treatment, trial an H2-antagonist or a prokinetic (e.g. domperidone, metoclopramide) for one month. Referral can be considered at this point.
- If there is no response to the above steps refer for further investigation with endoscopy

- If symptoms recur, restart treatment with a PPI at the lowest effective dose and advise intermittent or as required treatment. Review maintenance treatment annually.[2]

Consider testing for *H.pylori* only after treatment failure

The pros and cons of a test and treat strategy (testing for *H.pylori* and then treating if positive) are widely debated and the decision to test for *H.pylori* is partly influenced by the likelihood of finding the infection.[2] The New Zealand Guidelines state that testing is recommended when there is a prevalence rate of greater than 30%.[3] As a guide, prevalence rates in the South Island are less than 30% but tend to be greater than 30% in adult Māori, Pacific and Asian people, people in lower socioeconomic areas and adult populations in Auckland.[3]

However, *H.pylori* infection rates are generally declining and a one month trial of a PPI is a reasonable approach for most patients with undifferentiated dyspepsia.

- An empiric trial of a PPI will treat the most common causes of dyspepsia, including GORD and peptic ulcer disease without the expense of *H.pylori* testing
- In populations with intermediate *H.pylori* prevalence (30 – 60%), empiric treatment and testing and treating are equally cost effective, but empiric treatment avoids the use of antibiotics and the possibility of resistance and adverse effects[2]
- A meta-analysis of randomised controlled trials that compared empiric PPI treatment with test and treat found no difference in treatment costs or symptoms when patients were followed up for one year[5]

Recommended test for *H. pylori* when indicated

If testing for *H. pylori* is indicated, the best test to use is dependent on the clinical setting. There are three tests, apart from performing endoscopy, to check for *H. pylori* infection. The most accurate test, in all clinical scenarios, is the Carbon-13 urea breath test. This test will determine if the patient has an active infection. However, this test is expensive and is not generally available. The faecal antigen test can also determine if active infection is present, but false-negative results are possible, which will limit interpretation when a diagnosis is required. Serology, using a blood sample, will show exposure to the infection, but this does not always mean that active infection is still present.

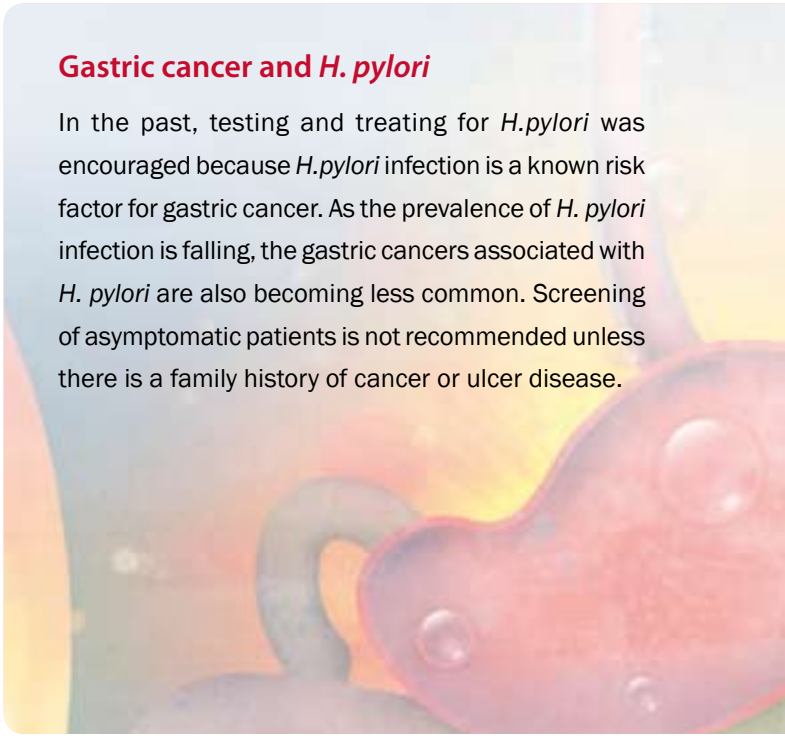
From a general practice perspective, serology is easy to obtain and is a reasonable approach for testing for *H. pylori*. A faecal antigen test is recommended to detect loss of infection after treatment.

Recommended treatment for *H.pylori*

For *H.pylori* eradication a seven day course of omeprazole 20 mg, clarithromycin 500 mg and amoxicillin 1 g (or metronidazole 400 mg, if allergic to penicillin), all taken twice daily is recommended. Note that the combination pack (Losec HP7 OAC) is no longer subsidised but triple therapy is subsidised if all three medicines are co-prescribed.

Gastric cancer and *H. pylori*

In the past, testing and treating for *H.pylori* was encouraged because *H.pylori* infection is a known risk factor for gastric cancer. As the prevalence of *H. pylori* infection is falling, the gastric cancers associated with *H. pylori* are also becoming less common. Screening of asymptomatic patients is not recommended unless there is a family history of cancer or ulcer disease.



Safety and long-term effects of PPIs

Many people have now been taking a PPI for several years and there have been a number of studies investigating long-term safety. Most studies are observational which cannot establish causality. There is no proven link with an increased risk of gastric cancer or nutritional deficiencies. From a general safety standpoint, PPIs should be used at the lowest effective dose for the shortest possible time and regularly reviewed.

Fractures of the hip, wrist, and spine

The data is conflicting as to whether PPI use is associated with an increased risk of bone fracture. There is a possible increased risk of fractures of the hip, wrist and spine.

In case controlled studies, long term PPI use has been associated with an increased risk of bone fracture, and this increased risk depends on the duration and dose of chronic use of the PPI. Use of a PPI for five years or more can increase the risk of osteoporotic fractures by 1.62-fold (95% CI: 1.02-2.58).[9] Other studies have shown that use of a PPI for seven years or more increases the risk of osteoporotic hip fractures by 4.55-fold (95% CI: 1.68-12.29).[9] PPI use for six to 12 months has been reported to be associated with an increased risk of osteoporotic hip and spine fractures.[9] If there is concern regarding the risk of bone fracture, such as for older adults who require long term PPI therapy, use the lowest effective PPI dose and ensure adequate dietary calcium intake.[10]

Vitamin B12 deficiency

Long-term use of PPIs does not lead to vitamin B12 deficiency except possibly in elderly people, or in people with Zollinger-Ellison Syndrome who are on high doses of a PPI for prolonged periods of time.[9] Routine testing for vitamin B12 is not advocated but may be advisable for such patients at increased risk.

Rare adverse reactions

PPIs are a relatively safe group of medicines and serious adverse events are rare. However, there have been case reports of interstitial nephritis with omeprazole, hepatitis with omeprazole and lansoprazole and visual disturbances with omeprazole and pantoprazole.[9]

Interstitial nephritis is characterised by acute renal failure, arthralgia, malaise and fever.

For further information see: **www.medsafe.govt.nz/profs/PUarticles/omeprazole.htm**

Interaction with clopidogrel

Omeprazole can be used to reduce the risk of gastrointestinal complications from antithrombotic treatment. However, omeprazole has been shown to decrease the formation of the active metabolite of clopidogrel and potentially reduce its anti-platelet effect. There is ongoing debate as to whether concomitant use of omeprazole and clopidogrel translates to adverse cardiovascular outcomes. Current advice from Medsafe is to avoid concomitant use. This advice may change as more evidence becomes available.

For further information see: **www.medsafe.govt.nz/profs/puarticles/clopidogrelandomeprazole.htm**

Functional dyspepsia is managed the same as undifferentiated dyspepsia

Defined pathology is unable to be identified in approximately half of the patients referred for endoscopy, and this is classified as functional dyspepsia. The cause of functional dyspepsia is not clearly understood and is likely to be multi-factorial. Some cases appear to be related to hyperacidity with associated heartburn and reflux symptoms, whereas others appear to be related to a disorder of gastrointestinal motility. Psychosocial and psychological factors may be involved but it is not known how significant these factors are on a population basis.

A PPI is considered first line treatment for functional dyspepsia, with or without symptoms of hyperacidity. Management follows the same approach as for undifferentiated dyspepsia.

Functional dyspepsia in patients, that have not responded to a PPI or prokinetic and are *H.pylori* negative (or have had the infection eradicated), is often challenging to treat.[2] There is some evidence that an antidepressant may be effective in reducing symptoms,[6] but it is not known if this is actually due to improved control of underlying depression. Either a tricyclic antidepressant (TCA) or a selective serotonin re-uptake inhibitor (SSRI) may be trialled.[7]

ACKNOWLEDGEMENT Thank you to **Dr John Wyeth**, Gastroenterologist and Clinical Director of Medicine, Capital & Coast DHB, Wellington for expert guidance in developing this article.

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Errors with methotrexate can be fatal

METHOTREXATE IS PRESCRIBED once weekly for rheumatoid arthritis or other autoimmune conditions. It is often initiated by a secondary care specialist, but is increasingly being initiated and prescribed in primary care. When used and monitored correctly methotrexate can be an effective and safe treatment, however, if an error occurs and it is taken as a daily dose rather than a once weekly dose it can be fatal.

The most common adverse effects of methotrexate are gastrointestinal. Folic acid is prescribed to manage these adverse effects (see opposite). Toxicity can occur with any dose of methotrexate, however, toxic effects are more frequent and more severe with increased dose or increased frequency of dosing.[1] Patients should be made aware of symptoms that may indicate methotrexate toxicity

A case report

A patient with rheumatoid arthritis presents to the general practice with a fever and chest tightness. After taking a history and examining the patient, you see in the medical record that the patient was last seen by another doctor in the practice, one week ago, for a repeat prescription of oral methotrexate.

The symptoms of chest tightness and fever could be unrelated to the methotrexate dose but should be further investigated.

Questions to ask: When did you last take your methotrexate? How many doses have you taken in the last seven days? How many tablets do you take at a time? Do you know what strength your methotrexate tablets are?

Action required: If questioning reveals that there has been an error in the methotrexate dose or frequency then the patient should be referred urgently to hospital for further tests and treatment, including chest x-ray, respiratory function tests and CBC.

