INFORMATION FOR AUTHORS
First page following cover

EDITORIALS
409 PHARMAC Mark 2: towards agreed solutions? Nick Bosanquet
410 Extended prescribing rights - a statutory right or hard-earned privilege? Tim Maling
411 Nurse prescribing The Editors

ORIGINAL ARTICLES
412 Anti-endomysial and anti-gliadin antibodies in screening for coeliac disease in children at greater risk of developing coeliac disease AS Day, HB Cook, M Whitehead, GD Abbott
414 A profile of alcohol and drug clients in New Zealand: results from the 1998 national telephone survey Simon J Adamson, J Douglas Sellman, Ann Futterman-Collier, Terry Huriwai, Daryle Deering, Fraser Todd, Paul Robertson
416 The accuracy of references in Australian and New Zealand Medical Journals Shaun Holt, Robert Siebers, Aneta Suder, Rachel Loan, Oliver Jeffery

CASE REPORT
418 Pulmonary thromboendarterectomy for thromboembolic pulmonary hypertension Philippa Shirtcliffe, Michael Nowitz, Alister Neill, Richard Beasley

SPECIAL ARTICLE
420 Guidelines for the use of flecainide in patients with supraventricular arrhythmias Warren Smith, Ian Crozier, Hugh McAlister, Tim O'Meeghan, Fiona Stewart

VIEWPOINTS
422 Reference pricing - is it in the public interest? Jennifer Martin, Evan Begg
425 Reimbursement of pharmaceuticals in New Zealand: comments on PHARMAC's processes Boyd Swinburn, Richard J Milne, Mark Richards, Evan Begg, Stuart Foote, Rod Jackson
Information for authors

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Abstract page – this must not exceed 200 words and should describe the core of the paper’s message, including essential numerical data. Use four headings: Aims, Methods, Results, Conclusions.

Body of the paper – there should be a brief introduction (no heading) followed by sections for Methods, Results, Discussion, Acknowledgements and Correspondence.

References – in the text use superscript numbers for each reference. Titles of journals are abbreviated according to the style used by Index Medicus for articles in journals the format is: Brawen GD. Outcome of managing impotence in clinical practice. NZ Med J 1999; 112: 272-3. For book chapters the format is: Marks P. Hypertension. In: Baker J, editor. Cardiovascular disease. 3rd ed. Oxford: Oxford University Press, 1998. p567-95. Note all authors where there are four or less; for five or more authors note only the first three followed by ‘et al’. Personal communications and unpublished data should also be cited as such in the text.

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The New Zealand experience with PHARMAC is of international interest, but it may also give signals about the local future. What lessons should be drawn about effective and appropriate policies in the future?

The paper in this issue of the Journal by Martin and Begg gives a local critique of how PHARMAC has carried out its task. This questioned PHARMAC’s assertion that reference pricing has had a sustainable effect on total expenditure. There is now ten years experience with reference pricing since it started in Germany and then extended to Sweden and the Netherlands. In Germany, reference pricing interventions were made in 1989, 1991 and 1992. These were followed by small reductions, but then spending returned to the trend. In Sweden, reference pricing was introduced in 1993. In the year after pharmaceutical sales growth was 1.6% less than the previous year. However, growth then rebounded to 16%. In the Netherlands, reference pricing had to be followed by a series of supporting measures which turned out to be troublesome, such as ‘voluntary’ price cuts, changes to the pharmacy incentive system, and eventually, a block on the entry of new products.

Other effects, such as cost shifting to new therapies without reference pricing and possible harmful side-effects leading to costs in treatment or hospital admissions, are even less easy to document than effects on total expenditure: however, such effects are quite likely. At the very least, we should be suspicious of any crude single solution over-riding local clinical judgement. Such solutions are best kept for emergencies rather than built into a permanent process.

Swinburn et al in their paper also in this issue of the Journal, make a useful start towards looking forward and setting an agenda for PHARMAC, which includes much more monitoring and evaluation of results. However, the decisions about the future need to be made against a wider background of what New Zealand might achieve. The focus for any new policy process should be on improving health outcomes. New Zealand, with its high level of professional skills and favourable environment, should surely be raising its sights towards a leadership role in the new challenges facing drug therapy worldwide.

New Zealand has a major opportunity to focus on achieving value with drug therapies. All countries are experiencing increased cost pressures, and New Zealand is not an exception. However, the question is whether New Zealand has made effective use of the new therapies to target high risk groups and to achieve the very real problems of budgetary control. Doctors and local managers should be willing to take ownership of the new therapies, but at the same time, it will have to face up to first base and to build on its potential strengths. It should become a beacon for effective drug treatment and timely use of new therapies, but at the same time, it will have to face up to the very real problems of budgetary control. Doctors and local managers should be willing to take ownership of budgetary control if given the opportunity.

Reference pricing has its attractions (it is easy to do), but the international evidence is that it is not very effective, it may in fact pre-empt the bargaining room for more local action. It also ties New Zealand to companies which may be the weaker partners for future development. The key focus for the future should be on local programmes to make most effective use of new therapies, especially through targeting their use on high risk groups.

Reference pricing also relies on the fallacy that there is no competition in the industry, and that local funders will be subject to intolerable price pressure - they will be ‘taken to the cleaners’ by the sellers. But the market is much more competitive than used to be the case, with much greater transparency of price information. New Zealand needs a low price, but it also needs to maximise its gains as an attractive partner which will be able to play a role in the developing new health programmes.

Access to medicines and access to knowledge and employment opportunities provided by pharmaceutical
companies are important to New Zealand. Unless PHARMAC exercises what is in effect monosponistic (sole buyer) power fairly, it will block New Zealand out of participation in one of the main growth areas in the 21st century new economy. PHARMAC should move towards agreed and negotiated solutions. PHARMAC has responsibilities for cost control and value for money, which are common to funders around the globe and are now well recognised by companies. There is scope for identifying common interests and meeting half way. Cost containment is a worldwide phenomenon: what is unusual to New Zealand is the relationship which is almost uniquely bad between industry and government. But there is an opportunity now to leave the past behind and to develop a new, more constructive approach which will serve the wider health interests of New Zealand.

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**Extended prescribing rights - a statutory right or hard-earned privilege?**

*Associate Professor Tim Maling, Clinical Pharmacologist, Wellington School of Medicine, Wellington.*

Modern medicines are generally cost effective. Without them, we would endure unacceptable incidences of serious diseases. We are fortunate that robust regulations exist to ensure that registered medicines in New Zealand are efficacious, when prescribed appropriately. There are also systems to monitor appropriate use and to ensure safety. To those who have never prescribed, the political decision to extend prescribing rights1 might seem to be relatively straightforward. However, for those of us who are authorised to routinely prescribe medicines, there is a flip side, which we learnt through a demanding course of undergraduate training in medical school and have re-learnt the hard way, in clinical practice.

In reality, medicines are expensive, inherently unsafe and difficult to use. Consider the not so simple decision to prescribe an antibiotic for the treatment of a bacterial infection. The prescription is the outcome of problem solving behaviour which involves diagnosis, the choice of antibiotic, and finally, the decision to prescribe or not. The remarkable variability in prescribing, amongst even the most skilled clinicians, is widely criticised by those who have never done it and who do not understand that the variability reflects the learnt components of widely differing clinical experience. Proponents of extended prescribing rights should not underestimate the complexity or the inherent difficulty of the prescribing process, especially in the context of national medicines utilisation.

**Where are we at?**

**Scopes of practice.** In January 2000, the new Government confirmed the concept of extended prescribing rights, embodied in the Medicines Amendment Act 1999. Cabinet agreed to the Ministry drafting regulations for nurse prescribing in Aged Care and Child and Family Health.2 The Ministry is also developing new proposals for Sexual Health, Palliative Care, Mental Health and Occupational Health.

**Limited medicine lists.** The Ministry is reviewing the composition of limited medicines lists, from which nurses may prescribe. The lists are meant to reflect the proposed scopes of practice, but there are some inconsistencies. The inclusion of broad spectrum antibiotics has been challenged by several expert groups, including the Ministry of Health Antibiotic Resistance Working Group. There is national concern for rapidly developing antibiotic resistance, at a time when there are several initiatives to minimise widespread antibiotic use. In contrast, antihypertensive drugs are not deemed to be safe for inclusion in the Aged Care list. Their adverse reaction profiles, compared with antibiotics and some other medicines included in the lists, need to be considered in the context of access to treatment of common problems - said to be one of the basic reasons for extending prescribing rights. Furthermore, if it is considered that the additional specialist training proposed for nurse prescribers will not permit safe prescription of an antihypertensives, then why are antibiotics included? Is the training for prescription of an antibiotic somehow different? Instead of a rather blurry preoccupation with medicines lists, the Ministry should recognise the importance of generic training for nurse prescribers, as already occurs for medical undergraduates. Nurse prescribers should be just as competent as medical practitioners, especially considering the risks inherent in paediatric prescribing and the high co-morbidity rates and propensity for poly-pharmacy in the elderly population.

**Standards for training programmes.** The move to extend prescribing rights has been strongly endorsed by the nursing profession, but there are nurses who remain concerned about the scope of their accountability and the still nebulous nature of the proposed training. In February 2000, the Nursing Council launched it’s Standards for Advanced Nursing Practice Programmes leading to Nurse Prescribing, to assess and monitor the new training programmes. The programmes will be delivered to Masters degree level and will include theory, research and current practice, and clinical pharmacology of the authorised medicines. The proposals are for a minimum of one year full time, although it is likely that the content will require a two year course. The Nursing Council has emphasised that entry requirements must include the demonstration of previously attained specialty nurse competencies, but it may be unwise to assume that the latter, even with additional experience, can substitute for the core knowledge needed to prescribe safely and effectively. The Council recognises that the programmes will require a lot of multidisciplinary input, it is unclear who will be doing the teaching, particularly in some of the Polytechnic based programmes.

**Dependent or independent nurse prescribing.** A key issue in the extended prescribing debate has been whether nurses should prescribe independently from medical practitioners, or whether they should be dependent prescribers.3 Dependent prescribers can continue to prescribe for a patient who has been clinically assessed, diagnosed and prescribed for initially by the doctor. An advantage of the dependent model is facilitation of a professional relationship between the nurse prescriber and the doctor. In a joint submission to the Parliamentary Select Committee, the Royal New Zealand College of General Practitioners and the Australasian Society of Clinical and Experimental Pharmacologists and Toxicologists endorsed the dependent
model in the context of a pilot study, to evaluate the health impact of extended prescribing. Senior nurses in the Ministry of Health see this as little more than ‘patch protection’ by the doctors and have pushed for independent nurse prescribing. The Parliamentary Select Committee are in favour of a post-implementation review, rather than a pilot study and are in favour of an independent, rather than dependent, prescribing model. However, there is no reason why a mix of dependent and independent nurse prescribers should not work well in New Zealand in the longer term, although it seems prudent to start with the dependent prescriber model and learn from the process. Independent prescribing status might be offered, for example, to family planning nurses, while dependent prescribers might include some specialist nurses and pharmacists. The Ministry stance, supported by the Nursing Council, could backfire as the nursing profession may find that nurses are discouraged, not only by the demands of the proposed course requirements, but also by the reality of the independent prescribing process.

