THE NEW ZEALAND MEDICAL JOURNAL
Journal of the New Zealand Medical Association

CONTENTS

This Issue in the Journal

Editorials

Original Articles

Viewpoints

Clinical Correspondence

Letters

100 Years Ago in the NZMJ

Proceedings

Methuselah

Notice

THE NEW ZEALAND MEDICAL JOURNAL
Journal of the New Zealand Medical Association

This Issue in the Journal

Access to new medicines in New Zealand compared to Australia
Michael Wonder, Richard Milne

This paper compares the public's access to new prescription medicines in Australia and New Zealand via their respective national medicines reimbursement schemes in the period 2000-2009. 135 new prescription medicines were listed in the Australian Schedule of Pharmaceutical Benefits, of which 59 (43%) were listed in the New Zealand Pharmaceutical Schedule. For these 59 new medicines, reimbursement occurred on average 33 months later in New Zealand. The 76 medicines not reimbursed in NZ cover many therapeutic areas. The differences between the 2 countries are largely due to the differing pharmaceutical reimbursement processes.

Over-the-counter codeine analgesic misuse and harm: characteristics of cases in Australia and New Zealand
Brian R McAvoy, Malcolm D H Dobbin, Claire L Tobin

This study has identified that controls on OTC codeine analgesics in Australia and New Zealand were not sufficient to limit non-medical use of these products. As a result, cases identified in these two countries escalated the number of self-administered tablets taken daily for misuse, resulting in codeine dependence and serious non-steroidal anti-inflammatory drug toxicity secondary to this dependence.

Usage and equity of access to isotretinoin in New Zealand by deprivation and ethnicity
Peter Moodie, Richard Jaine, Jason Arnold, Mike Bignall, Scott Metcalfe, Bruce Arroll

Oral isotretinoin, for severe acne, was until March 2009 fully funded in New Zealand only if the prescription was written by a vocationally registered dermatologist. This study was an audit examining the use of isotretinoin by deprivation level and ethnicity, in order to examine potential inequities in use. People living in more deprived (poorer) areas were less likely to use isotretinoin, as were Māori and Pacific people. Given there is no evidence for lower rates of acne for Māori and Pacific people, the reasons may include financial and other barriers.

Pharmacological management of children's asthma in general practice: findings from a community-based cross-sectional survey in Auckland, New Zealand
Sue Crengle, Elizabeth Robinson, Cameron Grant, Bruce Arroll

Between June 1999 and May 2001 the caregivers of 583 children aged 2 – 14 years were interviewed about the medications that had been given for their child's asthma in the previous 12 months. The results showed that there have been some improvements in the provision of medications for asthma since research was published in the early 1990s and suggested that some children with moderate, severe, and very severe asthma had not received preventive medications in the previous year. Some findings suggested that Maori and Pacific children did not receive the same quality of care as Other children.

Median sternotomy scar assessment
Hamesh Jina, Jeremy Simcock

Our study examined scarring from wounds over the breast bone following cardiac surgery 2-3 years after their operation. We found that 20% of patients had complaints about their scar and 10% of patients were noted by the plastics doctor to have a prominent scar. We could not find any reason to why some patients had symptoms or scarred poorly. We feel that this group of patients would benefit from treatment to prevent bad scarring.

Academic performance and career choices of older medical students at the University of Otago
William Shelker, Alison Belton, Paul Glue

The University of Otago is unusual amongst medical school, in that there is a process for admitting older students, who have relevant life- or work-experience. This study looked at how well these older students performed in medical school examinations, and what they did after graduation, compared with younger medical students. The older students performed as well or better than younger students in examination results and graduation rates from medical school. Compared with their younger classmates, after graduation, a greater proportion of these older students were practising in NZ, and were working as GPs. These findings may be relevant in planning for recruitment and training of the future NZ-trained doctors.

THE NEW ZEALAND MEDICAL JOURNAL
Journal of the New Zealand Medical Association

Sarcoma services in New Zealand

Gary Hooper

Soft-tissue sarcomas are rare (approximately 1% of all adult malignancies), and most practitioners may only see one in a practising lifetime. However, soft-tissue masses present commonly and are often accompanied by significant patient anxiety. Delaying the diagnosis or inappropriately investigating a soft-tissue sarcoma may compromise a patient's treatment and ultimate survival.[1] The case report from Blackett[2] in this issue of the *Journal* is a timely reminder on the appropriate investigation and treatment of soft-tissue sarcoma.

There are four internationally[3] accepted clinical criteria which are used to differentiate between malignant and benign soft-tissue tumours: a mass which is (1) greater than 5 cm in size; (2) increasing in size; (3) deep to the deep fascia; and (4) painful. Should any one of these factors be present then the clinician should consider the diagnosis of a soft-tissue sarcoma.

A magnetic resonance imaging (MRI) scan is the most useful diagnostic tool to investigate these tumours, but it is expensive and seldom available in the primary care setting. An ultrasound examination is often a helpful investigation which is relatively inexpensive and more readily available. It can give information to support the clinical findings (size and position of the mass) and can also comment on the density of the lesion which may help diagnosis.

The diagnosis is made on biopsy and all clinically suspicious lesions should have a tissue diagnosis. Fine needle biopsy is notoriously unreliable in soft-tissue sarcomas and is not indicated for primary diagnosis.[3,4] Multiple core-tissue biopsies, often under radiological control, or incisional biopsy, should be performed to give the best chance of providing a diagnosis without compromising the management options. Inappropriate or inadequate biopsy is one of the major reasons for poor outcomes in these patients and is associated with a significantly higher chance of local recurrence.[5] Indeed, specialist referral is important to improve patient outcome.

The best results in the treatment of soft-tissue sarcoma have been achieved with multidisciplinary teams[1,3] comprising pathologists, radiologists, oncologists and orthopaedic surgeons. The pathological diagnosis in these sarcomas can be difficult and often requires the correlation of both the clinical and radiological results. A close working relationship with the multidisciplinary team is important to make the correct diagnosis.

The successful treatment of soft-tissue sarcoma is dependent on complete surgical resection and therefore it is important that the surgeon is aware of the position of the biopsy tract to avoid local recurrence. Preoperative radiotherapy is often used to reduce the size of the lesion to allow wide resection and limb salvage which demands close communication between the radiation oncologist and the surgical team to stage treatment and initiate surgery at the optimal time for the best tissue response.

The National Institute for Health and Clinical Excellence[1] (NICE 2006) have provided management guidelines for patients with suspected soft-tissue sarcoma which have largely been adopted by the New Zealand Guidelines Group.[6] These guidelines indicate that all potential sarcomas should be referred for immediate specialist evaluation.

In New Zealand there are two established Sarcoma Units (in Auckland and Christchurch, respectively), which have been developed in conjunction with the New Zealand Orthopaedic Association and the Ministry of Health to give a comprehensive service throughout the country. Each of these Units has a multidisciplinary team who provide and coordinate a management plan for each patient. These Units offer access to both specialist and primary care physicians with patients being assessed within 2 weeks of referral.[4]

Practitioners working outside these two main centres should refer patients to their local orthopaedic surgeons. The outcome following soft-tissue sarcoma has improved largely due to the use of these teams to co-ordinate treatment options in a controlled and systematic approach.

Competing interests: None.

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THE NEW ZEALAND MEDICAL JOURNAL
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Why is publicly funded bariatric surgery still not fully supported?

Richard Flint, Steven Kelly

It is incredulous that New Zealand is still debating the merits of public funded bariatric surgery, when it is close to 40 years since it was introduced.[1,2] Back in the 1970s surgery was freely offered with little data justifying its efficacy.

Fortunately our surgical predecessors were right as we now know the perils of obesity; it reduces life expectancy (by 30% for every 5 kg/m^2 above normal BMI),[3] increases the risk of cancer,[4] is responsible for an alarming rise in diabetes,[5] reduces worker productivity,[6] and is destined to burden the health budget by over $300 million dollars per year.[7]

Furthermore we now know that bariatric surgery can result in significant, long-term weight loss;[8] reduce comorbidities;[9] improve quality of life;[10] improve mortality;[11] and improve health economics;[12] whilst maintaining a very safe perioperative profile.[13] So why is there now a hesitancy from the non-surgical community to adopt bariatric surgery as a viable option for those who are obese?

The first argument against surgery (and often the most fervent) is that obesity is just a product of free will and resources should not be spent to surgically correct a self-inflicted condition.[14] Whilst it is true that most food is ingested willingly, it is also true that factors promoting obesity are not experienced willingly.

Widespread obesogens like bisphenol-A (BPA),[15] prenatal factors such as poor maternal diet that increases the risk of future obesity,[16] socioeconomic status[17] and heavy commercial marketing of poor quality foods are all involuntary factors that have been implicated in the development of obesity.

The ethics of denying patients the chance for surgery because they have been too weak-willed to resist in a pro-obesogenic environment must be questioned. Even if this argument is accepted then it must surely raise a perturbing precedent.

What difference would there be in denying patients treatment for melanoma because they failed to use sunscreen, retrovirals for AIDS because they failed to adopt safe sexual practises, angioplasties for coronary artery disease because they failed to exercise 30 minutes a day, or oxygen therapy for COPD because they used to smoke? Most of healthcare is focused on conditions that could be ameliorated by healthy life choices, but it is disturbing that obese patients are judged on a premorbid sense of 'discipline' that is never debated as a prerequisite to treatment for other conditions.

A further argument against bariatric surgery is that it does not work. Anecdotal tales of a patient pureeing up Mars (chocolate) bars to sabotage their weight loss surgery are often garnered as proof (does anyone know who this patient really is?) However, this conclusion is not supported with scientific evidence.

Randomised controlled trials[18,19] and cohort studies[8,20] have shown bariatric surgery to be vastly superior to dieting. Weight loss is maintained for over a decade[21–25] that not only improves comorbidities but guarantees an increased survival.[8,11,26] However, if we are to accept that the single anecdote of a nameless patient can be used to reject the weight of evidence supporting bariatric surgery, then why is no-one questioning therapies for other conditions.

Why do we not deny drug-eluting cardiac stents when we know that over 10% of patients will fail to continue thienopyridine therapy within the first month so increasing stent thrombosis and subsequent mortality by a factor of 10.[27]

Why should we maintain solid organ transplantation when up to 38% of patients will fail to take their anti-rejection medication.[28] Is it because it is not acceptable to deny people an effective treatment when their survival is at risk. How much more inappropriate can it be to decline bariatric surgery that has been shown to improve annual survival by 80%![29]

But maybe the main reason that bariatric surgery is resisted is the concern that health resources may be overwhelmed. Estimates that a quarter of adult New Zealanders are obese[30] correlated to United States data showing rising popularity of bariatric operations[31] can cause concern over cost blow-outs unless surgery is withheld. Yet not doing anything has an inherent cost.

Obesity increases the cost of inpatient and outpatient care by 36%, the cost of medication by 77%,[32] and accounts for 2.5% of New Zealand's health spending.[7] This can be extrapolated to $344 million a year, yet the true cost can only be greater as this estimate is based on 1990 data that does not account for the recent rise in the rate of obesity. In the face of such sums it seems ironic that withholding surgery will actually cost the health system even more. Numerous studies have indicated that bariatric surgery leads to long-term savings[33–36] with the cost of surgery being recouped within 2 years.[37]

In recognition of such data the Ministry of Health published a business case in 2008 for New Zealand public funded bariatric surgery.[38] The recommendations that 0.5% of the morbidly obese population be offered surgery (equating to 915 operations over a 5-year time period) became closer to reality in October 2010 with the introduction of specific funding earmarked for bariatric surgery on a nationwide basis with geographical equality.[39] Despite being an admirable first step toward an effective treatment for obesity, it is uncertain to guarantee the adoption of bariatric surgery as a mainstream option. The funding is temporary and reliant on District Health Boards to pick up the future costs.