If no error has occurred in the methotrexate dose or frequency, consider other causes and advise the patient not to take any more methotrexate while awaiting the results of an urgent CBC, liver function and renal function tests. Review the patient again when the results are received.

such as fever, sore throat, abdominal pain, jaundice, chest pain or shortness of breath.

Routine baseline testing prior to initiation of methotrexate usually includes a complete blood count (CBC), liver function tests, serum creatinine, a chest x-ray and respiratory function testing.

Methotrexate-related pulmonary complications

Methotrexate use may cause significant pulmonary complications such as pneumonitis and pneumonia. Patients with methotrexate-induced pneumonitis typically present with fever, dry cough, chest pain and shortness of breath. It is not clear whether methotrexate-induced pneumonitis is due to direct toxicity, a hypersensitivity reaction or an underlying viral infection.[2] As methotrexate suppresses the immune system, people taking this medicine are more susceptible to opportunistic infections caused by pathogens such as *Pneumocystis carinii*, viruses or mycobacteria.[2] Both methotrexate-induced pneumonitis and *Pneumocystis carinii* pneumonia are potentially fatal.

Folic acid co-administration

Methotrexate use results in a decreased supply of folates. Folic acid is co-administered to minimise the adverse effects of folate deficiency (stomatitis, bone marrow toxicity, abnormal liver function tests and gastrointestinal intolerance). Total weekly doses of 5 – 27.5 mg have demonstrated efficacy in decreasing methotrexate adverse effects,[3] however, a pragmatic approach is the use of 5 mg, once weekly.

Scenarios for potential error

Prescriber error: The methotrexate prescription is inadvertently prescribed as a daily dose rather than a weekly dose.

Pharmacy error: The prescription is correctly written as a weekly dose but the pharmacist dispenses and labels it incorrectly as a daily dose.

Patient error: A prescription is changed from a large number of low dose methotrexate tablets to a smaller number of higher dose tablets (to help simplify the regimen for the patient). The prescription is dispensed correctly but the patient continues to take the same number of new higher dose tablets, as their weekly dose.

All of these scenarios have occurred in New Zealand and overseas, resulting in patient deaths.

Best practice for prescribing methotrexate

"Right strength, right dose, right frequency"

- Double check prescriptions (both on screen and printed)
- Prescribe in milligrams not number of tablets
- Specify on the prescription the day of the week that the methotrexate should be taken
- Consider only prescribing 2.5 mg tablets (unless the patient is already stabilised on 10 mg tablets)
- Confirm with the patient what their individual dose in milligrams is, the strength of their tablets, the number of tablets they should take and the day of the week they should take them
- Inform the patient of possible adverse effects and what they should do if they think an adverse effect has occurred

For further information about monitoring methotrexate use, see "Recommended investigations for some commonly used DMARDs" BPJ 17 (Oct, 2008).

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DETECTING MALIGNANT MELANOMA

Key concepts

- New Zealand has one of the highest rates of melanoma in the world
- Several factors can increase an individual's risk of developing melanoma including; a large number of naevi (moles), atypical naevi, frequent exposure to sun and sunburn during childhood and a family history of melanoma
- Early detection of melanoma involves clinicians being aware of the clinical signs of melanoma and algorithms that can assist with diagnosis, e.g. ABCDE, Glasgow checklist
- Encourage patients to report any suspicious skin lesions and invite at-risk patients for periodic full-body skin checks
- Refer, biopsy (depending on level of skill and clinical situation) or carefully follow up all suspicious skin lesions
- Dermatoscopy, digital photography and mole mapping are tools that can be used to aid in detection and surveillance

Melanoma in New Zealand

New Zealand has one of the highest rates of invasive melanoma in the world, with an incidence rate of approximately 41 per 100,000 people, per year.[1, 2] The most recently available data shows that in 2007, malignant melanoma accounted for approximately 11% of all cancer registrations in New Zealand.[3] Melanoma was the most commonly registered cancer for males aged 25 to 44 years and the second most common for females in this age group and all people aged 45 to 64 years.[3]

In New Zealand in 2007, 292 people died from malignant melanoma, making it the tenth most common cause of death from cancer (accounting for 3.4% of all cancer deaths).[3] The mortality rate from invasive melanoma is approximately 15%. Malignant melanoma is more common in males than females in New Zealand. Registrations are 16% higher and mortality rate is 90% higher in males.[3]

Melanoma in Māori and Pacific peoples

Melanoma is significantly less common in Māori than in non-Māori people in New Zealand.[3] There is evidence that melanoma is also uncommon in Pacific peoples, with a combined incidence rate in 2004 for Māori and Pacific peoples of 2.7 per 100,000 people, per year.[2,4]

Māori and Pacific peoples, however, present with melanomas that are thicker (>3 mm thickness) than those in non-Māori people and therefore are likely to be at increased risk of death.[4] It has been suggested that lesions at presentation are thicker because Māori and Pacific peoples present late to primary care.[2,4] However, evidence from studies of melanoma in other darker skinned populations consistently show poorer outcomes and it is likely that a complex mix of factors is responsible, including both biological (genetic and tumour type) and social aspects.[5]

In contrast to the non-Māori population in New Zealand, melanoma in Māori is more often found in women than men.[6] This female predominance is seen in other populations that have a low incidence of melanoma.[7]

In both Māori and non-Māori, melanoma is most frequently found on areas of the body that have been exposed to the sun. In darker skinned populations in other parts of the world, approximately two-thirds of melanoma are found on the palms, soles of the feet and under nails.[5,6]

Risk factors for melanoma

Screening for melanoma at a population level is not indicated but raising awareness of the factors that increase individual risk is important for both patients and clinicians.

The following factors increase the risk of melanoma.

Age: The risk of melanoma increases with age, particularly over age 60 years.[2,8] Incidence is higher in older men who tend to present with melanoma that are thicker and therefore are more at risk of metastasis.[9] Although melanoma is rare in children (estimated to be 1–2% of all melanoma cases), there is evidence that they may present with thicker lesions.[10] This has been attributed to a higher incidence of atypical lesions and a possible delay in presentation and diagnosis, due to the rarity of melanoma in this age group.[11]

Past history of melanoma or non-melanoma skin cancer: A person with a history of melanoma has a greater than ten times increased risk of developing another melanoma.[7,12] A past history of non-melanoma skin cancer increases the risk around four-fold.[9]

Family history of melanoma: A history of melanoma in a first degree family member almost doubles an individual's risk of developing melanoma.[9] It is estimated that approximately 10% of people with melanoma have a family history of melanoma in a first degree relative.[13] This increased risk may be attributed to, in part, by behavioural and environmental factors that are shared by these families but it is likely that there are also underlying genetic factors.[13]

What is malignant melanoma?[1]

Melanoma is a type of skin cancer that develops from melanocytes (melanin-producing cells), which are normally located in the basal layer of the epidermis or within the dermis. Although melanoma is less common than non-melanoma skin cancers, e.g. basal cell carcinoma and squamous cell carcinoma, it causes far more deaths. Melanoma may develop within an existing melanocytic naevus but more often arises from skin that appears normal. Melanoma can occur anywhere on the skin and on rare occasions, in other tissues such as the eye, central nervous system and the mucosa of the gastrointestinal, genitourinary and respiratory systems. Aggressive forms of melanoma can metastasise to almost any organ in the body.

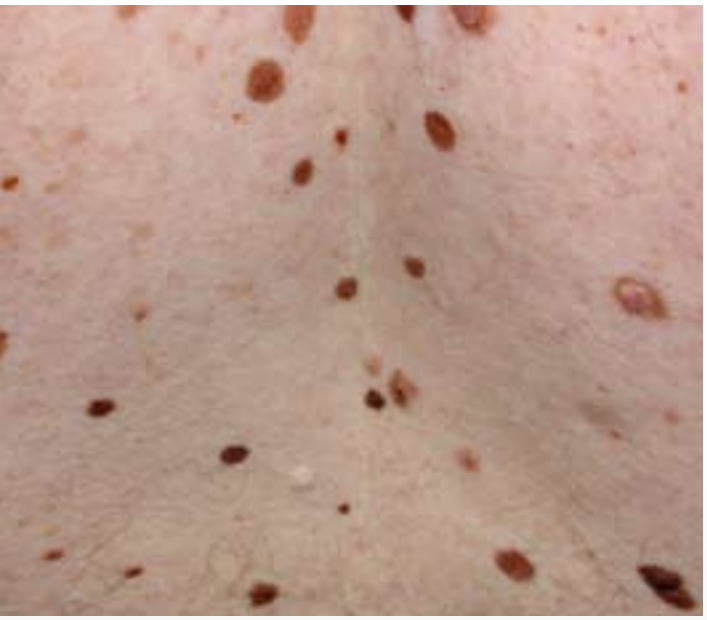


Figure 1: Mutiple benign but atypical melanocytic naevi. Image provided by DermnetNZ

What is a mole?[1]

A mole (melanocytic naevus) results from benign proliferation of melanocytes. Most European New Zealanders have 20–50 moles, depending on genetics and exposure to the sun. Some moles are congenital and others are acquired, particularly during childhood and adolescence. Development of a new mole later in life, e.g. after age 50 years, is less common.

An atypical naevus (also called Clark's naevus) is a melanocytic naevus that is unusual in appearance – i.e. a "funny-looking mole" (Figure 1). Most atypical naevi develop during childhood. Generally people, particularly those with fair skin, have up to ten atypical naevi however some with a familial syndrome may have several hundred. A person with five or more atypical naevi is at higher risk of melanoma. However, an individual atypical naevus has very low risk of malignant change as most melanoma arise *de novo*.