New prescribers advisory committee. In August 1999, the then Minister of Health, the Hon Wyatt Creech, proposed the formation of a New Prescribers’ Advisory Committee, similar to a UK proposal, to assess applications from health professionals seeking prescribing rights. The new Government has now endorsed the proposal and nominations are being sought. Appropriate medical, as well as nursing representation on this committee will be fundamental in ensuring the quality of the whole extended prescribing initiative.

What does the future hold?

It is easy to cite the lack of evidence for real health gain from extended prescribing, and just as easy to retire into one’s professional shell, muttering “over my dead body”; but extended prescribing has major implications for ways in which development of shared responsibilities can improve standards of care of medical patients. Changes in the delivery of health services are evolving very rapidly, with increasing emphasis on delivery by teams, rather than individuals. In their submission to the Select Committee, the nursing organisations considered that the introduction of nurse prescribing “would provide further opportunities for collaborative practice with medical practitioners, whilst opening the way for improved access and timely treatment for patients.” There is much to commend this view, supported in principal by the Crown report from the UK, but one of the chief dangers of multidisciplinary teamwork is the loss of willingness of doctors to make decisions on their own.

Despite the lack of evidence, extended prescribing is being promoted as a logical step forward in the development of the multi-disciplinary team approach. For this to succeed, we will need to overcome the traditional professional barriers and deep rooted cultural differences between the nursing and medical professions, as well as ensuring that all prescribers are adequately trained. The final decision to proceed with independent or dependent nurse prescribing is crucial, since it will bear directly on the development of effective communication between the nurse, the doctor and the patient.

Nurse prescribing

It is the view of the editors of the Journal that the extension of prescribing rights to nurses, or any other group, should proceed with extreme caution. The scope of practice and degree of autonomy or independence given to new prescribers must be matched by an appropriate breadth and depth of education, if public safety and confidence is to be ensured. With the increasing complexity of prescribing, few doctors feel overtrained. Many feel increasingly inadequate in the face of multiple drug interactions, involving for example various cytochrome P450 enzymes, food-drug interactions (such as with grapefruit juice), and genetic and age-related variations in drug handling.

The political decision to commence nurse prescribing with the young and the elderly demonstrates a profound lack of understanding of the complexity and context of prescribing for these, the most challenging patient groups. Our concern is compounded by the political decision to promote independent and autonomous prescribing in preference to collaborative or dependent prescribing. Prescribers were largely excluded from the decision making process, and concerns expressed verbally and in writing seem to have been ignored. The rush to adopt autonomous independent nurse prescribing has pan-political party support in New Zealand and is part of an international trend. Some overseas academics (non medical) have observed that this political support has little to do with increasing access to appropriate drug therapy. “Politically it may well have more to do with saving money, transferring routine medical work to nursing, and importantly, a challenge to the professional monolith of Medicine,” state McCartney and colleagues. If implemented, independent nurse prescribing will inevitably increase fragmentation of care and stifle inter-professional cooperation. It is hard to see how this will advance nursing. Most of the medical organisations in New Zealand have expressed support for the development of collaborative or dependent prescribing, which most agree does have the potential to improve access to appropriate medications and to encourage greater collaborative teamwork.

Politics and professionalism aside, nurse prescribing must ultimately be evaluated in terms of its impact on the patient. We believe there are real safety concerns with the proposal to introduce independent prescribing. It is hard to conceive how courses that are so much shorter and less comprehensive than the current medical course will result in prescribing that is at least equivalent in safety to that practised by doctors. If the training proves inadequate, inevitably it will be the patients who will suffer. Is it reasonable for nurses to be expected to assume the professional and legal responsibility for this?

It is a source of great disappointment that the opportunity to develop collaborative prescribing models has been lost because of the pursuit of an anti-professional political ideology.

The Editors

Classically, coeliac disease is diagnosed in children following presentation within the first two years of life with progressive symptoms of malabsorption (failure to gain weight, diarrhoea, and abdominal distension) subsequent to the introduction of dietary gluten. It is now clear that children may present beyond the first years of life and may have either no symptoms or atypical symptoms. Atypical symptoms include: isolated difficulty gaining weight, short stature, and chronic abdominal complaints (for instance, abdominal pain or constipation). Furthermore, it is now recognised that coeliac disease occurs more frequently in conditions such as insulin dependent diabetes, and in association with a family history of coeliac disease.

There are suggestions that coeliac disease has not always been recognised or considered in New Zealand children. Awareness of the variable presentation of coeliac disease is therefore increasingly important in diagnosis and implementation of appropriate management. Early diagnosis may diminish or prevent complications associated with untreated coeliac disease, such as osteoporosis and anaemia. Furthermore, early institution and maintenance of a gluten-free diet may reduce the incidence of small bowel lymphoma in association with coeliac disease.

The aims of the study were to screen for coeliac disease with antigliadin antibodies (AGA) and anti-endomysial antibodies (EMA) in groups of children who may be at greater risk of developing the disease than the wider population, and to identify variable presentations of coeliac disease in children.

Methods

Patients. The study population comprised children seen as inpatients or outpatients at the Department of Paediatrics, Christchurch Hospital, over twelve months from March 1996. Children were identified prospectively by assessment of presenting symptoms, by previous history as documented in hospital clinical notes, or by the referral letter from their general practitioner. Children were considered to have a possible increased risk of coeliac disease when one or more of the following conditions was present: failure to gain weight without obvious cause (weight <3rd centile for age), short stature (height <3rd centile for age), chronic gastrointestinal symptoms (dyspepsia, abdominal pain, constipation, diarrhoea or intermittent vomiting), insulin dependent diabetes mellitus, or family history of coeliac disease. Children with known coeliac disease were excluded. In addition, children younger than six months and older than fifteen years of age were excluded. Infants younger than twelve months of age were included only if they had been on a gluten-containing diet for at least one month.

Results. Thirty-six of 153 children had abnormal antibody tests. Seven (4.5%) of 34 children who underwent small bowel biopsy were found to have histological findings consistent with coeliac disease. Five of these children had presented with symptoms not classically ascribed to coeliac disease (failure to gain weight or non-specific abdominal pain).

Conclusions. The possibility of coeliac disease should be considered in children with atypical symptoms and the diagnosis excluded by appropriate testing. Recognition of the variable presentations associated with coeliac disease in children is clinically relevant.
positive EMA had abnormal small bowel histology. Specific IgA deficiency was not present in any of the children with negative EMA.

Small bowel biopsy was recommended in each of the 36 children determined to have abnormal antibody tests, but was not performed in two children because of parental refusal. In seven of those who underwent small bowel biopsy, the histology of the small bowel biopsies was consistent with coeliac disease. The average age of those diagnosed with coeliac disease was 52 months (SD = 39, range 15-120 months). Of the children with abnormal SBB, only two had abnormal AGA and EMA together, three had positive EMA alone, and two had abnormal AGA alone. The latter two children were fifteen months of age and had markedly elevated IgG and IgA AGA antibodies with normal EMA results.

Five (10%) of 49 children with unexplained failure to thrive were found to have coeliac disease, as were two of fifteen children with abdominal pain (13%). Coeliac disease was not recognised in 38 children with short stature, 19 with a family history of coeliac disease, 25 with chronic gastrointestinal symptoms and 7 with insulin dependent diabetes mellitus. In two additional children, small bowel biopsy histology was inconclusive. One child had circumstantial support for a diagnosis of coeliac disease, with an equivocally positive EMA, a history of gastrointestinal symptoms and failure to thrive, and a family history of coeliac disease. The second child had elevated AGA levels, but negative EMA.

Discussion
Coeliac disease may be defined as a permanent intolerance to dietary gluten in those susceptible, leading to a typical morphological and histological appearance of the upper small intestinal mucosa, with associated changes in cell appearance and function, crypt hyperplasia and villous atrophy.11 In the present study, seven children were judged to have coeliac disease. Two of these children were diagnosed under the age of two years with typical duodenal histological features, following presentation with classic symptoms of coeliac disease. The remaining five children did not present with the classic spectrum of symptoms, but with isolated unexplained failure to gain weight or abdominal pain. Diagnosis of coeliac disease was not suspected prior to diagnosis in these five children and therefore would have been otherwise delayed.

The incidence of coeliac disease in children in Christchurch appears to be increasing.12 Whereas 22 children were diagnosed with coeliac disease over a twenty year period from 1970 to 1990, 22 further were diagnosed from 1991 to March 1997, and seven children were diagnosed within the year of this study. This may be due to increased recognition of coeliac disease, or due to a true increase in the disease.

Diagnosis of coeliac disease has been facilitated with the availability of antibody testing.11,14 In addition to use in diagnosis of coeliac disease in symptomatic patients, antibody tests have established utility in screening for coeliac disease in large unselected populations.15,16 The structure of the current study did not permit calculations of sensitivity or specificity. However, the results do suggest caution in reliance upon the results of EMA testing alone in children, especially in those less than two years of age. Only two children with abnormal small bowel biopsies had positive EMA in conjunction with positive AGA. In addition, a number of children with positive EMA results did not have histological changes consistent with coeliac disease on duodenal biopsy.

It is possible that several of the children with abnormal antibody tests and normal duodenal histology may have latent coeliac disease or mild enteropathy.17-19 In latent coeliac disease, individuals have normal SBB findings at one time-point (in association with symptoms or with abnormal antibody results), but subsequently develop abnormalities of the duodenal mucosa.17 As latent coeliac disease may be observed more commonly in individuals with a family history of coeliac disease,20 consideration should be made in these individuals for regular clinical review with repeat antibody testing and possibly repeat SBB.

While coeliac disease has been found in up to 10% of first degree relatives of individuals with coeliac disease,21 none of nineteen children in the current study proved to have coeliac disease (expected number = 2). In addition, coeliac disease was not diagnosed in the other groups included in the present study (insulin dependent diabetes mellitus, short stature and family history of coeliac disease). However, the numbers of children enrolled in these groups were small. In addition, the design of the study did not permit inclusion of children with other conditions (for example Down’s syndrome) that also have been associated with coeliac disease. These patient groups deserve further study in order to confirm the suggested associations and thereby provide optimal management.

This study demonstrates the diagnosis of coeliac disease in children who did not present with classical symptoms. Increased awareness of the variable presentations of coeliac disease in children is required.
A profile of alcohol and drug clients in New Zealand: results from the 1998 national telephone survey

Simon J Adamson, Lecturer; J Douglas Sellman, Director; Ann Futterman-Collier, Co-Director; Terry Huriwai, Lecturer; Daryle Deering, Lecturer; Fraser Todd, Senior Lecturer; Paul Robertson, Lecturer, National Centre for Treatment Development (Alcohol, Drugs & Addiction), Department of Psychological Medicine, Christchurch School of Medicine, Christchurch.

Abstract

Aims. To describe the profile of clients seen across the broad spectrum of dedicated alcohol and drug treatment services in New Zealand.

Methods. 217 randomly selected alcohol and drug treatment workers in New Zealand were interviewed by telephone, yielding a randomly selected sample of 291 clients. Workers were asked to identify the age, gender, ethnicity, main substance use problem and geographical location of clients.