Furthermore, it is difficult to see how District Health Boards will be 'convinced' on the utility of bariatric surgery when the results of just 13 operations a year in cities such as Christchurch are expected to influence the adverse effects of the 90,000 obese people in their district. So it is unsurprising that some have intimated that the restriction of bariatric surgery is prejudicial rather than based on a reasoned evaluation of the evidence.[40]

In a time when obesity has increased to near epidemic proportions, New Zealand has progressed from readily available bariatric surgery to a position of near

impossible access. And this is despite the overwhelming evidence that extol the merits of such surgery. Must it take another 40 years to get back to the position we enjoyed in the 1970s?

Competing interests: Both authors are bariatric surgeons.

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THE NEW ZEALAND MEDICAL JOURNAL
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Access to new medicines in New Zealand compared to Australia

Michael Wonder, Richard Milne

Abstract

Aim To compare access to new prescription-only medicines in New Zealand (NZ) with that in Australia.

Method The range of new prescription medicines and the timing of their regulatory approval and reimbursement in NZ and Australia in the period 2000 to 2009 were compared.

Results 136 new prescription medicines were first listed in the Australian Schedule of Pharmaceutical Benefits in the study period and 59 (43%) of these were listed in the NZ Pharmaceutical Schedule. Listing of these 59 medicines for reimbursement occurred later in NZ (mean difference=32.7 months; 95% CI 24.2 to 41.2 months; p<0.0001) due largely to a longer time from registration to listing (mean difference=23.7 months; 95% CI 14.9 to 32.4 months; p<0.0001). The remaining 77 medicines that are reimbursed in Australia but not in NZ cover a wide range of therapeutic areas, including some diseases for which there are no reimbursed medicines in NZ. Four new medicines were listed in NZ but not Australia.

Conclusion In the last decade, public access to new medicines in NZ has been more limited and delayed compared to Australia.

Access to new medicines is an ongoing public health issue in most developed countries. Many new medicines are costly and unaffordable for many patients; therefore public access is very limited. Governments are under continual pressure to provide timely access to new medicines, many of which are costly.

In New Zealand (NZ) the governmental Pharmaceutical Management Agency (PHARMAC) manages purchasing of pharmaceuticals on behalf of District Health Boards (DHBs) following their registration by Medsafe. PHARMAC develops and maintains the NZ Pharmaceutical Schedule (the 'NZ Schedule') of pharmaceuticals available in the community on prescription by a medical doctor, dentist, registered midwife, designated nurse practitioner or optometrist, and partly or fully subsidised from a national pharmaceutical budget. It also includes some pharmaceuticals purchased by DHBs for use in their hospitals, for which national prices have been negotiated by PHARMAC.[1]

In Australia, pharmaceuticals that are subsidised by the Federal Government are listed in the Schedule of Pharmaceutical Benefits (the 'Australian Schedule') and funded by the Pharmaceuticals Benefits Scheme (PBS) following their registration by the Therapeutic Goods Administration (TGA). A PBS prescription must be written by a doctor, a dentist, an optometrist, a midwife or a nurse practitioner. There are separate arrangements for PBS prescriptions in certain public hospitals in most States.[2]

New prescription-only medicines become available after the results of their Phase 3 clinical trials become known and pharmaceutical suppliers make submissions to the NZ and Australian governments for public funding. In NZ, decisions on listing, indication, subsidy levels, prescribing guidelines and conditions are made by the Board of PHARMAC with input from its Pharmacology and Therapeutics Advisory Committee (PTAC), its specialist sub-committees, the Hospital Pharmaceutical Advisory Committee (HPAC) and PHARMAC staff.

In Australia, a statutory body called the Pharmaceutical Benefits Advisory Committee (PBAC) reviews all submissions by pharmaceutical suppliers. The PBAC then makes recommendations to the Minister for Health and Ageing on the listing and subsidisation of medicines in the Australian Schedule. Restrictions may be applied to limit the use of medicines to certain registered indications.

The aim of this study was to compare access to new prescription-only medicines in NZ with Australia in the period January 2000 to December 2009. For the purposes of this analysis we define 'access' to a new medicine in NZ or Australia as listing in the respective Pharmaceutical Schedule.[3,4]

Methods

A 'new medicine' was defined as:

- A new chemical entity in a new pharmacological/therapeutic class (so called "first-in-class" medicine)
- A new chemical entity that represents a *pharmacological analogue* of an existing medicine, including an analogue of an existing (recombinant) biological medicine (so called "me-too" medicine)
- A new presentation (e.g. pre-filled syringe versus tablet) of an existing medicine that is to be administered by a *different* route (e.g. injection versus oral ingestion) for use by a *different* patient population ("new medicinal use")

This definition includes a medicine that was registered some time ago, only to be deregistered and subsequently reregistered (ostensibly for use by a different patient population).

The analysis excluded any existing medicine in the *same* presentation that was subsequently reimbursed for use by a *different* patient population (i.e. a new indication). It also excluded any existing medicine that was given access to a wider patient group, but in the same indication (e.g. moved from second-line to first-line use).

The following were also excluded from the analysis:

- A new formulation of an existing medicine (e.g. salt, ester, pegylated form, glycosylated form)
- A new presentation of an existing medicine that is to be administered by the *same* route (e.g. tablet versus capsule, cream versus ointment, etc.) and thus be used by the *same* patient population
- A new enantiomer of an existing medicine
- A new medicine that is the pro-drug of an existing medicine
- A new structural form of an existing biological medicine (e.g. beta versus alpha form)

For Australia, we examined serial editions of Section 2 (Ready-Prepared Medicines) of the Australian Schedule issued during the study period to identify new medicines and their respective dates of reimbursement. Medicines listed only in Section 4 (Extemporaneously-Prepared Medicines) or the Repatriation Schedule of Pharmaceutical Benefits were excluded. New combination products were also excluded from the sample as we assumed that patients should be able to access the respective components separately. Vaccines and medicinal products, such as test strips and infant formulae, were also excluded.

A medicine was considered to be 'new' if its first listing in the Australian Schedule occurred no more than 10 years after its initial registration by the TGA. This was done to exclude medicines that were likely to be out of patent in Australia when they were first listed in the Schedule.

TGA registration dates are not readily available. When the initial registration date for a medicine could not be determined, the on-line version of the Australian Register of Therapeutic Goods (ARTG) was used to determine the date a medicine was first entered into the register; this date was used as a proxy for the TGA registration date. Medicines are generally entered in the ARTG within days of registration.[5] The core data set for Australia comprised new prescription-only medicines that were first listed in the Schedule in the study period.

Serial issues of the NZ Schedule were then searched for medicines in the core data set. A medicine listed in the NZ Schedule was considered to be the same medicine as that listed in the Australian Schedule if its registered form was the same chemical entity in the same or similar registered form. Tablets and capsules were considered to be sufficiently similar, and differences in registered dosage were ignored. A medicine listed in NZ was deemed to be different from that listed in Australia if it was available in a *different* presentation for use by a *different* patient population.

A new medicine was considered to be 'accessible' in New Zealand if it was listed in Section B (Community Pharmaceuticals) and/or in Part II (Pharmaceuticals Under National Contract) of Section H. Accessible medicines also include oncology products included in Part V (Pharmaceutical Cancer Treatments) of Section H (Hospital Pharmaceuticals) in the period January 1, 2000 to June 30, 2008 or into Section B or H after June 30, 2008. It was considered to be 'accessible' in Australia if it was listed in the Australian Schedule. A medicine listed in the NZ Pharmaceutical Schedule only under 'Special Access' provisions (i.e. reimbursed despite not yet being registered) was not considered to be 'accessible' as there are no such provisions in Australia.

The *New Zealand Gazette* and Data Sheets (Consumer Medicine Information) were examined to determine the registration status of all medicines in the core data set. Data Sheets were also used to determine which medicines in the core data set were prescription-only in New Zealand.[6]

The date that a medicine first appeared in the *New Zealand Gazette* was considered to be its registration date. Medicines in the core data set that have been reimbursed in NZ comprised the common data set.

The following descriptive analyses were performed on the medicines on the common data set.

- Breadth of access was determined by counting the number of medicines and their classification by therapeutic area (World Health Organization (WHO) Anatomical Therapeutic Chemical (ATC) main group) in each country.[7]
- Timeliness of registration and access were estimated by comparing the respective dates of registration and reimbursement in both countries.

The medicines in the core data set that were reimbursed only in Australia in the study period (unique data set) were then analysed by their ATC main group and therapeutic area (reimbursed use).

Finally, listings of all the new, prescription-only medicines that were reimbursed in NZ were compared with listings in Australia in the study period.

Single sample t-tests of differences were used for between-country comparisons of registration dates, reimbursement dates and the time from registration to listing. Analyses were conducted as two sided tests with an α of 0.05, using GraphPad.[8]

Results

Breadth of access—136 new, prescription-only medicines (core data set) were listed in the Australian Schedule in the study period (Table 1).

Table 1. New medicines listed in the Australian Schedule of Pharmaceutical Benefits in the period 2000–2009

WHO ATC Main Group[a]	Code	Number	Percentage (%)
Alimentary tract and metabolism	A	12	9
Blood and blood forming agents	B	9	7
Cardiovascular system	C	14	10
Dermatologicals	D	2	1
Genito-urinary system and sex hormones	G	4	3
Systemic hormonal preparations	H	3	2
Anti-infectives for systemic use	J	15	11
Anti-neoplastic and immunomodulating agents	L	30	22
Musculo-skeletal system	M	9	7
Nervous system	N	23	17
Respiratory system	R	3	2
Sensory organs	S	7	5
Various	V	5	4
Total		**136**	**100**

[a] WHO ATC classification system.

Another medicine (troglitazone) was listed in the 1 May 2000 issue of the Schedule but it was deregistered before the listing took effect.

Timeliness of access—Table 2 shows all 59 medicines that were listed in both NZ and Australia in the period 2000-2009 (common data set; Table 2).

Registration occurred on average sooner in Australia than in NZ (mean difference 9.0 months; 95% CI 3.6 to 14.4 months; p=0.0012). 43 (73%) of the 59 medicines in the common data set were registered in Australia before NZ and 53 (90%) of the 59 medicines in the common data set were reimbursed in Australia before NZ (mean difference 32.7 months; 95% CI 24.2 to 41.2 months; p<0.0001).

Importantly, the lag between registration and listing was almost 2 years longer in NZ than in Australia (mean difference 23.7 months; 95% CI 14.9 to 32.4 months; p<0.0001).

Earlier registration of ursodeoxycholic acid, dorzolamide and ezetimibe in NZ was followed by earlier reimbursement. In the case of four medicines in the common data set (pravastatin, meloxicam, donepezil and levetiracetam), their listing in the NZ Pharmaceutical Schedule was so delayed that the first entrant was a generic brand.

77 medicines of the core data set were reimbursed only in Australia in the study period (unique data set; Table 3). They encompass most therapeutic areas; the largest group is WHO ATC Main Group L (anti-neoplastic and immunomodulating agents) with 15 (20%).

Limited access to new medicines in NZ cannot be attributed to non-registration because 64 (84%) of the new medicines registered in Australia are currently registered in NZ. The medicines in the unique data set that are not registered in NZ have not been reimbursed by way of ‘Special Access’ provisions.

