BEST PRACTICE

40

NOVEMBER 2011

Atypical antipsychotics
Reflux and GORD in infants
Nausea and vomiting in pregnancy

bpac nz
better medicine

We would like to acknowledge the following people for their guidance and expertise in developing this edition:

Dr Anna Alderton, Christchurch
Dr Chris Leathart, Christchurch
Dr Hywel Lloyd, GP Reviewer, Dunedin
Andrew McKean, Christchurch
Dr Erik Monasterio, Christchurch
Dr John Newman, Auckland
Dr Helen Paterson, Dunedin
David Rankin, Wellington
Associate Professor David Reith, Dunedin
Professor Robin Taylor, Dunedin
Dr Neil Whittaker, GP Reviewer, Nelson

Best Practice Journal (BPJ)
ISSN 1177-5645
BPJ, Issue 40, November 2011

BPJ is published and owned by bpac^{nz} Ltd
Level 8, 10 George Street, Dunedin, New Zealand.

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

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

Bpac^{nz} Ltd is currently funded through contracts with PHARMAC and DHBNZ.

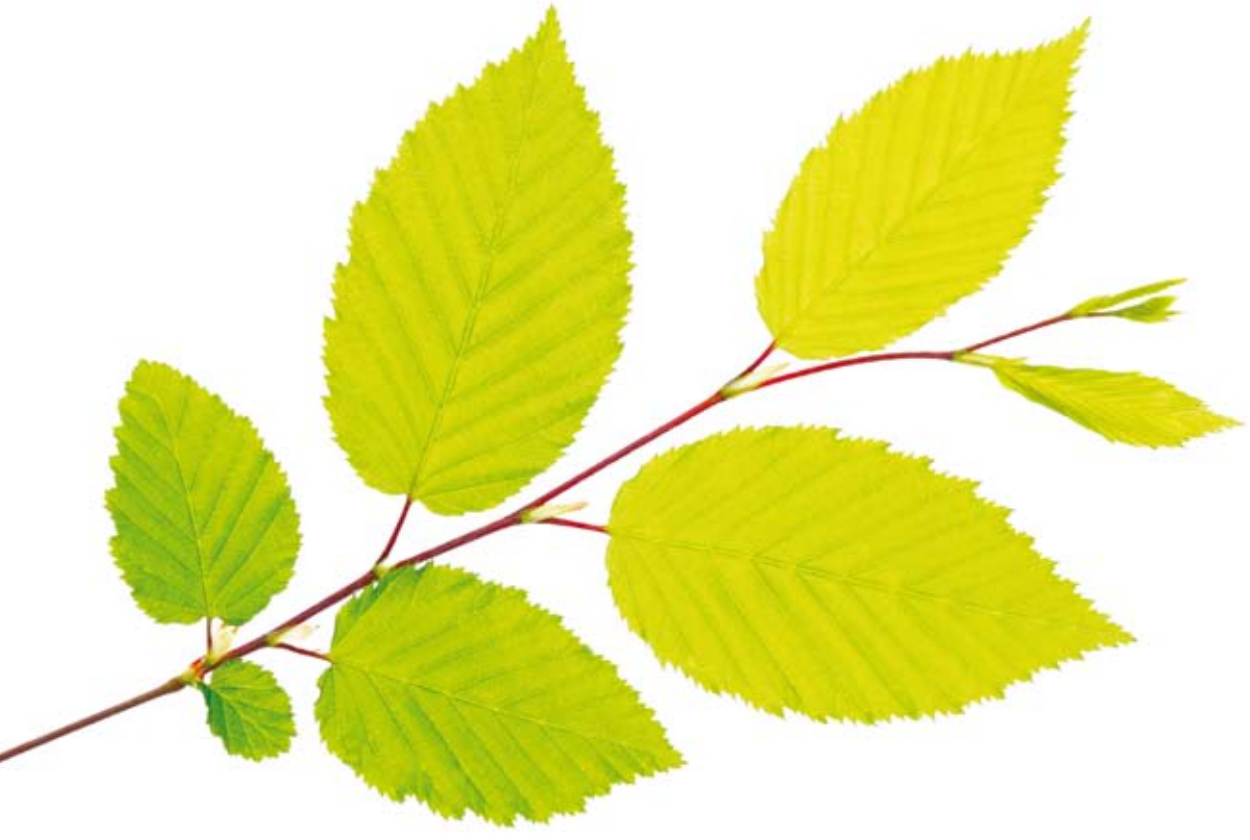
Bpac^{nz} Ltd has five shareholders: Procare Health, South Link Health, General Practice NZ, the University of Otago and Pegasus Health.

Contact us:
Mail: P.O. Box 6032, Dunedin
Email: editor@bpac.org.nz
Free-fax: 0800 27 22 69

www.bpac.org.nz

CONTENTS

CONTENTS



CONTENTS

Essentials

All web links in this journal can be accessed via the online version.

www.bpac.org.nz

Mental health issues in adolescents who have experienced abuse and neglect

In the fourth article in our series on vulnerable children and young people in New Zealand, we discuss the complex mental health needs of adolescents who have experienced violence, neglect and other forms of abuse.

The mental health needs of adolescents

Adolescence is a complex biophysical process. Dramatic and rapid physical changes with the onset of puberty are accompanied by longer and more subtle emotional, cognitive and social developments, often all evolving asynchronously. These challenges are further complicated in young people who have experienced violence, neglect and other forms of abuse and challenging behaviours, which have resulted in them coming into the care of Child, Youth and Family.

Receiving love is the most important mental health need

The most basic mental health need for adolescents is to be loved. Each parent or caregiver experiences this differently and provides it in different ways, making this aspect of mental health difficult to study scientifically. However, there are some aspects of loving that can predictably help young people recovering from abuse and trauma.

The following points can be considered and applied also to the health professional-adolescent patient relationship:

1. **Listen** when they talk and encourage them to tell their stories. Treat their stories with respect even when they may be hard to believe. Not all young people are ready to talk about their traumas and so will not benefit from being specifically encouraged to discuss traumatic events, however, it is important to be ready to listen.
2. **Provide a place of safety** – both emotional and physical; a place where they will not be mocked, put down or physically harmed.
3. **Treat them with respect** even when they do things that are unacceptable.
4. **Forgive** the bad things they do (which is not the same as condoning).
5. Use a framework of **helping them to grow up** rather than just controlling their behaviour.

Other core needs for adolescent mental health

Need for safety from violence and abuse of all types

- Safety of the young person – from themselves, peers, caregivers and community
- Safety of other young people and their caregivers
- Safety of the community

Need for positive development

- Care in a protective environment
- Individualised education programme
- Positive relationships and experiences
- Identity development, self efficacy
- Sexual identity and sexual relationships
- Moral development
- Self extension and skills
- Creative expression

Need to align with society

- Pro-social skills
- Adherence to societal laws and constraints
- Belonging to a group or identity
- Contributing to family and society

Need to address specific potential health and development challenges

- Nutrition and activity
- Positive choices around risky behaviours
- Health conditions and disability
- Mental health and illness
- Addictive behaviours
- Education and skills deficits
- Lifestyle choices (e.g. smoking)

Identifying adolescents with mental health problems

Despite the best efforts of all, some young people go on to have mental health problems. Every district in New Zealand has a Child and Adolescent Mental Health Service via the local DHB and general practices can provide access to other mental health services in the community.

Characteristics of mental health problems in adolescents

Western medicine divides mental health from other aspects of health, but for many young people in New Zealand, mental health cannot easily be separated from family or whānau health, spiritual health or physical health. Rather than identifying that they have a mental health problem, many young people will express their distress through criminal behaviour, withdrawing from social life or school, self harm or drug and alcohol use. Often young people who are obviously distressed will deny having a mental health problem but attribute their distress to the actions of others. Therefore it is useful to have a broad rather than narrow definition of mental health problems.

We recognise mental health by its ordinariness: attending school, gaining skills, interacting socially. Happiness is often associated with mental health but is not necessary for it. The young person who is stressed out (unhappy) by high academic or sporting expectations will overall have better mental health and lower risks. The distressed young person who throws themselves into helping at the Marae or school may do better than those happily playing computer games by themselves. The young person who is angry but channels that anger into high performance or artistic endeavour will do well.

Common mental health disorders in adolescents in New Zealand include depression (and suicide), conduct disorder

and substance abuse. Often these occur together, but rather than thinking of these as co-morbidities, it may be useful to consider that young people who are distressed often find multiple ways of finding relief. In addition, the symptoms of mental health problems can vary with age, so that younger men might use marijuana but when they are older they might use alcohol. Younger women might cut (self-harm), but when older they might have depression.

Causes of mental health problems in adolescents

Common causes of mental health problems in adolescents include; a family or genetic pre-disposition, poor attachment, lack of love and affection, as well as exposure to violence. Some young people have mental health symptoms in perfectly ordinary circumstances and this might be attributed more to their temperament. Some young people are born with disabilities such as foetal alcohol or autistic spectrum disorder which give rise to mental health symptoms. Some co-morbidities, such as attention deficient hyperactivity disorder (ADHD), seem to be extremes of normal behaviour. Mental health symptoms in Māori youth have increased since the migration to the cities. Unfortunately many of the causes of mental health problems co-exist, so that the child with exposure to alcohol in the womb may also suffer from neglect and abuse.

Interventions for mental health problems in adolescents

Family/caregiver support and community activities

Regardless of the specific mental health problem or symptoms, all young people have some basic needs for their mental health:

1. The need to feel loved
2. The need to belong
3. The need for hope and faith in the future

These three needs can be provided by family/whānau, and where families cannot provide them, other sources such as schools, churches, sporting clubs or mentors may help. Without addressing these basic needs, mental health interventions often make limited progress.

The individualism of western culture often leaves young people feeling isolated and unsupported. This influence can be counteracted by encouraging the development of the wider family and its involvement in the lives of young people. For Māori, elements of belonging such as pepeha, visiting their marae, understanding tikanga or walking their land can be helpful.*

Mentors can be effective in some circumstances, particularly when working with adolescents with more severe problems. The availability of good mentor programmes (trained, supervised, regular and prolonged) is variable by region and demand often exceeds the capacity of the volunteers.

Culturally based programmes (particularly in acculturated youth) have been shown to be effective, particularly in adolescents with alcohol, drug and violence problems. These programmes are available through kaupapa Māori organisations.

Activities and exercise are useful for a range of symptoms but particularly those where the young person is feeling low. It is important that the young person finds an activity that suits their abilities, which could range from going for a walk with family or friends, to playing sport at an international level.

Positive youth development (assisting positive development in young people) is effective for individuals and groups. Youth development interventions that are

* Pepeha are traditional Māori sayings similar to proverbs or tribal boasts. They often refer to tribal history, embody the history of settlement and allude to the deeds of ancestors, tribal migrations, warfare and whakapapa. Tikanga can be described as general behaviour guidelines for daily life and interaction in Māori culture, commonly based on experience and learning that has been handed down through generations.

effective tend to be intensive, prolonged and involve multiple areas of a young person's life. Programmes are available in most communities and include, for example, groups focused on sports, conservation, culture, outdoor education and work experience. Participating in the group involves learning new skills and activities, being involved, socialising, having fun and taking risks within a safe environment.

Youth One Stop Shops are available in some regions, to allow young people to access the help they need on their own, with staff who are skilled in talking to, listening to and understanding young people. Sometimes the best one stop shop is at the high school (or alternative education), particularly if it has counsellors, nurses, general practitioners or mentors.

Psychological therapies

Cognitive behaviour therapy has been shown to be effective in a wide variety of situations. This teaches young people the relationships between their feelings, thoughts and actions and how to change their emotions and behaviours for themselves. Some general practices may offer these services or patients can be referred to specialist clinics.

Gateway assessments for adolescents with mental health needs

From 1 July 2011, Child Youth and Family began rolling out the Gateway Assessment process with the Ministries of Health and Education. It is anticipated that all adolescents with high needs, identified through Child, Youth and Family interventions, will receive an assessment. The concept behind the assessment process is an integrated approach to the health and wellbeing of these young people, to ensure that their needs are met. This involves input from families, social workers, teachers and health professionals.

Gateway Assessment services reflect the principles developed by the World Health Organisation.* These are that young people:

- Regardless of situation, should have opportunities for healthy physical, social and mental development. It is an inherent part of their human rights.
- Have a right to access good quality health services (including comprehensive healthcare, preventive services and health promotion)
- Should expect to live in a positive care environment that promotes health, wellbeing and development
- Should be consulted and listened to concerning their health and wellbeing, both as individuals and as a group
- Should have the opportunity to develop and maintain relationships with one or more suitable adults in the community
- Should have their cultural beliefs and identity respected
- Should have the right to education, training and healthy lifestyle skills and work skills opportunities
- Have the right to privacy

* World Health Organisation (WHO). Promoting the health of young people in custody. WHO Regional Office for Europe, 2003. Available from: **www.hipp-europe.org** (Accessed Oct, 2011).

"Talk therapies" can be effective and seem to rely more on the relationship with the therapist than the actual therapy involved. This is widely available in the community.

Motivational interviewing is a specific type of talk therapy targeting problem behaviours. It is effective for changing a range of unhelpful behaviours (that are associated with mental distress), from drug use to overeating. General Practitioners can assist patients to find a therapist who specialises in this method, such as a drug and alcohol counsellor.

Family interventions such as family therapy can be effective when the focus is on family dysfunction rather than the individual. This is offered by a number of organisations in the community.

Multi-systemic therapy and **Functional Family Therapy** have been shown to be effective in conduct disorder (persistent bad behaviour). Both are intensive family based interventions.

Medical treatment

In some circumstances, antidepressants may be considered for an adolescent with a mental health problem such as depression. However, antidepressants such as serotonin re-uptake inhibitors (SSRIs) are not approved for use in people aged under 18 years, so are used "off-label". If an antidepressant is used, fluoxetine is considered the best choice for adolescents. It is important to maintain regular contact with the young person and to monitor for suicidal thoughts or other negative behavioural changes, especially in the first few weeks following prescription of the antidepressant. It is recommended that antidepressant treatment in a person aged less than 18 years should not be initiated in primary care without consultation with a child and adolescent psychiatrist.

For further information see: "Depression in young people", BPJ Special Edition (Feb, 2010).

ACKNOWLEDGEMENT Thank you to **Dr John Newman**, Specialist Youth Physician, HealthWEST PHO and Raukura Hauora O Tainui and **David Rankin**, Senior advisor, Child, Youth and Family, for contributing to this article.

End-of-life care for patients with chronic disease: the need for a paradigm shift

Contributed by: Professor D. Robin Taylor, Professor of Respiratory Medicine, Dunedin School of Medicine, University of Otago

Death comes to all of us, and if we survive into our late 70s or 80s, progressive organ failure, often with multiple co-morbidities, usually characterises the pathway towards the end of life. The care of patients with end-stage cardiac, renal or respiratory failure feature increasingly in the provision of health services, and the costs are immense particularly in the last year of life.[1]

However, it is also increasingly apparent that our current model of care does not provide what is best for patients at end-of-life. No one clinical service is equipped to provide for the patient's needs at all stages of their illness trajectory. Indeed, the philosophy of care and management priorities often differ between service providers. This leads to discontinuity of care. The emergency department and medical teams are geared to dealing with acute deterioration: the model is predominantly curative or "patch up and mend". Palliative care and hospice teams focus on "end-of-life" much more readily, but tend to operate in another domain, often separated from acute services not just philosophically but often geographically or by cost-centre. Because each of us operates in our separate silos, moving from a "curative" to an "end-of-life" management approach is difficult. Even where the diagnosis of dying has been embraced, our behaviours are more powerfully governed by the context in which we work. Often the default position is to continue as before, however inappropriate that may be.