A mole with three or more of the following clinical features can be defined as atypical:

- Size that is > 5 – 6 mm in diameter
- Border that is blurry or ill-defined
- Unusual irregular shape
- Variation in colour
- Variation in profile i.e. flat and raised parts

For further information see:
www.dermnet.org.nz

Number of moles: The risk of melanoma increases as the number of melanocytic naevi (moles) increases, particularly if there are more than 100.[1, 7]

Type of moles: The risk of melanoma increases if the patient has atypical naevi, with a six-fold increase in risk for those with more than five.[1,7,9]

Ultraviolet radiation: Exposure to ultraviolet radiation from the sun (UVB, UVA) or from sun bed use (UVA) increases the risk of melanoma.[8] Frequent exposure to sun and sunburn during childhood and adolescence approximately doubles the risk of melanoma. Ongoing exposure in adulthood also contributes to risk, particularly if the exposure is intermittent in a person unaccustomed to the sun.[7,8] However, a history of sunburn has limited clinical predictive value in regions such as New Zealand where the prevalence of sunburn is high.[9]

Skin type: Skin type can be categorised by response to UV exposure. Table 1 describes the six Fitzpatrick phototypes and the response of each type of skin to UV exposure.[1] The paler the skin, the more likely it is to burn and therefore the more protection it needs from UV radiation.

Gender: Males (non-Māori) in New Zealand and in other countries with a high-incidence of melanoma, e.g. Australia, United States, are at higher risk of melanoma than females. This is in contrast to other areas in the world with lower incidence of melanoma, e.g. Germany, Mediterranean counties, where there is usually a female predominance.[2,14]

Although the number of Māori with melanoma is low, there is evidence that Māori females are twice as likely to have melanoma as Māori males.[6]

Men are more likely to have melanomas on the trunk (approximately 40%) and women more likely to have lesions on the legs (approximately 35%).[1, 15]

Geographical location: New Zealand's geographical location increases the risk of melanoma for several reasons, including :[2,16]

- Large number of fair-skinned people
- Mild climate allowing outdoor activities during the middle of the day
- Changeable weather resulting in intermittent rather than constant sun exposure, which may alter people's sun-seeking behaviour and potentially increase the risk of sunburn
- 40% higher levels of peak summer UV radiation compared to countries with similar latitude and altitude in Northern hemisphere

Incidence rates of melanoma also vary throughout New Zealand with lower rates reported in the Southland area (approximately 20 cases per 100,000 people per year) compared to the Taranaki area (approximately 70 cases per 100,000 people per year).[2] The reasons for this difference are not clear but are likely to relate to atmospheric factors.

Table 1: The Fitzpatrick skin types (adapted from Dermnet NZ)[1]

Skin type	Typical Features	Response to UV exposure
I	Pale white skin, blue/hazel eyes, blonde/red hair	Always burns, does not tan
II	Fair skin, blue eyes	Burns easily, tans poorly
III	Darker white skin	Tans after initial burn
IV	Light brown skin	Burns minimally, tans easily
V	Brown skin	Rarely burns, tans darkly easily
VI	Dark brown or black skin	Never burns, always tans darkly

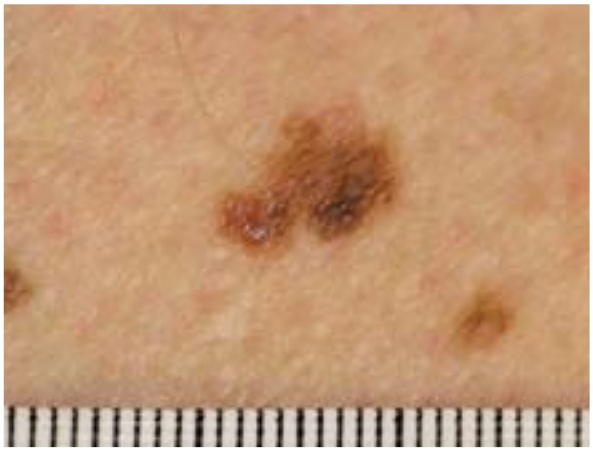
Types of melanoma

There are five main types of melanoma, distinguished by their clinical appearance, the growth and behaviour of the lesion and their location on the body. Approximately 10% of melanomas are non-pigmented (amelanotic) and this increases the difficulty in making an accurate diagnosis.[7] Once invasive, all types of melanoma can metastasise.

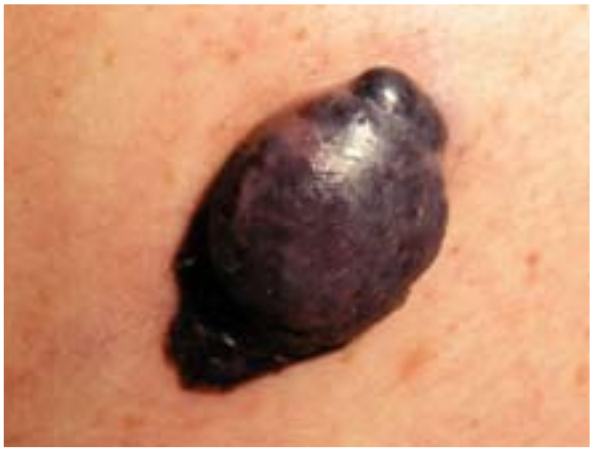
In addition to the five main types of melanoma there are a number of other more unusual types, such as desmoplastic melanoma and malignant blue naevus. Combinations of melanoma can also occur, such as a nodular melanoma growing within a superficial spreading melanoma.[1] Cutaneous metastatic melanoma may present as blue-black to pink-red solitary or multiple firm nodules. They may be close to the site of primary melanoma (satellites) or distant due to haematogenous spread. In some patients with metastatic melanoma, the site of the primary lesion may be unknown. Enquire about a history of skin lesion excision.

The five main clinical types of primary cutaneous melanoma are pictured.[1,7,17] (Images provided by DermnetNZ)

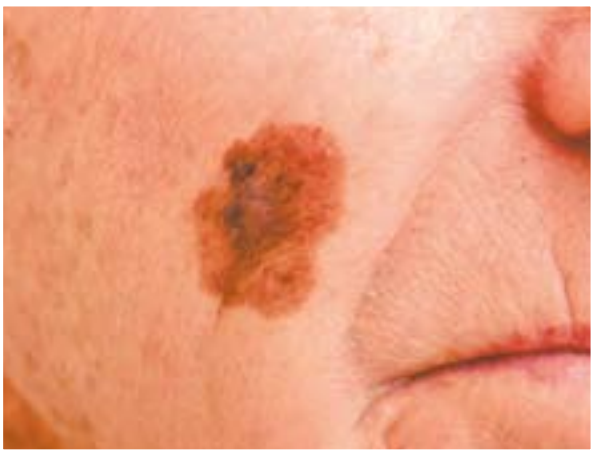
1. **Superficial spreading melanoma (SSM)** – the most common type of melanoma. Usually found on areas of the body which have been exposed to the sun. This type of melanoma is typically a flat patch that is irregularly shaped, irregularly pigmented and has an irregular outline. SSM frequently has a prolonged pre-invasive in-situ phase, growing slowly over months to years



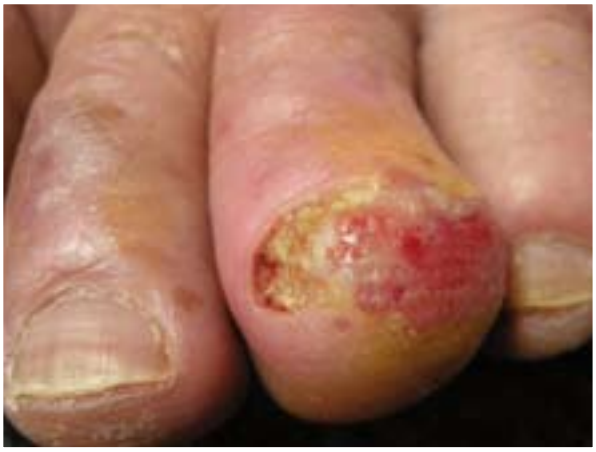
2. **Nodular melanoma (NM)** – this is the second most common type of melanoma and presents as a rapidly-growing (over several weeks to months) pink, red, brown or black nodule. The pigmentation within NM is often more uniform than in SSM. It may arise within an existing melanocytic naevus or in normal appearing skin. NM may be more likely to bleed or ulcerate than SSM. NM does not have an in-situ phase.



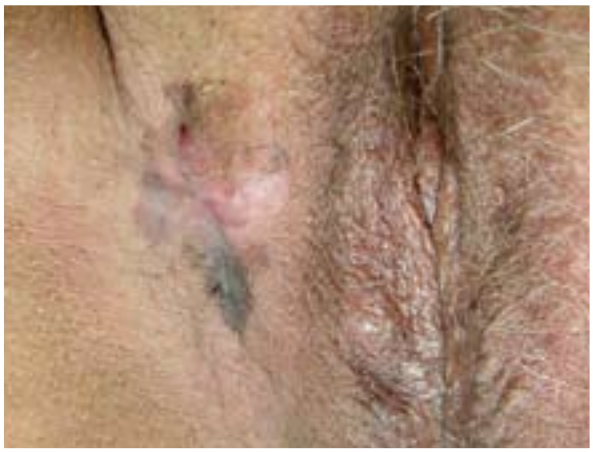
3. **Lentigo maligna melanoma (LMM)** – this type of melanoma is found on sun-damaged skin in older people, e.g. on the head and neck. The lesion typically has a long pre-invasive in-situ stage (years to decades), termed lentigo maligna (LM). LM presents as an enlarging, irregularly pigmented freckle.



4. **Acral lentiginous melanoma (ALM)** – this type of melanoma is found on the palms of the hands, soles of the feet and underneath the finger or toe nails. ALM account for less than 5% of all melanomas in New Zealand. Although still rare, ALM is the most common type of melanoma in dark-skinned people (Fitzpatrick phototype 5 or 6). Melanoma on the feet may not always demonstrate the characteristics associated with melanoma at other body sites and there is a higher rate of amelanotic (non-pigmented) melanoma among acral lesions (see sidebar: "Investigating lesions on the feet").[18]



5. **Mucosal lentiginous melanoma (MLM)** – these lesions arise from mucosal or paramuscosal sites including the vulva, vagina, penis, anus, eyelids, conjunctiva, oral cavity or lips.