Results. 60% of clients were male, 28% were Maori, the mean age was 31 years and the largest group of clients were seen for alcohol related issues (45%), followed by cannabis (27%) and opioids (17%). None of these variables differed significantly across residential/non-residential services. Significant trends to emerge were: that Maori clients were more likely to live rurally and to be in treatment for cannabis use, women were more likely to be in treatment for benzodiazepine use and less likely for cannabis use, opioid users were more likely to be seen at Crown Health Enterprise funded services, and cannabis users were (on average) younger than other clients, while alcohol users were older.

Conclusions. Alcohol and drug treatment services are dominated by clients seeking assistance with alcohol and cannabis use problems. Women are not under-represented in this population. Maori are over-represented. This contrasts with the absence of Asian clients and an under-representation of Pacific Island clients. There are some significant variations in the types of drugs used by different demographic treatment seeking populations. In contrast, client differences across treatment settings are minimal.

Alcohol and drug misuse in New Zealand carries a significant health burden to the general community. Reflecting the extent of this burden is the plethora of specialist alcohol and drug treatment agencies around New Zealand, with over 100 such services in operation.

New Zealand epidemiological studies indicate that substance misuse is common, particularly amongst men, Maori and young adults. The Christchurch Epidemiology Study reported six-month prevalence rates of DSM-III disorders in a household sample of 1498 adults, aged 16-64 years, in the Christchurch area in late 1986. For this study, 8.3% of the sample met criteria for an alcohol use disorder, while 1.5% met criteria for a drug use disorder.

The data from the Christchurch Epidemiology Study were not representative of the ethnic population of New Zealand. The sample was described as 96% ‘White’, 2% Maori, less than 1% Pacific Islander and 2% ‘Other’. Maori constitute 15.1% of the population and, consistent with other physical and mental health outcomes, are over-represented for first admissions to psychiatric hospitals for substance abuse or dependence by a factor ranging from 2.0 to 2.6 when compared to non-Maori.

The only previous New Zealand study to describe a cross-section of clients attending an alcohol and drug service examined an inpatient only population of 203 clients attending seven different residential programmes within the Canterbury region.

This telephone survey was conducted primarily for the purpose of gathering baseline data on New Zealand alcohol and drug workers, their practice, knowledge and attitudes, but was also recognised as an opportunity to gather a more comprehensive ‘snapshot’ of the clients seen by this workforce.

Methods

Following consultation with the treatment field, 90 services were identified as dedicated alcohol and drug treatment services. Dedicated services were defined as those employing paid staff (full time or part time) to do therapeutic work with people who have alcohol and drug problems. These staff must spend at least 70% of their clinical time working with people with alcohol and drug problems. The number of staff meeting this definition at these 90 services was 527. A random list of 288 staff, identified by first name and telephone number only, was drawn up and forwarded to interviewers. Of these 288 names, twelve were not used and 53 were ineligible due to having left the service, being managers/administrators or casual staff or could not be contacted in the time available. Of the remaining 223 eligible, there were six refusals, a response rate of 97.3%. The interviewers were four senior Clinical Psychology students.

All alcohol and drug treatment workers taking part in the survey were first asked a number of questions relating to the most recent client they had assessed in the two weeks preceding their interview, and then for the most recent client they had seen for a therapy session during the same period. Workers were asked the age, gender, ethnicity and main substance use of clients. Information pertaining to the geographic location and nature of the treatment service was gathered. Location was identified as either North Island or South Island, and one of New Zealand’s five main cities (Auckland, Hamilton, Wellington, Christchurch or Dunedin) or not. Services were defined as CHE (government funded Crown Health Enterprise) or non-CHE services, residential or non-residential, and for those residential services, whether or not the programme was primarily detoxification or post-detoxification.

In addition to the data discussed in this paper, respondents were asked questions in three further sections. The first asked a number of questions in relation to current and optimal practice, such as the use of formal diagnosis and the assessment of suicide risk. The second related to knowledge of alcohol and drug information, such as responsible drinking guidelines and key therapeutic models. The final section contained a number of questions, including abstinence orientation and the relationship of alcohol and drug services with mental health services. The interview took an average of 30 minutes to complete.

Because of the large number of grouping variables analysed, only p values less than 0.005 were reported as statistically significant. Grouping comparisons were performed for each question, but are only reported where results were significant at this chosen level.

Results

Of the sample of 217 workers, 130 had assessed a client in the preceding two weeks, while 169 had conducted a therapy session during that time period. In only eight cases was the last person seen for a therapy session also the last person assessed. Clients from both groups (assessment versus therapy) were compared on all variables displayed in Table 1 and no differences between the two groups were found. All
clients were subsequently combined to make a single sample. The eight clients in both groups were counted only once, resulting in a total of 291 clients who had been seen for therapy or an assessment in the two weeks preceding the research interview.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Percentage (n)</th>
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<td>Gender</td>
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<td>Male</td>
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</tr>
<tr>
<td>Pacific Islander</td>
<td>2.7% (8)</td>
</tr>
<tr>
<td>Latino</td>
<td>0.3% (1)</td>
</tr>
<tr>
<td>Main Substance</td>
<td></td>
</tr>
<tr>
<td>Alcohol Only</td>
<td>26.5% (77)</td>
</tr>
<tr>
<td>Mainly Alcohol</td>
<td>18.6% (54)</td>
</tr>
<tr>
<td>Mainly Cannabis</td>
<td>16.5% (48)</td>
</tr>
<tr>
<td>Alcohol &amp; Cannabis</td>
<td>10.7% (31)</td>
</tr>
<tr>
<td>Mainly IV Opioids</td>
<td>17.2% (59)</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>5.5% (16)</td>
</tr>
<tr>
<td>Other</td>
<td>5.2% (15)</td>
</tr>
<tr>
<td>Location</td>
<td></td>
</tr>
<tr>
<td>North Island</td>
<td>73.1% (211)</td>
</tr>
<tr>
<td>South Island</td>
<td>26.7% (77)</td>
</tr>
<tr>
<td>One of Five Main Cities</td>
<td>62.6% (181)</td>
</tr>
<tr>
<td>CHE</td>
<td>61.0% (177)</td>
</tr>
<tr>
<td>Non-CHE</td>
<td>39.0% (113)</td>
</tr>
<tr>
<td>Residential</td>
<td>26.5% (77)</td>
</tr>
<tr>
<td>Non-Residential</td>
<td>73.5% (214)</td>
</tr>
<tr>
<td>Detox</td>
<td>17.1% (13)</td>
</tr>
<tr>
<td>Post-Detox</td>
<td>82.7% (62)</td>
</tr>
</tbody>
</table>

The mean age of clients was 30.9 years. When clients were grouped into age tertiles (less than 26, 26 to 34, and 35 years and over) there were no significant age differences by ethnicity, gender or geographical location. Age did vary significantly by main substance used ($\chi^2 = 45.65$, df = 12, $p < 0.0005$), with alcohol use more common in the older group, and cannabis more common in the younger.

Just over a quarter of the sample were described as New Zealand Maori (27.8%), while the majority were Caucasian (69.1%). The remainder were 2.7% Pacific Island and one Latino (0.3%). When compared to Statistics New Zealand (1996) data on the ethnic mix of the general population, this is an over-representation of Maori, who make up 15.1% of the general population, an under-representation of Pacific Islanders, who make up 5.8% of the general population, and a complete absence of Asian clients, who constitute 5.0% of the general population.

Almost half of the clients were identified as presenting for alcohol or mainly alcohol use, with cannabis being the next most prevalent substance when ‘cannabis’ and ‘cannabis and alcohol equally’ were combined. Opioids and benzodiazepines were also significantly represented. The remaining 5.5%, classified as ‘Other’, included a number of individuals described as polysubstance users, plus those who used a range of individual substances, and one client who was being seen for a gambling problem. Women were less likely to be identified as cannabis users (12.8%) than men (36.8%), ($\chi^2 = 20.3$, df = 1, $p < 0.0005$). In contrast, women were more likely to be identified as benzodiazepine users (11.1%) than were men (1.7%) ($\chi^2 = 11.86$, df = 1, $p < 0.002$). Maori were more likely to be identified as cannabis users (40.7%), when compared to the remainder of the sample (21.9%), ($\chi^2 = 10.49$, df = 1, $p < 0.002$).

Clients seen mainly for cannabis or cannabis and alcohol equally were younger (25.0 years) than the remainder of the sample (33.1 years), (t = 6.50, df = 289, $p < 0.0005$). There was also a significant age difference for clients with alcohol or mainly alcohol (33.8 years), compared with clients seen primarily for other drug use problems (28.5 years), (t = 4.56, df = 289, $p < 0.0005$).

Close to three-quarters (73.3%) of the sample lived in the North Island and 62.6% lived in one of the five largest cities (Auckland, Hamilton, Wellington, Christchurch and Dunedin). This is comparable to New Zealand statistics, indicating that 75.4% of the population live in the North Island and 53.6% live in the five largest cities (Statistics New Zealand, data as of 30 June 1997). Maori were less likely to be represented amongst clients seen in one of the five main cities, with 46.9% of Maori clients living in cities, compared to 68.8% of non-Maori, ($\chi^2 = 11.88$, df = 1, $p < 0.001$). On closer examination, it was revealed that this difference was primarily due to the distribution of Maori in the North Island, 45.3% of whom attended services in one of the three main cities, compared to 70.7% of non-Maori = 12.38, df = 1, $p < 0.001$. In the South Island on the other hand, 52.9% of Maori were seen at services in one of the two main cities, compared to 63.3% of non-Maori ($\chi^2 = 0.60$, df = 1, ns). Location did not predict differences in any of the remaining client characteristics variables.

Information was also gathered as to whether workers were working for CHE or non-CHE services, residential or non-residential services; and for those in residential services, whether or not the programme was primarily detoxification or post-detoxification. Analysis found only one significant difference in client variables across these workforce locations. Intravenous drug users were seen at CHE services in 80% of cases, whereas 57% of non-intravenous drug users were seen at CHE services ($\chi^2 = 9.14$, df = 1, $p < 0.002$). There were no other significant differences for gender, ethnicity or age across workforce location.

**Discussion**

The picture revealed by this survey is that across locations and across services, alcohol and drug workers are assessing and treating essentially the same people. These clients are more often men than women, the mean age being 31 years, and over two-thirds are Caucasian. They are most likely to live in a North Island city where they are seen in outpatient CHE services. Problematic alcohol use is the most likely reason for presentation.

Women constituted a sizeable minority of the sample at 40.2%. Whilst this is an under-representation when compared to the general population in New Zealand, epidemiological data on substance misuse would suggest that this figure is actually an over-representation of women, given that women are less likely to suffer from alcohol and drug related disorders. The Christchurch Psychiatric Epidemiology Study found a six-month prevalence for substance use disorders (abuse or dependence) of 15.4% for males and 3.0% for females. Thus, of those meeting criteria for a substance use disorder, 16.3% were women. It therefore seems that New Zealand women who do meet criteria for a substance use disorder are more likely to seek treatment than are their male counterparts. This conclusion is reinforced by other findings from the Christchurch Epidemiology Study, where treatment seeking among those who met criteria for a diagnosis for alcohol abuse/dependence was compared with the remainder of the sample. Data were further broken down by gender, revealing that...
women in the alcohol use disorder group were significantly more likely to have accessed outpatient mental health services, inpatient mental health services and mental health services overall (including alcohol and drug services) than their male counterparts. Looking at alcohol related services specifically, 24% of the alcohol disorder women had accessed these services, while only 15% of the men with an alcohol disorder had, although this difference was not statistically significant.