A new model is required. Appropriate end-of-life care means less intensive, non-curative, symptom-relieving support in which preparing for death is seen as more important than clinging on to life. This means that "a good death" should be regarded as a quality outcome for *all clinical services* irrespective of where and by whom they are provided. It means striving to provide

continuity of care at the end-of-life. It means that chronic disease management, palliative care, end-of-life care and terminal care are regarded as a continuum to which all health care providers contribute. Whether in rest homes, primary care, emergency departments, medical wards or outpatient clinics, the "diagnosis of dying" should be entertained, sensitively communicated, and allowed to shape subsequent management.

In our own unit, a very bad death made us realise that there was a significant gap between our intentions and what we actually delivered. Since that incident, we have been attempting to improve end-of-life care in the Respiratory Medicine service in Dunedin Hospital. But we recognise that the obstacles are considerable, not because of attitudes on the part of individuals, but because "the system" militates against it. We have adopted several practical tools which can be applied to improving end-of-life care, but we realise that these have limited impact unless they are accepted across the wider organisation of a District Health Board. In isolation, progress is almost impossible. As well as specific tools, there is a need for strategic initiatives. The approach has to be "both... and" rather than "either... or".

The tools

An **Advanced Care Plan** provides the opportunity for patients, their family, and health care providers to enter into the territory of "end-of-life". Importantly, it opens up conversations. In many cases it is liberating – from denial of the reality that a patient is experiencing and from fear of what might lie ahead. The New Zealand Advanced Care Planning (ACP) Co-operative has been established through the Ministry of Health. Excellent guidelines on the principles and application of ACP have just been published.[2, 3] Advanced Care Planning is not the prerogative of a single professional group - specialists, General Practitioners or palliative care physicians.

In Dunedin, we have started a **Respiratory Failure Supportive Care Clinic** which includes, among other things, the opportunity to introduce the concept of ACP. The qualification for referral to the clinic is the so-called "surprise question", i.e. would we be surprised if the patient were to die within the next year? Areas for discussion include the medical prognosis, the patient's hopes and fears for the future, palliative treatments that are currently needed, as well as ACP, i.e. treatments that would be acceptable and those that would be excessive or futile in the event of acute deterioration. A generic ACP needs to be modified for specific disease groups such as patients with respiratory failure, and we have recently done so.

A generic Advanced Care Plan is available from the Advanced Care Co-operative website: **http://acp.hiirc.org.nz**

Try as everyone might, there are still occasions when acute-on-chronic deterioration is too distressing to be managed at home and patients present to hospital. The context of deterioration needs to be urgently considered (is this an end-of-life or terminal event?). The concept of **Ceiling of Care** is relevant in this setting, and derives from the ACP. The aim is to provide guidance to admitting staff who do not know the patient, so that there is continuity with the patients' previously expressed wishes, and/or limitations to their treatment are clear. We are currently working to have Ceiling of Care information electronically tagged to the patient's NHI (Figure 1), so that on admission the information is readily available. Of course patients may change their minds about how much intervention is desirable or appropriate – the approach cannot be rigid. But in our experience having the "ceiling of care" defined at the time of admission provides direction and security, particularly to nursing staff, as to how the patient is to be managed. In some centres, the **Liverpool Care Pathway** is also used, again providing a framework for appropriate in-patient management (and not abandonment) of patients who are terminally ill.

See "Liverpool Care pathway" BPJ 36 (Jun, 2011)

There is also immense scope for improving end-of-life care in the patient's home and in rest homes, and many in the primary care sector are working to this end. The

CEILING OF CARE / RESUSCITATION PREFERENCES FOR ACUTE ON CHRONIC RESPIRATORY FAILURE

NAME ..... NHI ..... DATE .....,,,,,.....

This patient has been attending the Respiratory Failure Support Clinic and / or has been an in-patient under the care of the Respiratory Service. The following Care Plan has been discussed and agreed with the patient, their family / whānau / carer, and has been confirmed and / or revised by the consultant specialist (electronically signed).

It should be used in the event of an admission to Dunedin Hospital with acute dyspnoea. Assuming that other diagnoses have been considered and excluded (e.g. pneumothorax), the patient's acute respiratory distress should or should not include the following:

SYMPTOM RELIEF: e.g. LOW FLOW OXYGEN / OPIATES / INTRA-NASAL MIDAZOLAM / HALOPERIDOL

Select one or more as appropriate for the patient's needs	ALWAYS
ANTIBIOTICS	YES / NO
PREDNISONE	YES / NO
NON-INVASIVE VENTILATION (BIPAP)	YES / NO
ICU / POSSIBLE MECHANICAL VENTILATION	YES / NO
CPR IN THE EVENT OF CARDIO-RESPIRATORY ARREST	YES / NO

Signed ..... (Consultant) ..... (Date)

Figure 1: Ceiling of care document (Southern DHB)

Table 1: Current goals for improving end-of-life care via DHB initiated strategic plans.

Goal #1:	To ensure that provision for end-of-life care and advanced care planning is included in the strategic and business plans for each clinical service operated by DHBs and PHOs
Goal #2:	To ensure that all clinical quality improvement initiatives within the DHB and PHO will address "quality of death" issues as much as they address "quality of life"
Goal #3:	To expedite nurse-led initiatives which will provide consistency in end-of-life care between the community and in hospital: ▪ Provide in-service training in palliative treatments for non-malignant diseases for community and practice nurses ▪ Adoption and implementation of the Liverpool Care Pathway across all adult medical and surgical hospital wards
Goal #4:	To explore mechanisms whereby patients in community rest homes have an Advanced Care Plan (where appropriate), and that these plans are central to their management in acute situations

N.B. This list is not exhaustive. These provide a unifying framework in which individual "tools" can be adopted and applied by different teams

introduction of ACP in rest homes is an obvious need. But the tool cannot be applied in isolation. Developing the palliative care skills of community and practice nurses as well as rest home carers is an obvious area where resources need to be allocated. In Otago/Southland criteria for providing "**Year of Care**" support is going to be extended in 2012 to include end-of-life patients, identified using the "surprise question". This is an example of how an appropriate philosophy of care and resource allocation can be integrated.

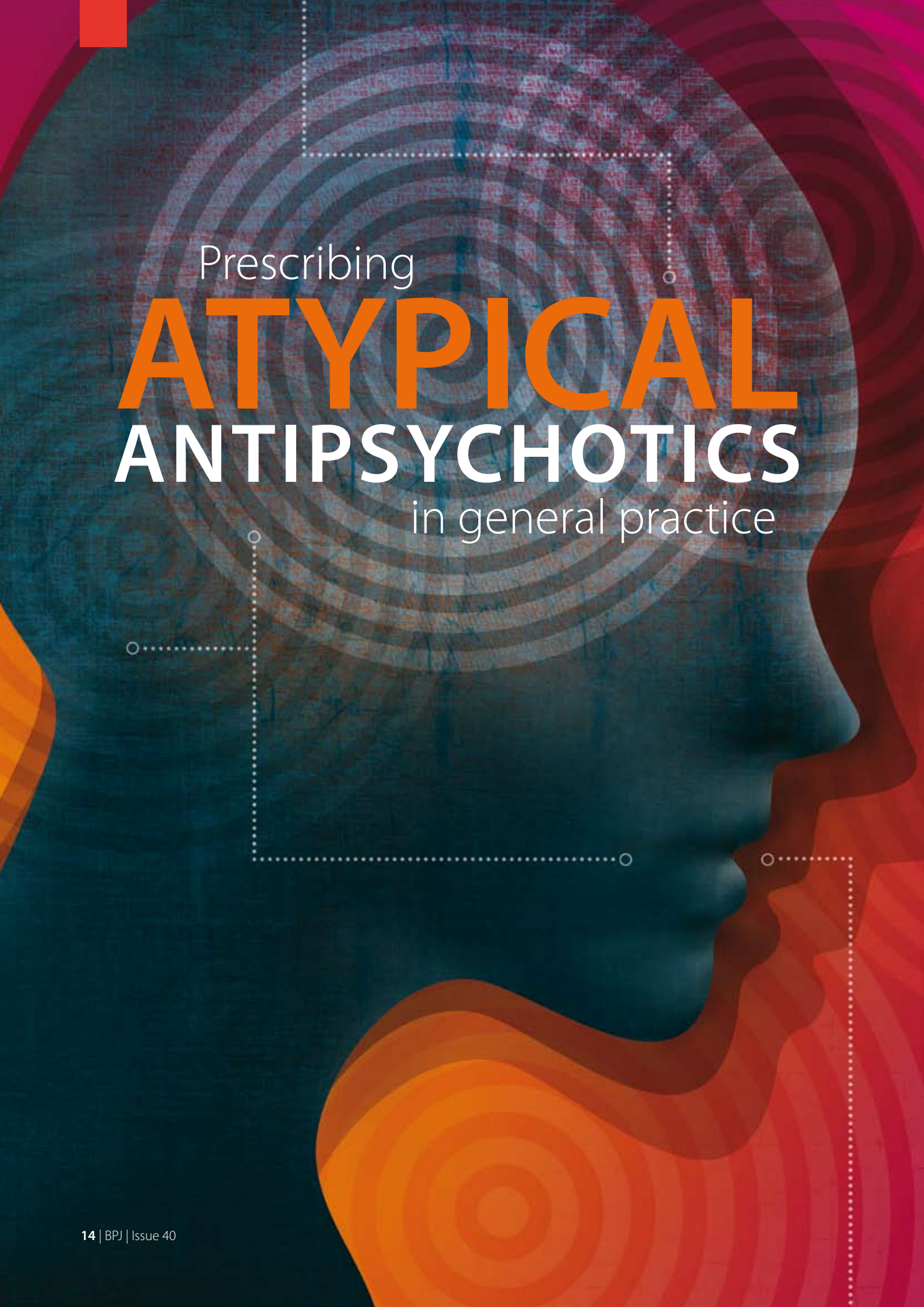
The strategies

Perhaps the most powerful incentive to improve end-of-life care is that this is what patients want,[4,5] and it is something that we would want for ourselves. Attitudes to death and dying from cancer have been powerfully and positively influenced by the hospice movement. But the philosophy of care which has been nurtured in that particular setting now needs to be extended and integrated into institutions where "cure and mend" has historically been the over-riding objective. The time has come for "both … and" rather than "either … or". The Southern DHB is currently considering proposals for its "Putting the Patient First" Strategic Plan (Table 1).

Patients at the end of life do not always want – and do not necessarily need – vigorous interventions but quality supportive care.[6] Quality improvement for such patients will be achieved not by straining indefinitely to extend life via acute medical services, nor by abandoning them when these fail. Adjusting what we do in the light of the diagnosis of dying, and managing the approach to death positively and meaningfully needs to be integrated into all clinical services, not just a few, so that a "good death" is included in what we mean by quality of life.

References

1. Chan W, Jackson G, Winnard D, Anderson P. Healthcare services funded by Counties Manukau District Health Board for people in the last year of life. N Z Med J 2011; 124; 1-12.
2. Ministry of Health. Advanced Care Planning; a guide for the New Zealand work force. Ministry of Health; Wellington, 2011.
3. Counties Manukau District Health Board (CMDHB). Advanced Care Plan. CMDHB; 2010.
4. Claessens M,Lynn Z, Zhong N, et al. Dying with lung cancer or chronic obstructive pulmonary disease: insights from SUPPORT. Study to Understand Prognoses and Preferences for Outcomes and Risks of Treatments. J Am Geriatr Soc 2000;48(5 Suppl):S146-53.
5. Curtis J, Wenrich J, Carline S, et al. . Patients' perspectives on physician skill in end-of-life care: differences between patients with COPD, cancer, and AIDS. Chest 2002;122(1):356-62.
6. Zhang B, Wright H, Huskamp M, et al. Health care costs in the last week of life: associations with end-of-life conversations. Arch Intern Med 2009;169(5):480-8.



Prescribing ATYPICAL ANTIPSYCHOTICS in general practice

Prescribing of atypical antipsychotics is increasing

Antipsychotic medicines are classified as "typical" or "atypical". Typical antipsychotics, also known as traditional or first-generation antipsychotics, include haloperidol and chlorpromazine. Atypical antipsychotics, also known as second generation antipsychotics, include quetiapine, risperidone and olanzapine. Both types of antipsychotics act in a similar way by blocking receptors in the dopamine pathway, but atypical antipsychotics are less likely to cause the extrapyramidal adverse effects associated with the older typical antipsychotics. However, atypical antipsychotics, along with typical antipsychotics, are associated with serious adverse effects, such as diabetes mellitus, stroke and cardiac death.[1]

Antipsychotics are indicated for the treatment of schizophrenia and related disorders and in some circumstances to treat the behavioural and psychological symptoms associated with dementia (risperidone only). International experience shows that antipsychotics are being increasingly used for off-label conditions (e.g. anxiety, insomnia).[2, 3]

The use of atypical antipsychotics has been increasing in New Zealand (Figure 1) and it is likely that off-label use is a factor in this increase. Special Authority prescribing restrictions have recently been removed from olanzapine (Page 22). Risperidone (excluding depot injection and dissolving tablets) and quetiapine have been available without restriction since 2009 and 2008 respectively.

Key concepts

- Use of atypical antipsychotics, such as quetiapine and olanzapine, is increasing and in many cases, they are being prescribed "off-label" – this is a worrying trend due to their potential to cause harm
- Atypical antipsychotics should only be used for specific indications and used with caution, especially in elderly people and young adults
- Atypical antipsychotics are indicated for the treatment of schizophrenia and related disorders and in some circumstances to treat the behavioural and psychological symptoms associated with dementia (risperidone only)
- Antipsychotics are not a first-line treatment for anxiety and are not recommended for post-traumatic stress disorder or insomnia

Traditionally, General Practitioners have been responsible for writing repeat prescriptions for patients, once an atypical antipsychotic has been initiated by a psychiatrist after confirmation of a diagnosis such as schizophrenia.

If a General Practitioner wishes to initiate treatment, then it is best to only prescribe for the recognised indications and to discuss the treatment plan with a psychiatrist (or other relevant clinician) before prescribing. Be particularly cautious when prescribing these medicines for elderly people, younger people and those at increased cardiovascular risk, especially as a result of obesity, diabetes or high cholesterol.

Adverse effects of atypical antipsychotics

Most adverse effects are common to all antipsychotics, both typical and atypical, but occur to varying degrees for individual medicines (Table 1).

