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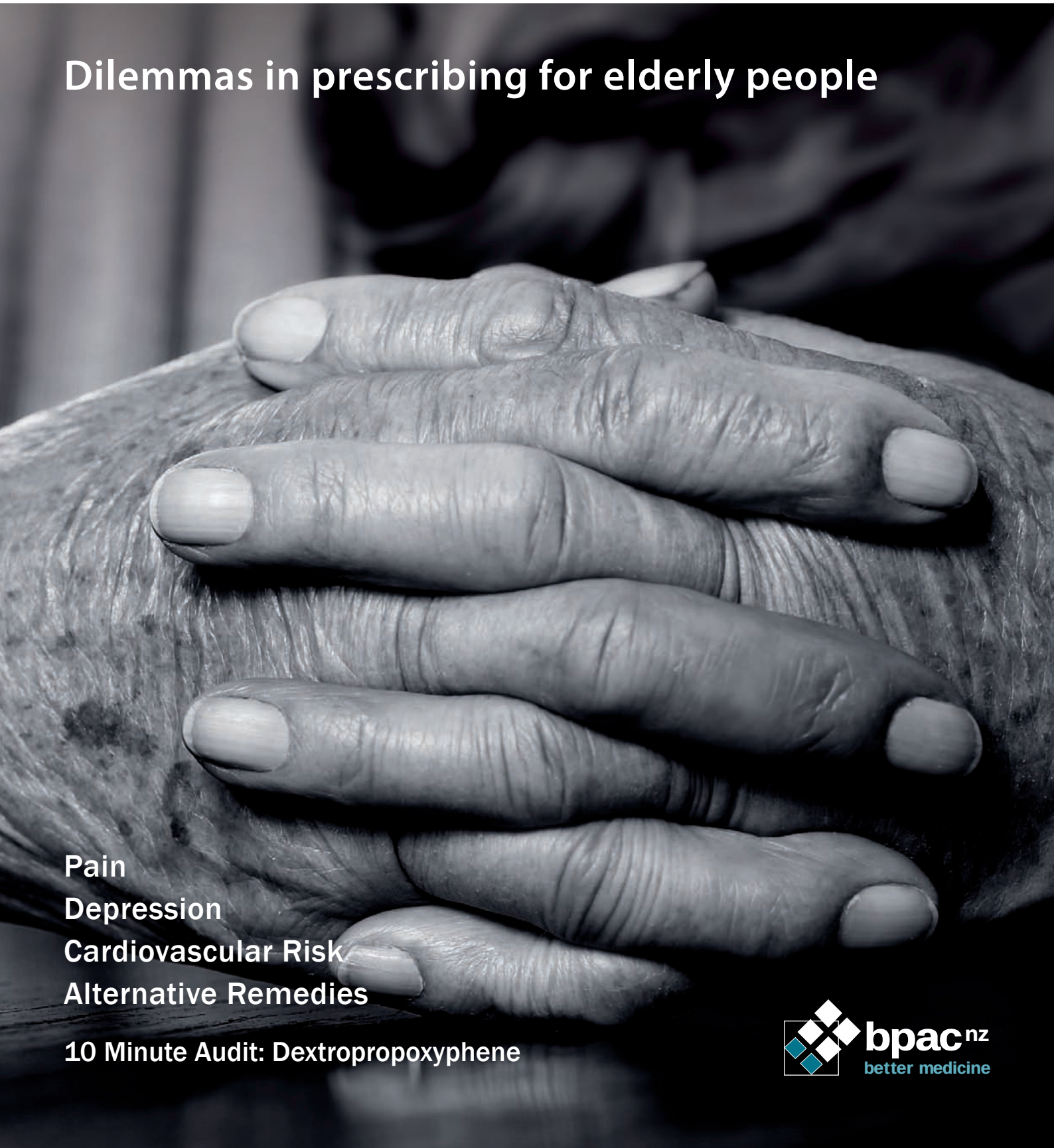

Dilemmas in prescribing for elderly people

Pain

Depression

Cardiovascular Risk

Alternative Remedies

10 Minute Audit: Dextropropoxyphene

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better medicine

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

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IMPACTS of an AGEING POPULATION on NEW ZEALAND SOCIETY

A Māori perspective

Adapted from an address by **Professor Mason Durie**, to the New Zealand Association of Gerontology 2007 conference: Ageing: The Everyday Experience

Perspectives on Ageing

Societal views on ageing are shaped by many experiences and prejudices.

A shift towards an ageing population has resulted in a greater visibility of older people within whānau and communities and has challenged society to rethink traditional attitudes towards older members.

When other New Zealanders might be contemplating withdrawal from public life, Māori elderly are often encouraged to accept new responsibilities expected by their own people - self interest will give way to the interests of whanau and hapu (sub-tribe).

Measuring Impact

Contrasting views on ageing and older people are also reflected in the ways that the impact of an ageing population on society is measured. Too often the context for discussing the implications of an ageing population on modern society is shaped only by the costs. What also need to be factored into the equation are the distinctive contributions of older people and the benefits that accrue to society as a whole.

Older People as Societal Assets

The costs of ageing are well documented but there have been fewer efforts to measure the contributions older people make to whānau, communities and future generations. A series of contributory roles can be identified and although many of them are more readily recognised within Māori society, all of them have some applicability to wider society and to all sub-populations within New Zealand.

Older People as Carriers of Culture

The standing of a tribe, its mana, as distinct from its size, relates more to the visible presence and authority of its elders than to the vigorous activities of its younger members. Without leadership at that level a Māori community will be unable to function effectively or to fulfil its obligations. The roles ascribed to older people are not only positive, they are critical for the survival of tribal mana.

Older People as Guardians of Landscape

Attachment to the land underpins indigeneity and in Māori society older people have responsibilities as kaitiaki (guardians) of the land. To many, the essence of being Māori is to be found in the nature of relationships with the environment. The quality of those relationships is largely dependent on the ways in which elders act as guides, so that the relationship can be experienced first hand and better understood by whānau.

Older People as Anchors for Families

In many cultures, older people act as anchors for families. They are accorded positions of responsibility and in turn provide avenues for family connectedness. Though they may have little active involvement in day to day activities,

their contribution to family events and to the family identity has the potential to be a major source of strength to younger members and especially to families with children.

Older Māori men and women live active lives, physically, socially and culturally. Contact with families is close and responsibilities and obligations are reciprocal.

Older People as Models for Lifestyle

Older people act as counters to younger generations especially those who are more inclined to adopt risk-laden lifestyles. For whatever reason, risk taking and risky lifestyles are less prevalent in later years

Older People as Bridges to the Future

Older people are not confined to living in the past. Laying the foundations for Māori health research for example was largely a function of older Māori women. They wanted answers to questions about the health of Māori women that captured Māori values, ideals and actual situations.

Older People as Bulwarks for Industry

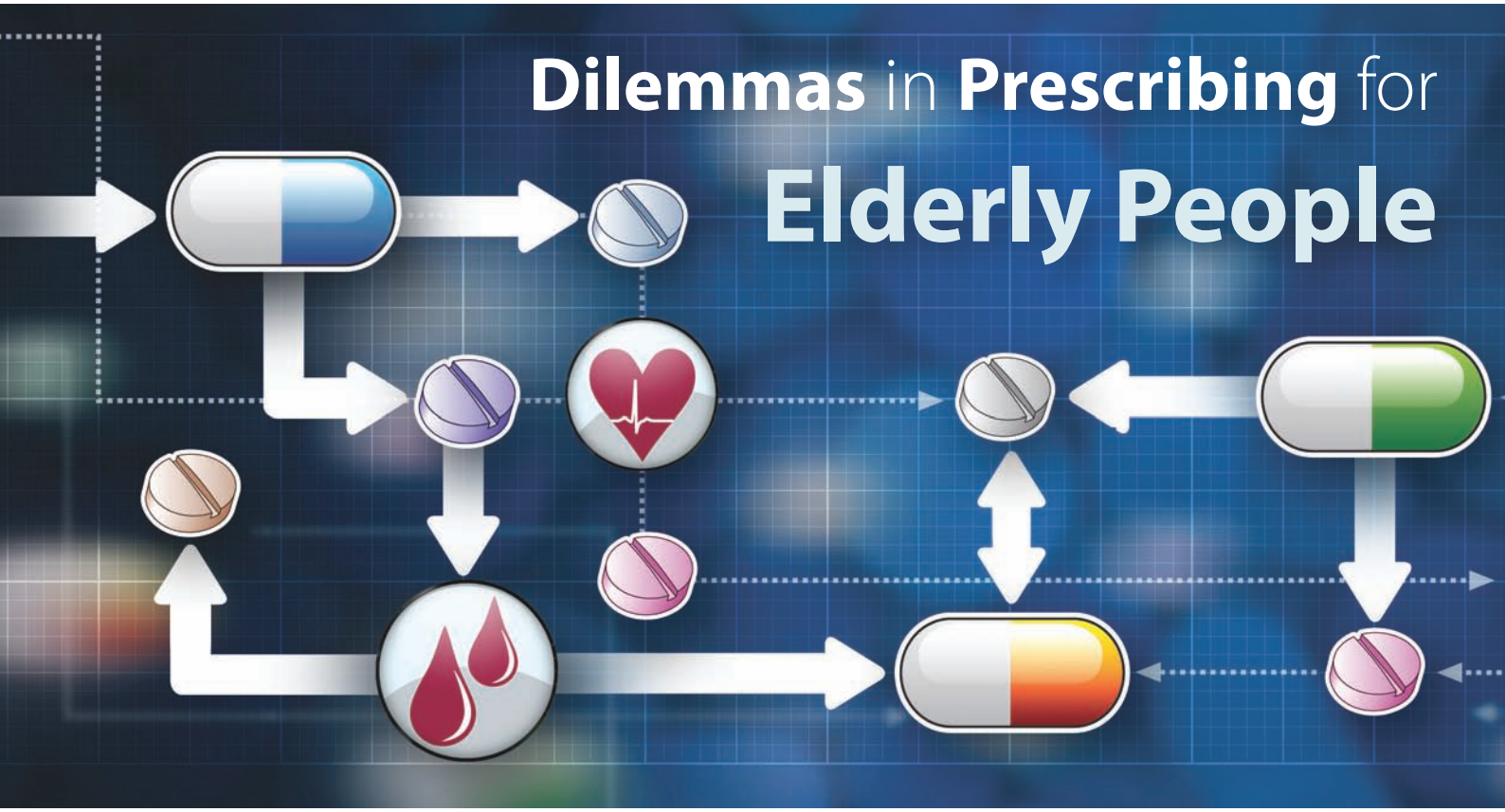
Compulsory retirement at age 65 robbed communities of accumulated expertise and wisdom. Skills gained over four or more decades were suddenly lost to the workforce and with them, product understanding, intuitive know-how and sector networking. Legislative changes have created opportunities for older people to choose when they will retire and to continue working alongside younger colleagues. Now around 40 percent of men and 20 percent of women aged between 65 and 70 years remain active participants in the workforce.

Older People as Leaders of Communities and Nations

At an age when retirement from public life might seem an attractive proposition, Māori elderly often find that life becomes busier rather than quieter. In contemporary Māori communities there are particular roles which are enhanced if they are filled by older people. Those roles include speaking on behalf of the tribe or family, resolving disputes and conflicts between families and between tribes, carrying the culture, protecting and nurturing younger adults and children and recognising and encouraging the potential of younger members. With advancing years both men and women are expected to demonstrate spiritual leadership and to satisfy tribal needs in either religious or cultural contexts.

Valuing Older People

Older people add distinctive elements to the life of the nation and enrich the quality of life for younger generations. Valuing older people from all cultures and allowing them to remain active members of society will bring consequential gains for the country as a whole.



Dilemmas in Prescribing for Elderly People

Why is it Difficult?

Prescribing decisions for elderly people are difficult because:

- **Physiological changes in elderly people often result in different and more severe drug related problems**
- **High rates of co-morbidity and polypharmacy increase the risk of interactions with other drugs and other illnesses**

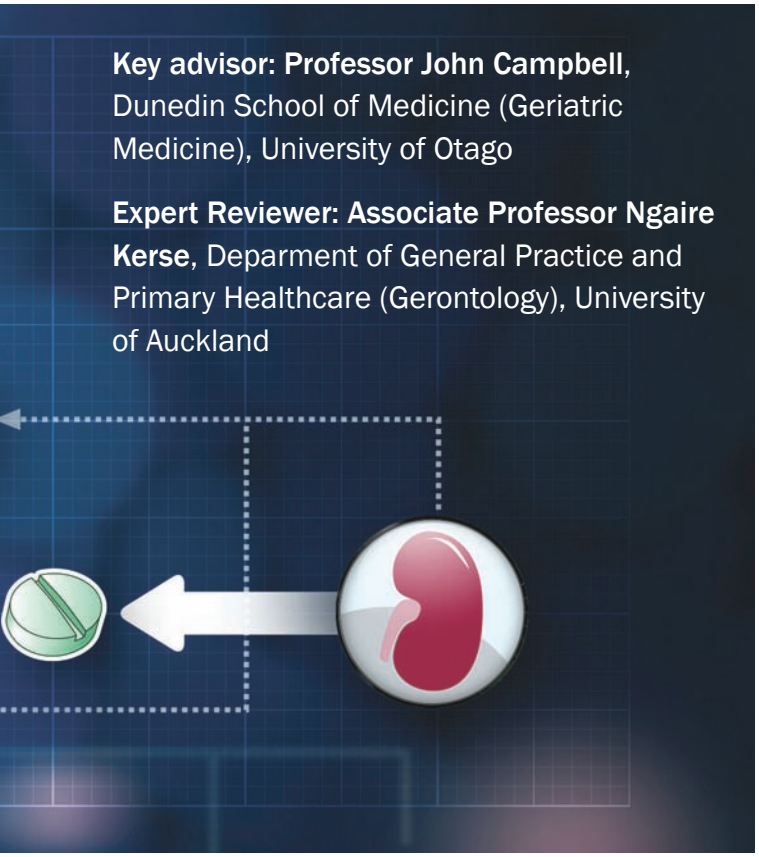
The results of drug trials are often difficult to apply to elderly people

www.bpac.org.nz keyword: elderlydilemma

Physiological changes in elderly people result in different and more severe drug related problems

Age related changes in pharmacokinetics and pharmacodynamics result in altered responses to many medications. These changes include decreased glomerular filtration rate, renal tubular filtration, gastric acid secretion, gastrointestinal motility, gastrointestinal surface area for absorption, splanchnic perfusion and hepatic size and perfusion.