Investigating lesions on the feet

The "CUBED" acronym can be used for investigating suspicious lesions on the feet.[18] The presence of any two features should trigger referral or excision. The "CUBED" acronym is:

- **C**oloured lesions where any part is not skin coloured
- **U**ncertain diagnosis
- **B**leeding lesions on the foot or under the nail, including chronic granulation tissue
- **E**nlargement or deterioration of a lesion or ulcer despite treatment
- **D**elay in healing (> two months)

Best Practice Tip: It can be difficult to determine the cause of subungual bleeding. Always ask about a history of trauma to the nail. An area of clear nail growth will develop at the base of the nail with time (weeks) if the subungual bleeding is a result of trauma (and not if the lesion is melanoma).[18]

Early detection of melanoma improves survival

Early detection of melanoma results in better outcomes for patients. The challenge for GPs is to accurately recognise skin lesions that are suspicious. Early detection also relies on the patient being aware of the need to have skin lesions checked. If a suspicious skin lesion is identified further treatment is essential. Depending on the level of clinical suspicion this may be immediate referral, biopsy or accurate documentation of the lesion and organised follow-up.

How can GPs help ensure melanoma is detected early?

- Be aware of the clinical signs of melanoma and algorithms that can assist with diagnosis, e.g. ABCDE, Glasgow checklist (Page 26)
- Be familiar with which patients are at increased risk of melanoma
- Educate patients who are at increased risk of melanoma about the clinical signs to watch for and encourage them to examine their skin monthly (see sidebar: "Skin self-examination")
- Consider periodically asking all patients if they are concerned about any moles or skin lesions, and offer full skin checks to older males
- When examining a patient for another clinical problem take note of any skin lesions with an unusual appearance (an "ugly duckling", Page 26) or scars from previous excisions of suspicious lesions
- A check of a single lesion that is of concern can be done quickly during a consultation for another clinical problem, although the entire skin surface should be examined if indicated, e.g. in high risk patients. Ensure access to good lighting when examining the skin.
- Refer, biopsy (depending on level of skill and clinical situation) or carefully follow up all suspicious skin lesions

- If a biopsy is taken, ensure that the results are followed up, e.g. place a recall or reminder in the patient notes
- Monitor clinically doubtful skin lesions for one to two months (but no more than three months).[9] Consider the use of digital photography to monitor changes. Ensure the patient knows to re-present sooner if there is any concern.
- Clinical photography with macroscopic and dermoscopic views can enable a second opinion from an expert (teledermoscopy)
- Consider taking a training course in dermatoscopy

Provide information about melanoma

Although mortality from melanoma decreases with early detection, some patients will still die from melanoma. Public health education and media reports have increased awareness about melanoma, however, some patients still do not seek medical advice at an early enough stage.[12] Where practical, information can be provided to help patients determine normal from abnormal moles.[19] Validate the usefulness of a skin lesion check as patients may feel that this is a trivial reason for visiting a GP.[19]

Encourage patients to report rapidly growing lesions

Some types of melanoma, e.g. nodular melanoma, grow very rapidly and are biologically aggressive from the outset.[12] Some, e.g. amelanotic melanomas, are more difficult to recognise because they do not usually display the classical clinical features.[20] Make patients aware that any rapidly growing or odd looking lesions should be checked. A few months of rapid growth may adversely affect prognosis.

Offer high risk patients a full-body skin check

Practical issues such as a lack of time, competing co-morbidities and patient embarrassment may limit the extent of a skin examination,[21] increasing the chance that lesions will not be detected. Population based screening using full-body skin examination is not recommended as there is no clear evidence that this is effective in reducing mortality.[9,12] However, patients who are at high risk of melanoma should be offered a full-body skin examination, that includes the scalp and skin folds. New Zealand guidelines recommend six-monthly full body skin examinations in high risk patients.[9] Patients may need to request a longer consultation time for a full body skin check or return for an additional consultation, particularly if they have other issues to discuss.

Although self-examination of the skin is beneficial and should be encouraged, there is evidence that full body skin examinations by doctors detect more melanomas than self-examination and also that the lesions found are more likely to be thinner or melanoma in situ.[22,23] In a study of well-motivated patients only 55% were continuing to examine their skin after one year.[22]

The use of clinical checklists may facilitate early detection of melanoma

Checklists of clinical features have been developed to assist in the detection of suspicious skin lesions by both patients and clinicians. Becoming familiar with the three most frequently used tools outlined below is advantageous, because a combined approach is most useful to detect malignant lesions.

The ABCDE criteria

Any combination of the ABCDE criteria may indicate a suspicious lesion:[24, 25]

- **A**symmetry – one half of the lesion does not match the other
- **B**order irregularity – notched, blurred or ragged edges
- **C**olour variegation - different colours such as brown, black, white, red or blue within the same lesion
- **D**iameter greater than 6 mm – the majority of melanoma are more than 6 mm in size although up to 25% of new lesions may be smaller
- **E**volution or Enlargement – any change in a lesion over time is suspicious (colour, shape or symptoms)

Skin self-examination

Self-examination of the skin should be seen as complementary to a skin examination by a health professional.[12] The aim of self-examination is for the patient to detect suspicious lesions early so that they present for a skin check by a doctor to enable reassurance, observation, excision or referral as appropriate.

A full self-examination of the skin requires assistance from another person or the use of two mirrors. A hair dryer can be useful when examining the scalp.

A guide to skin self examination can be found at: **www.cancernz.org.nz** Search term: Skin check

The disadvantage of the ABCDE criteria is that they are not very specific. Other types of skin lesions such as seborrheic keratoses can also exhibit the same features and early melanoma may not initially display these clinical characteristics.[20] In addition, not all skin lesions that change are melanoma. Moles undergo symmetrical enlargement, particularly in younger patients as they grow. Some skin lesions darken in a uniform manner after sun exposure and trauma or chronic rubbing may cause changes in colour or texture.[20]

The Glasgow seven point checklist

This checklist includes major and minor clinical features which are assigned a score. The checklist is:[7,26]

Major features (two points)

- Change in size
- Change in shape (irregular border)
- Change in colour (irregular pigmentation)

Minor features (one point)

- Inflammation
- Crusting, oozing or bleeding
- Sensory change or itch
- Lesion diameter ≥ 6 mm

Specialist referral or excision is indicated for patients with skin lesions which score three points or more.[27] Referral or excision should also be considered in the presence of any one clinical feature when there is a strong suspicion of melanoma, as major features are not always present.[7,27] The checklist is more complex and therefore less widely adopted than the ABCDE criteria.

The "ugly duckling" sign

The underlying clinical rationale for the "ugly duckling" sign is that most naevi in an individual are similar in appearance, therefore a lesion that is not like others should receive special attention, even though it may not raise suspicion on the basis of other clinical tools. The tool aims to improve specificity (i.e. reduce the number of benign lesions that are removed) but not decrease sensitivity (i.e. not miss detecting melanoma). It is most

useful in patients with large numbers of atypical naevi and may reduce the number of unnecessary resections. For example, in a patient with multiple but similar atypical lesions, e.g. red-brown with irregular borders, the "ugly duckling" lesion for that patient may be a small, well-defined black lesion.[28]

Dermatoscopy and digital technology

Dermatoscopy and forms of digital technology such as digital dermatoscopy or photography are additional tools that may be used by experienced clinicians to aid early diagnosis of melanoma.

Dermatoscopy (also called dermoscopy) is the technique of examination of the skin using a magnifying lens (usually 10×) and a light source. Modern dermatoscopes are small, portable, hand held devices that are used extensively in specialist practice and increasingly in primary care. When used by a trained clinician, dermatoscopic examination can reduce unnecessary excisions of benign skin lesions and increase the accuracy with which early melanoma is detected.[29]

Two forms of dermatoscopic systems are available:[1]

1. Fluid immersion systems where the lens is placed in contact with the skin and oil or alcohol is used to eliminate any light reflections from the skin. Contact dermatoscopy gives a better quality image but has the disadvantage of compression of vascular structures.
2. Polarised light non-contact systems which give better images of deeper structures and the vasculature. They do not require an immersion fluid and multiple lesions can be quickly viewed.

Effective dermatoscopy requires initial training, ongoing learning experience and access to specialist advice. Digital macro and dermatoscopic photography of suspicious lesions is highly recommended because it:

- Enables binocular evaluation of an enlarged view
- Enhances recognition of global and local dermatoscopic features
- Increases self-learning
- Allows more accurate follow-up than by memory and measurement alone
- Is easy to obtain a second opinion

Digital photography may be used to record the position and characteristics of skin lesions on a patient's whole body. The images can then be repeated over time to detect new lesions and lesions that may have changed in shape, size or colour.

Dermatoscopic images can be obtained and repeated over one to three months to assist in the follow up of suspicious skin lesions. For longer term surveillance, images can be repeated six to 12 monthly.

Mole mapping refers to a range of techniques that record the position and characteristics of skin lesions on the body. In its simplest form it may be the recording of lesions on a hand drawn figure. The use of digital photography, dermatoscopic images and computer software allowing serial monitoring has developed mole mapping to a new level. Mole mapping when used for surveillance combines digital technologies with risk assessment, patient education and regular specialist follow-up.[1] Mole mapping is most useful in patients with a large number of moles (> 50–100), atypical naevi, moles on the back that are hard to see and also in patients who are at increased risk of melanoma.[1]

The advantages and disadvantages of mole mapping (Table 2) should be discussed with the patient. A mole map is a diagnostic service and if a suspicious lesion is identified the patient is referred back to their GP or specialist for further treatment. In New Zealand, private mole mapping services, including assessment of the images by a dermatologist are available throughout the country, e.g. **www.molemap.co.nz**.

Table 2: Advantages and disadvantages of mole mapping (adapted from Dermnet NZ)[1]

Advantages	Disadvantages
Rapid assessment of change in a lesion	May miss melanoma in areas such as the scalp and genitals
Lesions of concern are detected early allowing careful follow up or early referral for surgery	False negatives (early melanoma may look benign and be missed)
Unnecessary excisions may be reduced	False positives (benign lesions may be excised unnecessarily)
Access to mole mapping may be quicker and easier than access to a dermatologist	The interval between mole mapping appointments may be too long for rapidly growing lesions
Patient and doctor reassurance	Cost (approximately $300)

The role of biopsy

Indications for excision of a suspicious skin lesion include:

- Lesion with typical clinical / dermoscopic features of melanoma
- Solitary atypical naevus (e.g. > 6 mm, irregular shape, asymmetry of structure and colour) in a site that is difficult to observe
- Atypical flat naevus that has been objectively observed to enlarge, e.g. by photographic comparison or observation by a reliable witness
- Enlarging pigmented or red nodule, particularly if symptomatic or if it is not possible to confidently diagnose a benign lesion such as dermatofibroma

Flat lesions can safely be observed if clinical concern is minimal.