Common, dose related adverse effects include:[4]

- Sedation – especially with clozapine, olanzapine and quetiapine
- Anticholinergic effects such as dry mouth, constipation and blurred vision – especially with clozapine and olanzapine
- Dizziness and postural hypotension – especially with clozapine, risperidone and quetiapine

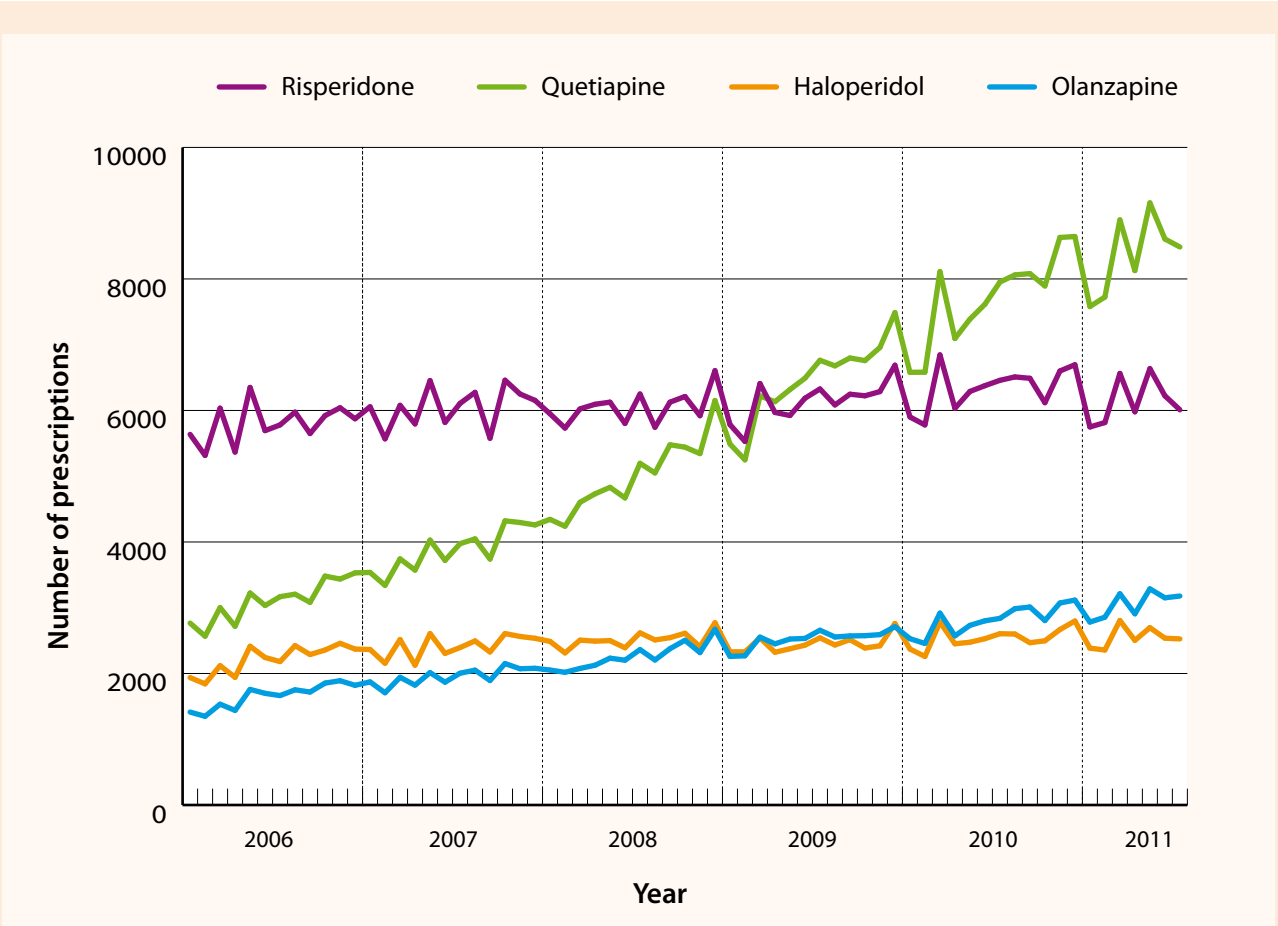


Figure 1: Use of selected typical and atypical antipsychotics by General Practitioners in New Zealand, 2006–2011 (dispensing data from the Pharmaceutical Warehouse database).

As experience has grown, significant adverse effects associated with atypical antipsychotics have emerged, such as the development of diabetes, dyslipidaemia, weight gain, metabolic syndrome, increased risk of stroke (particularly among elderly people), elevated risk of sudden cardiac death, seizures and tardive dyskinesia.[5] These adverse effects are also associated with typical antipsychotics.

Metabolic adverse effects

Metabolic adverse effects associated with antipsychotics are of particular concern because of the increase in cardiovascular morbidity and mortality.[4] Olanzapine and clozapine are particularly associated with substantial weight gain, dyslipidaemia and hyperglycaemia.[4] People taking these medicines often report that they always feel hungry. Weight gain can be substantial – a gain of 2 kg in two weeks should prompt a medicine review. All patients prescribed antipsychotics should be given appropriate advice on diet and lifestyle interventions and monitored carefully for diabetes.[7]

See: "Monitoring for metabolic disorders in patients taking antipsychotic drugs", BPJ 3 (Feb, 2007)

Extrapyramidal effects

Atypical antipsychotics are generally considered to cause fewer extrapyramidal adverse effects than typical antipsychotics. A meta-analysis showed clozapine, olanzapine and risperidone to be significantly less commonly associated with extrapyramidal symptoms than low potency typical antipsychotics (i.e. chlorpromazine 600 mg daily or equivalent).[8] The majority of studies have found no differences within the atypical group in terms of extrapyramidal effects.[5]

Table 1: Relative frequency of common adverse effects of antipsychotics (Psychotropic Expert Group, 2008).[6]

	Extrapyramidal	Sedation	Weight gain	Hyperglycaemia	Anticholinergic	Orthostatic hypotension
Atypical antipsychotics						
Risperidone	🟠🟠	🟠🟠 initially	🟠🟠	🟠🟠	🟢	🟠🟠 initially
Quetiapine	🟡*	🔴🔴🔴	🟠🟠	🔴🔴🔴	🟠🟠	🟠🟠
Olanzapine	🟡	🔴🔴🔴	🔴🔴🔴	🔴🔴🔴	🔴🔴🔴	🟡
Clozapine	🟡	🔴🔴🔴	🔴🔴🔴	🔴🔴🔴	🔴🔴🔴	🟠🟠
Amisulpride	🟠🟠*	🟡	🟡	🟡	🟢	🟡
Aripiprazole	🟡	🟡	🟡	🟢	🟢	🟡
Ziprasidone	🟡	🟠🟠	🟡	🟡	🟡	🟠🟠
Typical antipsychotics						
Haloperidol	🔴🔴🔴	🟡	🟠🟠	🟠🟠	🟡	🟡
Chlorpromazine	🟠🟠	🔴🔴🔴	🔴🔴🔴	🔴🔴🔴	🔴🔴🔴	🔴🔴🔴

Approximate frequency of adverse effects: 🟢 (<2%) = negligible or absent; 🟡 (>2%) = infrequent; 🟠🟠 (>10%) = moderately frequent; 🔴🔴🔴 (>30%) = frequent. * rarely a problem at usual therapeutic doses

Monitoring requirements for clozapine

Patients using clozapine require close monitoring as it can cause neutropenia, which may progress to a potentially fatal agranulocytosis.

Blood tests (white cell count and absolute neutrophil count) are required:[12]

- Ten days before commencing treatment
- Each week of the first 18 weeks of treatment
- Every four weeks during treatment
- Four weeks after discontinuation
- After discontinuation due to abnormal blood tests, until levels return to normal

Patients who present with evidence of infection, e.g. sore throat, fever or flu-like symptoms require an urgent complete blood count. Patients should also be advised to report any such symptoms.

Other adverse effects

Constipation is commonly associated with clozapine use and can be severe and even life-threatening. Co-prescription of a laxative for patients taking clozapine is recommended.

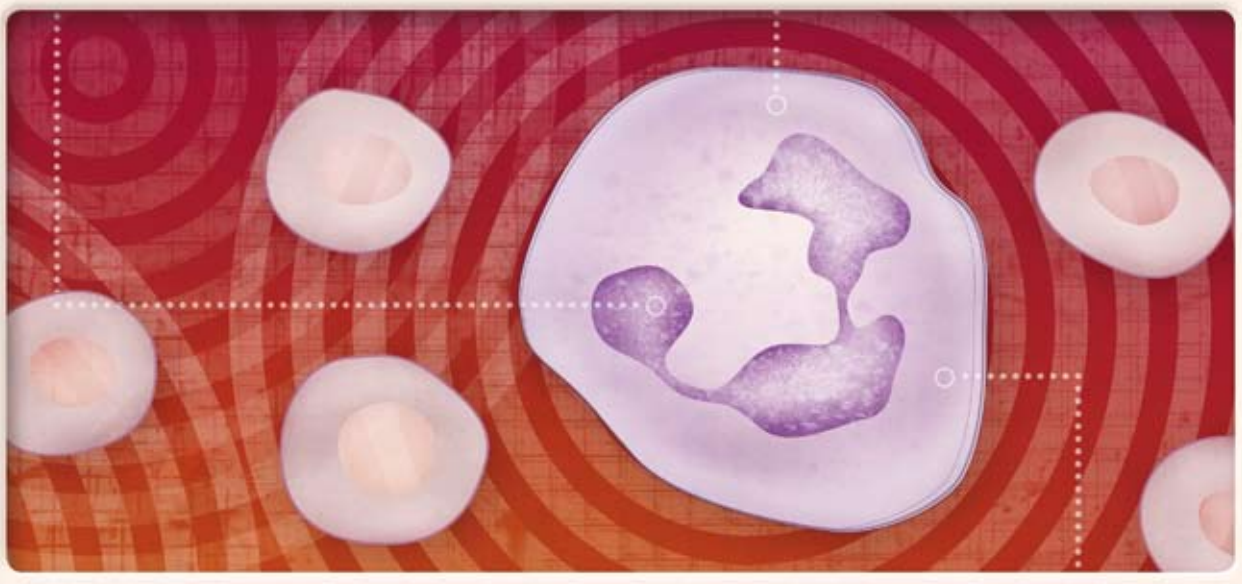
Additional adverse effects of clozapine are similar to other antipsychotics, but antimuscarinic effects (e.g. dry mouth, blurred vision, urinary retention), sedation and weight gain are often more pronounced.

The concomitant use of some medicines may increase the risk of adverse effects due to:

- A potential for bone marrow suppression, e.g. trimethoprim, co-trimoxazole, nitrofurantoin, sulphonamides, carbamazepine
- An increase in the plasma concentration of clozapine, e.g. erythromycin, ciprofloxacin

Clozapine is classified as a "hospital pharmacy" medicine which means it is only dispensed from a limited number of authorised pharmacies. ~~It is also currently monitored on the Intensive Medicines Monitoring Programme (IMMP)~~.

See "Clozapine: A reminder about safe and effective use". BPJ 14 (Jun, 2008).



* Removed November 2011

Tardive dyskinesia

Rates of new-onset tardive dyskinesia (orofacial and trunk movements) have been estimated at 3% with risperidone and 1% to 2% for other atypical antipsychotics.[5] In comparison, tardive dyskinesia develops in around 20% of people receiving typical antipsychotics.[9] Tardive dyskinesia is of particular concern as it may not be evident immediately, is often resistant to treatment, may be persistent and may worsen on treatment withdrawal.

Atypical antipsychotics for the treatment of schizophrenia and related disorders

Patients with schizophrenia should ideally be managed by a multidisciplinary team, including both primary and secondary care.[10] The early detection and prompt treatment of a first episode of schizophrenia is essential as this can improve health outcomes and possibly even the progression of the illness.[10]

Typical and atypical antipsychotics are used in the treatment of schizophrenia. Both types of antipsychotics are associated with adverse effects and there is also great variability in individual patient response. Therefore the same medicine cannot be recommended for every patient. As a general principle, an antipsychotic is started at a low dose and carefully titrated upwards to avoid or reduce the occurrence of adverse effects.[6]

Australasian guidelines recommend an atypical antipsychotic as first-line treatment for schizophrenia due to their lower risk of extrapyramidal adverse effects compared to typical antipsychotics.[10] However, more recently this recommendation has been challenged due to the concern that metabolic adverse effects associated with atypical antipsychotics are more problematic in the longer term.[11]

Clozapine is recommended in cases of treatment resistance, after the patient has trialled at least two other antipsychotics.[10] This medicine is not initiated in primary care, however, primary care clinicians have a role in monitoring for adverse effects (see opposite).

Pharmacological treatments for schizophrenia should always be used in conjunction with comprehensive psychosocial interventions.[10]

Atypical antipsychotics for the treatment of behavioural and psychological symptoms of dementia

Behavioural and psychological symptoms of dementia (BPSD) include; aggressiveness (verbal outburst, physical violence), activity disturbance (agitation, wandering) and psychotic symptoms. Non-pharmacological treatment is recommended first-line, but in some severe cases antipsychotics are used to manage BPSD.

Risperidone is the only atypical antipsychotic officially indicated for BPSD. Antipsychotics provide relatively few clinical benefits for people with dementia and in some cases pose a serious risk of an adverse outcome. A recent review predicts that for every 100 people with dementia given an antipsychotic only 20 will derive some clinical benefit and there will be one extra death and one extra stroke.[13]

Atypical antipsychotics should be used with extreme caution in older people, due to an increased incidence of adverse effects, and only used to treat severe symptoms. The decision to use an antipsychotic should be discussed with the patient, family and caregivers. Initial doses should be reduced to half the adult dose or less, taking into account factors such as the patient's weight, co-morbidities, and concomitant medication. Treatment should also be reviewed regularly.[14]

Antipsychotic treatment is not effective for symptoms such as wandering, social withdrawal, shouting, pacing, touching, cognitive defects and incontinence. Patients with these symptoms may respond to interventions such as improvements to the environment.[15]

See: "Antipsychotics in people with dementia – an update and reminder", BPJ 26 (Mar, 2010) and "Antipsychotics in dementia: best practice guide", BPJ Special Edition (Sep, 2008).

Off-label uses of atypical antipsychotics: insomnia, anxiety and post-traumatic stress disorder

In a recent survey in Canterbury, 96% of psychiatrists reported that they prescribed antipsychotics for off-label uses, with quetiapine being the most commonly used. The three most frequent indications for off-label prescribing of quetiapine were; anxiety (89%), sedation (79%) and post-traumatic stress disorder (57%).[16] Overall, it is estimated that between 43% and 70% of atypical antipsychotics prescribed are used for off-label indications.[16] It is generally accepted that there is limited evidence to support the use of antipsychotics for off-label uses, but this practice is now widespread and there is little guidance as to whether it needs to be reduced, or if patients are genuinely benefitting from the use of these medicines for these indications.

Drug company marketing has played a strong role in the increase in use of antipsychotics in recent years. In the United States, two drug manufacturers settled out of court, after being charged with illegally promoting the off-label use of olanzapine and quetiapine.[17, 18] There are reports that quetiapine is increasingly emerging as a drug of misuse in the United States. This trend has not yet been widely reported in New Zealand,[19] but may appear over time. There are some anecdotal reports that quetiapine is a drug of misuse in New Zealand prisons.

Off-label prescribing is legal in most countries, including New Zealand, therefore atypical antipsychotics can be prescribed for indications such as anxiety. However, the prescriber needs to carefully weigh up the risks and benefits and consider other appropriate medicines (or non-pharmacological options) first. The decision to prescribe should be discussed with the patient and their family and carefully documented in the patient's notes.

Anxiety

A selective serotonin re-uptake inhibitor (SSRI) is the first-line pharmacological treatment for generalised anxiety disorder.[20] Psychological treatments, such as cognitive behavioural therapy, are equally effective.[21] Patients should be treated for at least 12 weeks before assessing the efficacy of treatment with a SSRI. Treatment may need to continue for six to 12 months after symptoms of anxiety have resolved.[20]

Benzodiazepines are sometimes trialled for the treatment of anxiety if SSRIs or psychological therapies have been ineffective.[22] However, there is significant concern with tolerance, dependence and misuse associated with this medicine class. Buspirone is funded with Special Authority restriction, for use as an anxiolytic when other medicines are contraindicated or have failed. Tricyclic antidepressants may also be considered in some cases.

There is some evidence that quetiapine may be effective in the treatment of generalised anxiety disorder.[23, 24] Due to the adverse effects associated with quetiapine, it should only be considered for the short-term treatment of anxiety if all other appropriate pharmacological or psychological treatments had been trialled and were ineffective.

For further information see: "Generalised anxiety disorder in adults", BPJ 25 (Dec, 2009).

Post-traumatic stress disorder (PTSD)

PTSD is a psychiatric disorder which develops after exposure to a traumatic event. Three clusters of symptoms are typically present – re-experiencing, avoidance and hyperarousal. Treatment for PTSD involves a combination of psychological therapies, pharmacological treatment and social support. The first-line pharmacological treatment is an antidepressant, usually a SSRI.

There is a lack of evidence to support the use of quetiapine (or other antipsychotics) for the treatment of PTSD.[22]

Insomnia

Insomnia is usually secondary to an underlying cause such as an illness or poor sleep environment. Investigation and

treatment of the underlying cause will usually resolve symptoms of insomnia.

The first-line treatment is "sleep hygiene" intervention, e.g. advice to avoid alcohol, nicotine and caffeine, avoid stimuli before bedtime, avoid being in bed when not sleeping and learning relaxation techniques.