The current study found alcohol to be the primary substance of misuse, followed by cannabis, then opioids. This confirms earlier studies in New Zealand.\(^5,6\) It is also consistent with the reported prevalence of heavy alcohol consumption in New Zealand,\(^7\) with 89% of men and 85% of women aged 14 to 65 described as drinkers, with 31% of these men and 14% of these women drinking enough to feel drunk at least once a month.

Type of drug use was not evenly distributed across the sample. Cannabis was more of an issue for Maori and the young and less so for women. Clients seeking help for problematic benzodiazepine use were primarily women.

The under-representation of Pacific Island clients found in this study should not automatically be taken to indicate lack of assistance. It is important to acknowledge that ‘recognised specialist services’ are not the only assistance services available. In particular, the Church is an important part of Pacific Island communities and may be the first point of contact for many Pacific Islands people concerned about their alcohol and drug use, although it has been noted that to a large extent the role of alcohol in the lives of Pacific Islanders living in New Zealand has been ignored by the Church.\(^2\) This is an area that would benefit from further investigation. The complete absence of Asian clients is more of a concern. If we can assume that alcohol and drug problems do exist in this community, then this absence suggests a population that feels unwilling or unable to access treatment. There are no data at this time on drug and alcohol treatment needs of Asian communities within New Zealand. Clearly such research would be a valuable first step in developing and improving service access and delivery to a significant minority of the New Zealand population.

It should be noted that this is a sample of clients currently engaged in treatment, and is not representative of the substance misusing population at large. Also the fact that these data were collected over a single three month period may introduce a seasonal bias, with patterns of use of some drugs, such as cannabis and opioids varying across the year and therefore possibly influencing the make-up of clients presenting at a given time. Finally, the fact that data for this study were collected through interviews with workers, rather than clients, means that variables such as ethnicity and main substance used were not defined by the clients themselves. Data collected were also retrospective in nature. Despite these considerations, this sample can be viewed as broadly representative of clients seen within the dedicated alcohol and drug treatment field in New Zealand.

A further study is planned which will interview smaller groups of workers on a regular basis, the main purpose being to track changing patterns of substance use and client characteristics within New Zealand alcohol and drug treatment services. This study will employ a similar methodology.

**Acknowledgement.** This study was undertaken with the financial assistance of the Alcohol Advisory Council of New Zealand (ALAC).

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The accuracy of references in Australian and New Zealand Medical Journals

Shaun Holt, Clinical Research Fellow; Robert Siebers, Senior Technical Officer; Aneta Suder, Medical Student; Rachel Loan, Medical Student; Oliver Jeffery, Medical Student; Department of Medicine, Wellington School of Medicine, Wellington.

**Abstract**

**Aims.** Previous studies have found high error rates in references in biomedical journals. The aim of this paper was to assess the accuracy of references in three Australian and New Zealand general medical journals.

**Methods.** References from the August 1999 issues of the Medical Journal of Australia, the New Zealand Medical Journal and the Australian and New Zealand Journal of Medicine were assessed for accuracy using PubMed of the National Library of Medicine.

**Results.** This study found a high rate of reference errors in Australian and New Zealand medical journals. The reference error rate ranged from 33.5 to 48.8%. The most frequent errors were in the author’s names and in the title.

**Conclusions.** The reference error rate in Australia and New Zealand medical journals is high and is preventable. Authors should be more diligent and preferably verify cited references against the original article.

The accuracy of references in medical journals is important as mistakes can make it difficult for readers to obtain cited papers. Particularly, it is essential for the year of publication, volume number, first page number and journal title to be accurate in order to easily retrieve an article. Several studies have looked at the accuracy of references. De Lacey and colleagues found the reference error rate in...
leading general medical journals in 1984 to be 8-26%.1 Similar results were obtained in studies of specialist biomedical journals.2-4

The aim of this study was to assess the accuracy of cited references in three Australian and New Zealand general medical journals.

Methods

References from the August 1999 issues of the Medical Journal of Australia, the New Zealand Medical Journal and the Australian and New Zealand Journal of Medicine, were assessed for accuracy. This was undertaken using PubMed of the National Library of Medicine (http://www.ncbi.nlm.gov/PubMed). All references, which could be assessed for accuracy by this method, were included in the study. References excluded were those for electronic publications such as web sites, and those from journals before 1966, books, newspapers, theses and articles not yet published.

If there was an error in any part of the reference then the reference was classified as inaccurate. All inaccuracies were then further classified as to the part of the reference in which the error occurred ie author(s), title, journal, volume, year, page numbers. The reference error rate was calculated as the percentage of verifiable references containing one or more errors.

In addition, the Editors of the three journals were contacted in order to determine their journal’s policy for checking references, in order to possibly explain any differences in error rate.

Results

Table 1 shows the total number of references in the three journals, the number of references that were able to be checked with PubMed, the number of inaccurate references and the references error rate for each journal. The error rate ranged from about a third of references in the Medical Journal of Australia to almost half of the references in the New Zealand Journal of Medicine.

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Total number of references</td>
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</tr>
<tr>
<td>Number of references checked</td>
<td>188</td>
<td>430</td>
<td>404</td>
</tr>
<tr>
<td>Number of inaccurate references</td>
<td>84</td>
<td>144</td>
<td>197</td>
</tr>
<tr>
<td>Reference error rate</td>
<td>44.7%</td>
<td>33.5%</td>
<td>48.8%</td>
</tr>
<tr>
<td>Total number of errors</td>
<td>117</td>
<td>212</td>
<td>425</td>
</tr>
<tr>
<td>Authors errors</td>
<td>19</td>
<td>97</td>
<td>255</td>
</tr>
<tr>
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<td>65</td>
<td>41</td>
<td>97</td>
</tr>
<tr>
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<td>28</td>
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<tr>
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<td>16</td>
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</tr>
<tr>
<td>Year errors</td>
<td>2</td>
<td>9</td>
<td>15</td>
</tr>
<tr>
<td>Page number errors</td>
<td>11</td>
<td>19</td>
<td>16</td>
</tr>
</tbody>
</table>

Many references contained more than one error. For example, there were 197 inaccurate references in the Australian and New Zealand Journal of Medicine, but within these references there were a total of 425 errors, an average of 2.16 errors per inaccurate reference. From Table 1 it can be seen that the majority of errors occur in the author and title components of the reference.

Only one Editor of the three journals replied to our question relating to their policy with respect to checking references. The New Zealand Medical Journal does not have a system in place but is planning to institute a system of randomly selecting a proportion of references to be checked for accuracy.

Discussion

This study found a high rate of reference errors in Australian and New Zealand medical journals. The rate of 33.5 to 48.8% is similar to other published studies.1-4 We reasonably assumed that PubMed references were accurate. Nowadays, many of these are supplied directly by the publisher to PubMed, and the few inaccurate references would tend to be corrected following notification by database users.

Obviously some errors are more important than others are. Many were minor spelling mistakes in the title or authors names. However, there were some errors that were of more importance. These include errors in the journal name, year or first page number; all of which can make it difficult to retrieve an article. For instance, Table 1 shows that there were a total of 26 year errors in the three journals, which would make it frustrating and difficult, although not impossible, to retrieve the cited reference.

The accuracy of references, and indeed all parts of a paper, are the primary responsibility of authors. Indeed, one of the requirements of the "Vancouver" style of manuscript, which most biomedical journals conform to, is that authors must verify cited references against the original document.5 It is also possible for the journals themselves to improve the accuracy of references. There are several ways in which this can be achieved. Ideally, each reference would be checked ‘in-house’ for accuracy, but this is very time-consuming and therefore expensive. Alternatively, accuracy in references may improve if authors sign a covering letter when the manuscript is submitted, stating that all references have been checked against the original.6 Alternatively, authors could be required to enclose a copy of the first page of each cited article in order to prove this. With the use of modern databases, references can be downloaded directly and this should increase the accuracy of cited references.

In conclusion, an unacceptably high rate of reference errors was found in articles published in three Australian and New Zealand general medical journals. Greater emphasis should be placed on authors to ensure accuracy of references in their submitted articles.

Acknowledgements. A Suder, R Loan and O Jeffery were supported by summer studentships at the Wellington School of Medicine.

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On May 30, the British Medical Association released a report linking depictions of excessive slimness in the British media with eating disorders. The BMA stated that the media “should adopt a more responsible editorial attitude towards the depiction of extremely thin women as role models, and should portray a more realistic range of body images”.

Chronic pulmonary hypertension secondary to pulmonary thromboembolism has a poor long-term prognosis related to the level of pulmonary artery pressure. Pulmonary thromboendarterectomy represents the only effective treatment in severe cases, although it is not routinely available in New Zealand. We report a patient with this condition who successfully underwent pulmonary thromboendarterectomy at the University of San Diego Medical Centre (UCSD), to alert readers to the diagnosis, method of assessment and availability of this treatment option.

The patient
A 51-year old man was admitted to Kenepuru Hospital with a twelve-month history of progressively worsening shortness of breath and right leg swelling. These symptoms had begun six weeks following varicose vein surgery. Despite seeking a medical opinion for these symptoms on a number of occasions, the diagnosis of venous thromboembolism was not considered. His past history was unremarkable, apart from a family history of thrombocytopenia. At the time of admission, he had features consistent with pulmonary hypertension and was in respiratory failure. A Doppler ultrasound confirmed the diagnosis of right superficial femoral, profunda and popliteal vein thrombosis, and a ventilation perfusion (VQ) scan showed a high probability of pulmonary emboli. An electrocardiogram showed evidence of right heart strain and an echocardiogram confirmed significant dilatation of the right ventricle and septal flattening, suggestive of raised right ventricular pressure. He was treated with intravenous heparin, followed by long term warfarin. Domiciliary oxygen was commenced.

Following discharge, he made a modest improvement in terms of breathlessness; but whilst on warfarin, three months later, there were several episodes suggestive of further pulmonary emboli, which were confirmed with a repeat VQ scan. A Greenford filter was inserted and warfarin continued indefinitely. A thrombophilia screen was done at this stage, but was difficult to interpret due to the warfarin therapy.

During the next four months, following insertion of the filter, there was no improvement in his breathlessness, and he remained significantly limited in his daily activities. His resting oxygen saturation was 97% on room air, but this fell to 86% with two minutes of modest exercise. A repeat echocardiogram showed severe pulmonary hypertension, with an estimated right ventricular pressure of 54 mmHg.