Drug absorption, first-pass metabolism, protein binding, distribution and elimination are all affected. Overall this results in decreased clearance and greater exposure to



the drug. Due to these physiological changes, certain drugs are associated with an increased risk of adverse drug reactions (Table 1).

Reduced renal clearance in elderly people reduces excretion of many drugs, increasing the risk of adverse effects. Acute illness, especially dehydration, may cause further reductions in renal clearance, with the potential to move some drugs (e.g. digoxin) from the therapeutic to the toxic range without alteration in dose.

Elderly people have reduced ability to maintain homeostasis, often resulting in postural hypotension and impairment of thermoregulation, cognitive function and visceral muscle function. This means that increased symptoms may occur because of the body's inability to compensate for small perturbations in function from drug effects.

Altered molecular and cellular responses to drugs occur in elderly people. For example there are decreased density and/or affinity of receptors in specific receptor sites and target organs. Therefore, increasing the dose of a drug may have little effect on the target response but substantially increase adverse effects.

High rates of co-morbidity and polypharmacy increase the risk of interactions with other drugs and other illnesses

Increasing co-morbidity results in polypharmacy and increases the risk of:

- Drug-illness interactions
- Polypharmacy and drug interactions

Drug-illness interactions are common in elderly people

The increased frequency in elderly people of co-existing illnesses, places them at particular risk of drug-illness interactions. For example, many elderly people have both heart failure and arthritis. NSAIDs used for pain relief can adversely affect the heart failure, particularly if there is a degree of impaired renal function.

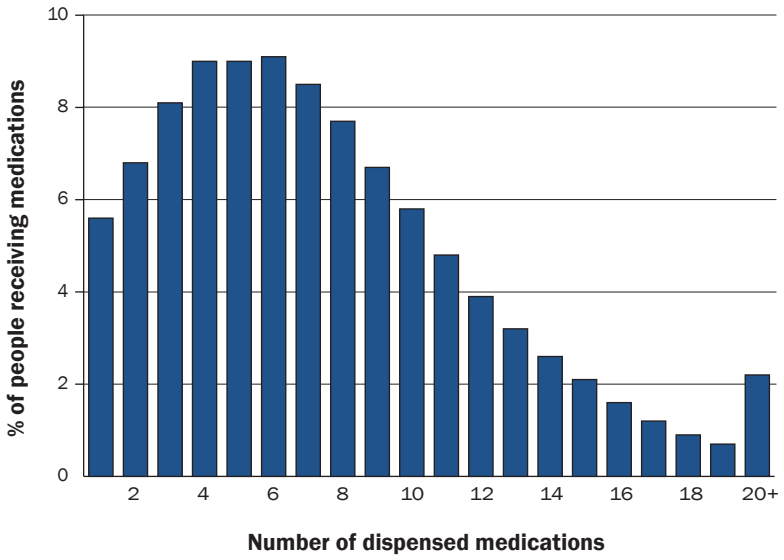
Polypharmacy increases the risk of drug interactions

The majority of elderly people take multiple medications. Latest data from the Pharmaceutical Data Warehouse (NZHIS) indicates that most people over 70 who have been dispensed any medication, are on at least four medications (Figure 1).

A steady increase in the likelihood of adverse reaction has been reported in a population of patients discharged from a hospital; from 10% of people taking two drugs to 100% of those taking twelve medications experiencing an adverse drug reaction. High prescribing rates were associated with more severe illness.[1]

Figure 1: Number of unique dispensed medications in patients aged 70 or over in a six month period.

(Notes: Study period was March to August 2007, study group included people over 70 who were dispensed one or more medication in the time period)



The results of drug trials are often difficult to apply to elderly people

As the absolute risk of many adverse outcomes increases with age, the number needed to treat (NNT) for interventions for these conditions might be expected to fall. The absolute risk of a cardiovascular event is high for elderly people, and there is evidence that anti-hypertensive treatment is beneficial. For example, the Hypertension in the Very Elderly Trial (HYVET) which commenced in 2001, was halted early due to detection of a significant reduction in strokes and cardiovascular mortality in the patients receiving treatment.

While the HYVET study is highly relevant to the elderly population, there is a lack of relevant evidence in other areas. Guidelines for clinical practice are largely based upon clinical trials which are problem focused, utilise single disease models, and exclude elderly people.[2] When elderly people are enrolled in a trial, they are usually a highly selected group, as people with co-morbidities and polypharmacy are excluded.[3] This means the results of drug trials are often difficult to apply to the elderly people seen in primary care.

Quality of life is the most relevant outcome to consider

Quality of life is the most relevant outcome to consider from treatment decisions and functional age is a much better predictor of quality of life than chronological age. In this way a functionally able person of 90 years may participate in treatment decisions and it may be appropriate to offer several drugs to manage co-morbidities.

"The good physician treats the disease; the great physician treats the patient who has the disease" —**Sir William Osler** 1849-1919

Table 1: Drugs commonly associated with adverse reactions in elderly people.

Drug or drug class	Comments
All drugs	Start low, go slow. Many drugs, e.g. oxybutynin, antipsychotics, TCAs and antihypertensives need much lower doses in elderly people.
Benzodiazepines	Those with a long half-life, such as diazepam and nitrazepam cause excessive and prolonged sedation. Temazepam is a better choice if necessary but all are best avoided.
Dextropropoxyphene	Can cause confusion and excessive sedation in elderly people. Avoid use.
Digoxin	Use low doses initially. Extra vigilance required for those who need to be on higher doses.
Indomethacin	This NSAID has a high incidence of CNS effects and gastrotoxicity.
Nefopam (Acupan)	CNS effects and marked anticholinergic actions. Avoid use.
NSAIDs	Use lowest effective dose for the shortest necessary duration. Avoid long-term use of full dose, longer half-life drugs such as naproxen and piroxicam.
Tricyclic antidepressants (TCAs)	Nortriptyline is the recommended first choice TCA in elderly people. Doxepin and amitriptyline are very sedating and have strong anticholinergic actions. They are not recommended as a first choice for depression in elderly people.

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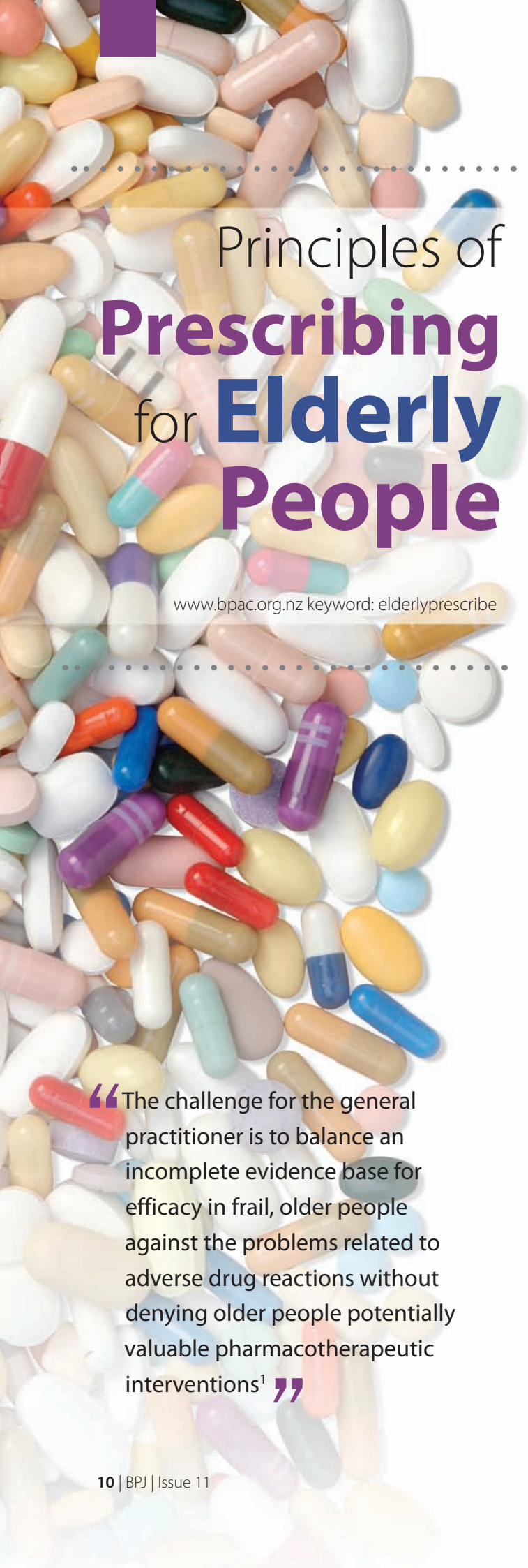

Principles of Prescribing for Elderly People

www.bpac.org.nz keyword: elderlyprescribe

> "The challenge for the general practitioner is to balance an incomplete evidence base for efficacy in frail, older people against the problems related to adverse drug reactions without denying older people potentially valuable pharmacotherapeutic interventions[1]"

The key principle when prescribing for elderly people is to consider quality of life as the most relevant outcome and:

- Treat the disease process rather than symptoms
- Be cautious about adding new medication
- 'Start low, go slow'
- Monitor closely for adverse effects
- Manage the whole of the patients treatment regimen

Treat the disease process rather than symptoms

Try to establish a diagnosis first. For example, treat the cause of pain rather than just the pain. Remember to consider whether any new symptoms and signs could come from drugs the patient is already on, to avoid a prescribing cascade.[2,3]

Be cautious about adding new medication

The decision to prescribe any drug is a complex one, especially in elderly people. Before we reach for the script pad or click the 'new script' icon, the following factors need consideration:

- Consider what you as the prescriber are trying to achieve for the patient and also if it is what the patient wants. Autonomy is often overlooked in prescribing guidelines.[4] Many older patients may be more concerned about the number of drugs they are on and the side effects of these, than whether "their disease or risk factor is managed according to the latest published guidelines".[1]
- Non-drug interventions such as lifestyle, activity, and mobility aids should be discussed with the patient and in some cases this will enable medication to be avoided.
- Check for the use of over the counter (OTC) and alternative medication.

- Regularly review long term medication to check that the indications for ongoing use are still appropriate and that they have achieved the desired effect.
- Optimise current drug therapies before adding a new drug.

Prescribing –'start low, go slow'

Once agreement is reached between prescriber and patient to initiate a new medication, the trusted advice 'start low, go slow' remains relevant and useful. This dosing axiom however, is not based on clinical trial data but on pharmacokinetics and the potential for adverse reactions.[5] Broad dosage guidelines which take into account age related pharmacokinetics may be available but individual titration will be required. As a general guide, "older people need 50–75% of the optimal dose for younger people."[6]

Monitoring for adverse effects is vital

Monitoring for problems requires consideration of the increased risk of doing harm in elderly people from altered pharmacokinetics, comorbidity and polypharmacy. Some drugs, when used in elderly people, are more likely to be associated with an increased risk of adverse events.

Assessing each individual patient for problems will generally mean knowing age, weight, general well being, cognitive function, use of OTC and complementary medications, specific renal and hepatic function, likely compliance, and an accurate understanding of the patient's other conditions and medications.

Serum levels for specific drugs, especially those with a narrow therapeutic index (eg. lithium, digoxin, warfarin, anticonvulsants) can help guide dosing.

Monitoring is required particularly when any new medication is started, with at least one follow up visit to check on response and look for adverse effects. Long term medications also need review because changes in

Ethical principles can be used to guide prescribing for elderly people.

The ethical principles that underpin many of our clinical decisions form the basis for appropriate prescribing principles in elderly people.

Beneficence —'what is the likely benefit for this patient?'

Nonmaleficence —'what harm could I do with this medication?'

Autonomy —'what does this elderly person want?'

Justice —'what is fair and just for the whole community?'

Many symptoms can be caused by medication. The common ones are:

- Falls
- Confusion or altered cognition
- Decrease in functional ability
- Dizziness
- Constipation
- Incontinence
- Unexplained tiredness
- Depression
- Tremor

the medical status of the patient over time can result in the medications becoming ineffective or unsafe.[6]

Many older people will be able to be titrated off medications that are no longer required. This should be discussed at yearly reviews.

Medication reviews are therefore recommended:

- on an annual basis
- with new medication
- after discharge from hospital
- after any change in condition of the patient (both exacerbations and improvements)

The assistance of a pharmacist can be very helpful for patients with complex regimens.

Manage the whole of a patient's treatment regimen

"Ideally a single GP should take overall responsibility for managing and coordinating the medication regimen for a patient."[7]

If you don't take charge, who will?

GPs are ideally placed to be able to manage all medications used by their patients. Never assume you are the only prescriber or that the patient is taking what you prescribed. There is evidence that elderly people visit multiple GPs and new medication may be prescribed at discharge from hospital, outpatient clinics, after hours clinics and emergency department visits.