If this approach fails to resolve the insomnia, pharmacological treatment may be considered for short-term use. Zopiclone or shorter-acting benzodiazepines (e.g. temazepam) are appropriate choices. Use the lowest effective dose for the shortest possible time (less than four weeks and preferably five to ten days).[25] Antidepressants are not recommended for insomnia in the absence of depression or anxiety.[26]

Quetiapine is not recommended for the treatment of insomnia in the absence of psychiatric disorder, e.g. schizophrenia. Quetiapine has been reported to increase total sleep time and sleep efficiency, however, adverse effects such as leg movements and akathisia (restlessness) limit its effectiveness.[27]

For further information see: "Managing insomnia", BPJ 14 (Jun, 2008).

ACKNOWLEDGEMENT Thank you to **Dr Erik Monasterio**, Senior Clinical Lecturer, Christchurch School of Medicine, University of Otago, Consultant in Forensic Psychiatry, Hillmorton Hospital and **Andrew McKean**, Acting Senior Pharmacist, The Princess Margaret Hospital, Christchurch for expert guidance in developing this article.

Olanzapine generic now available – weight gain and diabetes a concern

From 1 June 2011 two generic versions of olanzapine became available for prescription, without restriction – Olanzine and Dr Reddy's Olanzapine (tablet and dissolving forms). The Zyprexa brand of olanzapine is still available, but is now subject to a significant part-charge. Some patients may need to be counselled through the brand change. Inform patients that the orodispersible tablets taste different and may take longer to dissolve.

Olanzapine is approved for the treatment of schizophrenia and related psychoses and bipolar depression. Concern has been expressed, now that olanzapine can be prescribed without a Special Authority approval, that it will be prescribed for off-label indications in the same manner that has occurred for quetiapine. There are a number of conditions in which olanzapine has been used, or is under investigation for use, including Alzheimer's dementia, anorexia, autism, Asperger's disorder, insomnia, anxiety and agitation. As yet, there is no compelling evidence of its effectiveness for these conditions.

When prescribing olanzapine the clinician should be particularly aware of the metabolic adverse effects including weight gain, raised lipid levels, impaired glucose tolerance and new-onset diabetes.[5] Pancreatitis is also reported as a rare complication of olanzapine use.[28]

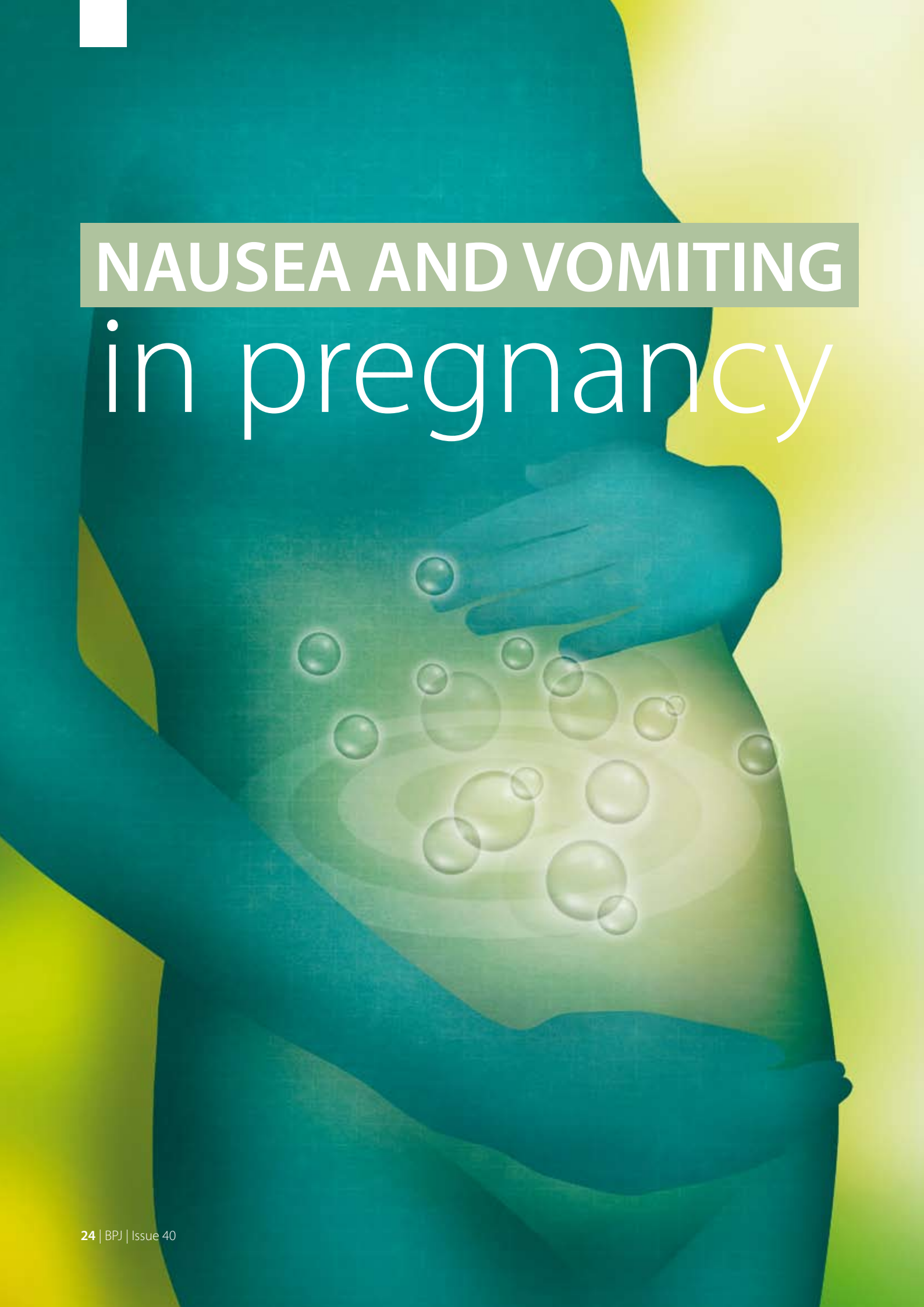
Table 2: Serious adverse effects of atypical antipsychotics that may be more troublesome with olanzapine[5, 29, 30, 31]

Adverse effect	Comment
Weight gain	Weight gain in people using olanzapine can be 1 to 3 kg greater than that associated with other atypical antipsychotics such as risperidone. In long-term studies (at least 48 weeks) the mean weight gain was 5.6kg. The proportion of patients with clinically important weight gain could be reasonably high as the number needed to harm has been calculated as 4 for a ≥ 7% gain in body weight. Teenagers (age 13–17 years) are more likely to gain weight and to gain more weight than adults. Potential consequences of weight gain should be considered prior to starting olanzapine. **Monitor** weight, waist circumference and BMI. If weight gain is more than 2 kg during the first two weeks then a change of antipsychotic may be necessary.
Diabetes	There is an increased risk of type 2 diabetes in people with schizophrenia. Olanzapine has been associated with a greater risk of new-onset diabetes compared with the other atypical antipsychotics. Use with caution in people with diabetes or other disorders of glucose regulation. **Monitor** HbA_{1c} for signs of worsening glucose control. Avoid use in people with risk factors for diabetes e.g. obesity or family history. If used, **monitor** fasting glucose levels before and periodically during treatment.
Serum lipids	Olanzapine has been associated with increases in triglycerides, LDL cholesterol and total cholesterol and decreases in HDL cholesterol. Use with caution in patients with pre-existing abnormal lipid profile. **Monitor** lipid levels during treatment.

References

1. Ray W, Chung C, Murray K, et al. Atypical antipsychotic drugs and the risk of sudden cardiac death. N Engl J Med 2009;360(3):225-35.
2. Domino M, Swartz M. Who are the new users of antipsychotic medications? Psychiatr Serv 2008;59(5):507-14.
3. Alexander G, Gallagher S, Mascola A, et al. Increasing off-label use of antipsychotic medications in the United States, 1995–2008. Pharmacoepidemiology and Drug Safety, 2011; 20: 177–84.
4. Mackin P, Thomas S. Atypical antipsychotic drugs. BMJ 2011;342:650-4.
5. McDonagh M, Peterson K, Carson S, et al. Drug class review: Atypical antipsychotic drugs. Update 3. Available from: http://derp.ohsu.edu/final/AAP_final_report_update_3_version%202_JUL_10.pdf (Accessed Oct, 2011).
6. Psychotropic Expert Group. Therapeutic guidelines: psychotropic. Version 6. Melbourne: Therapeutic Guidelines Limited; 2008.
7. Kessing V, Thomsen A, Mogensen U, Andersen P. Treatment with antipsychotics and the risk of diabetes in clinical practice. Br J Psych 2010; 197:266–71.
8. Leucht S, Corves C, Arbter D, et al. Second-generation versus first-generation antipsychotic drugs for schizophrenia: a meta-analysis. Lancet 2009;373:31-41.
9. National Institute for Clinical Excellence (NICE). Schizophrenia: core interventions in the treatment and management of schizophrenia in adults in primary and secondary care (update). National Clinical Guideline Number 82. The British Psychological Society & The Royal College of Psychiatrists, 2010. Available from: www.nice.org.uk (Accessed Oct, 2011).
10. Royal Australian and New Zealand College of Psychiatrists Clinical Practice Guidelines Team for the Treatment of Schizophrenia and Related Disorders. Royal Australian and New Zealand College of Psychiatrists clinical practice guidelines for the treatment of schizophrenia and related disorders. Aust N Z J Psychiatry 2005;39(1-2):1-30.
11. Kendall T. The rise and fall of the atypical antipsychotics. Br J Psych 2011;199:266-8.
12. Novartis New Zealand Limited. Clozaril (clozapine). Medicine datasheet. 2011. Available from: www.medsafe.govt.nz (Accessed Oct, 2011).
13. Banarjee S. The use of antipsychotic medication for people with dementia: A time for action. An independent report commissioned and funded by the Department of Health (England). October 2009. Available from: www.dh.gov.uk (Keyword Bannerjee) (Accessed Oct, 2011).
14. British National Formulary (BNF). BNF 62. London: BMJ Publishing Group and Royal Pharmaceutical Society of Great Britain, 2011.
15. Scottish Intercollegiate Guidelines Network (SIGN). Management of patients with dementia. A national clinical guideline. SIGN, 2006. Available from: www.sign.ac.uk/pdf/sign86.pdf (Accessed Oct, 2011).
16. Monasterio E, McKean A. Off-label use of atypical antipsychotic medications in Canterbury, New Zealand. N Z Med J 2011;124(1336).
17. Kmietowicz Z. Eli Lilly pays record $1.4bn for promoting off-label use of olanzapine. BMJ 2009;338:b217.
18. Tanne J. Astra Zeneca pays $520m fine for off-label marketing. BMJ 2010;340:c2380.
19. Wilkins C, Sweetsur P, Smart B, Griffiths R. Recent trends in illegal drug use in New Zealand, 2006-2010. Findings from the 2006, 2007, 2008, 2009 and 2010 Illicit Drug Monitoring System (IDMS). Auckland: Social and Health Outcomes Research and Evaluation (SHORE), School of Public Health, Massey University, 2011.
20. Baldwin D, Anderson I, Nutt D, et al. Evidence based guidelines for the pharmacological treatment of anxiety disorders: recommendations from the British Association for Psychopharmacology. J Psychopharmacol 2005;19(6):567-96.
21. National Prescribing Service Limited. Which treatment for what anxiety disorder? NPS News 2009;65. Available from: www.nps.org.au (Accessed Oct, 2011).
22. Gale C, Davidson O. Generalised anxiety disorder. BMJ 2007;334:579-81.
23. Ravindran A, Al-Subaie A, Abraham G. Quetipaine: novel uses in the treatment of depressive and anxiety disorders. Expert Opin Investig Drugs 2010;19(10):1187-204.
24. Ruelaz Maher A, Maglione M, Bagley S, et al. Efficacy and comparative effectiveness of atypical antipsychotic medications for off-label uses in adults. JAMA 2011;306(12):1359-69.
25. National Institute for Clinical Excellence (NICE). Guidance on the use of zaleplon, zolpidem and zopiclone for the short-term management of insomnia. NICE, 2004. Available from: www.nice.org.uk (Accessed Oct, 2011).
26. Laine C, Goldmann D, Wilson JF. In the clinic: Insomnia. Ann Intern Med 2008; 148(1).
27. Wine J, Sanda C, Caballero J. Effects of quetiapine on sleep in non-psychiatric and psychiatric conditions. Ann Pharmacother 2009;43(4):707-13.
28. Monasterio E, Bhalla R, McKean A. Olanzapine-induced acute pancreatitis and new diabetes mellitus. 2011: *In Print*.
29. Proietto J. Diabetes and Antipsychotic Drugs. Prescriber Update 2004;25(2):20-22.
30. Sweetman SC. Martindale: The complete drug reference. 37th edition. Pharmaceutical Press, London, April 2011.
31. Mylan New Zealand Limited. Olanzine & Olanzine-D. Medicine datasheet. 2011. Available from: www.medsafe.govt.nz (Accessed Oct, 2011).

NAUSEA AND VOMITING in pregnancy



Nausea and vomiting in early pregnancy is very common

Nausea and vomiting in early pregnancy is so common that it can be considered a normal part of pregnancy. It is colloquially referred to as "morning sickness" although this is a misnomer because symptoms will often persist throughout the day. Up to 85% of women experience nausea in early pregnancy with approximately half of women vomiting as well. Symptoms usually begin between the fourth and seventh week after the last menstrual period and resolve in many women by the twelfth week and in most women by the twentieth week of pregnancy.[1] A smaller number of pregnant women (approximately 0.3–1%), have a more severe form of nausea and vomiting – hyperemesis gravidarum, which is characterised by persistent vomiting, weight loss of more than 5%, ketouria, electrolyte abnormalities (hypokalaemia) and dehydration.[2]

While persistent nausea and vomiting in early pregnancy can be particularly debilitating for some women, it is not usually associated with any adverse pregnancy outcomes and in fact has been associated with lower rates of miscarriage.[2] Hyperemesis gravidarum is on rare occasions associated with maternal complications such as Wernicke's encephalopathy due to thiamine deficiency and foetal growth restriction.[3]

Evaluation of nausea and vomiting in pregnancy

Nausea and vomiting in pregnancy is usually a self-limiting condition, however, hyperemesis gravidarum should be distinguished from other conditions that may cause persistent vomiting, such as hepatitis, pancreatitis, pyelonephritis, peptic ulcer disease, thyroid disease and adrenocortical insufficiency. Investigations may include:[4]

- Midstream urine microscopy to exclude a urinary tract infection
- Ultrasound to exclude trophoblastic disease or multiple pregnancy
- TSH if there is suspicion of thyrotoxicosis
- Electrolytes and liver function tests

Nausea and vomiting that begins at or after 12 weeks gestation is unlikely to be caused by pregnancy so other causes should be investigated.[3]

Rehydration may be required

Women who present with mild to moderate dehydration can be managed with oral fluids. Women who are severely dehydrated will require referral to hospital for IV fluids and antiemetics, and in extreme cases nasogastric or parenteral

Key concepts

- Nausea and vomiting are very common symptoms of early pregnancy and usually resolve by 12–20 weeks gestation
- In most cases these symptoms can be managed with simple diet and lifestyle advice and reassurance that it will not have an adverse effect on pregnancy
- Women with more severe symptoms may require treatment with medicines and, in severe cases, referral to hospital for intravenous fluids and antiemetics

Aetiology and risk factors for nausea and vomiting in pregnancy

The causes of nausea and vomiting in pregnancy are unknown, however, it is thought to be associated with rising levels of human chorionic gonadotropin (hCG). This is based on the observation that the incidence of hyperemesis is highest at the time where hCG production reaches its peak and that conditions associated with higher hCG levels (e.g twin and molar pregnancies) are also associated with higher rates of hyperemesis gravidarum. Oestrogen is another suggested cause with the presence of a female foetus reported to increase the likelihood of severe nausea and vomiting during pregnancy.[4] One study found that women who were primiparous (first pregnancy), younger or were non-smokers were more likely to have nausea and vomiting in pregnancy.[5] Another study found that 63% of multiparous women who had nausea and vomiting had also experienced it in a previous pregnancy.[6] Chronic *H. pylori* infection has also been associated, in some studies, with nausea and vomiting in pregnancy.[3]

There is some evidence that hyperemesis gravidarum is more common in Pacific women. One study in Wellington found that the incidence of hyperemesis gravidarum was significantly increased among Pacific women (particularly Samoan women) and was associated with thyroid function test abnormalities.[7] Another study found that Pacific women were twice as likely to be hospitalised with hyperemesis gravidarum compared to other New Zealand women. The authors suggested that the higher prevalence of *H. pylori* in Pacific peoples could be a plausible explanation for the higher rates of hyperemesis gravidarum although they said psychosocial factors or thyroid function abnormalities could also be potential causes.[8]

nutrition.[9] Alternatively, IV fluids and antiemetics may be given at the general practice clinic, if appropriate facilities are available.