A CT pulmonary angiogram showed extensive thrombus in the right and left pulmonary arteries, and there was enlargement of the pulmonary trunk (Figure 1). There was also enlargement of lower lobe pulmonary arteries and right-sided heart chambers. High-resolution images demonstrated a ‘mosaic’ perfusion pattern produced by irregular pulmonary perfusion.1

With an estimated five year survival of 10%, the possibility of pulmonary thromboendarterectomy was considered. As no operative intervention could be offered in New Zealand, he was referred to the UCSD and transferred to San Diego two months later. An extensive pre-operative assessment included: repeat echocardiogram, perfusion scanning, arterial blood gas, walk test, pulmonary function studies, and thrombophilia screen. Right heart catheterization, pulmonary angiography and coronary angiography were also performed. In addition to confirming the nature and extent of the pulmonary obstruction, haemodynamic measurements were obtained. These revealed a right atrial pressure of 9 mmHg, a right ventricular pressure of 85/11 mmHg, a pulmonary artery pressure of 85/30 mmHg with a mean pressure of 50 mmHg, a pulmonary capillary wedge pressure of 11 mmHg, and pulmonary vascular resistance of 692 dyne/sec/cm5. Pulmonary angiography revealed segmental level disease in the right upper lobe. A pouch defect was present in the descending pulmonary artery at the right middle lobe level, with absent flow to the right middle lobe and the entire right lower lobe except the posterior and superior segments. Left-sided angiography revealed an irregular descending left pulmonary artery below the left upper lobe take-off. The lingular branch was quite irregular and lower lobe flow was confined to the posterior segment. Coronary angiography was normal.

He proceeded to pulmonary endarterectomy. This operation involves median sternotomy, high flow cardiopulmonary bypass with cooling to 20°C, a period of hypothermic cardioplegia and pulmonary endarterectomy. Endarterectomy is a complex technique and involves removing the organized thrombus along with its lining of neo-intima, while leaving the media and most of the original intima intact.1

In this case, extensive amounts of thrombus were removed (Figure 2). At the conclusion of the operation, pulmonary pressures and resistance were normal. The post-operative course was uncomplicated and he was discharged after eight days. At three months post-operative review, he was not limited by breathlessness on assessment.
daily activities and a limited exercise test showed no arterial oxygen desaturation.

Figure 2. Extensive thrombus removed during operation.

Discussion

The incidence of pulmonary hypertension secondary to unresolved emboli remains uncertain. Although it had previously been estimated at 0.1-0.2% of survivors of acute embolic events, a recent study based on serial echocardiographic and clinical follow up found about 5% with chronic pulmonary hypertension at five years. The reasons for the lack of resolution of pulmonary emboli in some patients are uncertain and cannot be predicted by the initial clinical presentation or presence of an underlying thrombophilia.

In the period following an acute embolic event, it is not sufficient to assess severity by symptoms, as a ‘honeymoon period’ often occurs until right ventricular function deteriorates. The prognosis is proportional to the degree of pulmonary hypertension. Riedel et al reported that patients with mean pulmonary artery pressures (MPAP) over 30 mmHg have a 30% five year survival. This has led to a recommendation of a routine echocardiogram at six weeks after an acute embolic event to identify patients with persistent pulmonary hypertension/right ventricular dysfunction who are potential candidates for pulmonary thromboendarterectomy. A repeat VQ scan is also recommended at this stage to estimate resolution of perfusion defects, and to provide a new baseline should the patient present with symptoms suggestive of recurrence.

Pulmonary thromboendarterectomy should be considered first line treatment for chronic major- vessel thromboembolic pulmonary hypertension. Medical options, including thrombolysis, are not effective, and the role of pulmonary vasodilator therapy is yet to be defined. The predominant worldwide experience is at the UCSD where this operation has been performed in over 1000 patients since 1970. Their operative mortality is 5-10%.

Most patients referred to the USCD have New York Heart Association (NYHA) class III or IV dyspnoea, a pulmonary vascular resistance of more than 300 dynes/sec/cm², and thrombi that are accessible as defined by angiography. All patients have inferior vena caval filters inserted and are maintained on lifelong anticoagulant therapy. They can expect significant improvement within a few weeks of surgery, with continued improvement over the next twelve months, by which time 95% are in NYHA class I or II. The proportion of patients with chronic pulmonary embolism that are surgical candidates is unknown. Factors that significantly increase the risk of death include: age greater than 70 years, marked obesity, the severity of the preoperative elevation of pulmonary vascular resistance, the severity of any heart failure, very high right atrial pressures and the presence of significant collateral disease.

This surgical procedure is not routinely available in New Zealand. A survey done amongst the five cardiothoracic units in New Zealand revealed that less than ten such operations have been performed in this country, most assisted by an overseas surgeon.

As a result, patients from New Zealand who require the operation must either have the means to meet costs of approximately NZS200 000 to NZS300 000, or be funded by the Health Funding Authority (or similar body).

In conclusion, pulmonary hypertension due to chronic pulmonary thromboembolism may be more prevalent than previously thought, with an up to one to twenty risk of this complication following an acute pulmonary embolic event. An assessment at three months, including a repeat VQ scan and echocardiogram, may help to identify these individuals. Until such time a pulmonary thromboendarterectomy is routinely performed in New Zealand, patients who are candidates for this procedure, and who have funding will need to be referred to other centres, such as the UCSD.

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The barrier to reducing the number of deaths from colorectal cancer is not a lack of scientific data, but a lack of organizational, financial, and societal commitment. All persons 50 years of age or older who are at average risk for colorectal cancer should undergo comprehensive evaluation of the entire large bowel. In my judgement, such screening is currently best accomplished by colonoscopy rather than by barium-enema evaluation, especially given the results of recent comparative studies. However, ensuring that all persons undergo some form of comprehensive screening is even more important than deciding whether colonoscopy or barium enema is used for the screening evaluation. If a patient has no abnormalities, colonoscopy need not be repeated for at least 5 years and perhaps up to 10 years. I believe it is time for both government and private insurers to provide coverage for colonoscopic screening for all persons 50 years of age or older who are at average risk for colorectal cancer. As many people have pointed out, relying on flexible sigmoidoscopy is as clinically logical as performing mammography of one breast to screen women for breast cancer. It is time to go the distance.

The results of the Cardiac Arrhythmia Suppression Trial (CAST) published in 1989, demonstrated a 2.5 fold increased risk of death in post-myocardial infarction patients treated with encainide or flecainide for suppression of non-sustained ventricular arrhythmias.1 Understandably, concerns arose about the risk/benefit ratio of antiarrhythmic drugs in general, and flecainide in particular, for treating supraventricular arrhythmias (SVT), even though this patient population is quite different to the CAST cohort. Central to these concerns was the concept of proarrhythmia. This label denotes the appearance of a new arrhythmia or aggravation of arrhythmia, after commencement of antiarrhythmic drugs therapy.2 Additional analyses of CAST data published more recently however, have emphasised the importance of placebo control, and suggest that a large portion of what has been termed proarrhythmia is spontaneous variability in arrhythmia frequency. Proarrhythmia is best defined as a net increase in mortality compared to placebo.1

For patients with SVT without a history of myocardial infarction, the absolute risk of proarrhythmia, as defined above, needs to be put in some perspective. Only two deaths (one from metastatic cancer, one unspecified) are documented in a combined cohort of 750 patients treated for SVT with flecainide for at least one year.4,5 These data suggest the risk is likely to be very small. By comparison, arrhythmic death occurred in 4.5% of 730 patients in the CAST study treated with flecainide or encainide, compared to 1.2% given placebo over an average exposure of 293 and 300 days respectively. Similarly, the initiation of antiarrhythmic therapy (flecainide, encainide or moricizine) in 3840 patients enrolled in CAST (I and II) and its pilot study, for an average exposure of 23 days, was associated with a three fold increase in arrhythmic death (0.5% in placebo cf. 1.6% for treatment).2 All CAST patients had a prior myocardial infarction and impaired LV function, which in some cases was severe.10

This working group undertook to review the available data on flecainide use in SVT, in order to provide practical guidelines for its prescription for this indication. Standard risk factors for proarrhythmia established predominantly in patients treated for ventricular arrhythmias (the presence of structural heart disease, a history of sustained ventricular arrhythmias, impaired left ventricular function) have been applied to the population of patients with SVT.11,12 The limitations imposed by a modest data base and largely retrospective analysis are acknowledged.

Low risk patients

Patients with SVT can be considered to be at very low risk of proarrhythmia if they have no evidence of heart disease on medical history and clinical examination, have a normal exercise tolerance, and a normal 12 lead ECG and chest x-ray. Echocardiography is not mandatory in all patients, but is recommended in those with atrial fibrillation or atrial flutter, and is strongly indicated for patients in whom clinical assessment raises suspicion of structural heart disease. Echocardiography is also recommended in patients with hypertension, to evaluate left ventricular hypertrophy.

Contraindications to flecainide treatment

Data quantifying the incremental risk of proarrhythmia from the factors listed in Tables 1 and 2 are incomplete. In respect of prior myocardial infarction, the CAST data cited above are persuasive. For impaired left ventricular function, the CAST study documented an increased risk of death or cardiac arrest from 13% to 16% to 33% for patients whose ejection fractions were >50%, 30-49% and <30% respectively.10 The presence of structural heart disease (eg valvular, congenital, hypertrophic, coronary artery disease) in the flecainide data base of 1330 patients with predominantly ventricular arrhythmias, followed for a mean of 292 days, increased the incidence of fatal proarrhythmia from 0% to 1.2%, and a history of sustained ventricular tachycardia or fibrillation from 0.1% to 3.1%.11,12

In choosing alternative antiarrhythmic agents, there are limited comparative data, and detailed discussion is beyond the scope of this article. In brief, amiodarone (and more recently dofetilide) has been shown not to increase mortality in heart failure and is quoted as having the lowest proarrhythmic risk for class III agents.5 Radiofrequency ablation may be a safer strategy in higher risk patients, bearing in mind a quoted serious complication rate of 3% in a recent large patient cohort.11

Relative contraindications

Relative contraindications to flecainide in patients with SVT are shown in Table 1. There is still a risk of serious or life-threatening proarrhythmia in all patients with relative contraindications to flecainide, so the drug should only be given after consideration of the clinical indications and balancing relative benefits and risks. If two or more relative contraindications exist, the risk is likely to be greater, and an alternative strategy should be considered.

**Table 1. Relative contraindications to flecainide therapy in patients with supraventricular arrhythmias.1,4,5,11,12,18**

- Mild systolic left ventricular impairment
- Mild left ventricular hypertrophy
- >Mild valvar heart disease with normal ventricular dimensions
- First degree atrioventricular block ≥0.28 sec
- QRS ≥0.12 sec and ≤0.15 sec
- Asymptomatic sick sinus syndrome without an artificial pacemaker
- Pacemaker-dependent patients
- Stable angina pectoris without a previous history of myocardial infarction
- Significant renal dysfunction (plasma level monitoring recommended)
- Severe hepatic dysfunction (plasma level monitoring recommended)
- Hypokalaemia (<3.5 mmol/L)

Treatment with flecainide should be initiated in hospital, with ECG monitoring for at least 48 hours in patients with first degree atrioventricular block (PR ≥0.24 seconds), sick sinus syndrome or QRS widening, and possibly also in patients with impaired left ventricular function.14
It is uncertain whether or not the chamber enlargement and/or left ventricular hypertrophy seen on echocardiography in some athletes is associated with an increased risk of proarrhythmia with flecainide (or any other anti-arrhythmic drug).