Sharing of information is vital. Accurate knowledge can only be acquired with good patient-doctor communication and relies heavily on effective communication between primary and secondary care.

Situations when patients are most at risk can become opportunities for taking control of a medication regimen

The key task is to identify those patients at risk. There are many risk factors likely to cause drug related problems in elderly people including;

- Recent discharge from hospital
- Use of multiple drugs
- Multiple prescribers
- Impaired cognitive status and/or communication problems
- Use of drugs with a narrow therapeutic index
- Use of drugs commonly associated with adverse drug effects
- Initiation of any new medicine
- Use of OTC or complementary medications
- A change in the condition of the patient

A 'brown bag review' can be the first step in regaining control

Once those at risk are identified, a useful initial tool is the "brown bag review".[8] As the name implies this is simply getting your patient to bring in all their medication in a bag –something GPs have been doing for years. GPs or practice nurses can then get an accurate understanding of all the medications the patients are currently on (and often many that they are not taking, but still have on hand).

Asking simple questions about what, why and how patients take their medication, can help reveal gaps in understanding and offer opportunities for patient education and improve compliance and outcome. Be prepared to stop unnecessary or inappropriate medication if it does not appear to be working or has the potential to do harm.

Discontinuing medication prescribed by others can raise uncomfortable feelings for the GP, but this should be balanced by the knowledge that you are likely to have the most complete picture of your patient's circumstances. Involving your patient in the decision will help overcome any resistance to change.

A "brown bag review" may uncover problems that require a more formal review. This review may involve GP, practice nurse and pharmacist in a team approach. Don't forget to complete an up-to-date medication card.

The overall goal when prescribing for elderly people should be appropriate monitored medication use that will "enhance functional ability and life expectancy and result in improved quality of life".[8]

Best practice tip

A Christchurch GP offers us his best practice tip for taking control of treatment for his elderly patients.

"After elderly patients are discharged from hospital for a non-routine event, they are phoned by my practice nurse and invited to make an appointment for a 'debriefing session' with me.

I review their medication and discuss what events and procedures took place at hospital and what, if any, problems were encountered.

This enables me to take control of my patients' overall treatment and facilitate understanding and communication flow."

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Recognition and Treatment of Pain in Elderly People

www.bpac.org.nz keyword: elderlypain

DECISION TO PRESCRIBE

Have I identified the cause of the pain?

- Treat the disease rather than the symptoms where possible.

What am I trying to achieve?

- Pain relief to improve quality of life.
- Increased function and wellbeing.

Is this what the patient wants?

- Some elderly people are reluctant to disclose pain and may perceive it as normal or that nothing can be done about it. Discussion with older patients about pain may help to reveal undiagnosed pain.

Is there evidence drugs will help achieve this?

- There is good evidence for regular use of analgesics, especially paracetamol.
- Short bursts of NSAID use may be acceptable for management of exacerbations of painful inflammatory conditions such as gout.
- Opioids at low doses are effective for long term pain control.

Are there non-drug therapies?

- Some elderly people will find non-drug therapies such as exercise, weight loss and alternative therapies more acceptable than medication.
- Often for elderly people it is the loss of function and interference with normal life that is more important than the pain itself. These issues can often be addressed separate to the pain itself.

Do the potential benefits outweigh harms?

- Untreated pain can cause significant suffering and reduce quality of life.

Chronic pain is often under-treated in elderly people

Chronic pain affects between 20–50% of elderly people and is more common in women. However, pain is often unrecognised, treated sub-optimally or not treated at all.[1,2]

Pain may significantly reduce quality of life and lead to depression, anxiety, increased suicide risk, increased dependence, reduced appetite, impaired gait, sleep disturbances and other problems.[1]

Reasons for under-treatment

There are many reasons why pain may be unrecognised or under-treated

- **Disclosure**. Patients do not or are reluctant to disclose pain. For example, an older person may perceive that pain is "normal". Elderly people often view pain as being less important than other medical problems.
- **Poor communication**. Cognitive impairment, hearing and speech problems may lead to poor pain assessment in elderly people. One study showed that people with cognitive impairment were prescribed less opioids by doctors and administered less opioids by nurses.[4]
- **Polypharmacy concerns**. Doctors may be reluctant to add another drug to an existing regimen due to concerns about interactions and adverse effects.
- **Inadequate risk/benefit analysis**. Using anything other than a simple analgesic may be mistakenly viewed as being too risky due to adverse effects and the possibility of drug related harm. For example, the use of an opioid often raises concerns about tolerance dependence, addiction and safety. This level of pain control may be necessary and the benefit outweighs the risk of adverse effects.

Recognition of pain in elderly people

Elderly people may not report pain

Pain may manifest as inactivity, agitation, unexplained decreased function or a lack of sleep. Studies show that older people may not mention pain without being prompted. Asking elderly people or their carers about pain and using an appropriate pain rating scale is a useful way of identifying people who may have undiagnosed pain.

Pain often goes unrecognised in people with dementia. However, even people with moderate to severe dementia are able to complete a verbal pain rating scale, which is more effective than just asking if pain is present.

The pain assessment tools used in one study included: [3]

- Verbal Rating Scale: none, mild, moderate and severe
- Numerical Rating Scale: 1–10 horizontal scale
- Faces Pain Scale: 7 faces
- Colour Pain Analogue Scale: graduated from white to red, no pain to worst possible pain
- Mechanical Visual Analogue Scale

Drug treatment of pain in elderly people

A good history will aid good management

Make a firm diagnosis of the reason for the pain. This can be difficult but management of the underlying disorder may be necessary. For example, spinal stenosis can cause excessive pain and decreased function and surgery may be helpful. Knowing the diagnosis and prognosis helps with decisions about long term management.

If the diagnosis is in doubt and pain is difficult to manage ask for help from a pain specialist or relevant diagnostician.

Identifying previous analgesic use, determining effective treatments, how previous treatments were taken, and if any side effects were experienced, can help to determine the appropriate analgesic and the correct dose.

Principles of analgesic use in elderly people

- Start low, go slow

A low initial dose, followed by slow titration to response, careful monitoring and regular review helps to optimise safe and effective drug therapy if indicated.

- Review and monitor use of analgesics regularly.

Effective monitoring involves not only measuring pain relief and adverse effects, but also monitoring functional status and quality of life. Regular review to adjust dose can result in more effective control of pain and minimise adverse effects.

- Good education is the key

Good education about the most appropriate way to use analgesics is essential to gain effective pain relief for elderly people. This is particularly the case with opioids.[1] A study investigating pain in arthritis found that self management improves pain control.[5]

Regular analgesic treatment preferred to 'as required' treatment

Regular analgesia is more effective than waiting for pain to break through. Adherence problems can be addressed by stressing the importance of regular doses to patients or caregivers.

Paracetamol is an effective analgesic in many cases, especially if given regularly instead of 'as required'.

Opioids are effective for non-malignant pain.

There is often a reluctance to use opioids for non-malignant pain but opioids can be very effective in managing other chronic pain conditions such as neuropathic pain if alternative agents have been unsuccessful.[1]

NSAIDs are effective and may be safe in short courses for acute exacerbations of inflammatory conditions. However, they are no safer than opioids and may in fact pose greater long term risks in elderly people than the appropriate use of opioids.[6]

International guidelines state that "opioid treatment should be considered for both continuous neuropathic and nociceptive pain if other reasonable therapies fail to provide adequate analgesia within a suitable timeframe." [7]

Codeine is normally used as initial therapy when opioids are indicated. Stronger opioids such as morphine or dihydrocodeine may be indicated for non-malignant pain that has not responded to other analgesics. Regular use of opioids is more effective for controlling pain than waiting for pain to break through.

Features of neuropathic pain

Neuropathic pain is commonly described as burning, cold, numb or stabbing in the distribution of a peripheral nerve or nerve root. It may be accompanied by paraesthesia, hypersensitivity or allodynia (pain on light touch). Involvement of the sympathetic system is indicated by a vascular distribution of the pain accompanied by localised pallor, flushing and/or disturbances of sweating.

Features of nociceptive pain

Nociceptive pain results from stimuli that damages or has the potential to damage normal tissues. When it arises from bone, joints, muscle or skin it is usually described as aching or throbbing and is well localised. Pain from visceral organs such as the GI tract may radiate to other areas of the body.

Adverse effects of opioids can be minimised and managed

Adverse effects can be minimised by starting with a low dose and slowly titrating to the optimal analgesic effect. Using the lowest effective dose can help minimise dose related adverse effects such as constipation and sedation. Constipation is often an inevitable side effect of opioid treatment and can be managed with a stimulant containing laxative (senna or bisacodyl, see Constipation BPJ 9), increased fibre, water and exercise.

Opioids increase the risk of falls. Those using them benefit from falls prevention strategies such as lower leg strengthening and balance retraining or home hazard assessment and modification.

Alternatives for neuropathic pain

Tricyclic antidepressants and anticonvulsants can be effective for neuropathic pain. These drugs interfere with the pain pathway and can make disabling pain bearable.

While they are effective they may cause sedation and/or postural hypotension and can increase the risk of falls. This can be minimised by using low doses. Amitriptyline is commonly used for neuropathic pain, however nortriptyline is equivalent and may be preferred as it is less sedating and causes less postural hypotension.[8]

Some analgesics are best avoided

- NSAIDs and COX-2 inhibitors can have adverse effects on renal function, particularly in elderly people. They are best avoided unless they are specifically indicated such as for people with bony secondaries or acute inflammatory pain. In those who need them, it is appropriate to use the lowest effective dose, review regularly and monitor renal function. NSAIDs and COX-2 inhibitors increase the risk of drug interactions therefore it is appropriate to review other medication before initiating therapy.
- Dextropropoxyphene with paracetamol is commonly prescribed in elderly people but the combination has negligible, if any, analgesic benefits over regular paracetamol. Dextropropoxyphene is best avoided as it causes sedation, dizziness, increases fall risk and interacts with many other drugs (see page 43).
- Pethidine is best avoided in elderly people as it has a toxic metabolite which can accumulate with impaired renal function.
- Tramadol has been associated with early reports of hallucinations and confusion.[9] This may be more of an issue in older people because of higher plasma concentrations than in younger people.[10]

Other treatments for specific pain syndromes

For some causes of knee pain, including osteoarthritis, exercise can be as effective as regular pain relief. Combinations of exercise, supports and strapping, TENS (Transcutaneous Electric Nerve Stimulator) and physiotherapy have anecdotal support in pain control. Each patient will respond to pain treatments in differing ways and trying different therapies can help in pain management.

Referral to a pain clinic

This may be necessary and should be offered if the cause of pain is untreatable and the pain is unmanageable with standard approaches.

Often appropriate management of depression will enable pain to be more easily controlled. An emphasis on self management techniques empowers the patient to increase function while managing pain.

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Depression in **elderly people**

DECISION TO PRESCRIBE

Have I identified the cause of the depression?

- Treat any underlying causes as well as the depression.

What am I trying to achieve?

- Relieve depression.
- Improve quality of life and functional ability.

Is this what the patient wants?

- Some elderly people perceive a low mood as normal and will not seek help. Discussion with the patient may help achieve appropriate management.

Is there evidence that drugs help achieve this?

- Elderly people respond as well to antidepressants as younger people.
- SSRIs are a suitable initial therapy for most depressed elderly people.
- TCAs are suitable in people who are unresponsive or intolerant to SSRIs.

Are there non-drug therapies?

- Psychological therapy used alone or as an adjunct to pharmacotherapy may improve outcomes.
- Social, environmental and household support is often just as important as pharmacological and psychological therapies in helping elderly people with depression.
- Exercise is beneficial and some people may choose to use alternative therapies.

Do potential benefits outweigh harms?

- Untreated depression can cause significant disability. Treating depression adequately can help to improve quality of life and relieve suffering. Harms can be minimised with the correct choice of drug and dose and adequate monitoring.

Medical conditions associated with depression

- Viral infection
- Certain endocrine disorders (e.g. thyroid disorders, Cushing's syndrome, adrenal insufficiency, hyperparathyroidism)
- Malignancy
- Cerebrovascular disease (e.g. stroke, vascular dementia)
- Parkinson's disease
- Myocardial infarction
- Metabolic disorder (e.g. B12 or folate deficiency, malnutrition)

Medicines associated with depressed mood

- Benzodiazepines or other central nervous system depressants
- Beta-blockers (especially lipid soluble e.g. propranolol)
- Steroids
- Anti-parkinsonian drugs
- Dextropropoxyphene

List adapted from Alexopoulos[3] and Prodigy[4]

Depression is common in elderly people

Depression in older people is common. It often goes unrecognised by both patients and doctors, is frequently under-treated, and can account for greater levels of disability than physical illness.[1]

Other causes of low mood may be even more common, can be more difficult to diagnose, and can still cause significant suffering.[2]

Depression in elderly people is a significant cause of disability

Depression is a significant cause of disability, causing suffering, family disruption and possibly worsening outcomes of other co-morbidities. The New Zealand Mental Health Survey established that mood related disability is greater than disability related to chronic conditions.[1] The causes of depression in older people may be different from younger people. Age-related disorders increase the vulnerability to depression; cancer, stroke, myocardial infarction and Parkinson's disease are all associated with depression in elderly people.[3] Various medications can cause a depressed mood, including, beta-blockers, corticosteroids and anti-parkinsonian drugs.

Depression in this population can be harder to treat due to increased clinical complexity.[5]

Depression is under recognised and under treated in elderly people

There are complex reasons for under-recognition of depression in elderly people. Barriers to diagnosis may include time constraints, other co-morbidities which complicate diagnosis and reluctance to discuss emotional problems. The stigma associated with depression may prevent elderly people seeking medical help and older people may also perceive that a low mood is normal.