Normal saline (0.9%; 150 mmol/L) or Hartmann's solution (sodium lactate) are appropriate choices for IV rehydration of pregnant women who are severely dehydrated. Dextrose containing fluids and hypertonic saline are inappropriate because they can precipitate severe neurological complications such as Wernicke's encephalopathy and central pontine myelinolysis.[3, 10]

Initial management in the majority of cases involves dietary and lifestyle advice

While there is limited evidence from clinical trials about the effectiveness of dietary and lifestyle interventions, the following recommendations may be useful and should be trialled first:

Dietary advice[4]

- Drink small amounts often – dehydration can exacerbate nausea so it is important for pregnant women to maintain hydration by drinking adequate fluids
- Trial different kinds of fluids - sometimes fluids such as flat lemonade or diluted fruit juice are managed better than water
- Avoid fatty or spicy food – this may exacerbate symptoms
- Avoid having an empty stomach – eat a light snack every one to two hours between meals
- Avoid very large meals -– small amounts of food more often are usually better tolerated
- Early morning nausea may be helped by eating a dry biscuit or cracker before getting out of bed
- Salty food such as potato chips or salted crackers may help, especially before meals

Lifestyle advice[4]

- Eat well when feeling the best or whenever feeling hungry
- If the smell of hot food worsens nausea, try cold food instead, avoid cooking if possible or cook in well ventilated areas so that odours do not accumulate; ask for help from family and friends with cooking
- Lie down when nauseated
- Avoid stress
- Take pregnancy vitamins (including folic acid) at a good time of the day (when feeling well)
- Keep physical activity gentle, getting too hot may exacerbate nausea

Alternative therapies – ginger, pyridoxine and acupressure

Ginger has been shown in some studies to improve nausea and vomiting compared to placebo, however, there is conflicting data on the efficacy of ginger which may be the result of different preparations and potencies used in studies.[3] The recommended dose of ginger is up to 1 g per day (in divided doses).[11] Products which contain ginger such as tea, biscuits or confectionary may also be trialled. Ginger may cause reflux and heartburn in some people.[1]

Pyridoxine (vitamin B6) is used first-line in many countries for nausea and vomiting in early pregnancy, however, there are large individual differences in its onset and action.[3] Studies have shown that pyridoxine improves mild to moderate nausea but does not significantly reduce vomiting.[12, 13] The recommended dose in pregnant women is 25–50 mg, up to three times per day.[11] Pyridoxine is available in 25 mg and 50 mg tablets, fully subsidised on the pharmaceutical schedule. Pyridoxine has been studied extensively as a combination product with doxylamine which was withdrawn from overseas markets, but has not proven to be associated with any teratogenic effects.[12]

Acupressure involves stimulation, either manually or with elasticised bands, of the P6 Neiguan point which is found on the inside of the forearm three fingerbreadths above the wrist. There is some evidence that P6 acupressure reduces symptoms of nausea and vomiting but some studies, which included sham acupressure, have found a strong placebo effect.[2]

Manage other conditions such as heartburn

Heartburn and reflux have been shown to exacerbate nausea and vomiting in pregnancy so managing these conditions, by making dietary changes or using medications, may help improve symptoms.[12] Treatment with a H2 antagonist or a proton pump inhibitor will also protect against the effects of persistent vomiting.[10] Omeprazole and ranitidine are considered safe to use during pregnancy.[14]

Pharmacologic treatment may be appropriate for women continuing to experience intolerable nausea and vomiting

Approximately 10% of women continue to experience significant nausea and vomiting during pregnancy, despite following dietary and lifestyle advice. In these cases, medications may be trialled.[1] Antiemetics used in pregnancy include; metoclopramide, prochlorperazine cyclizine, promethazine and ondansetron. These medicines are listed in Table 1 in a suggested order in which to try them, however, individual patient factors and adverse effect profiles may alter this. For example, a more sedating antiemetic may be of benefit to some women but may be inappropriate in others, such as those with small children. Any antiemetic should be used at the lowest effect dose for the shortest time it is required.

Metoclopramide is one of the most commonly prescribed medicines for nausea and vomiting.[4] It has been found to be more effective than placebo in the treatment of hyperemesis gravidarum and has not been associated with any significant increase in risk of major congenital malformations or other adverse pregnancy outcomes.[9, 12] However, it is associated with drug-induced movement

disorders and female gender is a risk factor for the development of this adverse effect.[12]

Phenothiazines (e.g. prochlorperazine) reduce nausea and vomiting compared with placebo and studies have found no association with teratogenicity.[2] Phenothiazines are more likely to cause drowsiness than the other antiemetics.[3] Extrapyramidal effects and oculogyric crises are reported with phenothiazines as well as metoclopramide.[3]

Antihistamines (e.g. cyclizine, promethazine) have been shown to significantly reduce nausea, however, they are associated with an increased risk of drowsiness. Studies have not found a significantly increased risk of teratogenicity with antihistamines.[2] Meclozine ("Sea-legs") was previously thought to be associated with cleft palate, however, recent studies have not shown an increased risk of malformation.[12]

Ondansetron may be considered in women with hyperemesis gravidarum

Ondansetron is an effective antiemetic which has been used in non-pregnant patients to treat nausea and vomiting. However, while animal data looks reassuring, there is very limited data on its safety in pregnant women.[12] Common adverse effects include, fatigue, headaches and drowsiness. Constipation is also very common and can exacerbate symptoms of bloating and abdominal discomfort.[10]

Corticosteroids are usually limited to women with intractable nausea and vomiting

Corticosteroids may be considered for women with intractable nausea and vomiting, but this is usually initiated in secondary care.[3] While the mechanism of action is not well understood, some women experience a very rapid resolution of their symptoms when treated with corticosteroids.[10] Oral corticosteroids have been associated with cleft palate when administered to pregnant women before ten weeks gestation so they are best avoided until after this time if possible.[1]

Best practice tip: Antiemetics can be taken according to when the pregnant woman experiences the most symptoms. For example, many women benefit from having a dose of antiemetic 30 minutes before getting out of bed to prevent vomiting while having a shower or after having breakfast. Late afternoon symptoms associated with tiredness may be improved by a second dose around 1–2 pm.[10]

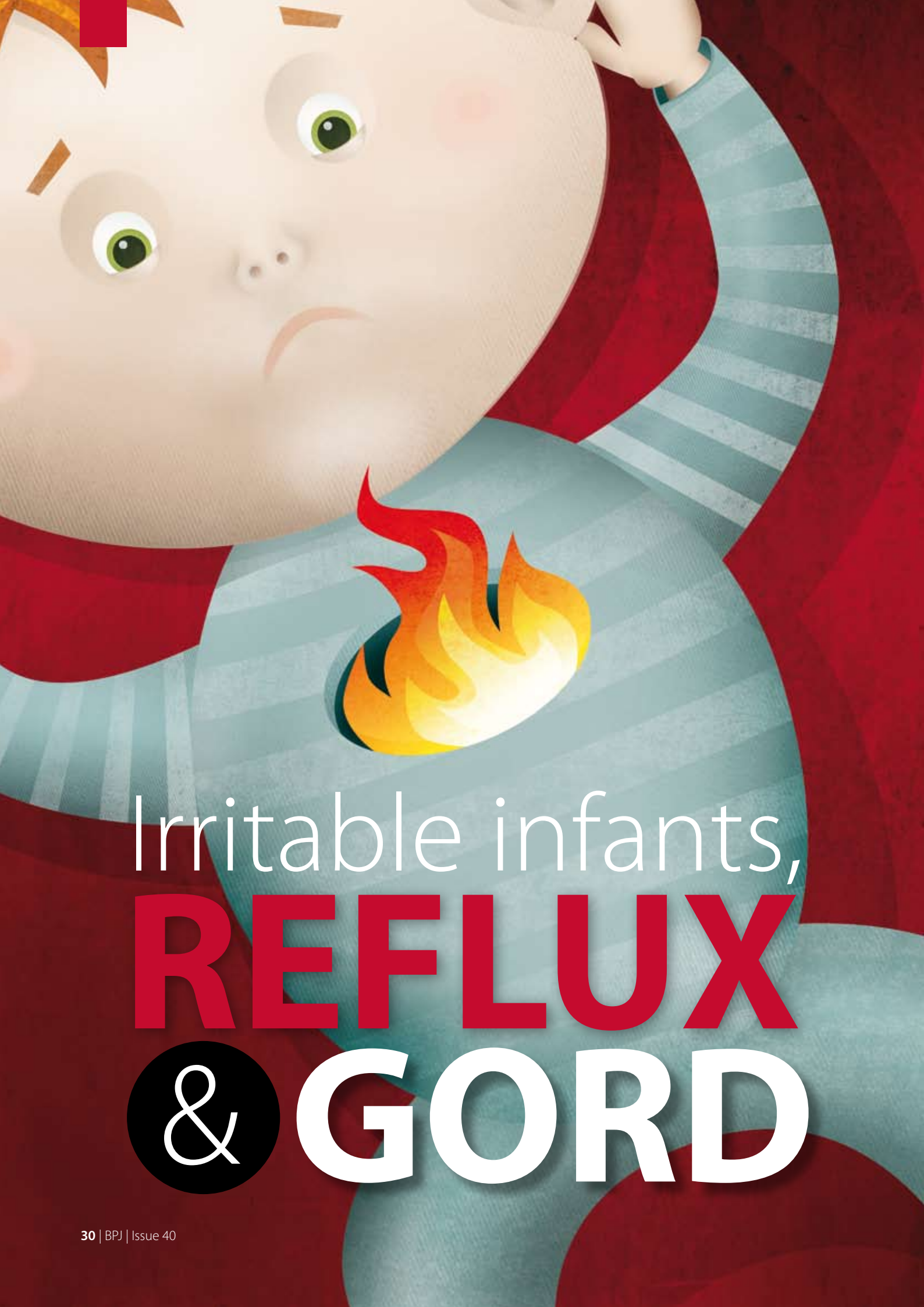
ACKNOWLEDGEMENT Thank you to **Dr Helen Paterson**, Consultant in Obstetrics and Gynaecology, Senior Lecturer, Department of Women's and Children's Health, Dunedin School of Medicine, University of Otago for expert guidance in developing this article.

Table 1: Antiemetics suitable for use in pregnancy (in order of preference)[3, 4, 10]

Medication	Dose	Adverse effects
Metoclopramide	10 mg three times daily	Extrapyramidal symptoms Tardive dyskinesia especially if used for more than 12 weeks
Prochlorperazine	5 mg three times daily	Extrapyramidal symptoms Sedation
Cyclizine	50 mg three times daily	Sedation
Promethazine	25 mg at bedtime, increased to maximum 100 mg daily in divided doses	Extrapyramidal symptoms Sedation
Ondansetron (hyperemesis gravidarum)	4 – 8 mg two to three times daily	Constipation

References:

1. Niebyl JR. Nausea and vomiting in pregnancy. N Engl J Med 2010;363(16):1544-50.
2. National Institute for Health and Clinical Excellence (NICE). Antenatal care: routine care for the healthy pregnant woman. 2008. Available from: www.nice.org.uk (Accessed Oct, 2011).
3. Jarvis S. Management of nausea and vomiting in pregnancy. Br Med J 2011;342:d3606.
4. Sheehan P. Hyperemesis gravidarum: assessment and management. Aust Fam Physician 2007;36(9):698-701.
5. Klebanoff MA, Koslowe PA, Kaslow R, Rhoads GG. Epidemiology of vomiting in early pregnancy. Obstet Gynecol 1985;66(5):612-6.
6. Gadsby R, Barnie-Adshead AM, Jagger C. A prospective study of nausea and vomiting in pregnancy. Br J Gen Pract 1993;43:245-8.
7. Jordan V, MacDonald J, Crichton S, et al. The incidence of hyperemesis gravidarum is increased among Pacific Islanders living in Wellington. N Z Med J 1995;108(1006):342-4.
8. Sopoaga F, Buckingham K, Paul C. Causes of excess hospitalisations among Pacific peoples in New Zealand: implications for primary care. J Primary Health Care 2010;2(2):105-10.
9. Quinlan JD, Hill DA. Nausea and vomiting of pregnancy. Am Fam Physician 2003;68(1):121-8.
10. Lowe S. Nausea and vomiting in pregnancy. O&G Magazine 2007;9(4).
11. Australian Medicines Handbook (AMH). Adelaide; AMH Pty Ltd, 2011.
12. Smith JA, Refuerzo JS, Ramin SM. Treatment of nausea and vomiting of pregnancy (hyperemesis gravidarum and morning sickness). UpToDate 2011. Available from: www.uptodate.com (Accessed Oct, 2011).
13. Festin M. Nausea and vomiting in early pregnancy. Clin Evid 2009;6:1405.
14. British National Formulary (BNF). BNF 62. London: BMJ Publishing Group and Royal Pharmaceutical Society of Great Britain, 2011.



Irritable infants, REFLUX & GORD

Crying and irritability: a normal part of infancy or a pathological cause?

The phrase "sleeping like a baby" is intended to mean peaceful sleep, however, the reality is that babies frequently wake, cry and require feeding. Although much variation occurs, crying generally increases at age two weeks before peaking at age six to eight weeks while a diurnal sleep/wake cycle is established.[1] Some infants will display excessive crying and irritability which may cause parental anxiety – particularly for first time parents. Sometimes parents suspect a pathological reason for their infant's distress with up to 20% of parents reporting a problem with infant crying or irritability in the first three months of parenthood.[2] However, in most cases, no medical intervention is required.

Gastric reflux

"Reflux" is commonly blamed for infant irritability, however, this is a normal occurrence in an infant and generally does not require medical treatment. Parents can be provided with reassurance and practical advice for managing the symptoms (over page).

An infant's body weight roughly triples in their first year of life and their caloric intake is high. Due to the frequency and relative size of an infant's feeds, their stomach is often distended and may require relief through transient oesophageal sphincter relaxations – otherwise known as gastric reflux.[3]

Uncomplicated reflux is a normal process involving the involuntary passage of gastric contents into the oesophagus. This occurs asymptomatically throughout the day, and may involve movement of food, drink and saliva, as well as gastric, pancreatic and biliary secretions. Reflux is less acidic in infants than in older children and adults, as the stomach contents are buffered by the frequent consumption of milk.

Key Concepts

- Uncomplicated gastric reflux is common in infants and generally resolves over time without pharmacological treatment
- In New Zealand, empiric treatment with omeprazole for infant irritability and reflux is increasing, despite the fact that it is not approved for this condition, is unlikely to improve symptoms and the potential adverse effects are largely unknown
- Omeprazole should only be considered for infants in cases of gastro-oesophageal reflux disease (GORD) associated with severe reflux oesophagitis or failure to thrive

Regurgitation

Regurgitation is the appearance of refluxed material in the mouth. Approximately 40% of infants regurgitate at least once a day.[4] In most cases, regurgitation resolves over time without treatment.