Table 2. New medicines listed in both the Australian and the New Zealand Pharmaceutical Schedules in 2000-2009

Medicine	WHO ATC Main Group	Australia			New Zealand			Difference (months)[a]		
		Date of Registration	Date of Listing	Time from Registration to Listing (months)	Date of Registration	Date of Listing	Time from Registration to Listing (months)	Registration	Listing	Time from Registration to Listing
entacapone	N	12/05/1999	01/02/2000	8.7	17/02/2000	01/11/2005	68.5	9.2	69.0	59.8
leflunomide	L	28/09/1999	01/02/2000	4.1	23/03/2000	01/05/2002	25.3	5.8	27.0	21.1
temozolomide	L	08/06/1999	01/02/2000	7.8	17/12/1998	01/05/2006	88.5	-5.7	75.0	80.7
irinotecan	L	17/09/1997	01/05/2000	31.5	29/05/1997	01/12/2002	66.1	-3.6	31.0	34.7
naltrexone[b]	N	06/01/1999	01/02/2000	12.9	18/03/1999	01/06/2004	62.5	2.3	52.0	49.7
insulin aspart	A	25/05/2000	01/08/2000	2.2	10/02/2000	01/11/2002	32.7	-3.5	27.0	30.5
quetiapine	N	27/01/2000	01/11/2000	9.2	11/12/1997	01/05/2001	40.7	-25.5	6.0	31.5
tramadol	N	29/04/1998	01/11/2000	30.1	17/10/1997	01/06/2003	67.5	-6.4	31.0	37.3
ursodeoxycholic acid	A	19/05/1999	01/11/2000	17.5	07/09/1995	01/02/1999	40.9	-44.4	-21.0	23.4
brinzolamide	S	24/10/2000	01/02/2001	3.3	23/11/2000	01/06/2004	42.3	1.0	40.0	39.0
bupropion	N	22/08/2000	01/02/2001	5.4	18/05/2000	01/07/2009	109.5	-3.2	101.0	104.2
dorzolamide	S	18/04/1996	01/02/2001	57.5	17/11/1994	01/07/1998	43.5	-17.0	-31.1	-14.1
donepezil	N	09/03/1998	01/02/2001	34.8	19/04/2001	01/11/2010	114.5	37.4	117.0	79.7
exemestane	L	30/11/2000	01/05/2001	5.0	30/05/2002	01/08/2007	62.1	18.0	75.1	57.1
levetiracetam[f]	N	22/02/2001	01/08/2003	29.3	23/12/2004	01/11/2010	70.3	46.0	87.1	41.1
oxaliplatin[e]	L	27/02/2001	01/12/2001	9.1	05/02/2004	05/02/2004	0.0	35.3	26.2	-9.1
imatinib	L	13/08/2001	01/12/2001	3.6	18/10/2001	01/12/2002	13.4	2.2	12.0	9.8

meloxicam	M	23/02/2001	01/02/2002	11.3	23/07/1998	01/09/2010	145.4	-31.1	103.0	134.1
pioglitazone	A	03/01/2001	01/11/2003	33.9	06/06/2002	01/09/2004	26.9	17.1	10.0	-7.0
eptifibatide[d]	B	18/11/1999	01/02/2004	38.5	30/11/2000	01/02/2007	74.1	12.4	48.0	35.6
zoledronic acid	M	15/03/2001	01/05/2002	13.5	22/02/2001	01/12/2002	21.3	-0.7	7.0	7.7
amisulpride	N	1/02/2002	01/08/2002	6.0	13/09/2001	01/12/2008	86.7	-9.6	76.1	85.7
tenofovir	J	08/08/2002	01/10/2002	1.8	10/11/2005	01/04/2007	16.7	39.1	53.0	13.9
tiotropium	R	23/05/2002	01/02/2003	8.4	18/10/2001	01/02/2005	39.5	-7.1	24.0	31.2
travoprost	S	21/01/2002	01/08/2002	6.3	14/02/2002	01/06/2004	27.6	0.8	22.0	21.2
bimatoprost	S	20/08/2002	01/02/2003	5.4	15/08/2002	01/08/2005	35.6	-0.2	30.0	30.1
moxifloxacin[c]	J	21/12/2000	01/02/2003	25.4	22/02/2001	01/12/2010	117.3	2.1	94.0	92.0
etanercept	L	09/09/2000	01/07/2003	33.7	31/01/2002	01/02/2004	24.0	16.7	7.1	-9.7
infliximab[d]	L	02/08/2000	01/11/2003	39.5	16/11/2000	01/02/2007	74.6	3.5	42.1	38.6
ezetimibe	C	18/06/2003	01/08/2004	13.5	24/04/2003	01/07/2004	14.3	-1.8	-1.0	0.8
deferiprone	V	02/04/2003	01/02/2004	10.0	21/05/2009	01/10/2010	16.4	73.7	80.0	6.3
adalimumab	L	03/12/2003	01/05/2004	4.9	30/09/2004	01/01/2006	15.1	9.9	20.1	10.1
aripiprazole	N	21/05/2003	01/05/2004	11.4	01/02/2007	01/08/2008	18.0	44.4	51.1	6.6
bosentan	C	20/11/2002	01/03/2004	15.4	16/12/2004	01/07/2009	54.5	24.9	64.0	39.2
sirolimus	L	21/05/2002	01/04/2004	22.4	11/01/2001	01/07/2007	77.7	-16.3	39.0	55.3
adefovir	J	10/09/2003	01/12/2004	14.7	11/08/2005	01/05/2006	8.6	23.0	17.0	-6.1
atazanavir	J	08/01/2004	01/12/2004	10.8	13/01/2005	01/11/2006	21.6	12.2	23.0	10.8
enfuvirtide	J	27/08/2003	01/12/2004	15.2	10/03/2005	01/09/2006	17.8	18.4	21.0	2.6
aprepitant	A	13/04/2004	01/04/2005	11.8	19/08/2004	01/10/2009	61.4	3.9	54.0	50.2
emtricitabine	J	21/12/2004	01/04/2005	3.3	27/10/2005	01/04/2007	17.1	10.2	24.0	13.8

iloprost	B	12/01/2004	01/04/2005	14.6	19/04/2007	01/07/2009	26.4	39.2	51.0	11.8
thalidomide[e]	L	03/10/2003	01/02/2006	28.0	18/12/2003	18/12/2003	0.0	2.5	-25.5	-28.0
insulin glargine	A	19/01/2001	01/10/2006	68.4	21/06/2001	01/07/2006	60.4	5.0	-3.0	-8.1
entecavir	J	05/04/2006	01/12/2006	7.9	19/03/2009	01/08/2009	4.4	35.5	32.0	-3.5
imiquimod	D	18/08/1998	01/12/2006	99.5	01/04/2004	01/09/2008	53.1	67.5	21.0	-46.5
trastuzumab	L	04/09/2000	01/10/2006	72.9	08/11/2001	01/07/2005	43.8	14.1	-15.0	-29.2
atomoxetine	N	16/01/2004	01/07/2007	41.5	13/01/2005	01/04/2009	50.6	11.9	21.0	9.1
sildenafil	G	07/08/2006[g]	01/03/2007	6.8	19/07/2007	01/07/2009	23.4	11.4	28.0	16.7
ziprasidone	N	24/10/2001	01/04/2007	65.3	20/04/2000	01/08/2007	87.4	-18.1	4.0	22.2
dasatinib	L	15/01/2007	01/08/2007	6.5	15/03/2007	01/08/2009	28.6	1.9	24.0	22.1
insulin glulisine	A	02/05/2005	01/07/2007	26.0	01/02/2007	01/08/2010	42.0	21.0	37.1	16.0
darunavir	L	15/03/2007	01/12/2007	8.6	23/08/2007	01/11/2010	38.3	5.3	35.0	29.8
varenicline	N	15/02/2007	01/01/2008	10.5	08/03/2007	01/11/2010	43.9	0.7	34.0	33.3
erlotinib	J	30/01/2006	01/08/2008	42.0	23/03/2006	01/10/2010	54.3	1.7	14.0	12.3
raltegravir	J	30/01/2008	01/07/2008	5.1	04/09/2008	01/10/2009	12.9	31.2	3.0	-28.1
sunitinib	L	14/09/2006	01/05/2009	31.6	26/10/2006	01/11/2010	48.2	1.4	18.0	16.7
etravirine	J	19/12/2008	01/07/2009	6.4	02/07/2009	01/11/2010	16.0	6.4	16.0	9.6
rivaroxaban	B	24/11/2008	01/08/2009	8.2	13/08/2009	01/12/2010	15.8	9.6	16.0	6.4
ambrisentan	C	18/11/2008	01/12/2009	12.4	13/08/2009	01/04/2010	7.6	8.8	4.0	-4.8
Mean				+20.2			+43.9	+9.0	+32.7	+23.7
95% CI				14.9 – 25.4			35.6 – 52.2	3.6 – 14.4	24.2 -41.2	14.9 – 32.4

[a] A positive sign denotes a shorter time in Australia; [b] New medicinal use; [c] Delisted on 1/01/2007; [d] Section H (hospital pharmaceutical) in NZ; [e] Date of reimbursement in NZ =date of registration'; [f] first listed on 1/08/2008 under Special Access provisions; [g] Date of registration for patients with pulmonary artery hypertension (*Revatio*)

Table 3. Medicines in the core data set that are reimbursed in Australia but not NZ

Category	Disease	Pharmacological Class	Medicine
No listed treatment (n=7)	Age-related macular degeneration	Light-activator for photodynamic therapy	verteporfin
		Monoclonal antibody to vascular endothelial growth factor	ranibizumab
		Cortisol analogue	anecortave[a]
	Facial lipoatrophy	Dermal filler	poly-L-lactic acid
	Hyperphosphatemia	Phosphate binder	sevelamer, lanthanum[b]
	Motor neurone disease	Glutamate antagonist	riluzole
New pharmacological class (n=29)	Acute coronary syndromes	Platelet aggregation inhibitor	prasugrel
		Direct thrombin inhibitor	bivalirudin
	Advanced hepatocellular carcinoma	Protein kinase inhibitor	sorafenib
	Alzheimer's disease	NMDA receptor antagonist	memantine
	Asthma	Leukotriene receptor antagonist	monteleukast
	Atopic dermatitis	Calcineurin inhibitor	pimecrolimus
	Chronic kidney disease	Anti-parathyroid agent	cinacalcet
	Depression	Serotonin and norepinephrine reuptake inhibitor	duloxetine
	Epilepsy	Sulphonamide	zonisamide[a,b]
	Kidney transplantation	mTOR inhibitor	everolimus
	Metastatic breast cancer	Protein kinase inhibitor	lapatinib
	Metastatic colorectal cancer	Monoclonal antibody to vascular endothelial growth factor	bevacizumab
	Multiple myeloma	Reversible inhibitor of 26S proteasome	bortezomib
	Multiple sclerosis	Monoclonal antibody to α4-integrin	natalizumab
	Non-small cell lung cancer	Epidermal growth factor receptor antagonist	gefitinib
	Osteoarthritis	Coxib	celecoxib, lumiracoxib[a], rofecoxib[a]
	Osteoporosis	Anti-resorptive agent	strontium
		Recombinant human parathyroid hormone	teriparatide
	Plaque psoriasis	Monoclonal antibody to CD11	efalizumab[a]
	Prevention of thromboembolic events following surgery	Inhibitor of activated Factor X	fondaparinux
	Pulmonary arterial hypertension	Prostacyclin analogue	epoprostenol[b]
	Rheumatoid arthritis	Interleukin-1 antagonist	anakinra[a]
		Monoclonal antibody to CD80 & CD86	abatacept
	Sepsis	Recombinant human activated protein C	drotrecogin
	Squamous cell cancer of the larynx	Monoclonal antibody	cetuximab
	Thyroid ablation	Thyrotropin	thyrotropin[b]
	Type 2 diabetes mellitus	Dipeptidyl peptidase 4 inhibitor	sitagliptin
New addition/s to an existing pharmacological class (n=38)	Alzheimer's disease	Cholinesterase inhibitor	rivastigmine, galantamine
	Hypertension and heart failure	Angiotensin II receptor antagonist	irbesartan, eprosartan, olmesartan[b], valsartan