If biopsy is indicated, an excision biopsy of the complete lesion with a 2 mm rim of normal skin and a cuff of fat is recomended.[7,9] The depth of the excision biopsy should extend to the deep fascia. This method provides sufficient material for histological examination and does not compromise a wider excision if required.[7]

Punch biopsy or other forms of partial biopsy of suspicious skin lesions is not recommended because it may not give sufficient material for an accurate pathological assessment of the lesion.[7,9] A partial biopsy or multiple biopsies may be appropriate in clinical situations such as a large facial lesion or acral lesion. However, expert advice should be obtained first.[9] Biopsy can also be useful to differentiate the lesion from a non-melanocytic tumour such as seborrhoeic keratosis. If it reveals a melanocytic lesion, particularly if there is atypia, complete excision should then be undertaken. The risk of seeding or dissemination of the melanoma with a partial biopsy is no longer thought to be significant.[9]

Best Practice Tip: Histological diagnosis of melanoma is often difficult. Provide the pathologist with a careful description of the lesion and explain why it is suspicious. Some pathologists find clinical photographs useful. Draw attention to areas of specific concern, e.g. eccentric pigmentation, as melanoma might be arising within an otherwise benign lesion. One way of doing this is by using a biopsy punch to score the skin around the suspicious area.

Sun protection and melanoma

Research to demonstrate the protective effect from sunscreen against melanoma has been difficult and at times controversial for several reasons including:[30]

- Individuals at higher risk of sunburn are at higher risk of melanoma
- Individuals at higher risk of sunburn are more likely to use sunscreen
- Sunscreen use may result in longer periods of sun exposure
- Previously the majority of sunscreens protected against UVB but not UVA (most sunscreens now provide protection from both)

The risk of melanoma can be reduced with avoidance of the sun at times of high UV levels and sun protective measures such as using sunscreen and wearing a hat and clothing that covers the skin. The "slip, slop, slap and wrap message" should continue to be promoted (see sidebar: "How to be SunSmart").[31]

Sun exposure, vitamin D and melanoma

Minimal exposure to the sun may result in a deficiency of vitamin D levels as UVB radiation is required for the production of vitamin D3 within the skin. Ideally, a balance can be achieved between safe levels of sun exposure and sufficient sun exposure to maintain adequate vitamin D levels. New Zealand guidelines recommend that short episodes of sun exposure, i.e. six to eight minutes in the summer and six to 50 minutes in the winter, depending on skin type and latitude, to 15–20% of the body most days, is required to maintain vitamin D levels.[9] Supplementation with vitamin D is likely to be safer than sun exposure for people who are at higher risk of melanoma, e.g. elderly people, people in residential care, people with a past history of melanoma or who are very sensitive to the sun and people who are on medications that increase photosensitivity.

How to be SunSmart

Encourage patients to be "SunSmart". In the middle of the day in summer it can take only 15 minutes for fair skin to burn. A wide range of information sheets on sun protection and skin cancer are available on the New Zealand Cancer society website: **www.cancernz.org.nz**

- **Avoid** exposure to the sun between 11 am and 4 pm, especially from September to March when UV levels are high. Also avoid sun beds.
- **Slip** on sun-protective clothing
- **Slop** on sunscreen that is broad-spectrum and SPF 30+ and reapply after every two hours in the sun and after swimming
- **Slap** on a hat
- **Seek** shade
- **Wrap** on some good quality sunglasses

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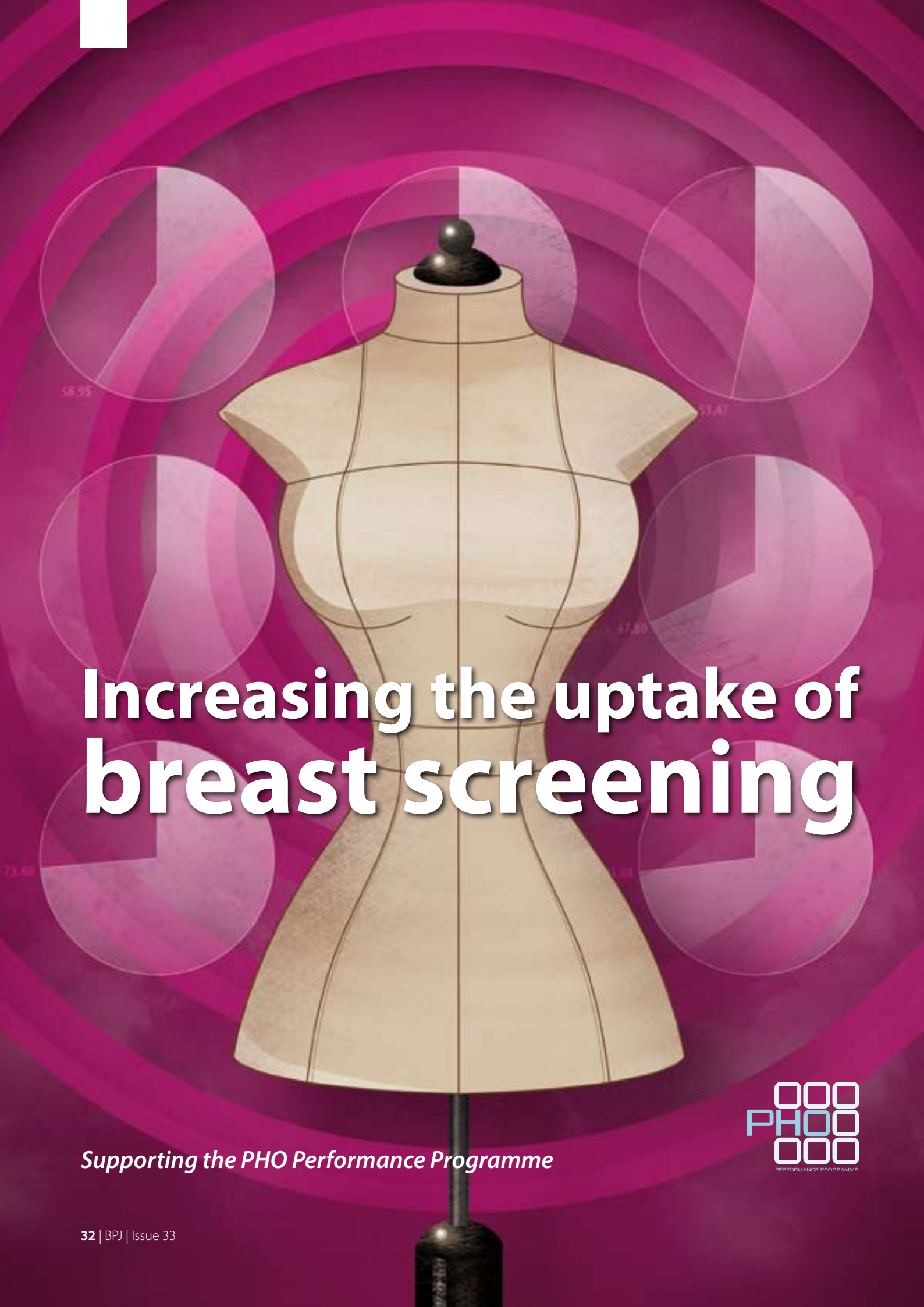


Increasing the uptake of breast screening

Supporting the PHO Performance Programme

PHO PERFORMANCE PROGRAMME

Achieving breast screening targets

Significant improvements are being made in the rate of screening for breast cancer, both in the high needs population and in the total population of New Zealand. However, breast cancer remains the most commonly diagnosed cancer[1] and one of the leading causes of cancer death in New Zealand women.[2] Māori females have a higher rate of breast cancer than non-Māori females and a mortality rate from breast cancer approximately 50% higher than non-Māori.[2] Overall the mortality rate from breast cancer is slowly decreasing in New Zealand, but continued efforts to improve the breast screening rate, especially among Māori and Pacific women, are still required.

Breast screening rates in New Zealand are improving

The rate of breast screening in New Zealand has improved incrementally over the past five years but is still below target. In the first six months of 2010 the national average rate for breast screening rose from 57.7% to 59.4% for women in the high needs population and from 65.7% to 66.6% for women in the total population.[3] During this reporting period 13 out of 78 PHOs achieved the PHO Performance Programme goal of at least 70% of high needs women having received a mammogram from a BreastScreen Aotearoa provider in the past two years.[3]

How can a practice increase the uptake of breast screening?

There is currently no national system in place that identifies and enrols eligible women for breast screening. Participation in breast screening relies on motivated, well-informed patients and a commitment from general practices to encourage and assist in enrolling all eligible women.