Gastro-Oesophageal Reflux Disease (GORD)

Infantile GORD is defined as; symptoms or complications of reflux (non-erosive gastro-oesophageal reflux and erosive oesophagitis) which may include frequent vomiting and regurgitation, poor weight gain, difficulty swallowing, abdominal or substernal pain, oesophagitis and respiratory disorders.[5] GORD is distinct from, and much rarer than normal infant reflux, however, the similarities between the two can lead to confusion. Frequent regurgitation (more than five times a day) and persistent feeding difficulties are the most specific clinical indicators of GORD.[6] Persistent crying is not a reliable indicator of GORD. One study found that only approximately one-sixth of infants presenting with persistent crying had GORD. Furthermore, the severity of irritability did not correlate with the severity of GORD. Cases of persistent crying and GORD, in the absence of frequent regurgitation and feeding difficulties were uncommon.[6]

The initial diagnosis of GORD is based on symptoms and the treatment is frequently empiric, due to a lack of diagnostic tools and inability to communicate directly with the patient.[7] The advantage of this approach is that the need for invasive procedures is avoided, however, using symptom severity as the diagnostic criterion for GORD can result in a significant number of cases of uncomplicated reflux being diagnosed as GORD and receiving unnecessary treatment.[8]

Suggested management plan for irritable, crying infants

Excessive crying and uncomplicated reflux are both common conditions in infants, therefore they often occur simultaneously, without necessarily being related. Primary care practitioners play an important role in providing parental reassurance and advice. In most cases, irritability and uncomplicated reflux resolve by age one year.[6,9] Infants without complications of reflux, who are otherwise well and thriving, do not usually require further investigation and treatment.[10]

Simple advice and reassurance may include the following points:

- Crying generally increases at age two weeks, peaking at around six to eight weeks. As infants age, they generally cry less and sleep for longer periods at night[1]
- Reflux and regurgitation are normal because infants ingest large quantities relative to their stomach size, symptoms usually improve as the infant grows and the digestive system matures
- "Winding" the infant several times during feeds and holding upright after feeds for a short period can improve symptoms – the parent can place the infant over their shoulder or hold the infant upright on the knee
- Placing the baby on their side decreases reflux, however, this is only appropriate when the baby is awake and closely observed, due to the risk of sudden infant death syndrome[11]
- Mothers should be encouraged to persevere with breast feeding
- Feed thickeners (e.g. rice cereal, carob-bean gum, carob-seed flour or carmellose sodium) can be added to expressed milk to reduce vomiting. Thickened formula is also commercially available, although breast feeding is always preferable. The evidence of the effectiveness of either of these treatments is limited.[11]
- Tobacco smoke should be avoided
- Medicines are not recommended

A primary care based study found that two weeks of conservative treatment (feeding modifications, positioning and avoidance of tobacco smoke) improved symptoms in 78% of infants with frequent regurgitation and irritability and symptoms completely resolved in 24% of infants during the study period.[12]

When to refer

Referral to a paediatrician (or paediatric gastroenterologist where available) for diagnostic investigations is indicated when an infant has excessive reflux and:[10]

- A failure of conservative treatment (such as feeding advice). N.B. PPIs and H2-receptor antagonists should not be diagnostically trialled in primary care
- Failure to thrive (see below)
- Suspected oesophagitis due to blood stained vomit, respiratory complications or abnormal posturing or movements
- Diagnostic uncertainty
- Extreme parental anxiety

Failure to thrive is an inability to gain weight in comparison to height. The infant may continue to grow but with reduced weight gain secondary to reduced caloric intake. Poor weight gain requires evaluation of caloric intake and ability to swallow. Failure to thrive is associated with multiple underlying conditions, including GORD.

Omeprazole is not a recommended treatment for reflux or uncomplicated GORD in infants

Omeprazole is a common treatment for gastric reflux in adults, but it is not approved for use in infants aged under one year. The safety, pharmacokinetics and bioavailability of omeprazole in young children is largely unknown.

Although omeprazole is effective at reducing gastric acidity and oesophageal acid exposure in infants, there is significant evidence that it is not effective in treating symptoms attributed to infant reflux or GORD. Two studies investigating the effects of omeprazole on infant irritability and reflux found that, while treatment groups had significantly reduced oesophageal acid exposure, there was no difference in irritability or crying.[15, 16] Similar results have been reported with other proton pump inhibitors (PPIs). Of 162 infants aged one to twelve months, there was no difference in the efficacy of lansoprazole or placebo, in

Investigations for infant GORD

If an infant is referred to secondary care for investigation of possible GORD, the following tests may be used:

Barium swallow: This procedure excludes structural abnormalities such as hiatus hernia, oesophageal atresia, tracheosophageal fistula and malrotation of the upper GI tract. Through imaging the oesophagus, it is possible to observe reflux and in some cases confirm or exclude oesophagitis or dysmotility. The limitation of this technique is that imaging is only possible for approximately five minutes therefore episodes of reflux may be missed.

pH monitoring: Performed over 24 hours, this technique is more reliable than a barium swallow at detecting reflux and is used when:

- Frequent reflux is suspected without regurgitation
- Apnoea is suspected to relate to undetected reflux
- Unexplained respiratory symptoms are thought to be related to undetected reflux
- Before or after surgery to correct reflux

Endoscopy and oesophageal biopsy: Used infrequently, these procedures are useful for diagnosing oesophagitis, but cannot detect mild reflux. They are considered when there is pain and irritability associated with an uncertain diagnosis, a poor response to treatment or GI blood loss.

Cows' milk allergy?

Cow's milk protein allergy (CMPA) is an immunologically mediated adverse reaction to cow's milk protein. The reaction can be IgE or non-IgE mediated and occurs in approximately 2% of infants aged under two years. It is estimated that CMPA is the underlying cause in up to 40% of infants referred for specialist management of GORD.[13]

CMPA is a cluster of syndromes which may include:[14]

- Immediate allergic reaction, anaphylaxis and food protein-induced enterocolitis
- Gastrointestinal syndromes such as CMPA induced GORD, constipation, enteropathy and allergic eosinophilic gastroenteritis
- Food protein-induced proctocolitis
- Eosinophilic oesophagitis

As many of these syndromes have overlapping symptoms, diagnosis can be difficult. However, eczema and a family history of atopy increase the risk of CMPA. Complete elimination of cow's milk from the diet (or the mothers diet if breast feeding) for two to three weeks and observing if symptoms resolve will usually confirm suspected cases.

For further information see: "Allergy to cow's milk protein and the appropriate use of infant formula", BPJ Special Edition (May, 2011).

alleviating symptoms attributed to GORD, including; crying, regurgitation, feeding difficulties, back arching, coughing and wheezing.[7]

Omeprazole is therefore not recommended for treating irritability, reflux or uncomplicated GORD. Omeprazole should only be considered in cases of severe infantile reflux oesophagitis or if GORD is causing complications such as failure to thrive. The decision to prescribe would usually be made in consultation with a paediatrician or gastroenterologist. Even in these circumstances, the administration of a PPI is unlikely to reduce the frequency of crying and gastric reflux.[17]

How is omeprazole given to infants when required?

In most cases, initiation of omeprazole treatment in infants should occur in secondary care with pharmacist and paediatric advice on the most appropriate delivery method. An appropriate dose of omeprazole for an infant is: 5 mg once daily for children weighing under 10 kg and 10 mg once daily for children weighing between 10 and 20 kg.[10]

Omeprazole suspension is extemporaneously compounded by mixing capsule contents into sodium bicarbonate solution (8.4%) and water, normally to a concentration of 2 mg/mL. The suspension should be stored in the refrigerator and discarded after 15 days.[18] There is some evidence to suggest that absorption of this formulation of omeprazole is incomplete.[20] In addition, infants often find the taste of this suspension unpleasant.[19]

An alternative preparation for infants involves sprinkling half the contents of a 10 mg capsule on a small quantity of apple or pear puree.[20] However, it is difficult to achieve an accurate dose with this method and care needs to be taken that the infant is able to swallow the mixture safely.

Omeprazole capsules and tablets should not be chewed, or dissolved in milk or carbonated water, as this can degrade the enteric coating.

Adverse effects of PPI treatment

PPIs are generally well tolerated in adults. Uncommon adverse effects include acute interstitial nephritis, hypomagnaesaemia and hypocalcaemia.[21] Little is known about the adverse effects of using PPIs in infants. The most commonly reported adverse effects of PPIs in children are headaches, nausea diarrhoea and skin rash.[22, 23]

Gastric acid plays an important role in both defending the body from foreign microflora and in regulating gastrointestinal microflora composition. Reducing acid secretion increases the likelihood of foreign microflora proliferation. A study of 186 children aged between four and 36 months, found that gastric acid inhibitors were associated with an increased risk of gastroenteritis and community acquired pneumonia, which persisted for at least two months following treatment.[24] Serious adverse effects, in particular lower respiratory tract infections, were also more frequent in infants symptomatic for GORD who were treated with lansoprazole compared to placebo controls.[7]

There are also suggestions that PPI use can cause rebound acid secretion resulting in PPI dependency. A study of 120

How much omeprazole is being prescribed to infants in New Zealand?

Between 2006 and 2010, the number of prescriptions of omeprazole dispensed for infants aged under one year in New Zealand increased from 4650 to 8231. The largest increases occurred in the age zero to three months (111%) and four to six months (80%) cohorts.

This increase is despite a lack of evidence to support the prescribing of omeprazole to infants for symptoms such as irritability and regurgitation associated with uncomplicated reflux. Omeprazole should only be considered in cases of severe infantile reflux oesophagitis or in cases of GORD accompanied with failure to thrive.

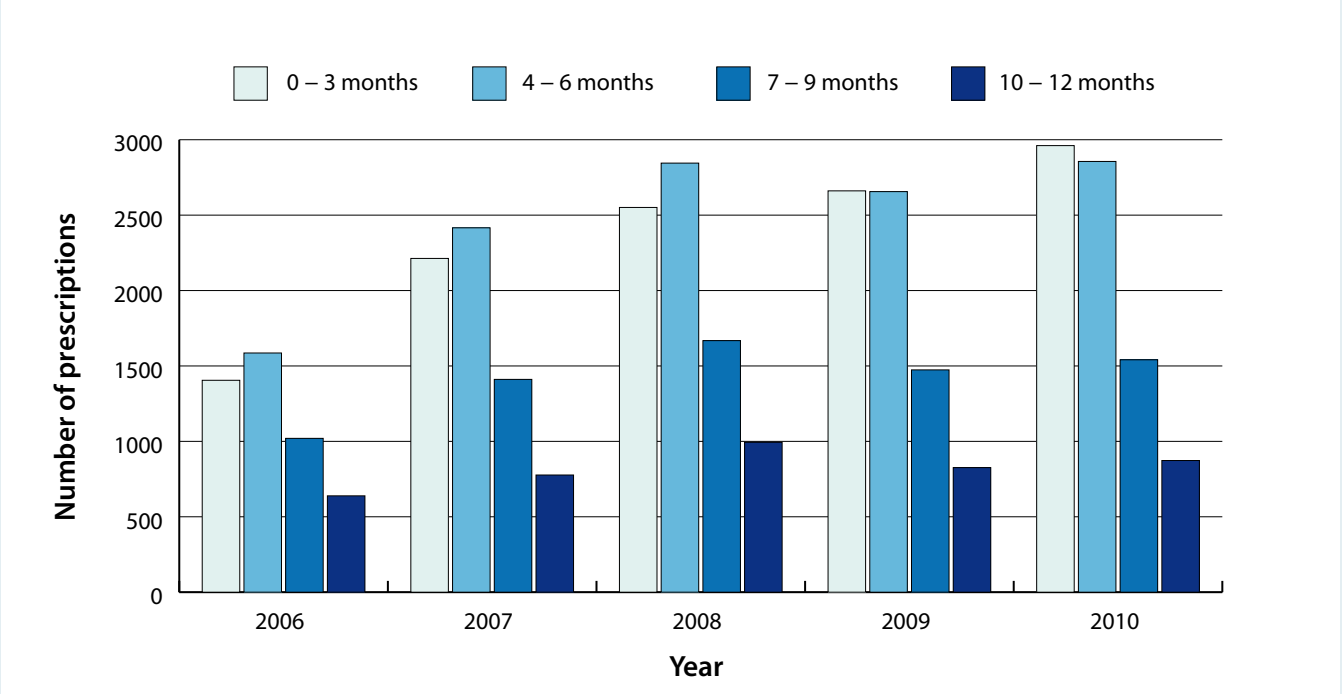


Figure 1: Number of omeprazole prescriptions dispensed in New Zealand from 2006 to 2010 for infants aged zero to three, four to six, seven to nine and ten to 12 months

adults with no history of acid related symptoms, found that more than 40% of subjects developed such symptoms following an eight week course of PPI treatment.[25] It is unknown if such an effect also occurs in infants.

It has also been speculated that PPI mediated reductions in gastric acidity and digestion, may increase the permeability of gastric mucosa to some food allergens, potentially increasing the risk of food allergy and eosinophilic esophagitis.[26]

The absence of long-term data concerning the safety of PPIs in treating infants, combined with reports of serious adverse effects, regardless of frequency, suggests that PPIs should only be prescribed to infants when the benefit outweighs any potential risks.

Granny told mother and mother told me... Is gripe water useful?

Gripe water is a traditional remedy that is used by parents for infants with reflux, colic and various other ailments. Formulations may contain alcohol, bicarbonate, sucrose, ginger, dill, fennel and chamomile. There is no evidence that gripe water is clinically effective for any of the conditions it is claimed to relieve. If parents wish to trial gripe water for their infant, they should be advised to avoid formulations that contain alcohol or sugars.

Blumenthal I. The gripe water story. J R Soc Med 2000;93:172-4.

Alternative pharmacological options for reflux and GORD in infants

Alginates such as a mixture of sodium alginate and magnesium alginate (Gaviscon infant) reduce acidity and reflux through increasing the viscosity of gastric contents. They can be used to relieve symptoms of regurgitation or reflux in infants. Alginates should not be used in infants at risk of dehydration (e.g. acute vomiting or diarrhoea) or intestinal blockage due to reports of constipation. Gaviscon infant powder is available in sachets. For infants weighing < 4.5 kg, use one sachet mixed into each feed, and two sachets for infants weighing > 4.5 kg.[10] Infants should not be given this medicine more than six times in a 24 hour period. Unlike adult versions of the medicine, Gaviscon infant does not contain bicarbonate frothing agents or aluminium hydroxide.

Histamine receptor antagonists such as ranitidine reduce histamine induced gastric acid and pepsin release. Ranitidine has been shown to be effective in the treatment of some cases of oesophagitis in children,[27] and is associated with a low incidence of adverse effects. However, as with omeprazole, there is no evidence to support empiric treatment of infants with symptoms of irritability and reflux. In New Zealand, ranitidine is not registered for use in children aged under eight years and discussion with a paediatrician is recommended before prescribing this medicine to an infant. Ranitidine is available in a syrup formulation that can be administered to infants at a dose of 2 to 4 mg/kg, two times daily.[10] N.B. ranitidine syrup contains 7.5% w/v ethanol.