Some studies report that less than 30% of elderly depressed patients receive adequate antidepressant therapy.[6] Antidepressants prescribed at insufficient doses and for an inadequate length of time contribute to treatment failure. Adherence is a major factor influencing the success of treatment and is often complicated by complex medication regimens, disability and cognitive impairment.[3,4]

Diagnosis of depression

Symptoms of depression in elderly people can often be mistakenly attributed to "normal" old age. On the

other hand some symptoms frequently associated with depression may be caused by other problems. For example, pain may contribute to a decreased interest or pleasure in activities, denture related eating difficulties can contribute to weight loss and many elderly people have disruptions in sleep patterns that may not be related to depression.

Tools such as the Geriatric Depression Scale (page 25) have been specifically developed for older populations to address these issues and give more weight to mood-related symptoms.[7]

Pharmacological treatments

Elderly people respond as well to antidepressants as younger people

Once a diagnosis is made it is important to treat depression in elderly people adequately. This includes using the correct antidepressant at adequate doses for a sufficient treatment period. Maximal response may not be reached for up to 8–10 weeks and uptitration can continue for longer periods. Evidence suggests that depressed elderly people respond as well to antidepressants as younger people with depression.[3]

SSRIs can be used initially for most depressed older people

SSRIs are generally considered first line in depressed older people. SSRIs have a similar efficacy to TCA antidepressants but SSRIs may be better tolerated by elderly people.[8]

Starting with a low dose and increasing gradually reduces the risk of adverse effects. Although initial doses of SSRIs should be lower in older people, maintenance doses may be similar to those used in younger people.[3]

Fluoxetine has a long half life and can take three to four weeks to reach steady state which can complicate dose titration. Paroxetine and citalopram have shorter half lives but withdrawal reactions are a disadvantage which requires tapering on discontinuation. Citalopram would be a suitable choice because it has less potential for interactions, which may be a particular concern in elderly people already on complex regimens.

It is important to trial any antidepressant for four to six weeks after reaching the recommended dose, before it is determined ineffective and another drug is tried.

TCAs used if unresponsive or intolerant to SSRIs

Tricyclic antidepressants may be considered in those who do not respond or who are not tolerant of SSRIs. Again initial doses should be low and increased gradually. TCAs may be more appropriate initially if a concurrent medical condition exists such as urinary incontinence, where a TCA may be substituted for oxybutynin.

Nortriptyline is a suitable choice of TCA because it has less sedative and anticholinergic effects, and may cause less orthostatic hypotension. It is safer to use in elderly people than other TCAs, such as amitriptyline, dothiepin or doxepin.[3]

Table 1 (page 22) compares these two different classes of antidepressant.

Other pharmacological treatment options

The reversible monoamine oxidase inhibitor (MAOI), moclobemide, can be used but there is limited evidence of its efficacy in elderly people.[6]

Irreversible MAOIs should only be considered in those who have had a previous good response to them or who are intolerant of other agents. They have many interactions, including food interactions, making them difficult to use safely.

Elderly people with treatment resistant depression can use venlafaxine but special consideration should be given to the potential for adverse cardiovascular effects (see BPJ 1 – Venlafaxine).

Table 1: Comparison of SSRIs and TCAs

	SSRIs	TCAs
Side effects	Common - nausea, vomiting, diarrhoea, dizziness, drowsiness, insomnia, agitation, and anxiety. Often these can be prominent in the initial phase of treatment but may improve with time. Increased risk of falls. Uncommon – hyponatraemia. Symptoms are usually non-specific and include anorexia, nausea, fatigue, lethargy, and confusion. If patients develop any of these symptoms hyponatraemia should be considered and electrolyte levels should be measured.	Common - Anticholinergic side effects which include dry mouth, blurred vision, urinary retention, constipation, and sedation. Increased risk of falls and associated fractures in elderly people. Uncommon – cardiotoxicity. This is an important consideration in elderly people with co-morbid cardiac disease.
Interactions	Fluoxetine and paroxetine inhibit the hepatic cytochrome P450 isoenzymes and interact with other drugs metabolised by these enzymes such as TCAs. Citalopram has a relatively low risk of interactions in comparison. SSRIs may increase the risk of bleeding and the risk may be further increased by concurrent use of other medicines that increase bleeding risk such as warfarin, NSAIDs or aspirin.	Increased anticholinergic effects if other anticholinergic drugs are taken in combination. These include other antidepressants, some antiparkinsonian drugs, antihistamines, antipsychotics, and antiemetics.
Cautions	Withdrawal symptoms may occur if antidepressants are discontinued abruptly. Doses should be tapered over at least four weeks.[6]	Co-morbid cardiac disease History of epilepsy TCAs are very toxic in overdose

Antidepressants and co-morbidities

Depression with a mental or physical co-morbidity is common in elderly people and is likely to respond to antidepressant treatment. Prescribers may have concerns about interaction of the treatment with the co-morbid condition.

- Cardiac disease – TCAs may induce arrhythmia and can cause hypotension. Caution is required with venlafaxine. SSRIs appear to be generally safer but this has not yet been subject to large-scale trials.
- Epilepsy – SSRIs and TCAs may lower seizure threshold; use low doses and titrate slowly.
- Glaucoma – TCAs can precipitate acute narrow-angle glaucoma, SSRIs are less implicated.
- Prostatism – TCAs may lead to urinary obstruction for men with prostatism.
- Parkinson's disease – SSRIs and TCAs may be used although caution is required with TCAs because of their side effect profile.
- Dementia – Depression can be treated in people with dementia as it can in other older people with depression. Depression responds to antidepressants even in the presence of dementia.[4]

Falls and depression go hand in hand

Depression is a significant risk factor for falls and falls predispose development of depression. Drug treatment for depression is also an independent risk factor for falls, SSRIs are no safer than TCAs.[9]

The exact reason for this close association between falls and depression is not known. Whether depression results in decreased activity, deconditioning and physical frailty and subsequent falls, or whether there is a central mechanism associated with depression that causes falls, is not known. Some people with depression have an abnormal gait pattern.[10,11]

Non-pharmacological treatment options

Psychological therapy should be considered in all elderly patients with depression. Psychological and pharmacological therapies initiated together are ideal for moderate depression although either treatment alone may be considered in mild depression. Some suitable psychological therapies for elderly people with depression are; cognitive therapy, supportive psychotherapy, problem-solving therapy and interpersonal therapy.

Electroconvulsive therapy can also be used in severe, unresponsive depression although there are risks associated and antidepressant therapy is usually required to maintain remission.

Exercise benefits people with depression and several trials have had promising results as long as the "dose" and intensity of the activity is adequate. Attention to compliance is important for people with depression and the successful trial interventions were intensive and supervised.[12]

A review of complementary therapies for depression shows St Johns Wort, QiGong, and massage have some evidence of benefit.[13] St Johns Wort is the most studied of these; however few trials have included older people. It is important to take into consideration potential adverse effects and interactions with conventional treatments.

A range of interventions are required to improve the quality of life for elderly people with depression

Elderly people with depression are often struggling to cope with the activities of daily living and co-morbidities or major life events may add to the problem. Social, environmental and household support is often just as important as pharmacological and psychological therapies in helping elderly people with depression.

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Geriatric Depression Scale

Instructions: Choose the best answer to describe how you have felt over the past week.

1.	Are you basically satisfied with your life?	**YES**	**NO**
2.	Have you dropped many of your activities and interests?	**NO**	**YES**
3.	Do you feel that your life is empty?	**NO**	**YES**
4.	Do you often get bored?	**NO**	**YES**
5.	Are you in good spirits most of the time?	**YES**	**NO**
6.	Are you afraid that something bad is going to happen to you?	**NO**	**YES**
7.	Do you feel happy most of the time?	**YES**	**NO**
8.	Do you often feel helpless?	**NO**	**YES**
9.	Do you prefer to stay at home, rather than going out and doing new things?	**NO**	**YES**
10.	Do you feel you have more problems with memory than most?	**NO**	**YES**
11.	Do you think it is wonderful to be alive now?	**YES**	**NO**
12.	Do you feel pretty worthless the way you are now?	**NO**	**YES**
13.	Do you feel full of energy?	**YES**	**NO**
14.	Do you feel that your situation is hopeless?	**NO**	**YES**
15.	Do you think that most people are better off than you are?	**NO**	**YES**

To score, count one point for each answer in the right-hand column. A score >10 is almost always depression.

Managing cardiovascular risk in elderly people

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DECISION TO PRESCRIBE

What am I trying to achieve?

- Prevent possible future cardiovascular events.
- Maintain quality of life.
- Maximise function or functional potential.

Is this what the patient wants?

- Discussing the potential risks and benefits with older people may help them decide which risk modifying factors they wish to implement. If an older person believes that reducing cardiovascular risk is likely to improve quality or length of their life they may choose active treatment.

Is there evidence that drugs will help achieve this?

- There is undisputed evidence that antihypertensives reduce the risk of cardiovascular events in elderly people. The case for low-dose aspirin and statins is less certain. However clinical judgement will weigh the risks and benefits of these treatments taking into account the health and longevity of the elderly person.

Are there non-drug therapies?

- There is limited evidence of the cardiovascular effect of lifestyle modification in elderly people, however eating a healthy well balanced diet, increasing activity and smoking cessation is likely to help and have other health benefits.

Do potential benefits outweigh harms?

- The risks and benefits must be balanced for each individual older person. Older people with advanced chronological or physiological age or severe co-morbidities may not be suitable for intensive treatment. In contrast those older people in good health with a reasonable life-expectancy may be more suitable.

There is less evidence about the management of cardiovascular risk in older people than younger age groups. Most elderly people over the age of 75 will have a five year cardiovascular risk of greater than 15% according to New Zealand Cardiovascular Risk Assessment guidelines. However calculation of risk, using the tables, can be useful when discussing risk modification with elderly people. In this article we discuss:

- Lifestyle modification
- Antihypertensives
- Statins
- Aspirin

Lifestyle modification

Lifestyle modification may reduce cardiovascular risk but also has benefits for other common conditions in elderly people. A study showed a significantly lower mortality rate in older people who combined a diet rich in fruit and vegetables and low in saturated fat (the Mediterranean diet), with non-smoking, moderate alcohol consumption, and at least 30 minutes of physical activity per day.[1]

Increasing physical activity is likely to be beneficial for elderly people

Although there is limited evidence about the effectiveness of exercise and physical activity in the prevention of cardiovascular disease, it is widely recommended because of other potential benefits for conditions such as hypertension, obesity, diabetes, and musculoskeletal disorders.[2] There is also some evidence that physical activity may reduce the risk of falls. In elderly people the ability to participate in physical activity can often mean the difference between independent living and living with assistance.[3]

Variation in the ability of elderly people to become physically active requires the intensity, frequency and duration of physical activity to be adjusted to the capabilities of each individual. Gradual increase in activity is recommended because there is some evidence of an initial increased risk of adverse events, particularly in people who have been sedentary.[2] The social aspect of group physical activities may encourage elderly people to participate.

Diet interventions and weight loss are often beneficial to elderly people

Although there is limited evidence of the effect of diet on cardiovascular risk in elderly people, eating more fruit and vegetables and reducing fat and salt intake is likely to be beneficial. Diet is part of therapy and more important for those with diabetes.

Weight loss may help modify cardiovascular risk in overweight individuals, and may be beneficial for other conditions that are common in elderly people such as osteoarthritis, and may also increase mobility.

Reducing salt intake may reduce blood pressure but not overall cardiovascular risk

A Cochrane review found that salt restriction in adults produced a minimal decrease in blood pressure; however there was not enough evidence to show a decrease in cardiovascular mortality.[4]

It is possible that reduced salt intake would be more effective for lowering blood pressure in elderly people than in younger people, because arterial compliance decreases with age and any change in intravascular volume relating to sodium intake, could result in a greater change in blood pressure.[5]

Elderly people are prone to hyponatraemia but when associated with drugs, such as thiazides or SSRIs, it is usually a dilutional hyponatraemia. It is due to a failure to clear water.

Reducing total and saturated fat is recommended

There is evidence that modifying dietary fat intake by reducing total fat intake, or replacing some saturated fat with unsaturated fat, may reduce the incidence of cardiovascular events in the general population.[6] However there is limited evidence that this also applies to older people. Older people are more at risk of unplanned weight loss than obesity and advice about reduction in dietary fat may be more suitable for those who are overweight or have dyslipidaemia.

Increasing fruit and vegetable consumption is recommended

Diets that are rich in fruit and vegetables and low in saturated fat, such as the Mediterranean diet, have been shown to reduce cardiovascular risk in elderly people[7] as well as in the general population.[8]

Smoking cessation is beneficial to elderly people

Smoking cessation is beneficial at all ages with immediate effect. The results of one study in elderly men showed the risk of all-cause mortality was the same in ex-smokers as in those who had never smoked.[9] Smoking is one of the most modifiable risk factors for lung cancer, chronic obstructive pulmonary disease and cardiovascular disease.

Smoking cessation advice should be offered to all patients regardless of age or co-morbidity.

Antihypertensives, statins and low dose aspirin in elderly people

In the general population there is evidence that antihypertensives, statins and low dose aspirin can modify risk of cardiovascular events. While antihypertensives have good evidence of effectiveness in elderly people, the evidence for statins and low dose aspirin is either of poor quality or lacking.