To be eligible to receive a mammogram from a BreastScreen Aotearoa provider once every two years, a woman must:

- Be aged between 45 and 69 years
- Have no symptoms of breast cancer
- Have not had a mammogram within the past 12 months
- Not be pregnant
- Be eligible for public health services in New Zealand

PHO Performance Programme: Breast screening

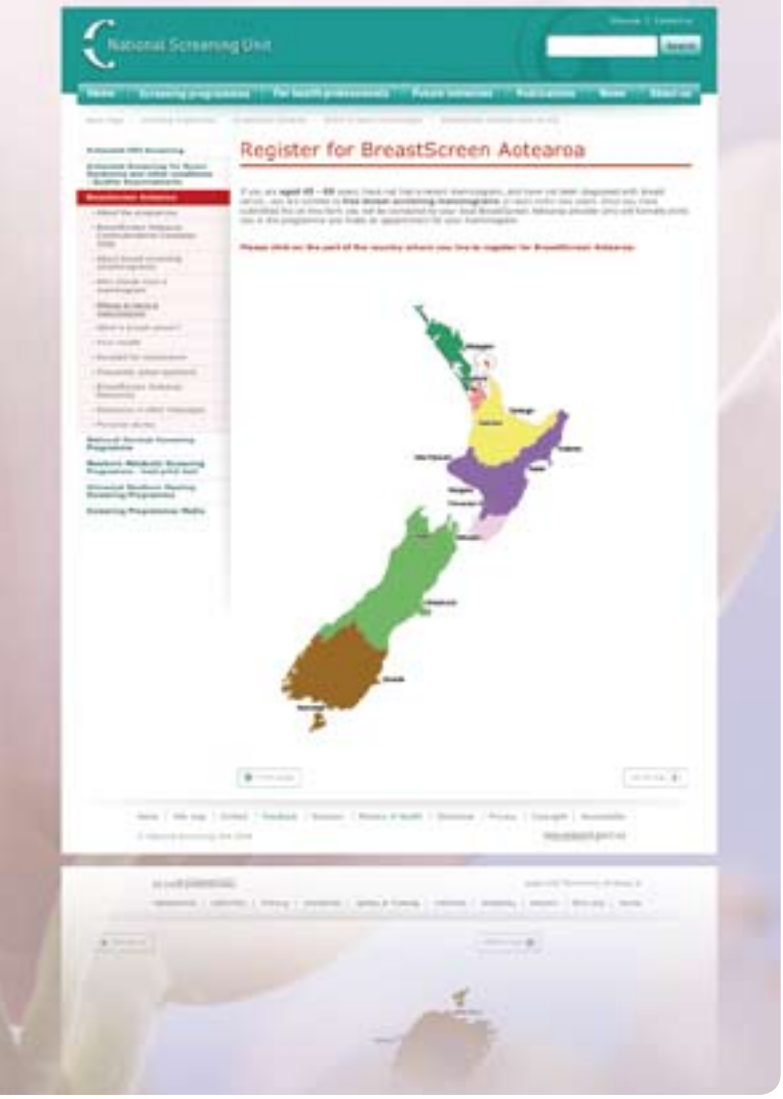
The PHO Performance Programme goal commencing from 1 January 2011, is for at least 70% of enrolled female patients, aged between 50 and 69 years, who are classified as high needs, to have received a screening mammogram from a BreastScreen Aotearoa provider within the last two years. Patients defined as high needs include Māori and Pacific women and those living in decile 9 or 10 areas. Data will also be collected for all women aged between 45 and 69 years who are eligible for a mammogram, as an information only indicator. These extended age bands now reflect the BreastScreen Aotearoa guidelines for screening women aged 45–69 years.

Calculation of breast screening rates is made using data extracted from the PHO enrolment data base and the National Screening Unit breast screening data base. It is important that all demographic information such as accurate ethnicity and gender are collected and entered.

Enrolling with BreastScreen Aotearoa

To enrol women with BreastScreen Aotearoa:

1. Gain consent
2. Telephone BreastScreen Aotearoa on **0800 270 200**
3. Complete the online form at: **www.nsu.govt.nz/Current-NSU-Programmes/1528.asp**
4. Post or fax an enrolment form to the BreastScreen Aotearoa lead provider in your area



Tips for encouraging and assisting enrolment for breast screening

Be able to identify and contact eligible women in your practice:

- Use your practice management system to identify eligible women
- Send invitations/information letters that encourage women to enrol for breast screening
- Have a system to ensure that when female patients reach age 45 years, they are sent an invitation to enrol in breast screening
- Have a system to ensure that new patients enrolling in the practice are included
- When an eligible women attends the practice for any reason, ask about her breast screening status and record it in her notes in a way that is accessible/searchable

Consider barriers that may prevent or discourage women from participating in breast screening such as cultural beliefs, language difficulties, shyness, fears (e.g. pain), costs and childcare arrangements. Strategies to overcome some of these barriers may include:

- Contact BreastScreen Aotearoa on behalf of the patient (with her consent) and make an appointment for a mammogram for her
- Ensure eligible women know that breast screening is free
- Provide women with appropriate information about breast screening. Free patient information in a variety of languages can be ordered online at: **www.healthed.govt.nz**
- Allow enough time to talk through a woman's concerns or arrange for her to speak to the practice nurse
- Support women who are shy, apprehensive or have communication difficulties
- Encourage women to bring a support person if needed
- Ensure all practice staff are aware of transport

options in your area. Your PHO may have a financial assistance programme which could be used to help cover the cost of transport, if this is a barrier.

Become familiar with local breast screening services, including mobile breast screening vehicles:

- Information about mobile breast screening units is available from: **www.nsu.govt.nz/health-professionals/1388.asp#**

  Click on your region on the map, then select "mobile screening unit schedule" to bring up a list of dates and locations of mobile screening. Consider printing this out and ensuring all practice staff are aware when the mobile screening unit is in your community.

- Consider coordinating with other practices to increase uptake of the mobile breast screening unit services in your community.

Once a patient has been enrolled with BreastScreen Aotearoa, place a recall in their clinical record to ensure that they continue to attend for regular mammograms and update the recall each time a result is received. Follow up patients who are overdue to ensure they are enrolled with BreastScreen Aotearoa and encourage them to make an appointment for their mammogram.

For further information, see BPJ 24 (Nov, 2009) "Breast screening - achieving equity"

Frequently asked questions about breast screening

What does a screening mammogram involve?

A standard screening mammogram involves x-ray imaging of two different views of each breast. When there are signs or symptoms of breast cancer (see sidebar), or a screening mammogram has shown a potential abnormality, diagnostic breast imaging is performed which usually includes additional views of the breast and ultrasound as required. Breast biopsy may also be indicated.

Possible signs or symptoms of breast cancer:

- A thickening or a lump in the breast
- Skin dimpling or ulceration
- Nipple discharge or new nipple inversion
- Persistent nipple rash
- Non-cyclical or focal breast pain
- Redness or changes in skin colour of the breast(s)

It is important for patients to understand that mammograms can detect most breast abnormalities, but cannot prevent breast cancer. However, the mortality rate from breast cancer is reduced by approximately one-quarter to one-third in women aged 50 years and over who have mammograms every two years as part of a screening programme.[4, 5] Women aged 45 to 49 years, have a smaller overall risk of death from breast cancer, but regular breast screening reduces this risk by approximately one-fifth.[4, 5]

Mammograms involve a small exposure to radiation and are described as uncomfortable or even painful by some women. Women who are concerned about the pain involved with the mammogram can be advised to take paracetamol or other analgesia prior to the procedure, however, there is limited evidence that it is effective for this indication.

What other imaging options are available?

Mammography is the only screening tool for breast cancer that is known to reduce deaths due to breast cancer through early detection.[4] Even so, mammograms do not detect all breast cancers. Some breast lesions are not easily visible or are difficult to interpret on mammograms. Cancers can be difficult to detect using mammography in breasts that are dense, with more glandular tissue and less fat. These are some of the reasons that patients and

clinicians may consider seeking possible alternatives to mammography such as the use of ultrasound.

Breast ultrasound

Breast ultrasound is primarily used in New Zealand to help diagnose or give further information on breast abnormalities that have already been detected by screening mammography and clinical breast examination. Breast ultrasound may sometimes detect small breast cancers that are not easily visible with mammography. Conversely, some cancers are not visible on ultrasound such as micro-calcifications which may be the first indications of breast cancer. Breast ultrasound is not used routinely with (or without) mammography for screening purposes and has not been validated in the medical literature as a screening tool.

One study has shown that adding a single screening ultrasound to mammography would allow detection of cancer in an additional 1.1 to 7.2 per 1000 high-risk women. However, it would also substantially increase the number of false positives.[6] In the study, 3% of women who received a mammogram alone were referred for breast biopsy, compared to 9% of those who received ultrasound in addition to a mammogram. Breast cancer was subsequently diagnosed in 23% of the women indentified through mammogram alone and in 9% of the women who had ultrasound.[6]

Some women may elect to use private services to undergo breast screening with ultrasound. Advantages of the ultrasound method are that it is a painless procedure and it does not involve radiation. Women who choose to have ultrasound, should be strongly encouraged to also undergo two yearly mammography screening. The only situations when breast ultrasound might be preferable to mammography as a screening tool (i.e. when there are no signs or symptoms of breast cancer) are for women who:

- Are pregnant (and therefore should not be exposed to x-rays)
- Have silicone breast implants (as x-rays cannot penetrate silicone)
- Have very dense breasts (as abnormalities are more difficult to detect with mammography)

N.B. Private breast screening is not included in national data collections.

Thermography

Thermography is currently being promoted as an alternative breast screening tool. The National Screening Unit, the Cancer Society of New Zealand and The New Zealand Breast Cancer Foundation do not support the use of thermography as a breast cancer screening or diagnostic tool as there is insufficient evidence that it is effective for either of these purposes.[7]

Thermographic imaging records the heat distribution on the surface of the breast. In theory, a tumour would appear as a temperature abnormality on the breast due to increased metabolism and blood flow in that area. Thermograms are frequently associated with both false positive and false negative results and therefore are not considered a clinically reliable method for breast cancer detection or diagnosis.

Is self-examination of the breast worthwhile?

Although once strongly advocated, breast self-examination has now begun to fall out of favour. There is limited evidence, from either clinical trials or observational studies, that breast self-examination is an accurate method for identifying lesions or that it actually decreases deaths from breast cancer. There is also some concern that self-examination may result in anxiety, or conversely, provide false reassurance and influence subsequent screening behaviour.[4]

Women can be advised that breast self-examination is unnecessary if they are receiving regular mammograms. It is possible that self-examination may provide some benefit in women outside of the recommended screening age-range, i.e. under 45 or over 70, or those who decline mammography.

What is the evidence for breast screening in women aged in their 40s?

The recommended age range for breast screening in New Zealand was extended in 2005 to include women aged between 45 and 49 years and 65 to 69 years (from the previous recommended age range of 50 to 64 years).