Antacids such as magnesium hydroxide and aluminium hydroxide reduce gastric pH, but cases of elevated plasma aluminium levels in infants combined with a lack of data to confirm efficacy means that these medicines are not recommended for use in infants.[28]

Prokinetics such as metoclopramide and domperidone are not recommended for use in infants and there is little evidence of their effectiveness in the management of GORD.[26]

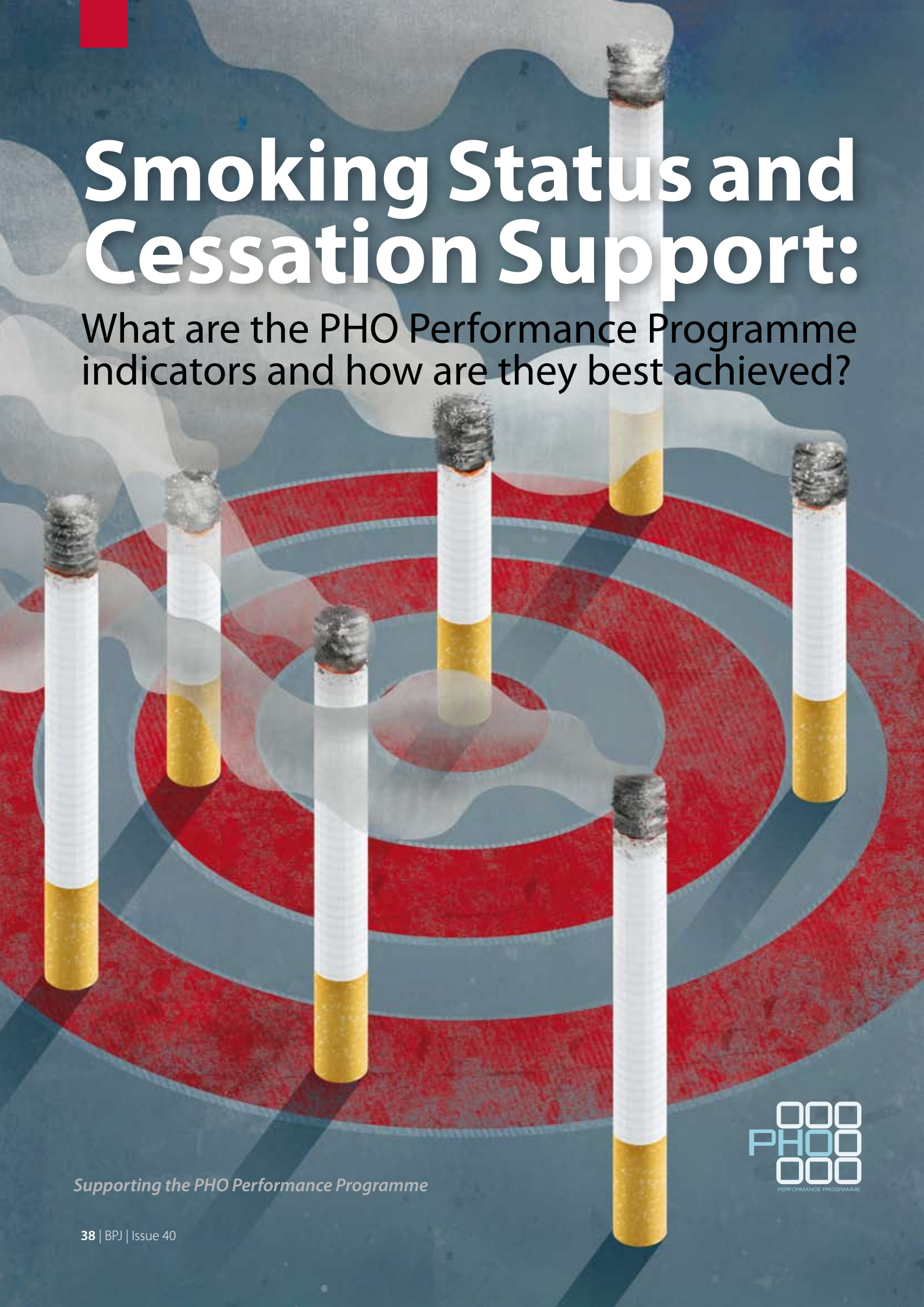
ACKNOWLEDGEMENT Thank you to **Associate Professor David Reith**, Paediatrics & Child Health, Dunedin School of Medicine, University of Otago, **Dr Chris Leathart**, General Practitioner, Christchurch and **Dr Anna Alderton**, General Practitioner and Clinical Facilitator, Pegasus Health for expert guidance in developing this article.

References

1. Michelsson K, Rinne A, Paajanen S. Crying, feeding and sleeping patterns in 1 to 12-month-old infants. Child: care, health and development 1990;16:99-111.
2. Hiscock H, Jordan B. Problem crying in infancy. Med J Aust 2004;181(9):507-12.
3. Vandenplas Y, Hassall E. Mechanisms of gastroesophageal reflux and gastroesophageal reflux disease. J Pediatr Gastroenterol Nutr 2002;35(2):119-36.
4. Orenstein SR. Infantile reflux: different from adult reflux. Am J Med 1997;103:114S-19S.
5. North American Society for Pediatric Gastroenterology and Nutrition (NASPGN). Pediatric reflux clinical practice guidelines. J Pediatr Gastroenterol Nutr 2001;32(Suppl. 2):S1-S31.
6. Heine R, Jordan B, Lubitz L, et al. Clinical predictors of pathological gastro-oesophageal reflux in infants with persistent distress. J Paediatr Child Health 2006;42(3):134-9.
7. Orenstein S, Hassall E, Furmaga-Jablonska W, et al. Multicenter, double-blind, randomized, placebo-controlled trial assessing the efficacy and safety of proton pump inhibitor lansoprazole in infants with symptoms of gastroesophageal reflux disease. Pediatrics 2009;154(514-20).
8. Finkel Y. Am I a heretic if I don't believe in GERD? J Pediatr Gastroenterol Nutr 2006;43:3-4.
9. Fike F, Mortellaro V, Petitford J, et al. Diagnosis of gastroesophageal reflux disease in infants. Pediatr Surg Int 2011;27:791-7.
10. Starship Children's Health. Gastro-oesophageal reflux 2007. Available from: www.starship.org.nz/clinical-guidelines/ (Accessed Oct, 2011).
11. BMJ. Best Practice: Disorders of infant feeding 2011. Available from: www.bestpractice.bmj.com (Accessed Oct, 2011).
12. Orenstein SR, McGowan JD. Efficacy of conservative therapy as taught in the primary care setting for symptoms suggesting infant gastroesophageal reflux. J Pediatr 2008;152(3):310-4.
13. Kemp AS, Hill D, Allen K, et al. Guidelines for the use of infant formulas to treat cow's milk protein allergy; An Australian consensus panel opinion. Med J Aust 2008;188(2):109-12.
14. Allen KJ, Davidson GP, Day AS, et al. Management of cow's milk protein allergy in infants and young children: An expert panel perspective. J Paediatr Child Health 2009;45:481-6.
15. Moore D, Tao B, Lines D, et al. Double-blind placebo-controlled trial of omeprazole in irritable infants with gastroesophageal reflux. J Pediatr 2003;143:219-23.
16. Omari T, Haslam R, Lundborg P, Davidson G. Effect of omeprazole on acid gastroesophagel reflux and gastric acidity in preterm infants with pathological acid reflux. J Pediatr Gastroenterol Nutr 2007;44(1):41-4.
17. Van der Pol R, Smits M, van Wijk M, et al. Efficacy of proton-pump inhibitors in children with gastroesophageal reflux disease: a systematic review. Pediatrics 2011;127(5):925-35.
18. HealthCare Otago. Formulation in pharmacy practice. Dunedin: HealthCare Otago, 1993.
19. Sharma V.K, Peyton B, Spears T, et al. Oral pharmacokinetics of omeprazole and lansoprazole after single and repeated doses as intact capsules or as suspensions in sodium bicarbonate. Aliment Pharmacol Ther 2000;14:887-92.
20. Pegasus Health. Irritable infants - reflux and constipation GP Small Group Education. Pegasus Health, 2011.
21. Oh S. Proton pump inhibitors. Aust Fam Phys 2011;40(9):705-8.
22. Hassall E, Kerr W, El-Serag H. Characteristics of children receiving proton pump inhibitors continuously for up to 11 years duration. J Pediatr 2007;150(3):262-7.
23. James L, Walson P, Lomax K, et al. Pharmacokinetics and tolerability of rabeprazole sodium in subjects aged 12 to 16 years with gastroesophageal reflux disease: an open-label single and mulitple-dose study. Clin Ther 2007;29(9):2082-92.
24. Canani R, Roggero P, Romano C, et al. Therapy with gastric acidity inhibitors increases the risk of acute gastroenteritis and community-acquired pneumonia in children. Pediatrics 2007;117(5):e817-20.
25. Reimer C, Sondergaard B, Hilsted L, Bytzer P. Proton-pump inhibitor therapy induces acid-related symptoms in healthy volunteers after withdrawal of therapy. Gastroenterology 2009;137:80-7.
26. Merwat S, Spechler S. Might the use of acid-suppressive medications predispose to the development of eosinophilic esophagitis? Am J Gastroenterol 2009;104:1897-902.
27. Tighe M, Afzal N, Bevan A, Beattie M. Current pharmacological management of gastro-esophageal reflux in children. Pediatr Drugs 2009;11(3):185-202.
28. BMJ Group. BNF for children: 2010-2011.London: BMJ Publishing Group and Royal Pharmaceutical Society of Great Britain, 2010.

Smoking Status and Cessation Support:

What are the PHO Performance Programme indicators and how are they best achieved?



Supporting the PHO Performance Programme

Programme objectives

The PHO Performance Programme has now been running for five years. It was established to pursue two primary objectives:

1. To encourage and reward improved performance by PHOs in line with evidence based guidelines
2. To measure and reward progress in reducing health inequalities by including a focus on high need populations

PHOs receive performance based payments which are linked to key performance indicators. These indicators are reviewed annually and adjusted to take into account factors which may vary from region to region, such as age and ethnicity. The indicators which have been funded since 1 July are shown in Table 1.

Smoking status recorded

The purpose of the smoking status indicator is to encourage health providers to ask about and record the smoking status of their patients.[1]

Targets and funding

The PHO Performance Indicator and target is: For at least 90% of the number of enrolled people aged 15 to 74 years to have had their smoking status recorded.[1]

Recording of smoking status accounts for 7% of a PHO's performance payment, with 5% allocated for achieving the target in the high needs population,* and 2% for achieving the target amongst the rest of the population.[1]

* High needs is defined as Māori and Pacific peoples and people living in New Zealand deprivation decile 9 or 10 socioeconomic areas (most deprived).

Table 1: Funded PHO Performance Indicators with annual weighting for the period commencing 1 July, 2011[1]

Chronic conditions	Cervical cancer screening	9%
	Breast cancer screening	6%
	Ischaemic cardiovascular disease detection	9%
	Cardiovascular disease risk assessment	20%
	Diabetes detection	9%
	Diabetes follow-up after detection	9%
	Smoking status	**7%**
	Smoking advice and/or cessation support	**13%**
Infectious disease	Influenza vaccine in people aged over 65 years	9%
	Age appropriate vaccinations for children aged two years	9%

How is it calculated?

The number of people enrolled in the PHO who have ever had a smoking status recorded (numerator) is divided by the number of people enrolled aged 15 to 74 years within the PHO (denominator).

How should smoking status be recorded?

In order for smoking status records to be retrieved from the Practice Management System (PMS) an appropriate Read code needs to be entered (Table 2).

How to achieve the target

The recording of smoking status can be achieved simply. For this reason, it is important that every practice meets the performance target in order for the PHO to receive maximum funding. A simple routine of checking and if necessary recording or updating the patient's current smoking status, at the start of every consultation is all that is required.

Table 2: Read codes for smoking status[2]

Category	Read code
Never smoked tobacco	1371
Current smoker status	1372–137S (excluding 137D, 137E and 137I)
Tobacco dependence	E251.
Smoking history	ZPSA.

Smoking advice and cessation support

This indicator was funded in July 2011 for the purpose of prompting providers to give brief advice to stop smoking to all current smokers, and to provide evidence-based cessation support. There is a natural progression between the two smoking indicators. Once smoking status has been recorded, where applicable, a discussion can be initiated on smoking behaviour and smoking cessation following the ABC format (see below).

Targets and funding

The PHO Performance Indicator and target is: For at least 90% of enrolled patients, who are current smokers and have been seen in general practice, to have been given brief advice and/or provided with cessation support in the last 12 months.[1]

A minimum threshold applies

The smoking advice and cessation support indicator is categorised as phase two. Once 70% of the eligible population has had their smoking status coded, funding is then made available to the PHO.

When a PHO is eligible for funding the weighting is 13%, with 9% allocated for high needs and 4% for the rest of the population.

What qualifies as brief advice and cessation support?

Brief advice: Any documentation that a patient who currently smokes was advised to stop smoking. In many cases this will take the form of consultation notes relating to a smokers willingness to quit. If any offer of cessation support – whether it was accepted or refused - is documented then it is considered brief advice to quit was also given.

Cessation support: Any referral made to a smoking cessation support programme, prescribing of nicotine replacement therapy (NRT) and/or smoking cessation

pharmacotherapy, or provision of behavioural support either face to face or via the telephone.

How is it calculated?

The number of enrolled patients with a smoking status of current smoker recorded within the last 15 months, that have been given smoking advice and/or cessation support in the last 12 months (numerator) is divided by the denominator. The denominator is the number of enrolled people in the PHO who have had a smoking status of current smoker in the last 15 months, adjusted to account for the number of people aged 15 to 74 years expected to have presented to general practice in the last 12 months.

How should brief advice and cessation support be recorded?

To allow information to be extracted from a PMS an appropriate Read code must be entered for every patient who is given smoking advice and offered cessation support (Table 3).

How to achieve to the targets with the ABC

New Zealand guidelines recommend that smoking cessation advice should be strongly and repeatedly recommended to all people who smoke.[3] The ABC is an evidence-based, best practice smoking cessation intervention promoted for use in general practice. The aim is to gather information in order to provide advice and support to the patient.

A = **A**sk the patient about their smoking

B = Give **b**rief advice to quit

C = Offer evidence based **c**essation support

Health professionals are encouraged to use their judgement when implementing the ABC. Strategies that are personally relevant and emphasise the benefits to the patient and their family are more likely to be effective.

Table 3: Read codes included for brief advice to stop smoking and smoking cessation support or referral[2]

Brief advice to stop smoking	Read code
Health education – smoking	6791.00
Brief cessation advice given	ZPSB10
Patient refused cessation support	ZPSC90
Smoking cessation support or referral	
Referral to cessation support	ZPSC10*
Prescribed cessation medication	ZPSC20*
Provided cessation behavioural support	ZPSC30*

* If a brief advice to stop smoking Read code is not entered, however, a smoking cessation support or referral Read code is, then, it will automatically be assumed that brief advice to stop smoking has been given.

The benefits of participation

The proportion of smokers in New Zealand declined from 24.4% in 2006 to 21.8% in 2009.[4] In order to continue this trend it is important that primary care continues to push the "quit smoking" message. It is known that advice from a health professional increases the likelihood of a person quitting smoking.[5] In addition, providing appropriate access to resources such as nicotine replacement therapy (NRT), pharmacotherapy and specialist counselling services has been shown to further increase the chances of success of any quit attempt.[5]

A focus on smoking cessation

Case Study 1

A 20 year old female presents for a routine visit. The patient has a two-year-old child and she mentions that she is pregnant again. As part of a general health assessment, you ask her about her smoking status, she confirms she still smokes and her flatmates smoke. She is very reluctant to try to quit as she believes that smoking is safer for her baby than taking "chemicals" like NRT.

The risks of smoking while pregnant far outweigh any risk that NRT treatment presents. The adverse effects of smoking while pregnant include low birth weight, pre-term delivery, childhood respiratory disease and attention deficit hyperactivity disorder. In particular, children exposed to cigarette smoke in the womb are at much higher risk from sudden infant death syndrome (SIDS). Compared to smoking, NRT results in the foetus being exposed to less nicotine.

It is recommended that NRT products such as gum, lozenges, sublingual tablets and inhalers are used in preference to patches, as the amount of nicotine delivered is less.[6] NRT is available at a subsidised rate to the patient of $3 for an eight week supply through Quitline, a Quit Card provider or on prescription from a General Practitioner.