**Complete contraindications**

The contraindications to flecainide treatment in patients with SVT are shown in Table 2. These patients are at particularly high risk of serious or life threatening proarrhythmia. In this group, flecainide (or any Class I agent), should only be used in exceptional circumstances where the benefits clearly exceed the risks and where no alternative management is available for these patients.

<table>
<thead>
<tr>
<th>Table 2. Flecainide therapy contraindicated in patients with supraventricular arrhythmias.1,4,11,12,16</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Heart failure</td>
</tr>
<tr>
<td>• Prior myocardial infarction</td>
</tr>
<tr>
<td>• Unstable angina</td>
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<tr>
<td>• Moderate left ventricular systolic impairment</td>
</tr>
<tr>
<td>• Moderate left ventricular hypertrophy</td>
</tr>
<tr>
<td>• Hypertrophic cardiomyopathy</td>
</tr>
<tr>
<td>• Valvular heart disease with abnormal left or right ventricular dimensions</td>
</tr>
<tr>
<td>• Congenital heart disease</td>
</tr>
<tr>
<td>• First degree atrioventricular block (PR &gt;0.28 sec)</td>
</tr>
<tr>
<td>• Second degree atrioventricular block</td>
</tr>
<tr>
<td>• Bifascicular block†</td>
</tr>
<tr>
<td>• QRS &gt;0.15 sec</td>
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<tr>
<td>• Congenital long QT syndrome</td>
</tr>
<tr>
<td>• QTc on flecainide &gt;0.50 sec</td>
</tr>
<tr>
<td>• Previous cardiac arrest or history of sustained ventricular tachycardia</td>
</tr>
</tbody>
</table>

*Excludes patients with minor or repaired shunts; fn the absence of an artificial pacemaker.

**Monitoring**

Flecainide should be started at a dose of 100 to 200 mg/day, and in adults can be increased to a maximum of 300 mg/day. The patient should be assessed and a twelve lead ECG done within a few weeks. Development of first-degree atrioventricular block, QRS widening and QTc prolongation are an indication for urgent specialist review or withdrawal of therapy.

Long term follow-up is important, so specialist review is recommended at two-year intervals for patients without contraindications, and annually for those with relative contraindications. Monitoring of trough drug levels is recommended in patients receiving flecainide doses greater than 200 mg/day, for those with significant renal or hepatic impairment, and in children.

Stated laboratory upper limits for therapeutic trough drug levels are up to 2100 nmol/L. However, this is close to levels associated with flecainide toxicity in some patients and levels <1800 nmol/L are strongly recommended.

Flecainide should not be prescribed alone for patients with atrial flutter, because one-to-one atrioventricular conduction may occur secondary to slowing of the flutter cycle length and have minimal effect on the atrioventricular nodal refractory period. Concomitant treatment with digoxin, or a calcium - or beta-blocking agent is recommended. Combined treatment is not mandatory for atrial fibrillation, but consideration should be given to adding a second agent for rate control should a breakthrough arrhythmia occur.

Flecainide also has some potentially detrimental non-arrhythmic cardiac effects, eg negative inotropic effect and increased pacing thresholds in patients with permanent pacemakers. The latter group should be reviewed with a pacemaker check, following the institution of flecainide therapy and after any subsequent increase in the dosage. The risk of these adverse cardiac effects however, may be independent of the dose of flecainide.12

Flecainide is concentrated in human breast milk, but resultant infant blood levels are predicted safe with normal feeding practice. The American Academy of Paediatrics therefore considers flecainide treatment to be compatible with breast feeding.15

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Over 5000 scientists from around the world have signed a declaration saying that AIDS is caused by HIV. In the journal Nature the scientists make clear that the declaration is a direct response to the debate in South Africa sparked by its president, Thabo Mbeki, about HIV and whether or not it causes AIDS. Scientists fear that the debate will raise doubts and result in the loss of many lives.

The timing of the declaration is crucial. It comes in the week before the Durban AIDS 2000 conference opens and follows the release of alarming statistics by UNAIDS, the Joint United Nations Programme on HIV/AIDS. It also arrives at the moment when President Mbeki’s AIDS Advisory Panel (with many scientists who doubt that HIV leads to AIDS) has re-convened in Johannesburg to advise the president on the pandemic.
Reference Pricing is a tool adopted by PHARMAC in 1993 for managing prices of pharmaceuticals. We examined the effects of reference pricing as a pricing tool, and its implications for the health of New Zealanders. The historical background for the evolution of the reference pricing policy is outlined briefly and its effectiveness as a policy tool is examined. We also looked at whether some of the major decisions of PHARMAC have been consistent with their own Operating Policies and Procedures (OPP).

The Pharmaceutical Management Agency LTD (PHARMAC) was set up in 1993 to “manage and develop the Pharmaceutical Schedule” on behalf of the four Regional Health Authorities. The reference pricing policy was an evolution of the Department of Health’s ‘uniform subsidy’ and ‘therapeutic group pricing’ policies. Subsidies were to be based on the lowest cost drug in a group, in contrast to the earlier Department of Health concept, in which the cheapest drug in the group was not necessarily the one subsidised. Sometimes a more expensive medicine was subsidised because it had some advantages, such as having greater efficacy, less side effects, better compliance and less interactions than other medicines in the therapeutic group ie drugs were ‘priced and subsidised according to their merit’. Whilst it was difficult to use ‘merit’ in a consistent way, these important aspects of pharmacology were at least attributed some value.

Reference pricing divides pharmaceuticals into ‘therapeutic groups’ that include all pharmaceuticals used to treat the same or similar condition(s). A ‘sub group’ is a set of pharmaceuticals that produces the same therapeutic effect in the treatment of the same or similar conditions. All pharmaceuticals in a given subgroup are subsidised at the level of the lowest priced pharmaceutical in that subgroup (called the reference priced drug).

The specific aims of this review are first, to assess whether PHARMAC has followed its OPP when making reference pricing and other decisions; second to assess whether reference pricing has been successful at controlling pharmaceutical costs in New Zealand; and third to see if international experience with reference pricing is similar to that of New Zealand.

Has PHARMAC followed its Operating Policies and Principles?

Recent decisions made by PHARMAC were assessed against their OPP. The OPP set out the criteria that PHARMAC uses to make decisions about proposed amendments to the Pharmaceutical Schedule. Each criterion will be discussed in turn.

Criterion i) “the health needs of all the Regional Health Authorities’ populations”. There is little evidence that the health needs of the populations have been taken into account when reference pricing decisions have been made. Part of the problem is that the health needs were never defined by PHARMAC, nor were there any studies performed at the time of the decisions to see whether policy changes were having any impact. There are a few examples where funds have been reallocated (eg funding for atypical antipsychotics) but there are many other areas of health need (eg osteoporosis) that have been neglected. Examples of the lack of consideration of effects on health status includes ignoring the deleterious effects of switching and cost-shifting, and incorrectly assuming equivalence of drugs in the same subgroup (eg placing nefazodone in the select serotonin reuptake inhibitor [SSRI] group – for details see criterion iii). As well, any form of regulation (such as reference pricing) leads to incentives for bending the rules, and has the effect of improving the relative health status of a privileged few who know the rules and can work loopholes.

Criterion ii) – “the availability and suitability of existing pharmaceutical and other therapies to meet the health needs of those populations”. Although PHARMAC believe that this criterion is considered in its reference pricing decisions, several recent examples show that this may not be so. PHARMAC bases its decisions on a criterion of ‘same or similar effects’ which can be used at will to include or exclude important aspects of pharmacology. It is never clearly defined as to whether same or similar refers to surrogate or true endpoints of treatment eg whether or not a medication lowers blood pressure, or whether or not the lowered blood pressure actually reduces mortality or morbidity. Does same or similar take into account side effect profile, drug interactions, clinical effect or compliance? Is it primarily a funding tool for subsidisation purposes, or is it supposed to direct clinical prescribing?

Grouping within a subgroup implies that the scientific background for each drug is similar, that an individual patient will respond in the same manner as a previously studied population, and that the specific patient-drug fit would be similar for all drugs in the subgroup. Clearly this is too simplistic. History has shown that assuming a similar ‘class’ effect may have problems. A number of drugs have had to be withdrawn from common use because of the safety differences within the class eg mianserin, practolol, fenoterol, phenylbutazone and terfenadine. Subgroups have been defined in an inconsistent manner. They are sometimes based on chemical structure eg tricyclic antidepressants, and sometimes on mechanism of action eg angiotensin converting enzyme (ACE) inhibitors. Sometimes they have been defined very specifically, eg dividing the monoamine oxidase inhibitors into selective and non-selective inhibitors, and sometimes too generally eg classifying nefazodone with the SSRI drugs. Oral contraceptives have been divided into six groups, and calcium channel blockers into three groups.

Many of the benefits of reference pricing depend on how tightly different pharmaceuticals are clustered into subgroups. Excessively tight clustering restricts the ability of reference pricing to control costs, and too loose a grouping can lead to the wrong agent being prescribed. Reference pricing has had a deleterious effect on the availability of future pharmaceuticals, and on medical education in New Zealand. A number of companies have downsized or left the country (eg Pfizer), and new drugs have not entered, or have been withdrawn from New Zealand (eg famciclovir). Other
effects include the loss of funding of research (eg Bristol Myers Squibb) and consumer education (eg Glaxo physician workshops and the Herpes Foundation). Drug companies have an incentive to divert resources from innovation in pharmaceuticals that might improve the health of New Zealanders, to activities that ensure that any new pharmaceutical makes the Pharmaceutical Schedule as a first in its group (PHARMAC has a policy to fund one drug in each therapeutic subgroup). The first in a group will, by definition, be the reference priced drug because at this stage it is the only drug in the group.

Criterion iii) “the clinical benefits, risks and the costs of a pharmaceutical.” It is clear that although costs have been taken into account, benefits and risks have not. Examples include:

1. the reference pricing of erythromycin in the macrolide group. When adverse drug reactions, drug interactions and compliance issues are considered, as well as efficacy, erythromycin is not necessarily a cheaper drug.

2. the reference pricing of statins. It was known from the literature and from an independent consultant report commissioned by PHARMAC, that simvastatin and pravastatin had a greater evidence base, and were cheaper per percentage reduction in cholesterol, than the statin (fluvastatin) that PHARMAC reference priced. PHARMAC did not take into account the increased taxpayer costs of extra visits, extra lipid profile checks and the indirect patient costs of switching. There has been recent clinical research to show that there was an increase in serum lipids in some patients with established atherosclerosis after fluvastatin became the reference priced drug. Later, it was demonstrated that a significant increase in the frequency of thrombotic events paralleled the increase in serum lipids, compared with the previous six months of simvastatin therapy. This study did not have controls and true causality was not demonstrated, but it did highlight a potential danger with reference pricing.

3. the decision to include nefazodone in the SSRI subgroup. This may have been a useful decision in terms of cost, but other benefits and risks were not taken into account. Compared to the SSRIs, nefazodone is not strictly an SSRI, has different indications, different side effects and different drug interactions.