The value of screening women aged in their 40s for breast cancer is controversial because there is no definitive estimate of its benefit. In the UK, the age limit for the national breast screening programme is about to be lowered to 47 years. However, in the U.S. the Preventative Services Task Force has recently changed its recommendation to commencing breast screening at age 50 years, rather than at age 40 years. This decision was based on the opinion of the Task Force that the borderline statistical significance of effectiveness of breast screening in women aged 40 to 49 years is insufficient to advise screening in this age group.[8]

Accumulated research shows that a screening mammogram every one to two years in women aged 40 to 49 years results in a 15% decrease in breast cancer mortality rate after 14 years of follow-up.[9] This is compared to a 22% reduction in mortality for women who began screening at age 50 years. Researchers note that the 15% decrease could also be partly due to the effect of screening after age 50 years. In addition, the confidence interval associated with this estimate means that the reduction could be as much as 27% or as little as 1%.[10] The UK Age Trial included over 50 000 women undergoing breast screening from age 40 years. Early estimates are that screening from age 40 years has resulted in a 17% reduction in mortality from breast cancer. However this reduction is not statistically significant.[11]

A New Zealand analysis published in 2005 concluded that there is sufficient evidence that mammography reduces breast cancer mortality among women aged 40 to 74 years, but the benefit is greatest and harms the lowest for women aged over 50 years.[12]

The benefit of screening must outweigh any possible harm. Benefit is difficult to achieve when screening asymptomatic people as it is hard to improve their situation and easy to cause harm. False-positive tests can cause anxiety, unnecessary investigations and associated adverse effects of these investigations. Conversely, false-negative tests can result in women delaying seeking medical attention if symptoms later develop. Encouragingly, data from the UK Age Trial study, showed that in women who began breast screening aged in their 40s, experiencing a false-positive result did not compromise re-attendance for screening.[13]

Given the potential for benefit, although not statistically conclusive, it seems reasonable to begin screening women at age 45 years, however screening women below this age would require much more evidence on the benefits and harms.

Is there a risk of radiation-induced breast cancer from mammograms?

There is concern among some women that radiation exposure during a mammogram may result in radiation-induced breast cancer. However, this has never been conclusively proven.

A research model was recently developed to estimate the theoretical absolute risk of breast cancer from mammogram exposure. This estimate was calculated at a total of 86 cancers and 11 deaths per 100 000 women who received annual screening from age 40 to 55 years and screening every two years thereafter until age 74 years. It was concluded that the lifetime risk of radiation-induced breast cancer is small compared with the expected reduction in mortality from breast cancer that is achieved through screening.[14] Earlier estimate models give slightly differing results but similar conclusions. The International Agency for Research on cancer has estimated that the lifetime risk of radiation-induced death from breast cancer among women who began regular screening at age 50 years is 10–50 per million. This risk increases to 100–200 per million among women who began regular screening at age 40 years.[15]

The breast cancer gene

It is thought that in approximately 5% of cases of breast cancer, an abnormal gene is present – predominantly BRCA1 or BRCA2. Women who have an abnormality in either BRCA1 or BRCA2 have a much higher than average risk of developing breast cancer and/or ovarian cancer, but not all women with this gene mutation will develop cancer.

If a woman has a strong history of breast or ovarian cancer in her family, especially if family members developed the cancer before the age of 50 years, it is reasonable to consider referral for genetic counselling to determine her risk. Routine testing for BRCA mutations is not recommended.

Women who test positive for a breast cancer gene mutation can reduce their risk of developing breast cancer, with options including more frequent screening (and starting at a younger age), hormonal therapy (tamoxifen) or prophylactic mastectomy or oophorectomy (removal of the ovaries, which reduces both the risk of breast and ovarian cancer, but only with BRCA2 mutation).

Referral for genetic counselling within DHBs is funded, however, testing for the breast cancer gene is not and currently costs $2000 – $3000. It can take up to six months before results are available.

For further information visit:

- BreastCancer.org: **www.breastcancer.org/symptoms/testing/genetic/**
- National Breast Cancer Centre, Australia: **www.nbcc.org.au/resources/resource.php?code=BOG**

For referral to a Genetic Counselling service contact:

- Northern Region 0800 476 123
- Central Region 0508 364 436
- Southern Region 0508 364 436

Women can be reassured that the risk associated with radiation exposure during a mammogram is much less than the benefit derived from screening.

Which women are at higher risk of breast cancer and how often should they be screened?

The risk of breast cancer increases with age. Approximately 70% of breast cancers occur in women aged over 50 years.[2] A previous breast biopsy or a close family history (i.e. affecting a mother or sister) of breast cancer further increases risk. Other factors that increase the risk of breast cancer include older age at the time of a first birth and younger age at menarche.[10]

There is no evidence to support specific screening intervals for women at increased risk of breast cancer.[10] Early results from the UK-based FH01 study suggest that yearly mammograms in women aged under 50 years, with a close family history of breast cancer are effective in preventing deaths from breast cancer.[16]

In New Zealand, The National Screening Unit (NSU) recommends that women of any age who are at high risk of getting breast cancer, get their breasts checked regularly, e.g. with a yearly mammogram.

The NSU define “high risk” as those women with:

- A mother or sister who developed breast cancer before menopause or who developed cancer in both breasts
- A previous breast cancer
- A previous biopsy of breast tissue showing an at-risk lesion
- A breast lump or change which needs checking

N.B. Women aged under 45 years and women undergoing diagnostic rather than screening mammography, will need to be referred directly by their GP to a DHB breast screening service or private radiologist.

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Successful initiatives in men's health

Last year we asked for your feedback in regards to getting men to attend general practice. Here we present some of your responses.

Insights and perspectives on men's health

David Mitchell and Alison Horn from the Nelson Marlborough Institute of Technology conducted a research project that aimed to identify what Occupational Health Nurses believed were the health-related issues that affect the men they work with.

The research involved eight participants*, who attended two focus groups, held six weeks apart. At each session they were asked to respond to the question: "What are the main health related issues that affect the men that you work with?" This process and timeframe was planned to enable the participants to reflect over time and during their practice and to perhaps challenge some of their own assumptions.

*While this was a small number of participants the group represented a high percentage of the Occupational Health nurses in the Nelson area, especially those that worked with males. However the findings from the project should only be generalised to a wider population with considerable caution.

In the first session, the participants echoed the more stereotypical thoughts on men and their attitudes towards health care, e.g. being macho, not caring about their health and lacking in responsibility. In the second session, the participants explored the question in greater depth. This resulted in them presenting insights about men and their health that are not commonly understood. The participants talked about a delicate balance between men, employment and being a provider to their family. They talked about how these factors were linked to men's self esteem/self image and, importantly, how men viewed health assessments as presenting a threat to continued employment and subsequently a risk to their self perceptions (as an earner and provider).

> "And they do resist that [finding out about their health status], they're very anxious about it. They're worried about what the results [of the health assessment] might be and the implications

for working. For example, how long does it take for hearing to be lost? They're worried about the results." – Research participant

The participants also considered the workplace culture as critical in promoting the health of men. Here the important factor was whether there was a focus on a minimum level of compliance with Health and Safety legislation or whether the employer believed there were benefits in supporting a focus on health and wellness. A minimum level of compliance tended to result in interventions that were viewed as surveillance and this linked closely with the men's perception of a risk to themselves. In addition, the participants believed that nurses have a particular advantage in engaging with men as health professionals. They were able to specify educational preparation and skills that they felt were important in achieving this connection.

Findings from this project show that health professionals need to be vigilant in appreciating what factors motivate men to present, to present late or to not present to health services in order to avoid reinforcing the negative discourses around men and their health-related behaviours.

The participants in this project demonstrated that experienced nurses, given the opportunity, are able to clearly articulate a range of insights and skills in working with men that are not commonly understood. With the presence of a large population of nurses in the primary care health workforce it seems timely for this group to have the opportunity to take a greater responsibility in developing initiatives in the area of men's health.

It is of interest that this small, local project has acted, at least in part, as a catalyst for continued work. Nelson Bays Primary Health has now completed a project entitled "Getting Men In the Door", with the aid of funding through the Ministry of Health's "Men's Health Innovation Fund", as well as other initiatives that either directly or indirectly impact on men's health.

The benefits of inviting men to a male health check

Dr Pete Barwell from Muritai Health Centre, Wellington, conducted a research study on the benefits of inviting men to attend general practice for a health check. The invitations resulted in almost three times the usual number of men attending for a health check, increased numbers of male patients attending for a specific problem and increased implementation of preventative health screening. The practice received positive feedback from both the invited males and their partners. This was expressed even when the male had not attended– the initiative from the practice was appreciated and it generated discussion about health issues "over the dinner table".

The practice used the following approach:

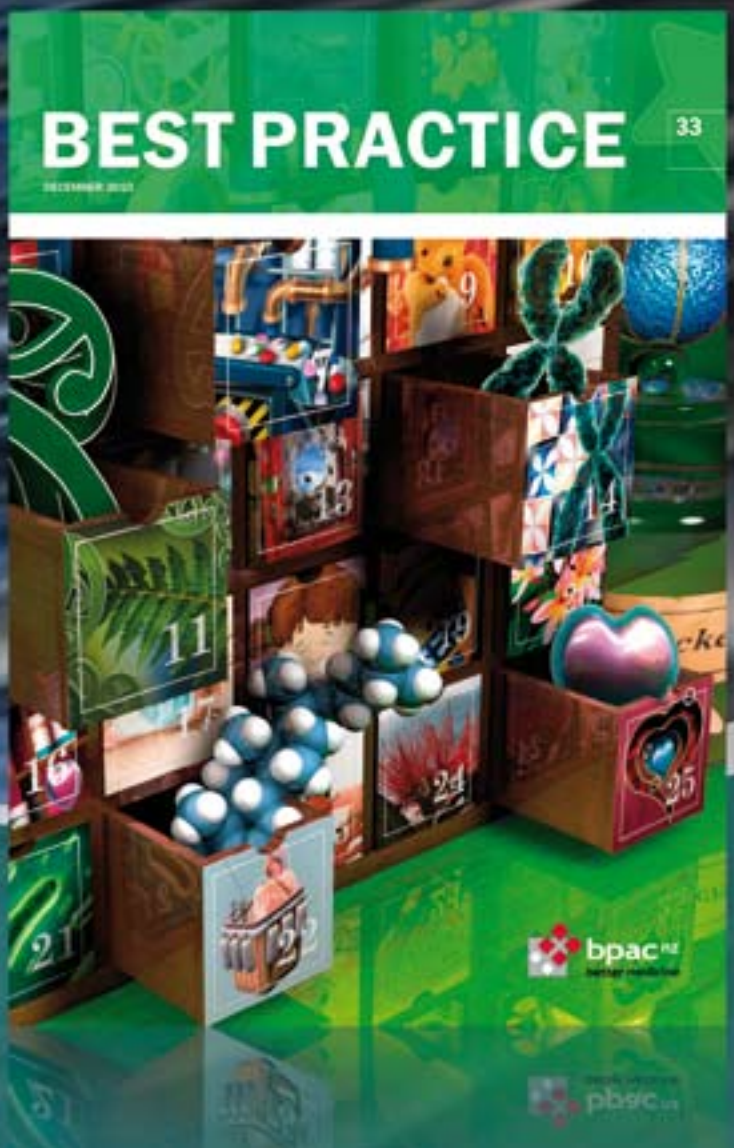
- Initial education sessions about the importance of male health issues, involving all practice staff
- Simple tick-box screening template ("Well Man Check") incorporated into the practice management system
- Guideline biopsychosocial screening process for individual staff to apply as they felt appropriate
- Men aged between 40 and 50 years were identified using the PMS and sent an invitation to attend for a Well Man Check. Patients with known conditions requiring regular follow-up were excluded, as were

those with recent health assessments.