Reducing blood pressure reduces cardiovascular risk in the elderly

Many trials have shown significant benefits of treating hypertension in elderly people, to reduce the risk of cardiovascular events, especially stroke. All trials have resulted in marked reductions in morbidity associated with stroke and myocardial infarction (MI). However they report conflicting results on the reduction of all-cause mortality; some report a significant reduction and some show no significant reduction.

The recent HYpertension in the Very Elderly Trial (HYVET) was stopped early after researchers observed significant reductions in both overall mortality and stroke, in those receiving therapy.[10] The HYVET trial is novel in testing the hypothesis that treatment of hypertension at advanced age (over 80) does not reduce events. The hypothesis was proven wrong and marked benefit was observed.

Antihypertensives lower cardiovascular risk, reduce blood pressure and prevent cardiovascular events. They may also reduce the development of dementia, as it is likely that most dementia is mixed dementia, and reducing the vascular component delays onset of symptoms.

Once dementia has reached an advanced stage, active management of co-morbidities should be reconsidered as it may not increase quality of life.

Treatment decisions that can reduce the risk of antihypertensive treatment:

- Starting with the lowest dose and increasing gradually reduces the risk of postural hypotension.
- More frequent monitoring in elderly people can identify potential problems with treatment, especially intolerable side effects such as postural hypotension. Elderly people may see their side effects, such as impotence with thiazides, as an unavoidable part of treatment and not report them.
- Thiazides are a good first choice as they may be particularly effective in elderly people.[11]
- Calcium channel blockers are less influenced by age and ethnicity compared with other agents (e.g. ACE inhibitors) and this may present a benefit for their use in elderly people.[12]
- ACE inhibitors may be considered initially in elderly people with co-existing conditions such as chronic kidney disease or diabetes.[11, 13]
- Beta-blockers have been shown to be not as effective as other antihypertensive agents in elderly people. Initial therapy with beta-blockers should probably be limited to those people who have compelling indications for their use, such as coronary heart disease or congestive heart failure.[11]

Modification of lipids may be beneficial

Data on primary prevention of cardiovascular events with statins in the elderly population is limited. Studies in older people report adverse effects inconsistently making it difficult to draw conclusions regarding the risk of treatment versus the benefit.

The Prospective Study of Pravastatin in the Elderly at Risk (PROSPER) showed no significant reduction in all-cause mortality, but suggested that statin therapy in high-risk elderly patients, can reduce coronary disease events.[14]

Other trials and sub-group analyses have shown a variable effect of statins on mortality as well as cardiovascular events.

Those with limited life expectancy due to co-morbidities will be unlikely to benefit from statin primary prevention.[14] Age alone is not a contraindication to drug therapy.[2]

The decision to treat elderly people with a statin should be made on an individual basis, taking into account cardiovascular risk assessment, patient choice, life expectancy and quality of life.

Treatment decisions that may reduce the risk of statin therapy:

- Start with low doses and increase gradually. Higher doses may place elderly people at increased risk of adverse effects.
- Monitoring therapy is especially important in elderly people. They are at increased risk of statin induced myopathy, even though the risk is still small. Patients should be advised to report any unexplained muscle pain, tenderness or weakness. This may occur without muscle enzyme rise.
- Elderly people are at risk of polypharmacy and may be taking drugs such as macrolides, amiodarone, cimetidine, or azoles (ketoconazole and itraconazole), which may increase the plasma concentration of statins.

Atrial fibrillation and anticoagulation

Anticoagulation with warfarin lowers the risk of stroke in people with atrial fibrillation (AF). Treating 1000 people with AF for one year with warfarin rather than aspirin would prevent 23 ischaemic strokes.[17]

However warfarin is associated with increased risk of major bleed including cerebral haemorrhage. This is particularly so in those 80 years and over and in the initial few months of treatment. In a recent trial the cumulative incidence of major haemorrhage in this group was 13.1 per 100 patient years.[18]

Low dose aspirin may be suitable for elderly people at high risk of cardiovascular events

The likelihood of benefit achieved from primary prevention with aspirin improves with increasing risk of cardiovascular events. Therefore in those at highest risk of cardiovascular events, the benefit of low dose aspirin prophylaxis outweighs the risks associated with aspirin therapy.

In people at lower risk of cardiovascular events, the excess bleeding risks, such as gastrointestinal bleeds or haemorrhagic stroke associated with aspirin, may outweigh any benefit of reduced cardiovascular outcomes.[15] A meta-analysis showed aspirin to increase the risk of gastrointestinal bleeding by a factor of 1.5–2.0. However higher rates (up to double) may be expected in elderly patients. The risk of bleeding may be higher in elderly people due to underlying conditions such as gastric ulcer or drug interactions, including concomitant NSAID or anticoagulants.[16]

People with uncontrolled blood pressure may be at greater risk of a cerebral haemorrhage with aspirin therapy[2] and the beneficial effects of low dose aspirin therapy may be attenuated in patients with poorly controlled blood pressure.[15]

Enteric coated preparations do not seem to reduce the risk of gastrointestinal bleeding.[2]

Factors relating to the use of low dose aspirin:

- Only use low dose aspirin in patients at high risk of cardiovascular events when the benefits outweigh the risks.
- Risks of bleeding are increased in elderly people taking other drugs such as NSAIDs or anticoagulants, or with underlying clinical conditions such as peptic ulcer or uncontrolled blood pressure.
- Enteric coated preparations are not protective.
- Doses as low as 75mg are effective.

Summary

Older people have a high absolute risk of cardiovascular disease and therefore appear to have the most potential to benefit from cardiovascular risk reduction. However they are often also at increased risk of adverse drug events and the decision to treat must be made on a case by case basis, taking into account the likely benefits and risk of treatment and the person's values.

Lifestyle measures should be implemented where possible as they may be beneficial to cardiovascular and other aspects of a patient's health.

Older people with advanced chronological or physiological age or severe co-morbidities may not be suitable for intensive treatment. In contrast older people in good health with a reasonable life-expectancy have a greater capacity to benefit from treatment and less risk of adverse effects.

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Alternative remedies and lifestyle measures for longevity

The "science" of anti-ageing

The development and marketing of anti-ageing products is a multi-million dollar industry. There is no shortage of remedies and lifestyle measures, claimed to slow, stop or reverse the process of ageing. More often than not, these claims are not supported by scientific evidence. At the very least, people may be financially burdened by purchasing ineffective products. At worst, these products may be harmful or interact with standard therapies.

A group of 52 internationally recognised researchers have developed consensus statements on several of the main issues related to ageing.[1]

Life span is defined as the observed age at death of an individual. The maximum lifespan of humans is increasing with time. However it is not people that have changed. Longevity is related to the protected environments that we live in and advances in biomedical science, which enables more people to approach their life span potential. The overwhelming majority of the world's population will die long before they reach the maximum possible age of a human.

Life expectancy is the average number of years of life remaining. Historically, advances in life expectancy were a reflection of dramatic declines in mortality risks in childhood and early adult life. Because this mortality risk is now close to zero, further improvements would have little effect on life expectancy. Advances in life expectancy now are due to decreases in mortality in middle and older ages. The researchers' concluded that it is unlikely that life expectancy could increase significantly unless future technological advances allow modification of the underlying processes of ageing.

However some disagree with this assumption and believe that life expectancy will continue to rise at a steady rate of 2.5 years per decade, as it has done over the past century and a half, with no signs of slowing.[2]

Immortality is not possible. Eliminating all age-related causes of death would perhaps increase life expectancy by a few years but accidents, homicides, suicides and the biological process of ageing would continue to result in death.

Geriatric medicine manages the treatment of degenerative diseases associated with ageing. These interventions treat the manifestations of ageing, not ageing itself. The biomedical knowledge required to modify the process of ageing does not currently exist.

Anti-ageing medicine does not exist, despite many advocates claiming otherwise. There are many false, misleading, or dramatic claims made about these products for commercial purposes. Some products may relieve the symptoms of age-related illness and some may mask the manifestations of ageing, but there are no pills or remedies that can slow, stop or reverse ageing.

Special note on free-radicals and antioxidants:
It is scientifically accepted that free-radicals play an important role in the ageing process and that antioxidants can counteract their effect. Ingesting fruit and vegetables, which contain antioxidants, can reduce the risk of age related disease such as cancer, heart disease, macular degeneration and cataracts. There is however, very little evidence at present that supplements containing antioxidants can provide any benefit additional to dietary

consumption and there is no evidence that they have any effect on human ageing.

Hormones such as testosterone, progesterone, oestrogen and growth hormone have been shown in clinical trials to improve some of the physiological changes associated with ageing. Hormones may be beneficial to some people but they will not affect the ageing process overall. Many adverse effects are associated with hormone use and there is some evidence that growth hormone may actually shorten life span. Hormone supplements should not be used unless they are specifically indicated for a diagnosed medical condition.

Supplements may be used with some success to alleviate the symptoms of age-related illnesses such as arthritis and dementia, however there is little evidence supporting their clinical effect. Gingko biloba is thought to have a beneficial effect on memory preservation, however a recently published Cochrane review concluded that evidence is "inconsistent and unconvincing".[3] St Johns wort is often used to treat symptoms of depression, however it has the potential to interact with other antidepressants and medications.

It is important to note that supplements are not regulated in New Zealand and are therefore not subject to quality control. A review of supplements used to treat the symptoms of osteoarthritis can be found on page 34.

Lifestyle measures, including healthy nutrition, exercise and avoidance of smoking, alcohol and excessive sun exposure can increase the chance of living longer by delaying or preventing the occurrence of age related illness. However these lifestyle changes do not affect the ageing process itself. There is good evidence of effectiveness for exercise in the prevention and treatment of osteoporosis and for diet, weight loss and smoking cessation in cardiovascular disease.

Caloric restriction is believed to increase longevity, however it has progressively less effect the later in life it is begun. The evidence for this association is based on animal studies and to date there is no human study that proves it works long term. The level of caloric restriction needed to effect longevity is intolerable for most people and very few have tried this method. Older people do not gain weight again after being malnourished, and giving advice to severely restrict food intake, is likely to increase frailty and falls and therefore shorten lifespan.

For most people, quality of life is preferable over quantity of life.

Life expectancy in New Zealand

The average life expectancy of New Zealanders continues to rise according to Statistics New Zealand. Figures from 2006 show that females can expect to live 81.9 years and males 77.9 years (from birth). Increases in life expectancy are largely due to reduced mortality rates in people over 50 years of age. Mortality rates among young adults (15–24 years) and infants also declined significantly between the periods 1995–1997 and 2000–2002.

Non-Māori have a significant longevity advantage over Māori. In 2000–2002 life expectancy for Māori females was 73.2 years, compared with 81.9 years for non-Māori females. For Māori males, life expectancy was 69.0 years and 77.2 years for non-Māori. This is an average difference between Māori and non-Māori of about 8.5 years, slightly less than the estimated difference of 9.1 years in 1995–1997. Lower non-Māori mortality rates at ages 50–74 years account for over 60 percent of the difference between Māori and non-Māori life expectancy at birth.[4]

As people get older their life expectancy increases. For example, a female aged 70 years can expect to live a further 16.5 years. If that person then reaches 85 years, they can expect to live a further 6.7 years and if they reach 90, a further 4.6 years.[5]

Alternative treatments for osteoarthritis

Do alternative treatments really work?

The simple answer to this question is that many alternative treatments do work, although whether this is due to an actual clinical effect or simply an investment in the hope that it will work, is debatable. It is difficult to apply usual scientific method to determine whether an intervention has made a difference. Few high quality trials of alternative therapies, involving large numbers of people, exist.

Questions to consider when assessing an alternative therapy for a patient may include:

- Is there clinical evidence of effect?
- Is it cost prohibitive?
- Are there adverse effects?
- Does it interact with other medications?
- Will it compromise conventional medical treatment?
- Will it reduce the need for conventional medications?

Evidence of effectiveness of commonly used supplements, herbal products or devices in the treatment of osteoarthritis

Osteoarthritis affects around 8% of the total population of New Zealand, and up to 50% of those over 65 years of age, with no difference between Māori and non-Māori in age-standardised prevalence rates.[6]

It is claimed that some supplements can modify the indication for surgery, time to disability or at the least, reduce the reliance on drugs such as NSAIDs.[7] While there is a lack of clinically significant evidence for many of these products, some hold promise.

Glucosamine and chondroitin for arthritis: some evidence of effect

The mainstay of current treatment for osteoarthritis is to reduce pain. Conventionally, NSAIDs, corticosteroids or simple analgesics are used but recently two alternative products, glucosamine and chondroitin, have been gaining favour.

Glucosamine is an amino sugar found in the body. The exact mechanism of its action is unclear but it is thought that it promotes the formation and repair of cartilage. The glucosamine in manufactured supplements is usually sourced from shellfish shells and is available in two different chemical forms.

Several trials have found an improved clinical outcome with a regimen of 1500 mg/day glucosamine sulphate. Evidence from a recent meta-analysis showed that glucosamine may be effective in preventing the long-term progression of osteoarthritis. This was assessed by measuring joint space narrowing associated with articular cartilage degeneration.[13] Glucosamine sulphate has an analgesic effect which may compare favourably to NSAIDs. In addition, its use results in improved joint mobility and functioning.[14] There is less evidence of effectiveness for glucosamine hydrochloride.

Glucosamine is generally well-tolerated and is not known to be associated with any serious adverse effects. The most common side effects are gastrointestinal disturbances including dyspepsia, abdominal discomfort and diarrhoea.[14] There have been some reports that glucosamine may exacerbate asthma, however there is no definitive evidence of this association. It has also been suggested that glucosamine may adversely affect insulin resistance, however this effect has not been observed in humans and requires further study.[7] As glucosamine is derived from shell fish, people with an allergy to seafood should use it with caution.