There is insufficient evidence to recommend the use of nortriptyline, bupropion or varenicline to women who are pregnant.[6]

It is important that this patient is given the opportunity to benefit from education, support, cessation strategies and NRT at a time when her foetus is particularly vulnerable to the harmful effects of smoking. Highlighting the benefits that her and her family would gain by quitting may motivate the mother to quit. These benefits include:

- Presenting a positive role model to her children of a parent who does not smoke will reduce the chances that her children will smoke
- Improving the health outcomes for her baby through reduced risk of still birth, postnatal complications and SIDS
- Improving the health of her children through reduced risk of asthma and bronchial complications
- Increasing the family's ability to save money
- Improving the patient's health
- Reducing the risk of dying early

It can often be worthwhile reminding patients that although it is nicotine which causes the addiction, it is the >5000 compounds that are inhaled during smoking that damages the body.[7] NRT in comparison is relatively harmless.

Case Study 2

A 56 year old Māori male patient has recently had a heart attack (15 days ago). He has been discharged from hospital and has not smoked since. The patient is now highly motivated to stop smoking completely. You discuss the range of treatment options available to the patient.

Often highly motivated people will want to quit by "going cold turkey". It is important that these people understand that this is one of a number of options available – it is also the least likely to succeed.[6] A good idea is to discuss the potential for a relapse with people considering quitting by "cold-turkey". One possibility for a person who wishes to avoid medication, is to prescribe NRT and to advise use only if they are strongly tempted to smoke again.

NRT can be safely used by almost anyone who wants to quit smoking. NRT approximately doubles a person's likelihood of quitting and is an appropriate cessation aid for this patient.[6] There is no evidence that one NRT product is more effective than any other and patient preference should be the primary consideration in treatment choice. However, heavier smokers do benefit from a higher steady-state dose (e.g. 24 hour 21 mg patches and 4 mg gum). Nicotine, by itself, is not a risk factor for cardiovascular disease (CVD) or acute cardiovascular events. Oral NRT is the preferred treatment option in this circumstance as nicotine levels can be reduced more rapidly if complications arise.[8]

Both bupropion and varenicline can be safely prescribed following a serious cardiovascular event. The possible adverse effects of these medicines need to be balanced against the risk of the patient relapsing into smoking. Uncommon cardiovascular adverse effects of varenicline include atrial fibrillation and palpitations.[9] The possible adverse cardiovascular effects of bupropion include; tachycardia, palpitations, vasodilation, postural hypotension, hypertension (severe in some case), flushing and syncope.[9]

Varenicline is available under Special Authority and in order to qualify, amongst other criteria, patients must first have made two or more unsuccessful quit attempts using NRT, or a failed attempt with bupropion or nortriptyline. Patients considering varenicline, particularly those with a history of mental illness, need to be advised of the possibility of personality and mood disorders developing, including suicidal ideation (see Case study 3).

Nortriptyline is contraindicated during the acute recovery period following myocardial infarction. Known adverse effects of nortriptyline include; hypotension, hypertension, tachycardia, palpitation, myocardial infarction, arrhythmias, heart block and stroke.[10]

The assistance of cessation support services such as Quitline, also increase the chances of becoming smoke-free. When cessation support is combined with NRT a person is four to five times more likely to quit.[6] Smoking cessation services available include:

- Quitline Ph. 0800 778 778 six days a week. For further information see: **www.quit.org.nz**
- Aukati Kai Paipa a service provided by Māori health providers for Māori who smoke. For further information see: **www.tehotumanawa.org.nz**
- DHBs and practices which have implemented their own cessation services

Case Study 3

A 53 year old man with depression who smokes 30 cigarettes a day is currently taking fluoxetine and attending counselling sessions. The patient is now motivated to make further changes in his life.

New Zealand guidelines report that quitting smoking does not worsen a mental health disorder, although close monitoring of a patient's mental health status is advised whenever behavioural changes are undertaken.[5] Given that the patient appears motivated, his depression is likely to be well controlled and counselling sessions are likely to reduce the impact his quit attempt might have on his depression. However, it would be advisable to ask about the frequency of counselling and confirm that the patient will also be supported by family and friends.

Smoking is known to induce some liver enzymes (e.g. CYP 1A2). When people stop smoking, some medicines are

metabolised more slowly and dosages may need to be reduced. Medicines that may be metabolised at different rates when a person quits smoking include; clozapine, olanzapine, chlorpromazine, imipramine and haloperidol.

For an extensive list of medicines affected by smoking (or cessation) see Appendix 9 of the New Zealand smoking cessation guidelines.[6]

The rate of smoking among people with mental health disorders is higher than the rest of the population. This group also appear to benefit from more intensive cessation interventions such as multi-session support.[6]

NRT can be safely used to assist people who have a history of mental illness to quit smoking, and in general, should be considered first line treatment for this patient group.

Caution is advised when prescribing nortriptyline, bupropion or varenicline to patients with a history of mental illness due to the potential effect on the underlying condition, adverse effects and possible interactions with other medicines. N.B. in the present scenario, fluoxetine does not have any clinically significant interaction with smoking cessation medicines.

Nortriptyline is contraindicated in patients taking other tricyclic antidepressants or monoamine oxidase inhibitors (MAOI), due to an increased risk of serotonin syndrome.[10] Bupropion is contraindicated in patients taking MAOIs and a minimum of 14 days needs to elapse between discontinuation of a MAOI and the beginning of bupropion treatment.[11] Bupropion and to a lesser extent nortriptyline may cause adverse effects in patients with a low seizure threshold.[11]

Varenicline has been associated with increased suicidal ideation. Patients taking this medicine (and their families), must be told of the need to monitor for serious changes in thoughts or behaviour, including; anxiety, psychosis, mood swings, agitation, aggression, depression and suicidal ideation. Further studies are required to understand the effect of varenicline in patients with serious psychiatric illnesses such as schizophrenia, bipolar disorder and major depressive disorder.[9]

For further information see “Smoking cessation – pharmacological therapy”, BPJ 20 (Apr, 2009).

References

1. DHBNZ. PHO Performance programme. Indicator definitions as at 1 July 2011. Version 5.3. Available from: www.dhbnz.org.nz (Accessed Sep, 2011).

2. DHBNZ. Code mappings for data transfer specification and clinical performance indicator data format standard document. Version 0.6. Available from: www.dhbnz.org.nz (Accessed Sep, 2011).

3. New Zealand Guidelines Group. New Zealand Cardiovascular Guidelines Handbook: a summary resource for primary care practitioners. Available from: www.nzgg.org.nz (Accessed Sep, 2011).

4. Ministry of Health. Tobacco use in New Zealand: Key findings from the 2009 New Zealand tobacco use survey. Wellington: Ministry of Health, 2010.

5. Stead LF, Bergson G, Lancaster T. Physician advice for smoking cessation. Cochrane Database Syst Rev 2008;2:CD000165.

6. Ministry of Health. New Zealand smoking cessation guidelines. 2007. Available from: www.moh.govt.nz (Accessed Sep, 2011).

7. Rodgman A, Perfetti TA, The chemical components of tobacco and tobacco smoke. CRC press, Florida, USA ,2009.

8. McRobbie H, Hajek P. Nicotine replacement therapy in patients with cardiovascular disease: guidelines for health professionals. Addiction 2001;96 (11) 1547-51.

9. Pfizer New Zealand Ltd. Champix (Varenicline as tartrate). Medicine Datasheet. 2009. Available from: www.medsafe.govt.nz (Accessed Sep, 2011).

10. Mylan New Zealand Ltd. Norpess (Nortriptyline). Medicine Datasheet. 2010. Available from: www.medsafe.govt.nz (Accessed Sep, 2011).

11. GlaxoSmithKline NZ Limited. Zyban (Bupropion hydrochloride). Medicine Datasheet. 2010. Available from: www.medsafe.govt.nz (Accessed Sep, 2011).

"The capacity to blunder slightly is the real marvel of DNA. Without this special attribute, we would still be anaerobic bacteria and there would be no music." — Lewis Thomas

Improve patient safety by sharing solutions and prevent these incidents from occurring again. Report patient safety incidents here:

www.bpac.org.nz/safety

Health literacy: a focus for the Health Quality & Safety Commission

Over half of New Zealand's adult population is believed to have difficulty understanding and interpreting health information. This includes four out of five Māori males and three out of four Māori females.[1]

Dr Janice Wilson, the Health Quality & Safety Commission's Chief Executive, believes this could be creating barriers to health care and putting the welfare of some health care consumers at risk.

"Health providers could be offering the best care in the world but if people don't understand their treatment plans or how to take their medication, that care could be compromised."

People's ability to understand and interpret health concepts, terminology and processes is known as "health literacy" and is recognised as an important determinant of an individual's ability to access quality health care.

Dr Wilson says the concept of health literacy is relatively new to New Zealand but very pertinent in today's complex health environment.

"What we mean by health literacy is the degree to which individuals can obtain, process and understand the health information they need to make appropriate health decisions."

"The Commission recognises the value of health literacy in delivering safe and quality health care, and will incorporate this thinking into our work."

The New Zealand Guidelines Group (NZGG) was recently contracted by the Commission to conduct a survey to find out how health providers are catering for patients with poor health literacy skills, in the area of medicine safety.

A range of health providers were asked to identify any initiatives being undertaken within their organisations, or at a regional or national level, which they felt addressed health literacy in the area of medication safety.

The *Health Literacy and Medication Safety* report found that most organisations supplied written resources and dedicated websites relating to medicine safety, but few did anything else to address the needs of patients who may be challenged by traditional forms of communication.

Researchers found only seven examples where organisations had deliberately intervened to address health literacy in the area of medicine safety.

These interventions were:

- A project being led by Mauri Ora Associates for the Ministry of Health (including a health literacy module developed by Workbase) that aims to increase cultural competence and health literacy awareness amongst health care practitioners and other professional bodies throughout New Zealand

1. Ministry of Health. Korero Marama: Health Literacy and Māori. 2010. Available from: www.moh.govt.nz/moh.nsf/indexmh/korero-marama-health-literacy-Māori-feb2010 (Accessed Oct, 2011)

HEALTH QUALITY & SAFETY COMMISSION NEW ZEALAND

Kupu Taurangi Hauora o Aotearoa

- The efforts of Ngaruawahia pharmacists, Mary and Steve Roberts, in addressing poor health literacy among the lower-socio economic communities they serve
- The use of DHB-funded Medication Utilisation Reviews, which use trained pharmacists to assist at risk patients to use appropriate medicines to manage their conditions
- The Workbase initiative, which uses a dedicated website to raise awareness of health literacy, especially amongst health care providers and health care organisations
- The Auckland University/Workbase international research project aimed at strengthening health literacy among Māori and Pacific people living with cardiovascular disease
- The joint health education venture between PHARMAC, Mauri Ora Associates and the Māori Pharmacists Association to increase awareness and understanding amongst Community/Māori Health Workers of the appropriate use, storage and disposal of medicines
- The emerging shift in emphasis of the Heart Foundation from using mainly written materials to employing more interactive resources which focus on patient's understanding of their heart condition and the medications required to manage it

These organisations have made a conscious effort to use adult learning concepts and to employ interactive communication methods, often including graphics and animation. However, the report revealed that the use of such tools certainly was not the norm.

"Much of the health sector appears largely unaware of the relevance of adult learning theory to health literacy (in either medicines safety or more broadly). For all patient-mediated self-management (such as taking medicines), an ability of health professionals routinely to create effective learning opportunities for patients in the course of meeting health needs appears underdeveloped."

The report has a list of recommendations on how the Commission can work towards improving levels of health literacy, particularly among Māori and Pacific peoples, and encourage health providers to develop innovative ways to communicate when health literacy is an obstacle.

Dr Wilson says there is little published data available on health literacy specific to New Zealand and the report provides valuable insights into an important emerging issue.

"We need to recognise that traditional communication methods don't work for all our patients and to constantly ask ourselves what we can do to simplify, de-jargonise and package information better. The Health Quality & Safety Commission will certainly be addressing these big questions which are central to the delivery of safe and high quality health care."

The full report is available on the Commission's website: **www.hqsc.govt.nz**

Treating candidiasis of the breast in a woman who is breast feeding

Dear Editor,

I have a female patient who is taking oral sporanox (itraconazole) for presumed candidiasis of the breast – she is continuing to breastfeed her seven-month-old baby while taking it. I initially prescribed it intending it to be a short course but she has kept asking for repeat prescriptions as she says that as soon as she stops it, the symptoms recur. She had been referred to the breast clinic for advice and they apparently told her it was "not their area" and suggested she see me. She is paying for it herself so I have not needed to involve a specialist. She is now asking if she can have a month's worth at a time with repeats. She wants to continue feeding for as long as she can. Please can you advise me whether this is safe?

General Practitioner, Wellington

Itraconazole is excreted in small amounts in breast milk, so it is recommended to avoid if possible during breast feeding. Fluconazole is also present in breast milk, but in amounts unlikely to cause harm, so it is preferred in breast feeding if an oral azole antifungal must be used.[1, 2] If itraconazole is used for more than one month, liver function needs to be monitored as it can cause hepatotoxicity.[2]

To manage candida infection of the breast, the mother and baby should be treated simultaneously. For the mother the first line option is miconazole 2% cream applied to the nipples after each feed with the excess wiped off before the next feed. This should be continued for two weeks.[3, 4] Miconazole oral gel applied four times daily is recommended for the infant.[4]

If symptoms do not improve or worsen during treatment, oral fluconazole is the next appropriate option for the mother. Fluconazole is given as a 150–300 mg single dose, followed by 50–100 mg, twice daily, for ten days.[4] Topical treatment for both the mother and the child should be continued at the same time.

If symptoms still persist, it would be appropriate to refer the patient to a specialist in the area which may be a lactation consultant.

During treatment for candidiasis of the breast, the patient can be advised to:

- Continue to breastfeed
- Wash hands frequently, especially after nappy changes
- Wash and sterilise dummies, teats, nipple shields and toys that are put in the infants mouth

Given the persistence of symptoms, it may be appropriate to re-think the diagnosis of candidiasis. Symptoms of candida infection of the breast include; intense pain (often described as deep shooting pain) after a period of pain-free breastfeeding, pain in both nipples or breasts, and pain after feeds or beginning near the end of a feed. These symptoms are not accompanied by pyrexia or inflamed areas of the breasts as in mastitis.[5]

It is difficult to confirm a *Candida* infection of the breast. One study compared a group of breastfeeding women with sore, inflamed or traumatized nipples or intense stabbing

or burning pain in their breasts with breastfeeding women without symptoms. They found that *Candida* species could not be cultured from either group suggesting that *Candida* infection is not present in milk ducts.[6] Despite this, based on the presence of symptoms, treatment is often effective and allows the mother to continue breastfeeding.[3]

Differential diagnoses for pain in the nipples and breasts include:[3]

- Feeding issues e.g. incorrect attachment, tongue tie in the infant (unlikely to be the cause in the present case given the mother has been breastfeeding for seven months)
- Eczema, including a reaction to creams or breast pads
- Raynaud's disease of the nipple
- A blocked duct which may appear as a white spot at the end of the nipple
- Bacterial infection (may be present at the same time as candida infection)

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

References:

1. Australian Medicines Handbook (AMH). Adelaide; AMH Pty Ltd, 2011.
2. British National Formulary (BNF). BNF 62. London: BMJ Publishing Group and Royal Pharmaceutical Society of Great Britain, 2011
3. The Breastfeeding Network. Thrush and breastfeeding. 2009. Available from: www.breastfeedingnetwork.org.uk (Accessed Oct, 2011).
4. Clinical Knowledge Summaries (CKS). Breastfeeding problems. CKS, 2011. Available from: www.cks.nhs.uk (Accessed Oct, 2011).
5. Jones W, Breward S. Thrush and breastfeeding. Community Pract 2010;83(10):42-3
6. Hale TW, Bateman TL, Finkelman MA, Berens PD. The absence of Candida albicans in milk samples of women with clinical symptoms of ductal candidiasis. Breastfeed Med 2009;4(2):57-61

visit us at **www.bpac.org.nz**

Call us on **03 477 5418** Email us at **editor@bpac.org.nz** Freefax us on **0800 27 22 69**