- The Well Man Check consisted of a 15 minute appointment with the practice nurse, where data was collected including weight, height, waist circumference, blood pressure and mid-stream urine test. Smoking, drug and alcohol history were taken when time allowed.
- This 15 minute check was then followed by a GP consultation, where the most appropriate assessment aspects were selected for that individual

"I think the multi-factorial causes of poor male attendance to general practice are pretty well understood, with male cultural roles, perceived child/female centric health centres, 'boys don't cry' attitude and poor understanding of their own body and when something is wrong, being well studied. A better focus may be on whether getting men to attend 'well man checks' actually provides any benefit. The findings of my research study show there is pathology out there to detect, but not whether resources exist to deal with it or any formal quantified assessment of whether men feel their wellbeing has been improved by an invitation to attend a health check, whether or not they took it up."– Dr Pete Barwell

For further details of this study see: Barwell P. Do invitations to attend Well Man Checks result in increased male health screening in primary health care? J Prim Health Care 2009;1(4):311-4.



Different strategies needed for getting men to attend general practice

Jean Harris, a community cardiac nurse from Horowhenua, recently undertook cardiovascular disease (CVD) risk assessments at a local general practice. Both men and women in the appropriate age ranges were invited to attend on a particular day for a CVD risk assessment, however, it was mostly female patients that attended.

> "The men were not good attendees, with less than 50% turning up. When it came to the women I had a really good response and some of the women asked me to make appointments for their husbands again as they were really cross that they hadn't attended." –Jean Harris

It was unclear why the men did not attend therefore uncertain what could have been done differently, but it is apparent that a different strategy would be required if CVD risk assessments for men were offered again.

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DECISION SUPPORT FOR HEALTH PROFESSIONALS

Lack of regulation for herbal medicines and supplements is concerning

Dear bpac,

Thank you for your reasoned and patient replies to the correspondence on Red Yeast Rice (BPJ 32, Nov 2010). Indeed the Becker study comparing simvastatin plus written diet and exercise advice, against red yeast rice tablets, plus fish oil supplements, plus a 12 week supervised and coached exercise programme, plus counselling from a dietician, is one of the best examples of the worst way to do a clinical trial, from which, no scientific conclusions can be drawn. A correct scientific study would have been comparing simvastatin, plus written diet and exercise advice, against red yeast rice tablets, plus the same written diet and exercise advice. In my opinion it is amazing that this study was even published.

A further matter for consideration is that to my knowledge, herbal medicines/supplements are not subject to any mandatory regulatory requirement for safety or toxicity testing prior to being launched on the unsuspecting public. Thus we doctors often may advocate to our patients herbal or nutritional supplement products which have no safety testing whatsoever.

Medicines such as simvastatin are required to conform to safety and toxicity testing including single dose toxicity lethal dose, repeat or ongoing dose toxicity, carcinogenicity, genotoxicity or mutagenicity and embryotoxicity or reproduction toxicity. If the regulators believe that a medicine is safe in all of these areas and the proposed medicine dosage for humans is significantly less than the dosages which could cause potential problems in animals, then the product is allowed to be safety tested on volunteer humans. Further clinical studies in efficacy and comparison with other therapies continue.

As well as this progressive safety hierarchy of medicine testing, we currently have post-marketing studies and intensive adverse drug reaction reporting to give us more data on any unexpected positive or negative effects once a medicine is registered and in use. Indeed, we usually think in terms of unexpected new negative effects showing up. However, the recent large scale study reported in the Lancet showing use of statins causing a significant 12% reduction in the incidence of bowel cancer, shows that such surveillance can bring up further positive effects that the initial pharmaceutical manufacturers and investigators never envisaged.

I know of no such safety procedures with any of the myriad of herbal and nutritional supplements, vitamins and "natural" remedies that I see marketed at present. If we GPs are going to follow the dictum "Primum Non Nocere", how can we confidently say to our patients it's safe just because it's natural? We may easily blame the pharmaceutical industry for withholding data, poor study design or investigations being done by people with vested interests. However, registered medicines that I use still have a markedly better basic consumer safety system than our "feel good natural products industry".

Dr Steve Culpan, GP
Auckland

Pityriasis versicolor

Dear bpac,

I often see patients present with pityriasis versicolor (especially at the end of summer when they have tanned skin). However I am never quite sure which treatment is most effective or evidence-based (and ideally funded). Can you help me with any guidance on treatment of this condition?

***GP**, Dunedin*

Pityriasis versicolor (also known as tinea versicolor) is a superficial infection of the skin caused by the yeast *Pityrosporum ovale*. This yeast can transform into a pathogenic form and turn off melanin-producing cells in the skin, producing asymptomatic flaky patches on the trunk, neck or arms. These patches appear pink or coppery on pale skin and pale brown on tanned skin.[1] A number of conditions can trigger conversion of *P. Ovale*, including hot and humid weather, use of oils, hyperhidrosis (excessive sweating) and immunosuppression.[2]

Topical antifungal medicines are the treatment of choice for pityriasis versicolor.[3] Two studies that compared topical therapy with systemic therapy, found that topical regimens were either equivalent to (clotrimazole cream for three weeks vs. fluconazole 300 mg/week for two weeks) or superior to (selenium sulfide shampoo for one week vs. itraconazole 200 mg/day for five days) oral therapy.[3]

Optimal treatment regimens have not yet been fully established, however, treatment for between one to four weeks is most common. Ketoconazole 2% shampoo (partly subsidised) or selenium sulphide shampoo (not subsidised) can be applied to affected areas, left on for at least ten minutes and then washed off. Treatment is ideally repeated daily for one to four weeks. Alternatively, imidazole creams such as clotrimazole 1% or miconazole 2% (both fully funded) can be applied once or twice daily, for one to four weeks.[2]

Systemic treatments for pityriasis versicolor include oral ketaconazole or itraconazole. Liver function must be monitored in patients receiving oral ketoconazole for more than one week or in patients prescribed oral itraconazole for any length of time.[4]

Recurrences of infection after successful treatment are common. To help prevent relapse, continued intermittent use of topical therapies can be useful.

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Is aqueous cream an appropriate leave-on emollient?

Dear bpac

An article was published recently in the British Journal of Dermatology which suggested that emollient creams worsen eczema rather than improving it. Have we been giving the wrong advice on the use of aqueous cream as a moisturiser?

Pharmacist, Auckland

Emollients are commonly used first-line for the treatment of eczema as they help to maintain the skin's barrier function, keeping moisture in and irritants, allergens and pathogens out. They should be applied liberally, frequently and continuously, therefore it is important that they are acceptable to the patient.

Aqueous cream is one of the most commonly prescribed and used emollients, however recent evidence suggests that it may not be appropriate for all people.

A recent study involving six people found that aqueous cream applied twice daily, to healthy skin on the forearm, for four weeks, reduced the stratum corneum thickness and increased the permeability to water loss (i.e. caused dry skin).[1] The aqueous cream used in this study contained 1% sodium lauryl sulphate which is a surfactant with soap like properties and a known skin irritant. The authors

suggested that sodium lauryl sulphate was a likely cause of the adverse effects on the skin and stated the following: "The fact that sodium lauryl sulphate is able to reduce the stratum corneum thickness of normal skin significantly following repeated, yet rather brief, application suggests an even more damaging action on diseased skin, the barrier function of which may already be compromised".[1]

An audit of 100 children attending a paediatric dermatology clinic found that an immediate cutaneous reaction (which included burning, stinging, itching or redness) was reported after use of aqueous cream in 56% of exposures in comparison with 18% of exposures to other emollients.[2] The authors noted that aqueous cream was not originally designed as a leave-on emollient, rather it was designed as a wash product, with brief skin contact only.[2]

These small studies suggest that aqueous cream may not be an appropriate choice as a leave-on emollient for some people. Aqueous cream is still a suitable option as a soap substitute because in this situation, the cream is washed off and is only in contact with the skin for a short time. What is clear is that it is important to allow patients to choose the emollient and soap substitute that suits them best because this will increase compliance.

In New Zealand, funded emollients include; aqueous cream, fatty cream (healthE fatty cream), emulsifying ointment and cetomacrogol cream. Partially funded options include; oily cream, glycerol with paraffin and cetyl alcohol (QV lotion) and wool fat with mineral oil (Alpha-Keri, Hydroderm BK and DP lotions). Urea cream (Nutraplus) is very effective at moisturising dry skin, but may sting if there is active eczema.

"Adverse reactions to currently available aqueous creams are rare in New Zealand but occasionally people complain about its greasiness. I have rarely considered it an irritant – except many years ago when there was a bad batch. The emulsifying wax contains very small amounts of sodium lauryl sulphate which allows it to act as a cleanser. But I agree, our patients need to be given options with a variety of soap replacements and emollients".

–Dr Amanda Oakley, Dermatologist

For further information, see BPJ 23 "Managing eczema"

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