> Glucosamine sulphate, 1500 mg/day may lessen the progression of osteoarthritis and provide pain relief and improved mobility.

Table 1: Supplements, herbal products and devices used for the treatment of osteoarthritis in New Zealand

Product	Evidence of clinical effect for OA?	What is the evidence?
Acupuncture	Inconclusive	A review of 10 randomised controlled trials (RCT) found mixed evidence of effectiveness for pain reduction. Acupuncture did not provide results superior to physical therapy. The placebo effect may play a major role.[8]
ASU (avocado soybean unsaponifiables)*	Yes (medium term)	Results from four trials show that ASU has a beneficial effect in reducing pain and NSAID use and increasing joint mobility. Ongoing benefit has been observed but evidence is for benefit in the medium-term (several months).[7, 9]
Boswellia (guggulu)	No	Only a few quality trials exist, but it has been observed that boswellia decreases severity of pain and swelling and increases joint mobility. No significant adverse effects are known.[7] A systematic review concluded that there is no current evidence of efficacy.[9]
Chondroitin sulphate	Inconclusive	There is evidence of effectiveness in reducing pain, improving function and reducing NSAID and analgesic use.[7] However a recent meta-analysis concluded that the benefit was minimal and only seen in mild cases.[10]
Collagen	No	Decreased pain compared to placebo has been observed.[7] Although promising, there is currently a lack of clinical evidence of efficacy.[9]
Deer Velvet	No	No clinical evidence of effect. A clinical trial found no significant difference between elk velvet and placebo for pain decrease in rheumatoid arthritis.[11]
Devils Claw (*Harpagophytum procumbens*)	No	Decreased pain compared to placebo has been observed with higher doses of the extract (60 mg), however a systematic review concluded that there is limited evidence of efficacy at present.[9]
Electromagnetic energy (pulsed electromagnetic field therapy)	No	Of five quality studies, none showed any benefit of this therapy over placebo for pain in osteoarthritis of the knee.[12]
Glucosamine sulphate	Yes	There is evidence supporting the efficacy of glucosamine in reducing pain and improving joint mobility and possibly in slowing disease progression.[13, 14]
Green lipped mussel	No	Decreased pain compared to placebo has been observed, however a systematic review concluded that there is limited evidence of efficacy.[9]
Homeopathy	No	Authors of meta-analysis of trials concluded that there was insufficient evidence that homeopathy is efficacious for any clinical condition.[15]

*Extract derived from one-third avocado oil and two-thirds soybean oil after hydrolysis

Table 1: (Continued from previous page). Supplements, herbal products and devices used for the treatment of osteoarthritis in New Zealand.

Product	Evidence of clinical effect for OA?	What is the evidence?
Ionised wrist band	No	A study found no difference in the reduction in pain for people wearing ionised bands compared to those wearing placebo bands. There was an overall decrease in pain for both groups.[16]
Laser therapy*	No	Four RCTs compared laser therapy with placebo and found no significant difference in pain outcomes.[17]
Methylsulphonylmethane (MSM)	Inconclusive	Based on two RCTs, 500mg of MSM significantly improved pain and joint mobility. There is moderate evidence of efficacy.[9] More evidence is needed.
S-Adenosylmethionine (SAMe)	Inconclusive	Clinical trials demonstrated a reduction in pain and functional limitation which was greater than placebo and comparable to NSAIDs. However, it is thought that SAMe may act by decreasing the perception of pain and therefore the effect may diminish over time. Onset of action is slower than with NSAIDs. Some documented cases of agitation and manic reactions in people with bipolar disorder.[7]
Shark cartilage	No	A reduction of pain has been demonstrated in vitro, however evidence of clinical effect is lacking.[18]
Withania/Ashwagandha	No	Only one RCT exists of this extract in combination with boswellia and zinc. There is a lack of evidence of efficacy.[9]

* Low level laser therapy uses a light source to generate "photochemical reactions in cells"

Chondroitin sulphate is also widely promoted for use in osteoarthritis. It is a carbohydrate component of cartilage, usually derived from cows and often combined with glucosamine in supplements. The dose most often used in clinical trials is 1200 mg/day.

In vitro and animal studies have found that chondroitin contributes to the cartilage matrix, inhibits proteolytic enzymes (that break down cartilage) and stimulates synthesis of collagen and glycosaminoglycan. Chondroitin has been shown to work in synergy with glucosamine.[7] There is a lack of evidence of an effect on joint space narrowing, but several trials concluded that chondroitin has significant analgesic properties when compared with placebo, as well as demonstrated improvements in joint mobility.[7] However, the authors of a recent meta-analysis of large-scale clinical trials, concluded that the symptomatic benefit of chondroitin is minimal, and likely to only be seen in mild cases of osteoarthritis.[10]

Chondroitin does not appear to be associated with any significant adverse effects, however it has a mild anticoagulant effect and may interact with drugs such as warfarin and heparin. The long-term safety profile of chondroitin remains uncertain.[7]

> Chondroitin sulphate at 1200 mg/day may have some analgesic benefit, especially when combined with glucosamine.

Bottom Line: It is likely that glucosamine sulphate has some benefit in reducing pain, improving joint mobility

and perhaps in slowing the progression of osteoarthritis. The evidence for chondroitin is conflicting. Both products have fewer (or less severe) side effects than NSAIDs, but it is unknown what the long-term effects of using these supplements are. In addition, it is perhaps unwise to promote widespread, long-term use of products that are not regulated or subject to quality control. A cautious approach is indicated.

ASU – the new kid on the block

Avocado soybean unsaponifiables (ASU) is a lipid mixture that has been gaining recent interest for its apparent beneficial effect on pain in osteoarthritis. It is an extract derived from the hydrolysis of one-third avocado oil and two-thirds soybean oil. The main component of the resulting mixture is plant sterols, therefore any adverse effects on lipid profile with use of ASU is unlikely - in fact plant sterols are known to be beneficial in lowering cholesterol.

Results from several randomised controlled trials were assessed in a systematic review and it was found that ASU 300 mg/day decreased NSAID use and resulted in improved joint mobility. In short-term (three to six month) studies, there was a two month delayed onset of action and residual effects persisted for two months after treatment ceased. In a long-term (two year) study, pain scores, mobility and concurrent NSAID intake were not different from placebo after one year. There is no evidence that ASU slows the narrowing of joint space, but there have been some observations of beneficial disease modifying effects in severe osteoarthritis.[9]

Bottom Line: There is good evidence that ASU has medium term (several months) symptomatic benefit in osteoarthritis, including reducing NSAID use, but there is currently a lack of evidence for its long term benefit. Further investigation is required.

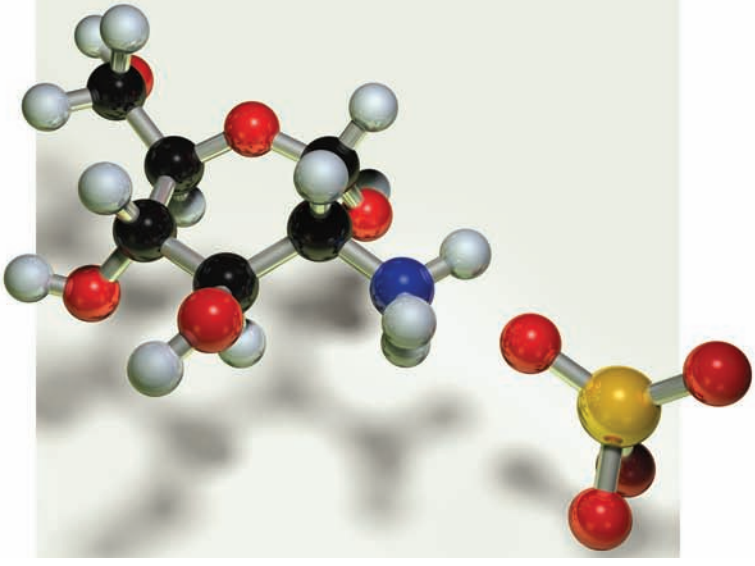
A special note on magnetic devices to treat pain

To date, over $5 billion has been spent worldwide on magnetic devices to treat pain.[19] However there is currently

Sulphur amino acids

Many supplements used in the treatment of osteoarthritis also contain large quantities of sulphur (e.g. chondroitin, glucosamine, SAMe). We require a certain amount of sulphur in our diet and this is usually ingested in the form of cysteine or methionine (amino acids). Protein-rich foods are a good source of sulphur, as are vegetables such as asparagus, onions, beans and cabbage. Sulphur deficiencies are rare.

Sulphur is used in our body for the synthesis of glycosaminoglycans which form the cartilage matrix. In osteoarthritis, the turn-over of glycosaminoglycans is greatly enhanced, and as a result sulphate levels in the body are rapidly depleted. Therefore, dietary sulphur may play an important role in the treatment of osteoarthritis. It is possible that at least some of the therapeutic value attributed to these supplements is due to their sulphur content. It is known that glucosamine hydrochloride has less therapeutic value than glucosamine sulphate. Increasing intake of dietary sulphates may have a similar effect to taking these products.[7]



no definitive evidence to support an association between magnets and pain reduction. It is claimed that magnetic fields increase circulation and therefore enhance healing of tissue, however this has not been proven. Magnetic underlays in New Zealand cost around $200 to $500.

Authors of a recent study concluded that exposure to a static magnetic field (magnets in a mattress) does not alter pain perception, sympathetic nerve function, blood pressure or heart rate. Study participants were tested once on a regular mattress and once on a mattress with imbedded magnets – participants were not aware which treatment they were receiving. Subjects first rested on the mattress for one hour, and then performed three interventions (isometric handgrip, muscle ischaemia induced by a blood pressure cuff and immersion of their hand in ice water). Exposure to the magnetic field did not alter pain perception during the three interventions and was not associated with increased muscle sympathetic nerve activity, heart rate or blood pressure at rest.[20]

It is interesting to note that the study most often quoted by companies selling magnetic mattresses did not actually involve the use of a magnetic mattress. Pain response was tested in people with post-polio syndrome with pre-existing knee pain. The 29 people assigned to receive the treatment had a credit card sized magnetic device applied directly to the site of their pain. These participants reported a greater reduction in their pain than the 21 participants assigned to the inactive device. Pain relief was achieved within 45 minutes and was assessed subjectively using a questionnaire. No physiological measurements were taken.[21] As the pain experienced by people with post-polio syndrome is unique, the results of this study cannot be extrapolated to other causes of pain.

Bottom line: It seems unlikely that magnetic mattresses have any clinically significant effect.

The placebo effect

Sometimes something which shouldn't work, according to science, does work. Belief in the value of alternative therapies is often very strong and this accounts for much of the success of otherwise ineffective treatments.[22]

- People may get better due to the natural course of an illness and attribute this "cure" to their coinciding alternative therapy.
- Many illnesses are cyclical and people often seek alternative therapy when symptoms are at their worst. When symptoms are better, this is attributed to the therapy, when it is the upwards side of the cycle.
- An alternative therapy may be tried after months of conventional medical treatment and when symptoms improve, it is attributed to the new therapy rather than the prior intensive medical treatment.
- If the original diagnosis is wrong, then claims of a cure are meaningless.
- Often the time and attention given by the provider of alternative therapy accounts for more improvement in wellbeing than the therapy itself.
- The psychological investment that people and their families put into believing that something will work may account for much of the perceived benefit of the treatment.[22]
- Alternative therapies may help to maintain hope.

Bottom line: If a person finds something to alleviate their symptoms and it does not cause financial burden, adverse effects or interact with or compromise their conventional therapy, then it is of benefit, whether or not a peer-reviewed meta-analysis proves that it works.

Further reading:

Bandolier knowledge library: a "down to earth" approach to assessing the evidence on many alternative therapies. Search by key word. Available from:

http://www.jr2.ox.ac.uk/bandolier

Mayo Clinic: Up to date information about developments in anti-ageing medicine (search by topic). Available from:

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Exploring the Everyday Experiences of **Older Māori** and their **Medication**

Key contributor: Bevan Clayton-Smith, Ngati Maniapoto, MClinPharm, PhD Candidate, Research Centre for Maori Health and Development, Massey University

www.bpac.org.nz keyword: oldermaori

Key Points:

- **Enquire about the views and perceptions of health and well-being of older Māori**
- **Reassure older Māori about the need for the medication in a way they can relate to**
- **Provide information that aligns with Māori beliefs, values and understandings**
- **Provide written information including the safe use, storage and disposal of the medication**

Older Māori negotiate the complexities of medication and its use through self-regulation and self-management – guided by their beliefs, values, and attitudes along with the issues they face on a day-to-day basis.

The 1997 Oranga Kaumatua Study about the health and well-being of older Māori people revealed a number of factors (Box 1).[1] There are a number of issues that need to be addressed.

Older Māori are likely to follow instructions, driven by trust and respect for the doctor's authority. This may lead to older Māori continuing to take medication when it is no longer needed[2, 3]

Older Māori are more likely than non-Māori to be treated for the symptoms of chronic conditions rather than the conditions themselves.[4, 5, 6, 7]

Insufficient information is provided to Māori concerning the safe use, storage and disposal of medicine. This is a particular concern if there are communication issues, they are living alone, are without social support, or are caring for mokopuna (grandchildren).[8]

Factors emerging from the 1997 Oranga Kaumatua Study about the health and well-being of older Māori people.[1]

- Two-thirds of older Māori were taking medication on a regular basis
- 75% recalled what it was they were taking
- 95% knew what the medication was for
- Almost 100% indicated that they knew when to take their medication
- 88% of older Māori received health advice/ information from their doctor
- 36% received information from their pharmacist
- Older Māori preferred or relied on non-medical sources of information
- Almost half indicated that they always followed the health information they received, 20% indicated they often followed advice and 26% sometimes followed medical advice
- Older Māori preferred information to be provided 'kanohi ki te kanohi' (face to face), in written form and through hui, although non traditional methods such as multimedia still rated highly
- Information provided by the health provider was most preferred (87%), followed by Māori health workers (26%), friends (11%) and whanau (2%)

Considerations for Older Māori and their Medication

Medication for Māori is more than just pharmacological and physical. For older Māori, medication may be viewed as a conduit to facilitate other important factors and events in their lives that enhance their well-being and enable them to live active and self-dependant lifestyles. Therefore medication use is not considered in isolation.