4. the reference pricing of felodipine within the dihydropyridines. Felodipine has the potential for greater fluctuations in plasma concentrations, when given with grapefruit juice and other interacting drugs, compared with most other dihydropyridine drugs. As well, because felodipine has a greater peak/trough ratio than amlodipine, it is not as well tolerated. Both of these points are important, as the control of blood pressure with calcium antagonists is linked directly to plasma concentrations.

Criterion iv) “the cost-effectiveness of meeting health needs by purchasing pharmaceutical services rather than by purchasing other health care and disability services”. PHARMAC has not produced any data to show that this has been taken into account. This is pertinent, because there are a number of studies showing that pharmaceuticals may be underutilised in the healthcare equation. In the UK, the Office of Health Economics showed that money spent on pharmaceuticals in one year was less than the amount saved by decreased hospital bed usage and hospital costs. There are several PHARMAC decisions that illustrate this, eg the failure to fund low molecular weight heparins (even though this enables early hospital discharge) and preloaded adrenaline syringes for anaphylaxis (which may prevent hospital admission or death). There may also be increased hospital costs from switching drugs to the reference priced product through loss of lipid control. Predicted savings on a ledger seemed to be based on the assumption that everything else remains the same.

Criterion v) “the overall budgetary impact of any changes to the Pharmaceutical Schedule”. The broader definition of the cost of a drug includes both the actual price and the quantity used (volume). Whilst prices may be controlled by reference pricing, behavioural responses that negate the primary gains may occur eg switching of usage patterns from older, less expensive products to newer more expensive drugs. Volume of drug use is not controlled by reference pricing. Patients and doctors have little incentive to economise on drug use when the drug is heavily subsidised. They may also feel encouraged to use the reference priced drug from a more expensive class, even if the cheaper drug may have been adequate. Volume has, in fact, increased (Figure 1), eg proton pump inhibitors (491% increase since 1991), SSRI antidepressants (564% increase since 1991) and antiviral drugs (270% increase since 1991). This is likely to be the result of preferential usage of these drugs when they achieved reference priced status. However, other factors may have been involved, such as increased recognition of gastroesophageal reflux disease (GORD) as an entity and perceived increased tolerability of the SSRIs over tricyclic antidepressants. Cheaper products from competing therapeutic subgroups may have been effectively prescribed in many circumstances. Capped budgets provide insurance for PHARMAC against runaway expenditure, but perversely may increase the prescribing of agents affected, because once the cap has been reached, they are perceived as being “free”.

When PHARMAC was set up, it was stated that the aim was to stabilise the growth of the subsidy bill to half that of the previous year. In fact, the growth rate continued to increase as a constant proportion of the overall health budget – the cost of both overall health expenditure and pharmaceutical expenditure both increased by 28% from 1993-1997. For the first time, in PHARMAC’s 1999 annual report, the actual expenditure reduced from $772 million in 1998 to $717 million in 1999. This is laudable from an accounting perspective, but must be balanced against the deleterious effects on society of cost shifting, drug switching and decreased new drug availability owing to withdrawal of some drug companies (and their drugs) from New Zealand. PHARMAC explains savings against projected costs, based on predicted future spending at previous rates of growth, assuming no compensatory behaviour and assuming that the other variables remain constant (which in health care does not occur).

Criterion vi) “The direct costs to the health service users”. Although subsidies benefit those who can tolerate subsidised drugs, costs to those who require non-subsidised drugs have increased. Although these figures may not be considered in the pharmaceutical bill, they are costs to New Zealanders.

Criterion vii) “any recommendations on core health and disability services made by the National Advisory Committee on Core Health and Disability services”. This committee no longer exists, but a new committee, the National Health Committee (NHC) has taken over a majority of its functions. We are unsure if PHARMAC has acted on any of the NHC recommendations.

Criterion viii) “such other matters as PHARMAC sees fit…” This is too loose to enable formal analysis and seems to negate the need for all the other criteria in the OPPs.

Has reference pricing controlled costs in New Zealand?

It was clear from the beginning that the main proponents of reference pricing regarded cost-control as a primary focus,
rather than the overall health needs of the population. Thus a judgement on whether reference pricing has been successful must focus on whether it has enabled costs to stabilise.

PHARMAC said that its “immediate challenge (was) to reduce the growth in public expenditure on pharmaceuticals in a way that optimises the health status of all New Zealanders”. In fact, overall costs have not been contained as well as planned (see analysis of criterion v), and there is little evidence (and some contrary data) that health status has been optimised, or that PHARMAC has ensured a stable market in pharmaceuticals. Perhaps PHARMAC should be more upfront in stating that its main focus is financial efficiency and leave decisions affecting health status to other groups.

Reducing growth in expenditure, through reference pricing was regarded as an optimal goal in itself. In the present climate of reducing costs in health, pharmaceuticals are an easy target for cost-containment (one of the points that makes reference pricing attractive). The result of price reduction is easy to see (as evidenced by PHARMAC’s focus on potential money saved in its Annual Reviews, although as noted, volume has been largely ignored), whereas the negative effects of the policies on wider health issues may take years to become evident. As well, the pharmaceutical industry is a relatively low risk political target.

**International experience of reference pricing**

Other countries experimented with reference pricing prior to it being introduced into New Zealand. Germany introduced it in 1989. Apart from an initial one-off gain in the year of introduction (which was mainly due to cost-shifting into categories that were not reference priced), there has been no reduction in the percentage of the health budget spent on pharmaceuticals. The results are similar in the Netherlands, Norway, Sweden and Denmark, where reference pricing was unable to control growth in pharmaceutical expenditure. Most countries have either abandoned reference pricing completely, or have had to institute policies that control the demand for pharmaceuticals. For example, budgetary restrictions and improved prescriber education were introduced into Germany in 1992. In 1996, the Netherlands adopted an international price-link which enforced adjustment of Dutch prices to the much lower average of four selected countries, in an attempt to contain costs.

**Summary**

Many of PHARMAC’s decisions do not appear to be consistent with its own Operating Policies and Procedures, largely because reference pricing has been the main policy tool by which decisions are made. We suggest that reference pricing is a flawed policy tool because it encourages compensatory behaviour patterns that negate primary cost gains.

The main problem with reference pricing is the excessive focus on cost. Other factors, like the transfer of costs to the patient, patient idiosyncrasies or favourable pharmacological characteristics of non-reference priced drugs, are not taken into account. The issue of switching, for many years accepted as a dangerous policy, has been introduced overnight for large numbers of patients.

The policy of reference pricing can allow decisions to be made that are not in the best interests of patient health eg through the misuse of ‘same or similar’. This concept of ‘same or similar effect’ has never been explicitly defined by PHARMAC.

How can PHARMAC policy be improved to ensure better health care, prescriber acceptability and future availability of suitable pharmaceuticals in New Zealand? It is likely that cost-containment could be achieved without such a dogmatic policy to contain prices in

![Figure 1. Graph of pharmaceutical price, volume and overall pharmaceutical expenditure, 1992-1998 (extrapolated to 2000) (with permission of PHARMAC, Wellington 1999).](image)
Reimbursement of pharmaceuticals in New Zealand: comments on PHARMAC’s processes

Boyd Swinburn, Associate Professor; Richard J Milne, Associate Professor; Mark Richards, Professor; Evan Begg, Associate Professor; Stuart Foote, General Practitioner; Rod Jackson, Professor, The National Heart Foundation Pharmacetical Advisory Committee.

PHARMAC was established in 1993 by the Regional Health Authorities (now the Health Funding Authority, HFA) to manage the Pharmaceutical Schedule, a list of medicines that are fully or partly subsidised by the HFA. It seeks to “balance the needs of patients for equitable access to health care with the needs of taxpayers for responsible management of the cost they ultimately bear.” There is no disagreement that healthcare at any cost is untenable and that there is a clear need to obtain the greatest good for the greatest number from every health dollar. This is particularly true for pharmaceutical costs, because it is one of the few areas of the health budget which is essentially uncapped.

The taxpayers’ annual investment in pharmaceuticals is large (over $800 million) and therefore, PHARMAC has a major responsibility to promote increased efficiencies in the spending of this money. PHARMAC uses a variety of policy instruments to reduce the price of drugs it subsidises. These include: reference pricing, tendering, two-part pricing, sole supplier agreements, subsidisation of preferred brands, targeting, limiting access through special authority and capped budgets. The savings gained from these better prices are available for funding more drugs and health services.

Recent experience with pricing policies on cardiovascular drugs

Over the last few years, there have been three major pricing policies which have involved cardiovascular drugs and affected over 100 000 patients. (Estimates of patient numbers quoted in this paper have come from PHARMAC). The first was the ‘statin decision’ about access to HMG-CoA reductase inhibitors. A judgement was made that the health gains (in terms of morbidity and mortality) of statins was proportional to their cholesterol-lowering effect (ie a ‘class effect’). This led, in July 1997, to a policy of ‘reference pricing’ statins to fluvastatin, a cheaper statin with no proven morbidity or mortality outcomes. This policy was coupled with a loosening of the stringent statin access criteria to allow general practitioner (GP) prescribing for some patients with known cardiovascular disease. Most of the criticisms of this statin decision were levelled at the assumption that fluvastatin improved clinical outcomes, the bureaucratic red tape associated with obtaining approval, and the lack of potency of fluvastatin which may result in loss of control of cholesterol levels and potential risk for patients. The full subsidisation of the potent statin, atorvastatin, in January 1998 addressed the last point, although the commercial deals that PHARMAC struck with Parke Davis meant that atorvastatin became subsidised at a higher level than simvastatin and pravastatin, both of which were backed by clinical outcome studies. Approximately 12 500-15 000 patients were affected by the decision, and the initial savings offset the increased numbers of statin prescriptions resulted from the wider access criteria. No evaluation of the statin decision other than counting prescription numbers and costs was initiated by PHARMAC.

The second initiative involved ACE inhibitor drugs, which are primarily used for treating hypertension. There was no placebo-based, randomised, controlled evidence available in hypertensive patients demonstrating that any ACE inhibitors reduced major cardiovascular events. By contrast, diuretics and β-blockers (which are also cheaper) do have this evidence. A recently published study suggests that ACE inhibitors have an effect equivalent to diuretics and β-blockers on reducing cardiovascular events. There is evidence that some of the ACE inhibitors improve clinical outcomes and are cost-effective in patients with heart failure and diabetic nephropathy. PHARMAC decided to reference price ACE inhibitors to the cheapest one available, which after the atorvastatin deal with Parke Davis was quinapril. On this occasion, the major criticisms were that this would involve the transfer of about 100 000 patients who were currently stable on ACE inhibitors, with possible consequences of side effects and (at least temporary) loss of blood pressure control; and that the cheapest ACE inhibitor drugs did not have clinical endpoint data for treatment of heart failure or diabetes. This was partly countered by PHARMAC providing two subsidised GP visits over the transfer period. In addition, patients with currently (but not newly) diagnosed heart failure were exempted from the part charge for the more expensive ACE inhibitors because of the...
evidence from randomised controlled trials of their effectiveness. Two evaluations of the decisions were funded by PHARMAC, and while these may be indicative, neither of them will give the sufficient prospective data needed to determine the effects of this massive drug switch.