	Hypertension	Calcium channel blocker	lercanidipine
		Imidazoline receptor agonist	moxonidine[b]
	Type 2 diabetes mellitus	Sulphonylurea	glimepiride
		Thiazolidinedione (PPAR agonist)	rosiglitazone
		Insulin analogue	insulin detemir
	Peptic ulceration and gastro-oesophageal reflux disease	Proton pump inhibitor	rabeprazole
	Acromegaly	Somatostatin analogue	lanreotide
	Acute myocardial infarction	Recombinant form of tissue plasminogen activator	tenecteplase
	Aspergillosis	Triazole derivative	voriconazole, posaconazole
	Asthma	Glucocorticoid	ciclesonide
	Bone metastases from breast cancer	Bisphosphonate	ibandronic acid
	Chronic myeloid leukemia	Protein kinase inhibitor	nilotinib
	Contraception	Progestogen	etonogestrel
	Depression	Serotonin-noradrenaline reuptake inhibitor	reboxetine
	Dyslipidemia	HMG-CoA reductase inhibitor	rosuvastatin
		Fibrate	fenofibrate[b]
	Heart failure	Aldosterone antagonist	eplerenone
		Beta blocker	bisoprolol[b]
	Hepatitis B	Nucleoside analogue	telbivudine
	HIV infection	Protease inhibitor	amprenavir[a], tipranavir
	Iron overload	Iron chelator	deferasirox
	Multiple myeloma	Thalidomide analogue	lenalinomide
	Narcolepsy	Centrally acting sympathomimetic	modafinil
	Nausea and vomiting following cytotoxic chemotherapy or radiotherapy	Serotonin antagonist	granisetron
	Non-small cell lung cancer	Antifolate antimetabolite	pemetrexed
	Pain	Opioid receptor agonist	hydromorphone
	Parkinson's disease	Dopamine agonist	pramipexole
	Prostate cancer	Gonadotropin releasing hormone analogue	triptorelin[b]
	Pulmonary arterial hypertension	Endothelin receptor antagonist	sitaxentan
	Osteoporosis	Bisphosphonate	risedronate
New presentation for use in a new patient population (New medicinal use) (n=3)	Luteal phase support in IVF	Progestogen	progesterone
	Opiate dependence	Opioid receptor agonist	buprenorphine[c]
	Superovulation prior to IVF	Gonadotropin	choriogonadotropin

[a] Since delisted; [b] Not registered in NZ; [c] Buprenorphine is registered by Medsafe in several formulations, but not for opiate dependence.

Other new medicines listed in NZ—In total, 80 new prescription-only medicines were listed in the NZ Pharmaceutical Schedule in the period 2000–2009. Excluding the 59 new medicines listed in both countries during this period (see Table 2 above), most of the remainder were registered in Australia prior to the study period and two (rizatriptan and mirtazipine) were registered in Australia subsequent to the study period. Five new medicines were reimbursed in NZ but not in Australia (Table 4).

Table 4. New medicines listed in NZ during the study period, and their reimbursement status in Australia[a]

Medicine	New Zealand	Australia
alendronate	01/02/2000	01/11/1996
bambuterol	01/07/2000	Not registered
brimonidine	01/08/2000	1/11/1999
topiramate	01/09/2000	1/08/1997
efavirenz	01/01/2001	01/10/1999
abacavir	01/01/2001	01/10/1999
gabapentin	01/04/2001	01/12/1994
carvedilol	01/04/2002	01/05/1998
levonorgestrel[b]	01/10/2002	01/02/2003
venlafaxine	01/01/2004	01/08/1996
capecitabine	01/07/2005	01/02/1999
rituximab	01/07/2005	01/11/1999
ropinirole	01/11/2005	Not reimbursed
glatiramer	01/12/2005	01/11/1999
pentostatin[c]	01/01/2006	Not registered
anagrelide[c]	01/02/2006	Not reimbursed
clopidogrel	01/10/2006	01/11/1999
pravastatin	01/11/2006	01/06/1993
rizatriptan	01/06/2008	01/03/2010
finasteride	01/10/2008	Not reimbursed
mirtazapine	01/11/2009	01/05/2001

[a] Excluding those listed in both countries during 2000-2009 (Table 2); [b] Intra-uterine device (*Mirena*) listed for heavy menstrual bleeding but not contraception in NZ; [c] Unregistered medicine

Inclusion of levonorgestrel in the form of an intrauterine device to prevent heavy menstrual bleeding (*Mirena*) is perhaps controversial, as levonorgestrel (in tablet form) was already listed in the NZ Schedule as a contraceptive (*Microlut*). Nonetheless, the tablet form is listed for systemic use as a contraceptive whereas the IUD is listed for localised slow release of levonorgestrel to prevent heavy menstrual bleeding. Levonorgestrel (as *Mirena*) was first listed in the Australian Schedule for use as a contraceptive device on 1 February 2003. It was not considered to be a new medicine, as the tablets were already listed in the Australian Schedule for use as a contraceptive.

The PBAC recommended the listing of ropinirole for the treatment of Parkinson's disease at its December 1997 meeting; however, it remains unreimbursed because its sponsor decided not to proceed with the listing. An application to list ropinirole for the treatment of patients suffering with severe primary restless legs syndrome was rejected by the PBAC in March 2006.[9]

Anagrelide was first registered in Australia on 23 November 1999.[5] At least 2 applications seeking its listing on the PBS have been rejected by the PBAC, the last in

June 2003.[10] Finasteride was first registered in Australia on 26 October 1993 but it has never been listed in the Schedule of Pharmaceutical Benefits.[5] No application has been made since June 2003.[9]

Although pentostatin was designated as an orphan drug by the TGA on 15 May 2009, it remained unregistered as at December 2010.[5,11]

Discussion

Over the previous 10 years, the NZ public has been given access through Government funding to less than half of the new medicines that have been reimbursed in Australia. The remaining 77 new medicines that are reimbursed in Australia but not in NZ cover a wide range of therapeutic areas, including some diseases for which there are no reimbursed medicines in NZ. For the new medicines that were listed in both countries, registration occurred on average 9.0 months later in NZ and listing occurred 32.7 months later, giving a 23.7 month difference in the interval between registration and listing (95% CI 14.9 to 32.4 months; $p<0.0001$). Sixteen of the new medicines listed in both countries (27%) were registered first in NZ but only three of these (ursodeoxycholic acid, dorzolamide and ezetimibe) were listed first in NZ.

Differences in access are probably due to both the financial constraints on the reimbursement agencies and the methods of assessment used. Both PHARMAC and the PBS aim to provide 'value for money'; however, PHARMAC is legislated to operate on a capped budget[1] whereas the Australian Government allows the expansion of the PBS budget in order to accommodate as many new medicines as can demonstrate clinical importance, clear evidence of effectiveness, affordability, cost-effectiveness and other qualities.[12]

PHARMAC assesses and prioritises new medicines against each other and against widened access to older medicines annually, and declines or defers listing of new medicines in the NZ Schedule in order to stay within its budget.[1] The result for the NZ public is delays in listing of new medicines, an expanding list of new medicines that are acceptable but deferred, and more predictable pharmaceutical expenditures. In contrast, the PBAC judges each new medicine on merit, regardless of other medicines that are competing for the same budget.[2] The result for Australia is better access to new medicines along with an expanding pharmaceuticals budget.

The methodologies for achieving value for money also differ. PHARMAC relies heavily on a wide range of relatively blunt commercial tools including reference pricing, expenditure caps, tendering for sole supply, multi product agreements, confidential rebates to suppliers and Special Authority provisions to restrict access.[1] Whilst reference pricing and prior authorisation provisions are also used in Australia, deeds of agreement containing risk sharing arrangements are increasingly being used by the Government to manage financial risk and to contain PBS costs.[13]

Both the PBAC and PHARMAC take into account the cost-effectiveness of new medicines as one of several listing criteria. The PBAC Guidelines require suppliers to provide a detailed cost-effectiveness and budget impact analysis of each new medicine compared with the treatment most likely to be replaced in practice. These analyses are scrutinised by PBAC's Economics Sub-Committee (ESC) comprised of academics and clinicians. Economic models are evaluated by the Pharmaceutical

Evaluation Section (PES) in detail, including all clinical and economic data used to populate the model, its construction and the auditing of any formulae. Suppliers are given the opportunity to comment on the PES report before this goes to the ESC, as well as the opportunity to comment on the ESC report before it goes to the PBAC.[14]

In contrast, PHARMAC encourages suppliers of new medicines to provide detailed cost-effectiveness and budget impact analyses of their products, then undertakes (generally) rapid economic analyses in-house, comparing new medicines with submissions for other new medicines and widened access to older medicines.[15,16] In short, while the PBAC evaluates each new medicine against current medical practice in a given therapeutic area, PHARMAC evaluates each new medicine against the range of funding options that are currently available to it across all medicines (old and new) and all therapeutic areas. Budget impact plays an important role in the listing decision in both countries.[12,15]

Since mid 2005, the PBAC has published all its decisions relating to submissions to list new medicines on the PBS in the form of public summary documents.[17] PHARMAC has defended some of its decisions to list or decline to list certain new medicines (or classes of medicines) in the NZ Schedule, including some that are now listed in both NZ and Australia [18-29] and others that are listed only in Australia.[30-36] However, most of PHARMAC's listing decisions have not been open to public scrutiny except for a limited number of unpublished health technology assessments.

Restrictions in access to new medicines have an opportunity cost for patients in terms of preventable mortality and morbidity and potential quality-adjusted life year (QALY) gains forgone. PHARMAC has estimated QALY gains achieved by listing or declining to list selected new medicines[29,37] but information is not available concerning the overall QALY gains and losses across all major funding decisions. Restricting access to new medicines also limits the opportunity to improve the overall efficiency of healthcare delivery through reducing hospital admissions and length of stay.[38]

On the other hand, expanded access to new medicines has a monetary opportunity cost. The cost of the PBS has increased steadily over the last decade[39] whereas PHARMAC has been successful in containing growth in the community pharmaceuticals budget in the face of volume growth, by driving down prices and limiting access.[40] Funds within PHARMAC's budget that are preserved by limiting access to new medicines are used to widen access to other medicines, and funds that might have been allocated to pharmaceuticals can potentially be used for non pharmaceutical healthcare delivery.[30]

A secondary benefit to PHARMAC of deferring the listing of new medicines is that prices inevitably decline with time and they can fall precipitously when a generic ultimately becomes available.[10] However, most of the medicines that are reimbursed in Australia but not NZ (Table 3) are unlikely to cause undue stress on PHARMAC's budget. Only 4 medicines that were listed in Australia but not NZ (ranibizumab, rosuvastatin, rabeprazole and celecoxib) were in the top 50 highest PBS cost items for the year ended 30 June 2010.[13]

The results from our study have some limitations. We chose new prescription-only medicines as our study sample because they are a major focus of current public

discourse on access to healthcare in both countries. We may well have obtained different results had we chosen a broader sample of medicines and medicinal preparations. We defined access as being listed in the respective national pharmaceutical schedules; we did not attempt to study the quality of access such as indications and patient groups. While the initial listing of most of the medicines in our study came with restrictions, we did not compare restrictions or examine whether restrictions were changed over time (within and/or across indications). These are all worthy areas of future research.