When prescribing for older Māori, it may be best to link the benefits of the medication with their ability to carry on with their lives – preserving and strengthening their social space and networks, their sense of well-being, their productiveness for themselves, their whānau and their community and their ability to function optimally. What may be important for older Māori are the improved health outcomes that result from taking medication rather than, for example, knowing their glycosylated haemoglobin is 8% after taking metformin for six months.

Understanding how older Māori perceive their well-being, by asking what is important for them may be an alternative approach to promote the benefits of their medication. Stressing patient-centered priorities, aligned with their health beliefs, goals and expectations rather than that of their doctor, is useful. The example using asthma and utilising Durie's whare tapa wha framework[9] explains this further (Table 1).

Conclusion

For older Māori, being provided with information about their medication that aligns with their needs, beliefs and understanding is essential. This optimises the benefits of the medication and ultimately improves health and well-being.

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Table 1: Managing asthma using the whare tapa wha framework

Wairua (Spiritual)	Hinengaro (Psychological)	Tinana (Physical)	Whanau (Family)
Improved asthma management allows a feeling of well-being which others will notice	Improved asthma management gives confidence for managing future attacks and reduces anxiety	Improved asthma management results in less problems with breathing and ability to participate in and enjoy a wider range of physical activities	Improved asthma management results in less distress for family and gives more energy for participation in family activities

Snippets

Topical or oral NSAIDs – a decision model

A recently published study in the BMJ suggests that taking the views of the patient into account when prescribing NSAIDs may improve adherence, judgement of efficacy and the doctor-patient relationship. It is important to closely monitor elderly people who use NSAIDs.

A model was developed for shared decision making about the prescription of oral or topical NSAIDs, taking into account both patients and clinicians beliefs about clinical benefit, adverse effects, preferences and costs.

Factors influencing patient treatment choice include:

- Relief of symptoms
- Adverse effects (or perceived risk)
- Availability of alternative treatments
- Perceived severity of condition
- Nature of pain
- Presence of other illness
- Practicality
- Medical advice

The authors found that people with mild, transient pain preferred topical NSAID treatment and people with serious, constant or widespread pain preferred oral NSAID treatment.

The main issues identified were a lack of understanding and knowledge about NSAIDs and the impact this had on informed choice, trust in the GPs advice, perception of risk and education about adverse effects.

Increasing patients' knowledge through education about the causes of their pain, the mode of action of their medication and its potential adverse effects, improves both adherence and informed choice.

In general, older people are relatively trusting and accepting of their GPs advice and decisions about their healthcare. The advice of the GP plays an important role in the type of medication used.

The participants in the study tended to normalise general malaise, aches and a lack of well-being as a result of being old rather than as a consequence of the treatment prescribed. This demonstrates the need to monitor elderly patients closely to ensure that symptoms really are minor and not adverse effects of the medication.

There is a difference between perceptions of GPs and patients of adverse effects of oral NSAIDs. The risk of adverse effects influences choice – patients may opt for less effective treatments to avoid the perceived toxicity of more effective medications.

In summary, GPs should ensure that information about NSAIDs is effectively communicated and the decision to prescribe is made jointly with patients, based on practicality, appropriateness and acceptability.

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Dextropropoxyphene/paracetamol combinations withdrawn in the UK

In January 2005 the UK Medicines and Healthcare products Regulatory Agency (MHRA) announced it was withdrawing dextropropoxyphene/paracetamol products from the market. This followed a review of the safety and efficacy of these products where it was found that the benefits of this medicine did not outweigh the risks.[1]

Authors of a study in England and Wales found that dextropropoxyphene/paracetamol combinations were used as the sole method of suicide in 18% of drug-related suicides and this accounted for 5% of all suicides. They also found that dextropropoxyphene/paracetamol combinations were more likely to result in death when compared with tricyclic antidepressants or paracetamol, and that death can result from relatively few tablets, especially when combined with alcohol.[2]

The minimum lethal dose of dextropropoxyphene is 0.5g (equivalent to 10 tablets of Paradex).[3] Overdoses can result in severe CNS depression as well as cardiac arrhythmias and death can occur very rapidly, in some cases within 15 minutes to an hour.[4]

The MHRA decided to withdraw dextropropoxyphene/paracetamol products over a phased period which ended with the cancellation of licences in December 2007. Patients can still be supplied this medicine off-licence.[5]

A study conducted in New Zealand on opioid poisoning deaths from 2001 – 2002 reported that 16 of 92 opioid poisoning deaths involved dextropropoxyphene. Six of these were unintentional. One of their recommendations was that restrictions in the availability of dextropropoxyphene be considered in order to reduce deaths.[6]

There is no evidence that the combination of dextropropoxyphene and paracetamol has any analgesic benefit over paracetamol alone, particularly when used

Snippets

for the treatment of acute pain.[7] While this combination is commonly prescribed to older people, it is particularly unsuitable in this population as it causes sedation, dizziness and increases fall risk. (See pain article page 14)

In October 2006 Medsafe released a prescriber update article that advised of changes to the New Zealand datasheets for dextropropoxyphene/paracetamol products including:

- Narrowing of the indication to "relief of chronic pain of moderate severity"
- Restriction to second-line therapy for patients who have inadequately responded to, or have not tolerated, therapeutic doses of alternative analgesics
- Restriction of the recommended dose to two tablets every four hours with a maximum daily dose of eight tablets

They also reminded prescribers that concurrent use of alcohol is contraindicated.[8]

Dextropropoxyphene/paracetamol combination products are currently on the Intensive Medicines Monitoring Programme (IMMP)

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8. Medsafe. Dextropropoxyphene-Paracetamol combination products and risk of overdose. Prescriber Update 2006; 27(2): 21-22. Available from; http://www.medsafe.govt.nz/profs/PUarticles/dextro.htm. (Accessed January 2007).

Reduced antibiotic prescriptions results in less resistance at practice level

A recently published study conducted in Wales showed that a reduction in antibiotic dispensing at general practice level resulted in a small but significant reduction in local antibiotic resistance.

The seven-year study involving 240 general practices investigated the number of dispensed antibiotics and antibiotic resistance in coliform isolates from urine samples.

General practices that reduced dispensed antibiotics the most, showed a significant decrease in antibiotic resistance to ampicillin and trimethoprim, compared with practices that reduced dispensed antibiotics the least.

Overall, for practices that reduced their amoxicillin prescribing by 50 items per 1000 patients each year, there was a statistically significant 1.03% decrease in ampicillin resistance. There was also a significant 1.08% decrease in trimethoprim resistance per decrease of 20 trimethoprim items dispensed per 1000 patients each year.

The researchers concluded: "Reducing antibiotic dispensing at general-practice level is associated with reduced local antibiotic resistance. These findings should further encourage clinicians and patients to use antibiotics conservatively."

Other international studies have shown a decrease in antibiotic resistance associated with a population level reduction in antibiotic use. However this is the first study to examine the local impact of reduced antibiotic prescribing on levels of antibiotic resistance.

This is very relevant to general practice and provides the important message to GP's that individual antibiotic prescribing patterns can influence antibiotic resistance in their own practice population.

Reference:

Butler C, Dunstan F, Heginbothom M, et al. Containing antibiotic resistance: decreased antibiotic-resistant coliform urinary tract infections with reduction in antibiotic prescribing by general practices. Br J Gen Pract 2007; 57(543): 785-792.

Evidence That Counts

Calcium and Vitamin D Intake and Risk for Breast Cancer

Animal experiments and observational human studies suggest that calcium and vitamin D may decrease risk for breast cancer. Researchers prospectively assessed this relation among 10,000 premenopausal and 20,000 postmenopausal women enrolled in the Women's Health Study. Calcium and vitamin D intake was determined from self-reported questionnaires about food and vitamin supplement intake. During a mean follow-up of 10 years, the overall incidence of invasive breast cancer was 2.6% among premenopausal women and 3.6% among postmenopausal women. The hazard ratio for developing invasive breast cancer was 0.61 for premenopausal women at the highest versus lowest quintiles of calcium intake and 0.65 for vitamin D intake. No relation was found between calcium and vitamin D intake and risk for invasive breast cancer among postmenopausal women.

Comment:

In this large, prospective study, a higher intake of calcium and vitamin D was associated with a lower risk for invasive breast cancer among premenopausal but not postmenopausal women. Although the hazard ratios appear relatively large, the absolute risk reduction was modest. Limitations of this study include ascertainment of calcium and vitamin D intake only once at baseline and the possibility that unmeasured confounding variables explain the findings in this nonrandomised assessment of diet.

— Jamaluddin Moloo, MD, MPH

Lin J et al. Intakes of calcium and vitamin D and breast cancer risk in women. Arch Intern Med 2007 May 28; 167:1050-9.

Long-Term Benefits of Reducing Sodium Intake

Reducing sodium intake has been demonstrated to lower blood pressure in people with hypertension and to prevent the onset of hypertension in people at risk for it. However, the effect of reducing sodium intake on cardiovascular disease outcomes and mortality remains somewhat controversial. This long-term follow-up study shows a beneficial effect on key outcomes. U.S. investigators followed up participants in two randomised trials (TOHP I and II) that were completed in the 1990s. All 3126 participants had high normal blood pressure at baseline and were randomised to a sodium reduction intervention or a control group. Follow-up information was obtained from 2415 participants at 10 to 15 years after the original studies ended. The risk for a cardiovascular event was 25% lower in the intervention group, after adjustment for clinic, race, age, and sex. The risk for death from cardiovascular disease was 20% lower in the intervention group, but this difference did not quite reach statistical significance. Intervention patients were significantly more likely to prefer low-salt foods and to monitor their salt intake.

Comment:

This study presents some of the strongest evidence yet to show that reducing sodium in the diet can reduce certain important clinical events, even in people without overt hypertension. The authors recommend less sodium for everyone as a public health measure, an approach endorsed in a recent review article on the role of sodium and potassium in the pathogenesis of hypertension (N Engl J Med 2007; 356:1966).

— Keith I. Marton, MD

Cook NR et al. Long term effects of dietary sodium reduction on cardiovascular disease outcomes: Observational follow-up of the trials of hypertension prevention (TOHP). BMJ 2007 Apr 28; 334:885. (http:// dx.doi.org/10.1136/bmj.39147.604896.55)

Low Bleeding Risk in Older Adults Receiving Warfarin for Atrial Fibrillation

Most patients with atrial fibrillation (AF) are older than 75. Clinical guidelines call for anticoagulation in these patients, although they are perceived to have increased risk for haemorrhage and are underrepresented in clinical trials. In this randomised trial, 973 patients (age ≥75) with atrial fibrillation or flutter were recruited from primary care practices in the U.K.; they received warfarin (titrated to an INR of 2–3) or aspirin (75 mg daily). After an average 2.7 years of follow-up, patients who received warfarin had significantly fewer fatal or disabling strokes, other intracranial haemorrhages, or clinically significant arterial emboli than those who received aspirin (1.8% vs. 3.8% per year). Warfarin was as effective in people older than 85 as in younger patients. Major haemorrhages were rare and occurred at similar rates in both groups (1.9% and 2.0% per year on warfarin and aspirin, respectively). Haemorrhage risk rose similarly with age in both groups.

Comment:
Several factors may help explain the infrequency of major haemorrhages in this trial: The target INR was lower than in some previous trials (with no reduction in efficacy), a large number of patients were taking warfarin before randomisation, and the frequency of crossover between treatments was high. In contrast, a recent observational study reported an extremely high rate of major haemorrhage — 13 events per 100 person years — during the first year of warfarin therapy among patients aged 80 and older (Circulation 2007; 115:2689), suggesting that anticoagulation may be safer in a controlled trial setting than in actual practice. Nevertheless, the results of this new trial suggest that some older adults from whom warfarin is withheld because of fear of bleeding might benefit from a less cautious approach.

— Bruce Soloway, MD

Mant J et al. Warfarin versus aspirin for stroke prevention in an elderly community population with atrial fibrillation (the Birmingham Atrial Fibrillation Treatment of the Aged Study, BAFTA): A randomised controlled trial. Lancet 2007 Aug 11; 370:493-503.

Early Treatment of MS Symptoms with Interferon-β May Reduce Later Disability

Several studies have shown that after a first neurologic episode highly suggestive of multiple sclerosis (MS), treatment with interferon-β delays occurrence of a second episode at a different location (i.e., clinically definite MS). In one such study, industry-funded investigators randomised patients to begin interferon-β or placebo within 60 days of a first suggestive clinical event and to continue treatment for 2 years or until progression to clinically definite MS, whichever occurred first. Upon completion of the study, 378 patients accepted open-label interferon-β and continued regular clinical assessments, allowing the researchers to compare progression of disease and disability between patients who received early and delayed treatment. After a total follow-up of 3 years, risk for progression to clinically definite MS was significantly lower in the early treatment group than in the delayed treatment group (37% vs. 51%). Most patients in both groups remained at a low level of disability, but risk for progression on a standardised 10-point MS disability score was significantly lower in the early-treatment group (16% vs. 24%).