The third policy related to the use of dihydropyridine calcium channel blockers (DHP CCBs) which are mostly used for managing hypertension, but are also used to treat angina. Only limited clinical outcome studies are available for DHP CCB treatment of hypertension, and because it is unclear whether their overall effects are neutral, beneficial, or harmful, closer monitoring and control of the use of these drugs is warranted. In the case of short acting DHP CCB’s as monotherapy for angina, there is evidence of overall harm. In addition, there are several niche areas where DHP CCB’s have been shown to be effective, such as the treatment of hypertension in the elderly, coronary vasospastic disease and subarachnoid haemorrhage, and with β-blockade, unstable coronary syndromes. Again the DHP CCB’s were reference priced to the cheapest drug on the assumption that there was a class effect. This policy was estimated to affect about 35 000 people from June 1999 and the transfer was also facilitated by subsidised GP visits. It is uncertain whether the evaluation processes will be adequate to determine the size of the positive and negative effects of the drug switch.

Concerns of the Pharmaceutical Advisory Committee of the National Heart Foundation

These three ‘supply-side’ (cost and access driven) initiatives from PHARMAC have directly affected about 150 000 New Zealanders, most of whom have switched medications as a result. This has caused an ongoing public debate. In general, the medical profession has emphasised the potential detrimental effects of switching the drug regimens of large numbers of patients, the continued restrictions or price disincentives on the drugs that are backed by evidence and the increase in paperwork generated by these changes. PHARMAC, on the other hand, has been emphasising the potential financial ‘savings’ and, in the case of statins, wider access for GPs. Unfortunately, the balance of this very important debate will never be known because the data needed to weigh up the pros and cons adequately were not collected. The Foundation’s Pharmaceutical Advisory Committee believes that it is time to reflect on the lessons learned from these major supply-side policies and to consider how the processes may be improved to maximise the benefits and minimise the harm to patients. While this paper focuses on PHARMAC’s role in the optimal use of pharmaceuticals, it is acknowledged that the other key players, particularly the pharmaceutical industry and the prescribers, also have a major influence in this regard.

Recommendations for PHARMAC’s processes

1. Transparent use of scientific evidence. Wherever possible, pharmaceutical policy decisions need to be based on scientific evidence that is graded to give due weighting. The highest grade of evidence of relative benefit of therapy comes from large randomised clinical trials with morbidity and mortality endpoints. This level of evidence should be used if it is available, but it is recognised that lesser forms of evidence will need to be incorporated into policy decisions. Where lesser evidence is used, it should be graded as such. Clear definitions of what constitutes a ‘class effect’ are essential. In addition, the absolute benefits of therapies need to be estimated for specific patient groups so they can be balanced by the costs and any detrimental effects. For example, there is high grade evidence that statins have a significant relative benefit in the primary prevention of myocardial infarction. However, the absolute benefit and cost effectiveness of treatment vary according to the underlying risk and age of the population sub-group, and thus some groups would warrant access to subsidised statins and some would not.

2. Full assessment of risks, benefits and costs. While one of PHARMAC’s main jobs is to get the best deal on drug prices, a full assessment of the risks and benefits of a given pricing policy is needed, including balance sheets for the economic, health and other effects. The economic balance sheet includes the effects on the drug bill (the current driving force for many of PHARMAC decisions and this is closely monitored), effects on other health care costs (not currently closely assessed), and hidden costs such as the added costs on doctors’ time to fulfil red tape requirements (not assessed at all). The health balance sheet would include health gains and health risks, such as the potential detrimental effects of increased side effects and loss of control of blood pressure or cholesterol. These are not being systematically estimated, and have been largely excluded from the decision-making process. The retrospective study by Thomas and Mann, suggested an increase in cardiovascular events occurred after patients were switched to fluvastatin. Despite its methodological flaws, this audit highlights our lack of knowledge of the effects of the mass transfer of tens of thousands of patients from one drug to another and suggests that they may be substantial. Estimating the size of the detrimental effects of mass drug transfers should not have to rely on anecdotes or ad hoc audits by clinicians. It should be systematically estimated from well-designed controlled studies and prospective monitoring.

The longer term impact of PHARMAC’s policies on pharmaceutical company funding for endpoint clinical trials and health professional and patient education also need to be included in the health balance sheet. Several major pharmaceutical companies have already down-sized or withdrawn their New Zealand presence, partly in response to the success achieved by PHARMAC in driving down drug prices. While New Zealand represents a tiny fraction of pharmaceutical sales world-wide, the ‘PHARMAC model’ is being watched by other countries that are struggling to contain their drug budgets. If clinical outcome evidence is not consistently given a high weighting by pharmaceutical regulatory bodies, this could potentially dissuade pharmaceutical companies from investing in these expensive, long-term clinical outcome trials in the future. Furthermore, the investment by pharmaceutical companies in research in New Zealand has been substantial, but has fallen sharply in recent years. While this research obviously has strategic value for the companies, it does produce important clinical information and supports investigator-initiated research projects. The drying up of these funds will have a significant negative effect on the capability and capacity of medical research in New Zealand.

The same can be said for health professional and patient education, the funding for which will increasingly need to come from the public purse. Perhaps some of the savings on the pharmaceutical bill could be diverted to education.

Lastly, other effects such as the impact on tens of thousands of patients of uncertainty, changing rules and ongoing disputes between doctors and PHARMAC is probably substantial. The code of rights for patients includes rights to effective communication, to be fully informed and to make an informed choice; and the ethical considerations of transferring many thousands of patients onto another drug (perhaps with less evidence behind it)
need closer consideration. These implications for patients do not appear to have been a significant factor in the decision-making process to date, and we believe they warrant a higher priority for future decisions.

3. Explicit assumptions and transparent decisions. The pricing policy decisions made by PHARMAC need to be fully transparent, and to achieve this, the scientific evidence, the full risk/benefit/cost assessment, and the assumptions made in the process would need to be explicit. One of the benefits of this transparency would be to allow for better detection of bias. Clinical and industry biases are well recognised, but managerial bias (preference for the cheapest option) also needs to be recognised. A good example of this occurred over the recommendations for targets for lipid lowering. The debate was whether the primary target for cholesterol lowering should be a percentage reduction (such as 20-25%), or a reduction below an absolute level (such as 5.0 mmol/L). Full analyses on this issue from the statin trials were not available at the time. Targets using absolute cholesterol levels could be based on the linear relationship between cholesterol levels and cardiovascular events in observational studies, whereas targets of 20-25% reductions could be argued on the basis of the average cholesterol reductions achieved in the trials. The clinical bias of wanting the maximum treatment for patients would favour the first option, and the managerial bias of wanting to contain the budget would favour the second option because the lower priced drug, fluvastatin, could only achieve these levels of 20-25% cholesterol reduction. In this case, the second option prevailed.

Economic modelling is required to link costs to evidence on health outcomes and to explore the short-term and long-term budgetary implications of reimbursement policies. Assumptions made in the modelling process need to be explicit and open to scrutiny, particularly when commercial deals become part of the reimbursement process. If cost-utility analyses are used to evaluate drug therapies, it is important to know the threshold at which therapies are considered affordable in New Zealand, the discount rate and the criteria that PHARMAC uses to assess reimbursement applications. Peer review of key pharmacoeconomic analyses are appropriate.

4. Wide consultation and interpretation of the evidence. Evidence is the most important ingredient needed for decision-making, but it is not the only one. Expertise is needed in interpreting the evidence and consultation is needed to ensure that when decisions are made they are workable and have as much buy-in and understanding as possible. In addition to the current consultation processes, a mechanism for seeking consumer input would be beneficial. A greater use of peer review on key issues is one way to increase the input of expertise at the critical early stages. As decision making depends increasingly on clinical epidemiology and pharmacoeconomics, it would be essential that these skills are available to PHARMAC’s key advisory committee, the Pharmaceutical and Therapeutics Advisory Committee (PTAC), either through its members or through its review processes. A review of the selection and training of PTAC members would be valuable.

5. Testing of major initiatives. All major initiatives that involve significant amounts of money or significant numbers of people would benefit substantially from prior testing. PHARMAC is already doing this in areas that may entail increases in pharmaceutical expenditure, such as nicotine replacement therapy, but did not consider it for the three mass transfer initiatives of cardiovascular drugs. Testing the processes (including the associated red tape) and outcomes (incidence of side effects, loss of control of blood pressure and lipids) would give doctors and their patients confidence that the potential for harm and cost shifting is minimised. Randomised controlled trials would be the method of choice for these studies, because this is the only methodology that can avoid confounding bias. Sufficient lead time is therefore needed to design, perform and analyse such studies. We cannot rely on international experience for this information because each country has a very different mix of health systems, drug reimbursement methods and prescribing patterns. For example, the US trial that favoured aggressive lipid-lowering therapy over angioplasty is clearly not applicable to the New Zealand situation where access to angioplasty is far tighter than in the US.

6. Close monitoring, especially of major policy initiatives. At present, PHARMAC invests a miniscule amount of its pharmaceutical budget in evaluation and monitoring the impact of pharmaceuticals on health outcomes. We propose that this should be substantially increased. Monitoring of major policy initiatives also need to be given sufficient lead time to be effective. Some monitoring of the ACE inhibitor and CCB initiatives has been put in place, but the time scale for getting the evaluations designed and in place was very rushed. In the case of the ACE inhibitor change, about 80 000 people had already been switched to the fully subsidised drugs before one of the evaluation studies could be started. The data from the monitoring of one initiative could then inform the processes for the next initiative, so that mistakes are not repeated.

7. Balanced communications. As part of the transparency of decision-making, balanced communications to health professionals and the public would involve an acknowledgement of the pros and cons of major PHARMAC decisions. A one-sided, ‘public relations’ version has tended to evoke an opposing and similarly one-sided view from the medical profession. Sound expenditure on pharmaceuticals can improve health outcomes and reduce hospital expenditure, and the concept of ‘dollars saved’ from the pharmaceutical budget will only become a persuasive argument for doctors and their patients when they can see the ‘savings’ being used to buy greater health gains.

8. Red tape minimised and not used as a rationing tool. One of the major concerns, particularly among specialists over the lipid initiative, has been the major increase in form-filling to get approval for statin drugs. Specialist assessment is still used by PHARMAC in many areas as a rationing tool, and this not only wastes time and money, but it also raises major financial barriers for those on low incomes. PHARMAC needs to give a high priority to developing a system for prescription endorsement which: 1) lets the pharmacist know whether or not the drug is subsidised for the patient, 2) is able to be monitored for prescriber compliance (possibly through random auditing) and 3) involves a minimal amount of red tape.

Conclusion PHARMAC has a critical job to do on behalf of the New Zealand public in achieving the greatest health gains it can from the pharmaceutical budget. The decisions it needs to make are often difficult and are often driven by the high or increasing costs of certain groups of drugs. The three major initiatives involving cardiovascular drugs have provided valuable lessons on the process of developing and implementing important pharmaceutical subsidy decisions. It is time to turn those lessons into action. We consider that PHARMAC’s decision-making processes need to be explicit and transparent, and have suggested a number of fundamental principles which, we believe, would improve them. These principles are
achievable and enacting them will help to restore the faith that PHARMAC’s partners (health professionals) and constituents (patients and taxpayers) should have in its processes.

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