Our definition of access did not consider prescription costs because we were more interested in studying whether (and when) new medicines were listed than whether patients could afford the requisite prescription co-payment. When they are reimbursed, medicines are more affordable to the NZ patient because patient contributions are lower and 3 months' supply may be dispensed for some medicines.[3,4]

We chose 2000-2009 as our study period rather than any single point in time. This strategy improved the size of our study sample and also showed that access to new medicines in NZ compared to Australia has been restricted and delayed over the recent decade.

Whilst others have also compared access to medicines in NZ and Australia (as well as in other selected countries), none have been as comprehensive as ours in terms of study sample and study period.

Danzon and colleagues recently published the results of their study on the impact of price regulation on the timing of the launch of new medicines in 25 major countries, including NZ and Australia. The study was conducted on 85 new chemical entities (NCEs). The outcome of interest was the launch date (i.e. the first possible date of supply), which could well be more of a registration issue than a reimbursement issue. Unfortunately, data limitations did not enable the analysts to distinguish between a delay due to market authorisation versus price/reimbursement approval.

The three countries that did not require price approval before launch had the highest number of launches. The USA led with 73 launches, followed by Germany (n=66) and the United Kingdom (n=64). At the other extreme, only 13 NCEs were launched in Japan, followed by Portugal (n=26) and NZ (n=28). Australia had 43 launches.[41]

A wide-ranging study (the Castalia Report) compared the number of new listings (new chemical entities, new products and new items) in Australia and NZ from June 1999 to June 2004.[42] The results for NZ were poorer for all three categories. Whilst some aspects of the findings of the Castalia Report have been challenged, criticisms were not directed at the results on the access to new listings.[43,44]

Morgan and colleagues compared the centralised drug review processes in four Commonwealth countries, including Australia and NZ. They examined the outcomes of the listing decisions by comparing the subsidised access, cost and use of 17 of the world's top-selling medicines in 2003 in each of the countries. They found that 15 of the 17 medicines were reimbursed in Australia whereas only 8 were reimbursed in NZ.[45] One of these was a combination product and another was already available in both countries as a generic. These results have since been updated. All of the 17 medicines were reimbursed in Australia and 9 were reimbursed in NZ.[46]

Researchers from the Karolinska Institute in Sweden studied the market introduction and total sales of 67 oncology products in 25 countries including the USA, UK, Canada, Australia and NZ. Uptake was slower in NZ than in Australia and Canada, and comparable to or slower than the UK.[47]

Our results contrast with those from a media release by PHARMAC showing that as at March 2006, NZ had listed more unique therapeutic chemicals than Australia (267 versus 217). NZ also had more funded chemicals or formulations of the same chemical entity with distinctly different uses (e.g. ketoconazole tablets versus ketoconazole shampoo) [717 versus 655].[48]

The methods and definitions used by PHARMAC have not been published, however the differences in results between PHARMAC's study and ours are not surprising given the differences in the questions being addressed and the study design. PHARMAC's study: (a) considered access only at one time point; (b) included both new and old medicines; (c) included medicines and medicinal preparations, such as nutrients/special foods, vitamins, non-hormonal contraceptives, barrier creams, emollients, etc, (d) included multiple strengths of the same or similar presentations of the same medicine/medicinal preparation and (e) excluded hospital pharmaceuticals that were not listed in the community pharmaceutical schedule.

Finally, declining to list highly cost-effective pharmaceuticals because of a pharmaceuticals budget cap, as in NZ, implies that such pharmaceuticals are intrinsically less cost-effective than any non-pharmaceutical interventions that they might displace if they were funded. This implicit assumption is clearly unsupported because rigorous economic evaluation is not available for most non-pharmaceutical healthcare interventions. There is a case for the expansion of PHARMAC's pharmaceuticals budget when highly cost-effective pharmaceutical interventions become available, rather than delaying listing indefinitely. PHARMAC would still benefit when the patent expires, and in the meantime patients would benefit.

Conclusion

Since 2000, the NZ public has been able to access fewer new medicines via its national medicines reimbursement programme than the Australian public. Access to new medicines in NZ is considerably slower than in Australia. The population health implications of the differences in access need further research.

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THE NEW ZEALAND MEDICAL JOURNAL
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Over-the-counter codeine analgesic misuse and harm: characteristics of cases in Australia and New Zealand

Brian R McAvoy, Malcolm D H Dobbin, Claire L Tobin

Abstract

Aim To describe the characteristics of clients addicted to over-the-counter (OTC) codeine analgesics presenting to an Auckland open-access clinic, and to compare them to clients admitted to a New Zealand detoxification unit, and in the Australian community.

Method Cross-sectional study of clients presenting to a regional, open-access detoxification clinic covering the Greater Auckland area between 1 January and 31 March 2010.

Results Fifteen clients were analysed, and compared to 77 similar clients identified in Victoria and five other Australian States, and 7 clients admitted to a New Zealand detoxification unit. Cases in each cohort were consistent with those in the published literature, and appear to be similar to each other both demographically and in terms of the high average tablets consumption (49–65 tablets per day), the serious non-steroidal anti-inflammatory drug (NSAID) adverse drug reactions identified, and the long duration of misuse. Many had a history of alcohol or other drug use and mental health disorder.

Conclusions This study has identified that controls on OTC codeine analgesics in both countries were not sufficient to limit non-medical use of these products. As a result, cases identified in these two countries escalated the number of self-administered tablets taken daily for misuse, resulting in codeine dependence and serious NSAID toxicity secondary to this dependence.

Internationally, the misuse of pharmaceutical drugs is a growing problem.[1] Whilst there is clear evidence of misuse of prescription drugs,[2] particularly those containing opioids, recent reports from the United Kingdom (UK),[3–5] Australia,[6–9] and New Zealand[10] indicate that there are also problems relating to misuse of over-the-counter (OTC) codeine analgesics.

The two main high-codeine content products available OTC in New Zealand are Nurofen Plus (codeine phosphate 12.8 mg and ibuprofen 200 mg) and Panadeine Plus (codeine phosphate 15 mg and paracetamol 500 mg).

This paper describes a study of clients identified prospectively presenting to a regional open-access detoxification clinic, and compares this population to their Australian and New Zealand counterparts.

Method

Over a 12-week period at the beginning of 2010, all clients presenting to an open-access detoxification clinic with a diagnosis of dependence on OTC codeine-

containing analgesics were identified. Details of the demographics, medications, codeine consumption patterns, associated morbidity, relevant history and management were recorded. The clinic covers the Greater Auckland region, involving three District Health Boards (Waitemata, Auckland, and Counties Manukau) with a combined population of approximately 1.4 million.

The clinic operates between 10am and 1pm Monday to Friday, and provides information, advice and support to individuals and families on detoxification from any substances. Comparisons were made between clients dependent on OTC codeine-containing analgesics, similar clients identified in Victoria and five other Australian states[6] and clients admitted to a New Zealand hospital detoxification unit.[10]

Results

Fifteen clients were identified (8% of all new attendances at the clinic). Details of these clients and their Australian and New Zealand inpatient counterparts are summarised in Table 1.

Table 1. Clients addicted to over-the-counter codeine products

Variables	New Zealand open access clinic	New Zealand detoxification unit[10]	Australia[6]
Number of cases	15	7	77
Male (%)	53	43	46
Average age (years)	44	44	33
Age range (years)	30–60	31–63	18–53
Aged <45 years (%)	53	43	95
Average daily intake of tablets	49	65	50
Daily intake codeine (mg)	627	832	640
Daily intake ibuprofen (grams)	9.8	13.0	10.0
Average duration of misuse (months)	27	22	30
Gastrointestinal bleeding/dyspepsia (%)	53	57	50
Renal tubular acidosis (%)	7	-	9
Alcohol or other drug use (%)	53	86	38*
Mental health disorder (%)	93	57	28*

*Many of the case reports did not provide information about this aspect of the medical history.

Amongst the New Zealand Auckland clinic clients, 66% had recently been hospitalised due to intoxication and/or physical problems associated with their OTC codeine preparation use. Of the 15 clients identified at the clinic, 47% undertook a community-based detoxification, 27% an inpatient detoxification, 13% self-detoxed and 13% were referred for methadone maintenance treatment.

Discussion

Although the three populations identified in Table 1 are not directly comparable, there appears to be many similarities between them (age range, average daily intake of tablets, average duration of misuse and associated gastrointestinal problems). A substantial proportion of the clients in the two New Zealand studies had a history of alcohol or other drug use and mental health disorders.

There was also a high prevalence of opioid dependence, consistent with cases published in the literature and in the Australian cohort. As would be expected from the large quantities of ibuprofen being ingested, more than half of the clients in the three surveys presented with gastrointestinal bleeding or dyspepsia.

These findings suggest that misuse and harm from combination codeine analgesics may be a growing problem in countries where they are available OTC. There are no official statistics for the UK but two websites have been identified which have over 4,000 people self-reporting having codeine dependency.[3] An Australian web-based online survey identified 180 recent users of OTC codeine, 17% of whom were classified as being codeine dependent (using the Severity of Dependence Scale)[4].

Despite this evidence there is considerable resistance from the pharmaceutical industry to further restrictions on sales of OTC codeine products. In a submission to the Medicines and Medical Devices Safety Authority's (MEDSAFE) Medicines Classification Committee, the New Zealand Self Medication Industry Association stated that it "believes that the needs and interests of the vast majority of responsible consumers need to be balanced against the risks of harm to a very small number of individuals".[11]

Similar arguments have been put forward in the past relating to temazepam capsules, flunitrazepam (Rohypnol) and paracetamol/dextropropoxyphene (Paradex). More explicit reasons have been given by an industry consultant in Australia: "This analgesic category generates almost the highest gross profit margin of all the categories in your pharmacies. It is an area definitely worth defending. There are some dollars at threat (average loss of $17,000 per pharmacy per year").[12] Last year OTC codeine products accounted for AU$84 million sales in Australia[12] and NZ$13 million in New Zealand.[13]

As awareness of the problems of OTC codeine preparations has grown, regulatory authorities have been examining their policies. In September 2009, the UK Medicines and Healthcare products Regulatory Agency (MHRA) updated its advice on non-prescription medicines containing codeine or dihydrocodeine.[14] The MHRA recommended that warnings on labels and leaflets should be further clarified and strengthened—*Can cause addiction. For 3 days use only*, pack size be restricted to 32 tablets, and that the existing advertising self-regulatory code should be strengthened.

In Australia, the National Drugs and Poisons Schedule Committee (NDPSC) recommended that from May 2010 OTC codeine analgesics be rescheduled to pharmacist only, thus preventing advertising to the public and self-selection in the pharmacy, and that pack sizes should be reduced to 30 tablets.[15]

In New Zealand, MEDSAFE's Medicines Classification Committee recommended that from 4 October 2010 pack sizes should be reduced to 30 tablets, and there should be behind the counter sales only. Sales should be restricted to qualified pharmacists, and warnings on labels should be strengthened—*Risk of addiction. Do not use for more than 3 days unless on medical advice* (from 1 May 2011).[16]

Although these responses are laudable, the lack of supportive pharmacological evidence for combinations of lower-dose codeine in compound analgesics, and the risk of adverse effects,[10] have prompted some authorities, including the United States' Food and Drug Administration's Acetaminophen (paracetamol) Advisory Committee,

and a leading US gastroenterologist, to question the continuing availability of non-prescription and prescription acetaminophen (paracetamol)/opioid combination products.[17,18] If recent tightening of the regulations in New Zealand, Australia and the UK does not have an impact on the trends described in this article, more drastic measures may need to be considered.