Comment:
Although these data seem to support treatment with interferon-β after an initial episode suggestive of multiple sclerosis, an editorialist advises caution, noting that the absolute differences in disability scores were small, and the number needed to treat (12) to prevent one patient from progressing to increased disability was large. This study will continue for 2 more years and may yet provide more robust results.

— Bruce Soloway, MD

Kappos L et al. Effect of early versus delayed interferon beta-1b treatment on disability after a first clinical event suggestive of multiple sclerosis: A 3-year follow-up analysis of the BENEFIT study. Lancet 2007 Aug 4; 370:389-97. Pittock SJ. Interferon beta in multiple sclerosis: How much BENEFIT? Lancet 2007 Aug 4; 370:363-4.

Does Recurrent Hypoglycemia Affect Long-Term Cognition?

In the landmark Diabetes Control and Complications Trial (DCCT), patients with type 1 diabetes (mean age 27) who received intensive insulin therapy had fewer microvascular complications than conventionally treated patients (JW Oct 15 1993, p. 57, and N Engl J Med 1993; 329:977). After this 6-year randomised trial ended in 1993, intensive treatment was recommended for all participants. Now, after 12 more years of follow-up (during which glycaemic control became similar in the 2 groups), 1144 subjects have been reexamined to determine whether an increased incidence of severe hypoglycaemia among intensively treated patients affected long-term cognition. During total follow-up of 18 years, 896 episodes of hypoglycaemic coma or seizures occurred in 262 patients in the original intensive-treatment group, and 459 episodes occurred in 191 patients in the original conventional-treatment group. The 6-year randomised portion of the study — when glycemic control was tighter with intensive than with conventional treatment — accounted entirely for this difference in hypoglycaemia. Scores on cognitive function tests (performed at baseline and 18 years later) remained similar over time, with no significant difference between groups.

Comment:

In this study, a higher rate of severe hypoglycaemia associated with intensive insulin therapy did not affect cognition adversely. However, the two groups were exposed to different intensities of glycaemic control — and thus differing rates of hypoglycaemia — during only 6 of the 18 years of observation; it remains possible that a longer-term comparison of intensive versus conventional treatment would result in a different outcome.

— Allan S. Brett, MD

The Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) Study Research Group. Long-term effect of diabetes and its treatment on cognitive function. N Engl J Med 2007 May 3; 356:1842-52.

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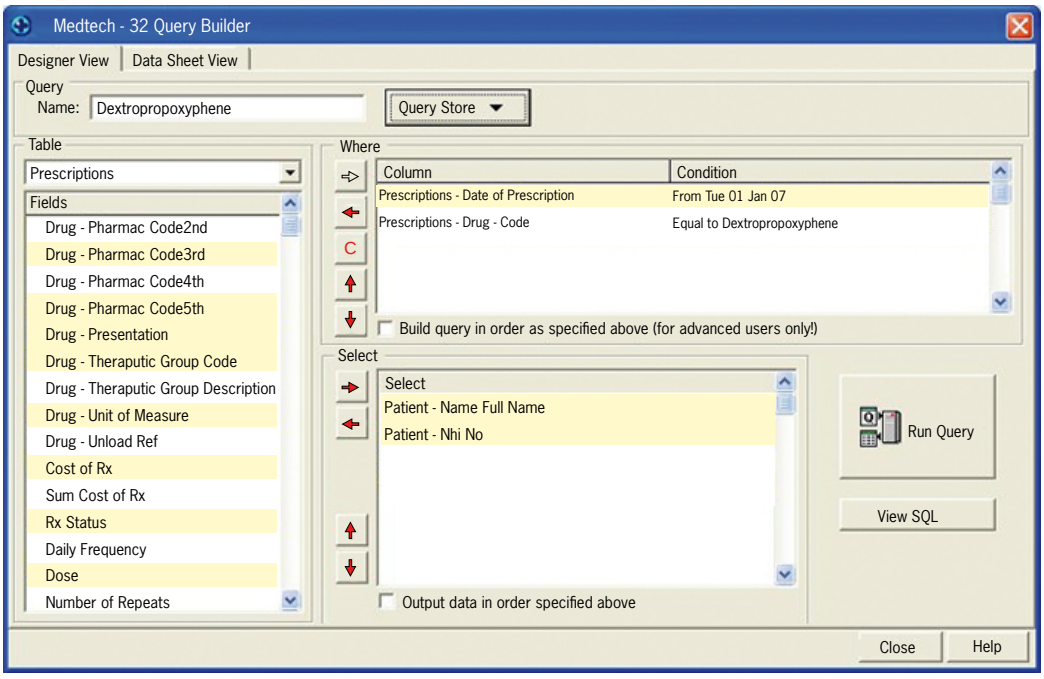
Ten Minute Audit

Identifying your patients on dextropropoxyphene

There has long been concern over the safety and efficacy of combination products containing dextropropoxyphene and paracetamol.

There is no evidence that this combination has any more analgesic benefit than paracetamol alone. In addition, it is particularly dangerous in overdose as it causes respiratory depression and cardiac arrhythmias and relatively few tablets constitute a toxic dose.



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The combination is especially unsuitable for elderly people as it causes sedation, dizziness and can increase the risk of falls. (See pain article page 14 and snippet page 43)

In 2005, following a review of the safety and efficacy of dextropropoxyphene/paracetamol combination products, the UK Medicines and Healthcare products Regulatory Agency (MHRA) decided to withdraw them from the UK market. In April 2006 the New Zealand datasheets for Capadex and Paradex were updated to contain more restricted dosing information.

While dextropropoxyphene products are still available in New Zealand, it may be a good time to check the suitability of these products for your patients. These products are now on the intensive medicines monitoring programme (IMMP). Follow the instructions to identify your patients for review.

Where now with cramp?

Dear bpac

We are having prescribers declining to continue quinine prescriptions for cramp, yet unable to offer any alternative beyond referral to us for OTC products. What is the current "Best Practice" for treatment of night cramp in the elderly?

Bruce Stimpson, MPS

The short answer is that unfortunately there is no real alternative to quinine for treating cramp.

There have been both local and international reports of thrombocytopenia associated with quinine use. This is thought to be an idiosyncratic hypersensitivity reaction which has a short time to onset and can be severe. Discontinuing quinine, should symptoms of thrombocytopenia occur, may not necessarily prevent serious consequences. For these reasons quinine is no longer indicated for the treatment of leg cramps.[1]

The first step for treating cramp is to exclude other possible causes. Some medicines that have been reported to cause leg cramp include diuretics, calcium channel blockers (especially nifedipine), beta-agonists, steroids, and fibrates.[2, 3, 4] Medical conditions associated with leg cramps include fluid and electrolyte disturbances, uraemia, diabetes, and thyroid disease.[2 ,3 ,4]

There are limited options to prevent leg cramps however some suggestions include:[2, 3, 4, 5]

- General measures to improve sleep such as avoiding alcohol and caffeine-containing drinks before bed, and not going to bed until tired.
- Stretching calf and foot muscles before going to bed and intermittently during the day.
- Drinking plenty of fluid during the day to avoid dehydration. But avoid drinking too much as this can dilute the concentration of sodium in the blood which can also cause leg cramps. About six to eight glasses may be appropriate.
- Wearing good shoes may help as flat feet and other structural problems may make some people more susceptible to leg cramps.
- Avoiding tight or heavy bed covers may help as this can tighten calf and foot muscles. Loosening the covers or sleeping on the stomach with feet hanging over the bed can keep muscles relaxed.

While there is limited evidence of the effectiveness of these measures they are generally safe and worth suggesting to patients suffering from leg cramps.

Dietary supplements such as magnesium and vitamin E have been suggested as possible remedies for leg cramps however the evidence of their effectiveness is lacking.[6]

Note: tonic water contains a very small amount of quinine. There have been isolated reports of adverse effects such as thrombocytopenia and skin reactions in people drinking large quantities, however, this is rare. Consuming normal quantities is unlikely to offer any benefit for treating leg cramps.

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5. Harvard Medical School Health. Five ways to prevent night time leg cramps. Harv Health Lett 2004; 30(2): 6.
6. Clinical Evidence. BMJ Publishing Group Limited 2008. Available from http://clinicalevidence.bmj.com/ceweb/conditions/msd/1113/1113.jsp (Accessed January 2008)

Should we prescribe fibrates?

Can't quite get my head around whether consensus is that fibrates are a waste of time and money in everyone nowadays or if there may still be subgroups of hyperlipidaemics who might derive benefit. Have you come across any reviews that may help?

Patch Graham.
GP, Nelson

Large trials of fibrates in recent years have generally shown significant positive changes in lipid levels however this has not consistently resulted in a reduction in cardiovascular events or all-cause mortality. Overall most trials have shown a trend towards a reduction in non-fatal cardiovascular events but most have not shown a significant reduction in mortality. This coupled with increasing evidence for statins to prevent cardiovascular events has resulted in a limited role for fibrates.[1,2,3]

Some guidelines suggest that fibrates may be used:

- As first-line therapy for severe hypertriglyceridemia (10 mmol/L or more), as these individuals are at high risk of pancreatitis.[2]
- For patients with high cholesterol only if other effective agents, such as statins, are contraindicated or not tolerated.[2]
- In combination with a statin for mixed dyslipidaemia that has not responded to initial statin therapy. However this combination must be monitored and is best initiated by a specialist as it carries an increased risk of muscle-related adverse effects such as rhabdomyolytis.[3]
- For some subgroups of patients such as those with type III genetic dyslipidaemia which is rare.[4]

References:

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3. Clinical Knowledge Summary. Lipids management. Available from: http://www.cks.library.nhs.uk/lipids_management/view_whole_guidance. Accessed January 2008.
4. Benatar JR, Stewart RA. Is it time to stop treating dyslipidaemia with fibrates? NZ Med J 2007; 120(1261): 65-68.

Safety of LABAs

I was surprised to find no mention of the increased risk of asthma exacerbations and asthma-related deaths with the use of LABAs in your article on Symbicort Maintenance and Reliever Therapy.

The Salmeterol Multicenter Asthma Research Trial (Chest 2006;129;15-26), which compared the safety of salmeterol or placebo added to usual asthma care, showed a two-fold increase in life threatening asthma exacerbations and a four-fold increase in asthma-related deaths in the salmeterol group.

A meta-analysis of the effect of LABAs on severe asthma exacerbations and asthma related deaths (Ann Intern Med. 2006;144:904-912) also found a 3.5-fold increase in asthma related deaths, a 2.6-fold increase in exacerbations requiring admission and a 1.8-fold increase in life-threatening exacerbation with the use of LABAs.

It is suggested that this increased risk is not seen with concomitant use of inhaled corticosteroids. However, in the above meta-analysis, when the evaluation was restricted to studies in which >75% of participants used inhaled

corticosteroids, a four-fold increased risk of hospitalisation was still demonstrated in the LABA treated group.

It seems that there is still sufficient concern about the safety of these agents to advise caution in their use even when combined with an inhaled steroid. The increase in their administration which is likely when used as part of the SMART regimen is therefore worrying and, I believe, warranted a mention in your article.

GP, Christchurch

Yes we agree, and it is possible that the effectiveness of the SMART regimen may be partly due to the change in use of corticosteroids. People may receive corticosteroids earlier in an exacerbation with the new single inhaler technique.

As you state, it appears from the recently published SMART trial, that LABAs may increase the risk of severe asthma exacerbations or death, particularly in those people on LABA monotherapy or of African American descent.[1]

Your letter has given us the perfect opportunity to reiterate the advice we gave in BPJ 2 (December 2006), where we included an update on the use of LABAs for the treatment of asthma. Our key points in that article were:

- Long acting beta agonists (LABAs) are not indicated as first-line therapy for any asthmatic patient.
- Adverse reactions to LABAs such as hyper-responsiveness, bronchospasm and respiratory arrest are rare but patients should be closely monitored for the first 6 - 12 weeks after the initiation of treatment.
- LABAs should only be prescribed for people who are already on inhaled corticosteroids (ICS).
- LABAs may be indicated as add-on therapy if symptoms do not respond to low to moderate doses of ICS (e.g. in adults 400 - 800 micrograms beclomethasone or equivalent).
- Patients on LABAs should be counselled and reminded of the importance of continuing their ICS.
- LABAs should be discontinued after a trial period if no benefit is seen.
- Patients with acutely deteriorating asthma should not be started on a LABA.
- Review the asthma management plans of people on combination LABA/ICS inhalers.

The November 2007 Prescriber Update contained a similar reminder about safe prescribing of LABAs and gave the following advice: [2]

- LABAs should not be used as monotherapy or first-line treatment for asthma; a LABA should be added to asthma treatment only if an appropriate dose of an inhaled corticosteroid does not provide adequate control.
- Patients should be warned not to stop or reduce corticosteroid therapy without medical advice, even when symptoms improve.
- LABA therapy should not be initiated, or the dose increased, in patients with significantly worsening or acutely deteriorating asthma.
- Patients should be advised to seek medical attention immediately if their asthma deteriorates suddenly.
- A reassessment of therapy should be undertaken if asthma worsens despite regular use of a LABA and an inhaled corticosteroid.

References:

1. Nelson H, Weiss S, Bleecker E, et al. The salmeterol multicenter asthma research trial: A comparison of usual pharmacotherapy for asthma or usual pharmacotherapy plus salmeterol. Chest 2006; 129: 15-26.

2. Prescriber Update 2007; 28(1): 3. Available from: http://www.medsafe.govt.nz/profs/PUArticles/PDF/PrescriberUpdate_Nov07.pdf. Accessed December 2007.

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