There is limited evidence of analgesic benefit from the incorporation of low-dose codeine into combination analgesics. As noted by Ferner and Beard, there are "disadvantages when relatively safe and effective analgesics such as paracetamol and ibuprofen are combined with small doses of an opioids that are likely to bring trivial therapeutic benefit, but increase the risks of abuse, addiction and adverse effects".[19]

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Usage and equity of access to isotretinoin in New Zealand by deprivation and ethnicity

Peter Moodie, Richard Jaine, Jason Arnold, Mike Bignall, Scott Metcalfe, Bruce Arroll

Abstract

Aims Oral isotretinoin, for severe acne, was until March 2009 fully funded in New Zealand only if the prescription was written by a vocationally registered dermatologist. This funding restriction was argued on the basis of complexity of management and an appreciable risk of teratogenicity if given during pregnancy or within a month of conception. However, this funding restriction had the potential to create inequitable access barriers. This study was an audit examining the use of isotretinoin by deprivation level and ethnicity, in order to examine potential inequities in use.

Method Dispensed prescription data for funded isotretinoin, for the year ending June 2008, held in a national repository was analysed using simple descriptive methods based on ethnicity and deprivation level. The same analysis was carried out for cyproterone acetate with ethinyloestradiol, another acne pharmaceutical available on prescription with no funding restrictions. There was demographic data on 60% of prescriptions based on the health identification number NHI.

Results People living in more deprived areas (as defined by NZDep Index) were less likely to use isotretinoin, as were Māori and Pacific people. The association with deprivation level was not present for cyproterone acetate with ethinyloestradiol, although disparities in use by ethnicity remained.

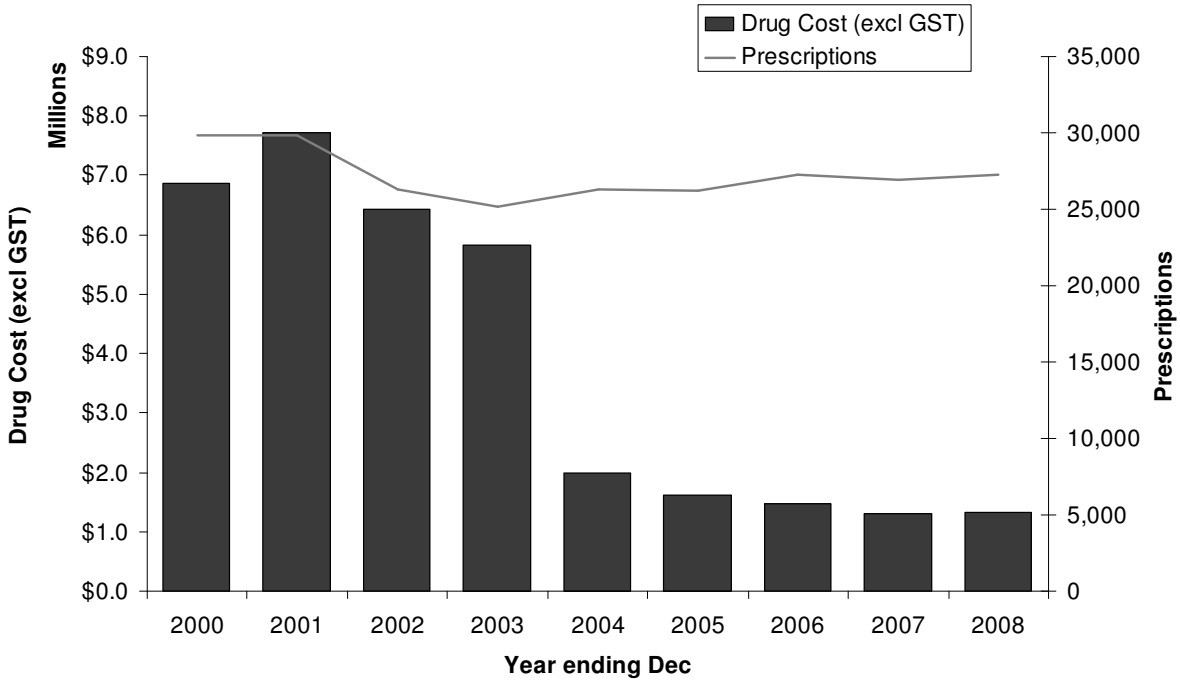
Conclusions Given there is no evidence for lower rates of acne for Māori and Pacific people, the reasons may include financial and other barriers.

Oral isotretinoin is a recognised treatment that has been available for over 20 years for severe refractory cystic and conglobate acne; however, until recently, funded access in New Zealand has been available only through prescriptions written by vocationally registered dermatologists. This funding restriction was created on the grounds that the medication was difficult to use and that there was an appreciable risk of teratogenicity if given during pregnancy or within a month of conception.[2] A number of other countries, including the United Kingdom and Australia, have similar restrictions.

As with many countries there is a shortage of dermatologists in New Zealand and access to them within the public health system is restricted because of long outpatient waiting times,[2,3] along with the prioritisation of other cases ahead of acne consultations. Therefore it is likely that the majority of prescriptions have been issued by dermatologists working in their private capacity where there is no funding subsidy for their consultations. Anecdotally these private practices are usually located in more affluent neighbourhoods while public dermatology services can be considerable distances from some suburbs.

Despite this funding restriction, other prescribers have always been allowed to issue prescriptions, albeit with a patient having to pay the full direct cost of isotretinoin along with pharmacy mark-ups and dispensing fees. Over recent years, with the arrival of generic isotretinoin, the actual cost of the medication has fallen quite significantly (Figure 1), to a point where the net cost to a patient for a consultation and a prescription issued by any primary care provider (usually a GP) would have been cheaper than a private dermatology appointment. It appears not many GPs or patients were aware of this option and GPs may have felt that they lacked experience in the use of this potentially difficult medication. The total number of prescriptions filled has not changed since this price reduction (Figure 1).

Figure 1. Expenditure and usage of isotretinoin in New Zealand, 2000–2008



In March 2009, the agency that manages New Zealand's community pharmaceutical budget, PHARMAC (Pharmaceutical Management Agency), widened funded access to oral isotretinoin such that vocationally trained general practitioners and nurse practitioners acting within their scope of practice were able to write fully subsidised scripts for their patients.

In making this decision, it was proposed that the funding restriction had led to unequal access to isotretinoin by deprivation level. Although moderate and severe acne is common amongst New Zealand school children with estimates ranging from 67% to 91% of school students,[4,5] there is no known association to deprivation level. However, previously unpublished data[6] from Auckland suggests deprivation level affects access to isotretinoin: 15% of students at a girls' school in and near affluent

neighbourhoods, had accessed isotretinoin, while no students from a school with students from poorer neighbourhoods, had.

When acne rates by ethnicity are considered, there is only minimal evidence for differing rates of acne amongst any ethnic groups. One study based on self-reported acne found that Pacific students more frequently reported 'problem acne'.[4] The same study found that Māori and Pacific students were more likely to report difficulty accessing treatment for acne. We identified no New Zealand-specific research examining ethnic differences in use of or access to isotretinoin in particular.

Despite this lack of New Zealand-specific research on differential access to isotretinoin, there is a large and well-documented New Zealand research base on the inequities in accessing health care and services. Māori have unequal access to diabetes care,[7] cancer services[8] and mental health services,[9] among others.

Access to health services also tends to be poorer for Pacific people.[10] Inequity of access is associated with deprivation level for a variety of services including primary health care.[11] Reasons that have been proposed for these inequities include financial barriers,[11] mobility, cultural and language issues—but it is likely to be a complex mix of a variety of factors.[12]

Given this background of limited research into this issue and the recent widening of funded access the aims of this study are to examine isotretinoin use in the year leading up to this funding change. The study aims to focus particularly on deprivation level and ethnicity. The study also aims to examine if use of isotretinoin is similar to other fully-funded pharmaceuticals used for the treatment of acne (in particular, cyproterone acetate with ethinyloestradiol).

Methods

Once a funded prescription is dispensed in New Zealand the data is collected in a national repository and available for analysis. In addition to prescriber details, the medication name, strength, quantity and dosage are recorded, along with an encrypted National Health Index (NHI) number where this is available.

The NHI number is a unique identifier for virtually everybody in New Zealand who has ever had contact with the health service. The number is linked to New Zealand census data and contains information about the individual's date of birth, ethnicity and socioeconomic status.

Most general practitioners in New Zealand have computerised prescribing systems and over 95% of all prescriptions recorded in the New Zealand Health Information Service (NZHIS) database have an NHI number attached. The one prescriber group that do not use NHI numbers routinely is private specialists because they do not have easy access to the numbers; however, the dispensing pharmacist will often know the NHI number of the patient (from previous prescriptions) and if they do they must transmit it along with the prescribing information to the national database.

Prescription data for isotretinoin and cyproterone acetate with ethinyloestradiol for the year ending June 2008 was accessed through PharmHouse. The PharmHouse database is a subset of the NZHIS database that contains records of all the claims for medicines dispensed within New Zealand.

The data was analysed using simple descriptive methods based on ethnicity and deprivation level. Age standardisation of ethnicity, deprivation level and gender results was completed using direct standardisation. Populations were standardised to the Segi World population. We used prioritised ethnicity so that if patients reported more than one ethnicity they would be classified as Māori, then Pacific then Other.

Individuals were assigned the deprivation level (a measure of socioeconomic status) of their area of residence based on the New Zealand Deprivation Index (NZDep). The NZDep Index is a population level index based on nine variables recorded on the 2001 New Zealand Census.[13]

There are other uses of isotretinoin and cyproterone acetate with ethinyloestradiol which may affect the comparisons made between them. For instance while only registered for use in acne a dermatologist may, although rarely, use isotretinoin for other skin conditions such as hydradenitis suppurativa. Cyproterone acetate with ethinyloestradiol is registered for use in androgen-dependent diseases in women (including acne), for oral contraception in women requiring treatment for androgen-dependent diseases and polycystic ovary syndrome.

Results

In the year ending June 2008 there were 27,056 funded isotretinoin prescriptions (approximately 3,000,000 capsules) dispensed. Of those prescriptions, only 60% contained a valid NHI number (Table 1). Once the available NHI information was scaled up it was estimated that 15,900 patients received a funded prescription for isotretinoin of which 43% were male and 57% female.

Table 1. Prescriptions of Isotretinoin by deprivation quintile and ethnicity

	Other	Māori	Pacific People	Unknown	Total
Q1	4,508	95	31	0	4,634
Q2	3,473	102	33	0	3,608
Q3	3,032	115	64	0	3,211
Q4	2,142	167	37	0	2,346
Q5	1,807	214	114	0	2,135
Unknown	0	0	0	11,122	11,122
Total	**14,962**	**693**	**279**	**11,122**	**27,056**

Although unfunded prescriptions are not recorded in the NZHIS database, a review of IMS Health New Zealand (personal communication, 2008) data suggests that less than one hundred unfunded prescriptions were dispensed. IMS Health New Zealand is a private organisation that provides data on pharmaceutical use in New Zealand.

Deprivation level—In New Zealand, there is a clear linear association between use of isotretinoin and deprivation level. People from the least deprived quintile are more than two and a half times as likely to access isotretinoin compared with people from the most deprived quintile (Figure 2 and Table 2).

Figure 2. Isotretinoin prescription rates by deprivation level, year ending June 2008

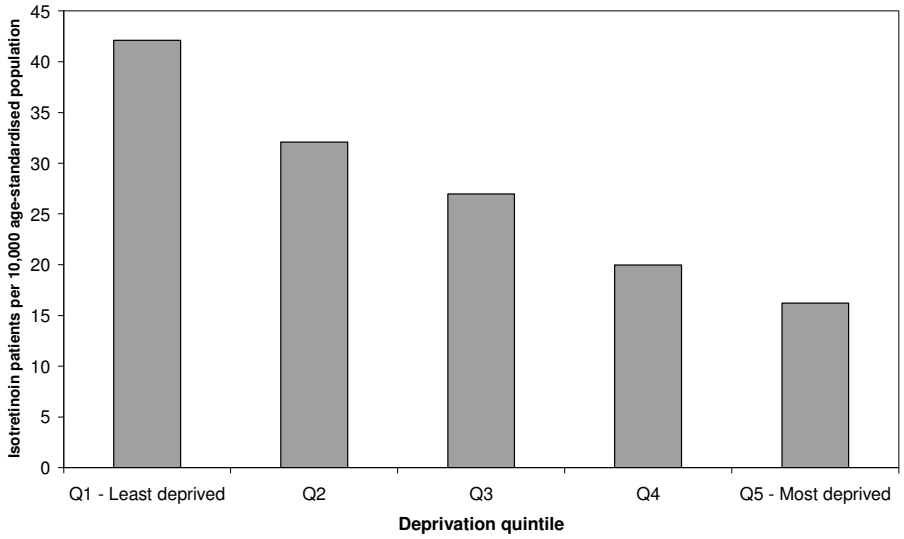


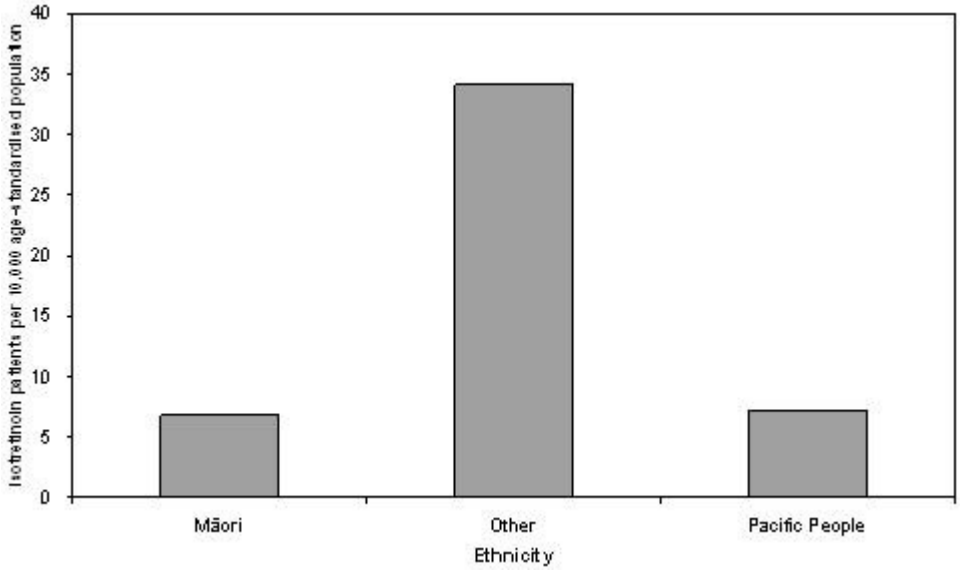
Table 2. Isotretinoin prescription rates and rate ratios by gender, deprivation level and ethnicity, year ending June 2008

Category	Rate*	Rate ratio
Gender		
Male	23.3	ref.
Female	30.1	1.3
Deprivation quintile		
Q5 – most deprived	16.2	ref.
Q4	20.0	1.2
Q3	27.0	1.7
Q2	32.1	2.0
Q1 – least deprived	42.1	2.6
Ethnicity		
Māori	6.8	ref.
Pacific people	7.1	1.0
Other	34.1	5.0

* All rates age-standardised and per 10,000 population

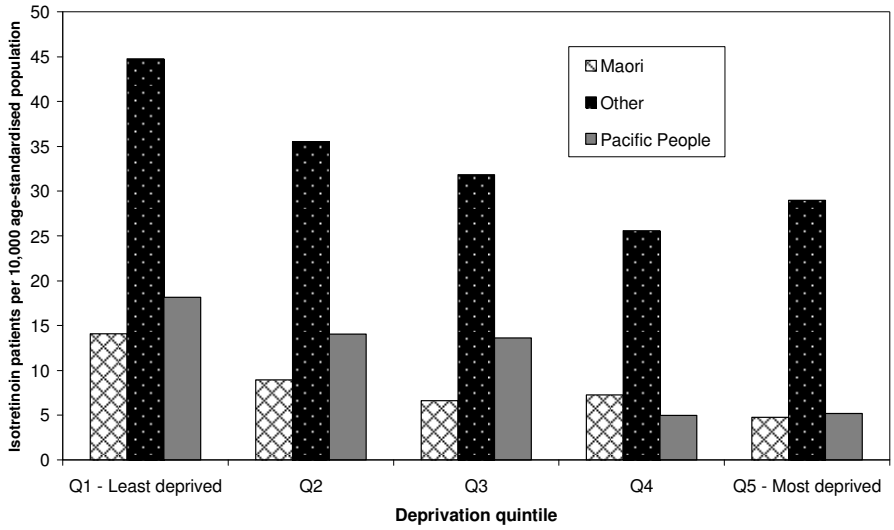
Ethnicity—Māori and Pacific people were far less likely to access isotretinoin than those of Other ethnicity (mainly New Zealand European) (Figure 3). Māori and Pacific people had similar levels of access to isotretinoin.

Figure 3. Isotretinoin prescription rates by ethnicity (isotretinoin patients per 10,000 age-standardised population), year ending June 2008



Deprivation and ethnicity—When comparing ethnicity across deprivation level it is clear that at all levels of deprivation Māori and Pacific people have far lower use of isotretinoin than the rest of the population (Figure 4). In fact, Māori and Pacific people in the *least* deprived quintile are using isotretinoin at about half the rate of the Other group in the *most* deprived quintile. Relative ethnic inequalities also appear greatest in the most deprived quintile.

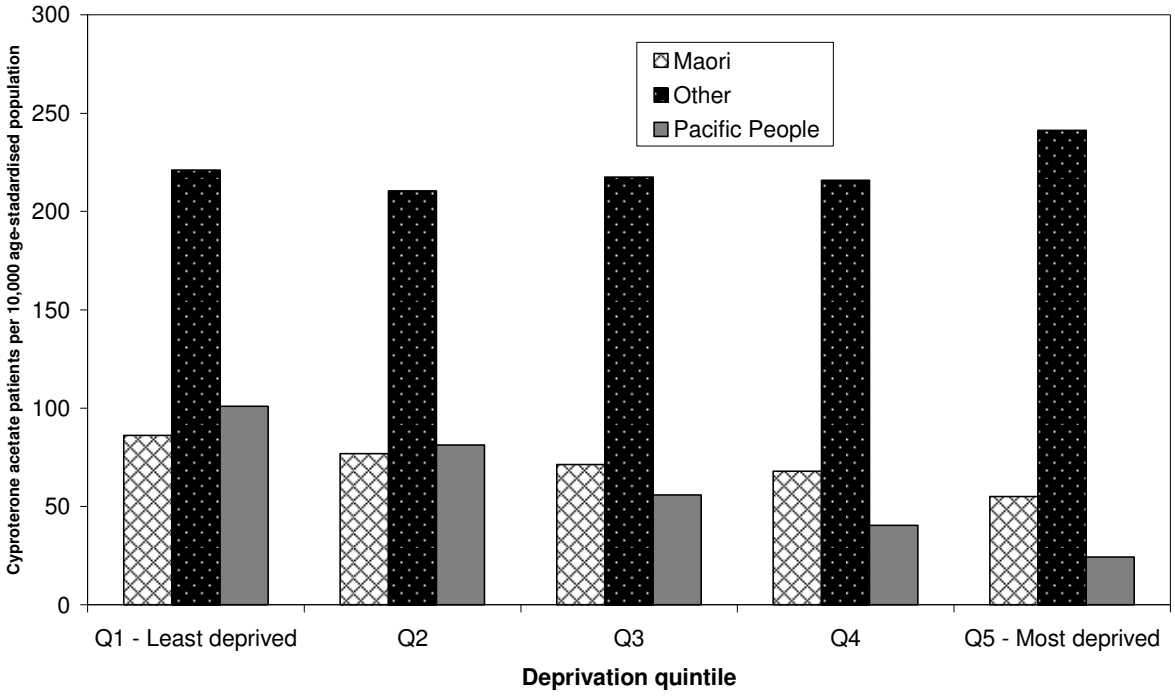
Figure 4. Isotretinoin prescription rates by deprivation level and ethnicity, year ending June 2008



Cyproterone acetate with ethinyloestradiol use—The association between cyproterone acetate with ethinyloestradiol and deprivation level is less clear than for isotretinoin (Figure 5). The clear association between deprivation level and pharmaceutical use identified for isotretinoin disappears for cyproterone acetate with ethinyloestradiol for those of Other ethnicity. However, this association is still present for Pacific people, and to a lesser extent for Māori.

There continues to be differences in use of cyproterone acetate with ethinyloestradiol by ethnicity as was seen for isotretinoin. That is, a far lower use by Māori and Pacific people.

Figure 5. Cyproterone acetate with ethinyloestradiol prescription rates by deprivation level and ethnicity, year ending June 2008



Discussion

This study has shown that the use of and access to isotretinoin in New Zealand varies by deprivation level and ethnicity. Those living in the most deprived areas and Māori and Pacific people have the poorest access to isotretinoin. Ethnic differences remain even when accounting for deprivation (by restriction). Similar access issues are not as pronounced for cyproterone acetate with ethinyloestradiol also used for the treatment of acne.

Equity of access by deprivation level—Inequity of access can occur for a variety of reasons, with financial barriers being commonly cited.[11] In the New Zealand setting it is likely that restriction of funded access for isotretinoin to dermatologists has unintentionally created this barrier. This is supported by the fact that the access disparity is not seen in the use of cyproterone acetate with ethinyloestradiol (which is fully funded and normally prescribed in primary care). While we suspect financial barriers play a large role in this disparity, we acknowledge that other barriers may influence this access disparity. These barriers could include the location of dermatologists' surgeries (and subsequent transport issues) and knowledge of the health service, amongst others.

Equity of access by ethnicity—Māori and Pacific people accessed isotretinoin less than Other groups (mainly New Zealand European), despite there being no evidence for lower rates of acne in these groups. This disparity held true regardless of deprivation level and also for the use of cyproterone acetate with ethinyloestradiol.

Clearly, the role ethnicity plays in access is different to the role of deprivation, although it is unclear why the ethnic disparities exist for both pharmaceuticals. Although financial and other barriers discussed above may play a part, it may be that cultural issues around the provision of the health service, cultural differences in the perception and importance of acne, or issues related to ethnicity and access to health services may be significant. These results support previous New Zealand research that suggests Māori and Pacific people have greater difficulty accessing treatment for acne and health care in general.[4,7,10]

Limitations—This data needs to be treated with some caution as 40% of prescriptions did not have an NHI number attached. Although our data set was not complete, we attempted to account for this by scaling through linear extrapolation. The relatively low proportion of prescriptions with NHI numbers is likely due to the non-routine recording of NHI numbers by private dermatologists.

This study was only a brief description of access differences by deprivation level and ethnicity, and (while providing hypotheses) cannot conclusively identify causes for the disparities shown. There is a theoretical bias with missing prescriptions from private dermatologists related to the ethnicities of the patients they see. If they were seeing predominantly Māori and Pacific patients, while anecdotally this is unlikely, the ethnic disparities may be less than observed.

The bias is more likely in the other direction and is likely to underestimate ethnic disparities (i.e. Māori and Pacific people are [presumably] less likely to visit a private dermatologist). Further research would be required to examine these issues. This is particularly so for Māori and Pacific people where disparities in access are present independent of deprivation level and regardless of pharmaceuticals compared.

It is also important to understand that the measure of deprivation used in this study (NZDep) is a population level measure. As such, it is not possible to identify the deprivation level of the individual for whom the prescription was written, rather the deprivation level of their resident neighbourhood.

Implications—As of March 2009, fully funded prescriptions of isotretinoin have been available through primary care providers. It is expected that the widening in access to funded isotretinoin will improve access to people in more deprived areas,

whereby the inequity of access no longer exists (as for cyproterone acetate with ethinyloestradiol). However, the extension of isotretinoin funding is unlikely to fully address the inequity of access by ethnicity. Other strategies will be required to address the ethnic disparities in access to acne-treating pharmaceuticals. Further research could attempt to identify the reasons behind this inequity and help inform future strategies.

Future implications include that with the funding restriction lifted, primary care providers who have had little or no experience using isotretinoin will have to upskill in this area. With the easier access it will be important that they are alert to the risks as well as the need to gain experience in the day-to-day use of isotretinoin. To support this, PHARMAC has arranged for training seminars along with a number of publications on the matter. Given the risks of isotretinoin use during pregnancy, it is a very real challenge for primary care providers to ensure that contraception is managed well in this group. It will be equally important for dermatologists to act as a backup to primary care in the use of isotretinoin.

The widening of access to isotretinoin funding has been made conditional on more rigorous reporting requirements; specifically, funded access will only be available if a written Special Authority application is made. This will mean that the recording of NHI numbers will be compulsory for all prescribers including dermatologists. In addition to accurate data on usage this will also mean that the prescribing data can be correlated to New Zealand termination of pregnancy data.

It would be important to continue to monitor isotretinoin use in the coming years to evaluate whether the extension of funding has had the desired effects on access. As such an appropriate area of further research would be a repeat audit post-funding changes as data becomes available.

Conclusions

The study aimed to examine isotretinoin use in the year leading up to a funding restriction change particularly with regard to deprivation level and ethnicity and then compare this to cyproterone acetate with ethinyloestradiol use. It found that the use of and access to isotretinoin varies by deprivation level and ethnicity.

Ethnic differences remain even when accounting for deprivation (by restriction). These results echo the well known disparities in broader health care access in New Zealand.

There are likely to be several reasons for the disparities seen, including financial barriers. Given there is no evidence for lower rates of acne for Māori and Pacific people, it is not clear why inequitable access to both pharmaceuticals existed for ethnic groups.

Competing interests: None.

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Pharmacological management of children's asthma in general practice: findings from a community-based cross-sectional survey in Auckland, New Zealand

Sue Crengle, Elizabeth Robinson, Cameron Grant, Bruce Arroll

Abstract

Aim To describe the pharmacological management of children's asthma and to assess whether there were ethnic differences in pharmacological management.

Methods A community-based, cross-sectional, interviewer administered face-to-face survey. The sample (n=583) included the caregivers of 221 Māori, 173 Pacific, and 189 European/other children. Data collected included sociodemographic information, and medications received and medication delivery devices used in the 12 months prior to interview. Descriptive and logistic regression analyses to investigate ethnic differences in pharmacologic management were undertaken.

Results Spacer devices were used by 80% of children under 7 years of age and 34% of children 7 years or over. No ethnic differences in the use of these devices were observed. Māori (58%) and Pacific (65%) were significantly ($p<0.0001$) more likely to have been given a nebuliser (European/other 34%). Most (96%) children received inhaled beta-agonists and there were no ethnic differences for these medications. Overall, 69% of children had received inhaled corticosteroids (ICS) and there were no significant ethnic differences in receipt of these medications. However, only 68–78% of children in the moderate, severe, and very severe morbidity groups reported inhaled corticosteroids use in the previous 12 months, suggesting that this group is being under-treated. Morbidity stratified analyses suggested that Māori and Pacific children who had experienced severe morbidity in the previous 12 months were less likely to have received ICS.

Conclusions Some aspects of the pharmacological management of asthma are more consistent with recommendations in evidence-based guidelines than previously reported in NZ. The proportion of children with asthma who were receiving beta agonists and ICS were higher than that previously reported in NZ and the reported use of anticholinergics was low. However, other findings show there is still room for further improvements to be made, particularly with respect to the use of inhaled corticosteroids among children who experience significant morbidity, the use of nebulisers, and the use of spacer devices. The implementation of clinical quality assurance activities that support primary health organisations and providers to monitor and improve the delivery of evidence-based asthma care could further improve asthma outcomes.

Asthma is a significant issue for children in New Zealand. Ethnic-specific estimates of the prevalence of asthma symptoms among children aged 6 to 7 years and adolescents aged 13–14 years have been reported using data collected in the International Study of Asthma and Allergies in childhood (ISAAC).[1-3] ISAAC Phase

III data estimated the prevalence of 'current wheeze' among children were European/Pākehā 21%, Māori 29%, and Pacific 25%. Among adolescents the prevalence of 'current wheeze' were European/Pākehā 29%, Māori 30%, and Pacific 21%.[4]

Asthma hospitalisations are higher for Māori and Pacific children. Between 2003-2005, hospitalisations rates (per 100 000) for Māori children were significantly higher than for non-Māori in the 1 to 4 year age group (Māori 1877, non-Māori 1175; odds ratio 1.60) and in the 5-14 year age group (Māori 329, non-Māori 232, odds ratio 1.42).[5]

Ethnic differences in prevalence do not fully account for ethnic differences in asthma hospitalisations.[3] Other factors hypothesised as contributors to ethnic disparities in asthma outcomes include differences in access to care, asthma education and knowledge and differences in medications.[6-9] Prior to the collection of data for this study some publications included information about asthma-related medication use by ethnicity[9-12] and three found ethnic differences in medication use.[9,10,12] However, none of these studies were designed to specifically address the questions 'are there ethnic differences in the pharmacological management of children's asthma?' The study from which the data presented in this paper is drawn was specifically designed to examine the management of children's asthma in primary care and asthma-related health service utilisation by Māori, Pacific and European/other children. This paper presents findings about pharmacological delivery mechanisms and pharmacological management.

Methods

We conducted a cross-sectional survey in Auckland, New Zealand (NZ). The caregivers of eligible children were invited to participate in the survey. Children were eligible if: aged 2 to 14 years; and had experienced asthma symptoms in the 12 months prior to interview; and they had a doctor diagnosis of asthma or had experienced wheeze or whistling in the chest. The University of Auckland's Ethics Committee approved the study.

Eligible children were identified using random residential address start points with cluster sampling of consecutive dwellings to the right of each start point. The householder was asked if there was an eligible child in the household and, if there was, the study was explained and the child's caregiver was invited to participate. If no one was at home, dwellings were visited on different days and at different times on up to three occasions. At the time of recruitment, the child's ethnicity data was obtained from the caregiver using a modified version of a NZ census ethnicity question. Multiple ethnic group choices were possible. Where multiple groups were nominated, the ethnicity data was prioritised into Māori, Pacific and European/other groups using Statistics New Zealand's prioritisation process.[13, 14] An ethnically stratified sampling ratio was applied to eligible children to identify those who would be enrolled into the study. The sampling ratios were used so that approximately equal numbers of Māori, Pacific and European/other children would be enrolled into the study. Only one eligible child from each household was enrolled in the study.

Data were collected in the home during a face-to-face interview with the child's main caregiver, after written informed consent was obtained. All interviewers were provided with study protocols outlining the study and the administration of the questionnaire, and were trained to administer the questionnaire in a standardised manner. During the interview, data were collected that described the child's ethnicity, household sociodemographics, asthma-related health service utilisation in the previous 12 months, and the medications and medication delivery systems used in the previous 12 months. Asthma morbidity in the previous 12 months was assessed using a morbidity scale designed and validated in New Zealand.[15] Data were collected between June 1999 and May 2001.

Medication delivery system outcomes were: use of inhalers, spacer devices, nebulisers, and oral medications. The following medication outcomes were used: inhaled beta-agonists, inhaled

anticholinergics, inhaled corticosteroids, cromoglycates, and oral steroids. The time period used for all outcomes was 'in the 12 months prior to interview'.

Caregiver-reported ethnicity data was collected during the interview following the same processes employed to collect and categorise ethnicity data during recruitment. Possible confounders were identified *a priori* and included in multivariable analyses. The confounders were age, sex, measures of socioeconomic position (SEP), whether the child had a regular source of primary care, and parental prior knowledge of asthma due to a history of asthma in a parent or the child's sibling. Four measures of SEP were employed: household income, the caregiver's highest education level, parental occupation, and the NZ Index of Deprivation 1996 (NZDep96) decile. The NZDep96 is a small geographic area based measure of socioeconomic deprivation.

Sample size estimates were based upon published estimates of the proportions of NZ children receiving preventive medications.[9] A sample of 170 children in each ethnic group was sufficient to have at least 80% power at the 0.05 significance level to detect ethnic differences in the proportions receiving preventive medications, assuming a prevalence of 4% for Pacific, 13% for Māori, and 25% for European/other ethnic group children.

Data were double entered using Epi-info and analysed using the survey procedures in SAS-PC software (version 9.2; SAS Inc. Cary, NC, USA). Estimates were adjusted for design effects associated with clustering and weighted for the number of eligible children in each household. Initially chi-square tests for categorical variables and analysis of variance for continuous variables were used to investigate ethnic differences. Logistic regression modelling was employed to further explore the association between ethnicity and the outcome variables after adjustment for potential confounding variables (age, sex, four measures of SEP, whether the child had a regular source of primary care, parental history of asthma, and sibling history of asthma).

Results

Of the 649 eligible children invited into the study, data were collected from 583 (90%) (Figure 1). The caregivers of 64 enrolled children did not complete the interview. Reasons for non-completion were caregivers no longer wanting to participate in the interview (n=45; 70%), not being contactable for an interview (n=9, 14%), having moved (n=6, 9%) or were ineligible (n=4, 6%). There were no significant differences in either the distribution of ethnicity or NZDep96 decile among completers and non-completers. The children whose caregivers were enrolled into the study but did not complete the interview were younger than those who did complete (8.7 versus 9.8 years; p=0.009) (data not shown).

Study sample demographics and source of primary care (Table 1)—The study sample (n = 583) included 221 (38%) Māori, 173 (30%) Pacific and 189 (32%) European/Other children. Males accounted for 55% of the sample. The mean age of the child at the time of interview was 7.6 years. Neither sex nor age varied with ethnicity.

Significant ethnic differences were observed in all four measures of socioeconomic position. Higher proportions of the Māori and Pacific ethnic groups lived in more deprived NZDep96 decile areas, had household incomes of $40,000 or below, had caregivers with no high school qualification, and were in occupations associated with lower socioeconomic position.

A parental history of asthma was more common (p=0.002) among Māori (51%) than European/other (47%) and Pacific (33%). A sibling history of asthma was also more common (p<0.01) among Māori (45%) than the Pacific (34%) and European/other ethnic groups (30%). Just over half of the total sample reported they had a regular source of primary care that was used all the time, with the remainder reporting they

did not have a regular source of care (6%) or used other GPs in addition to their regular source of care (43%). There were no significant ethnic differences in the use of a regular source of care.

Figure 1. Summary of enrolment and completion of interviews

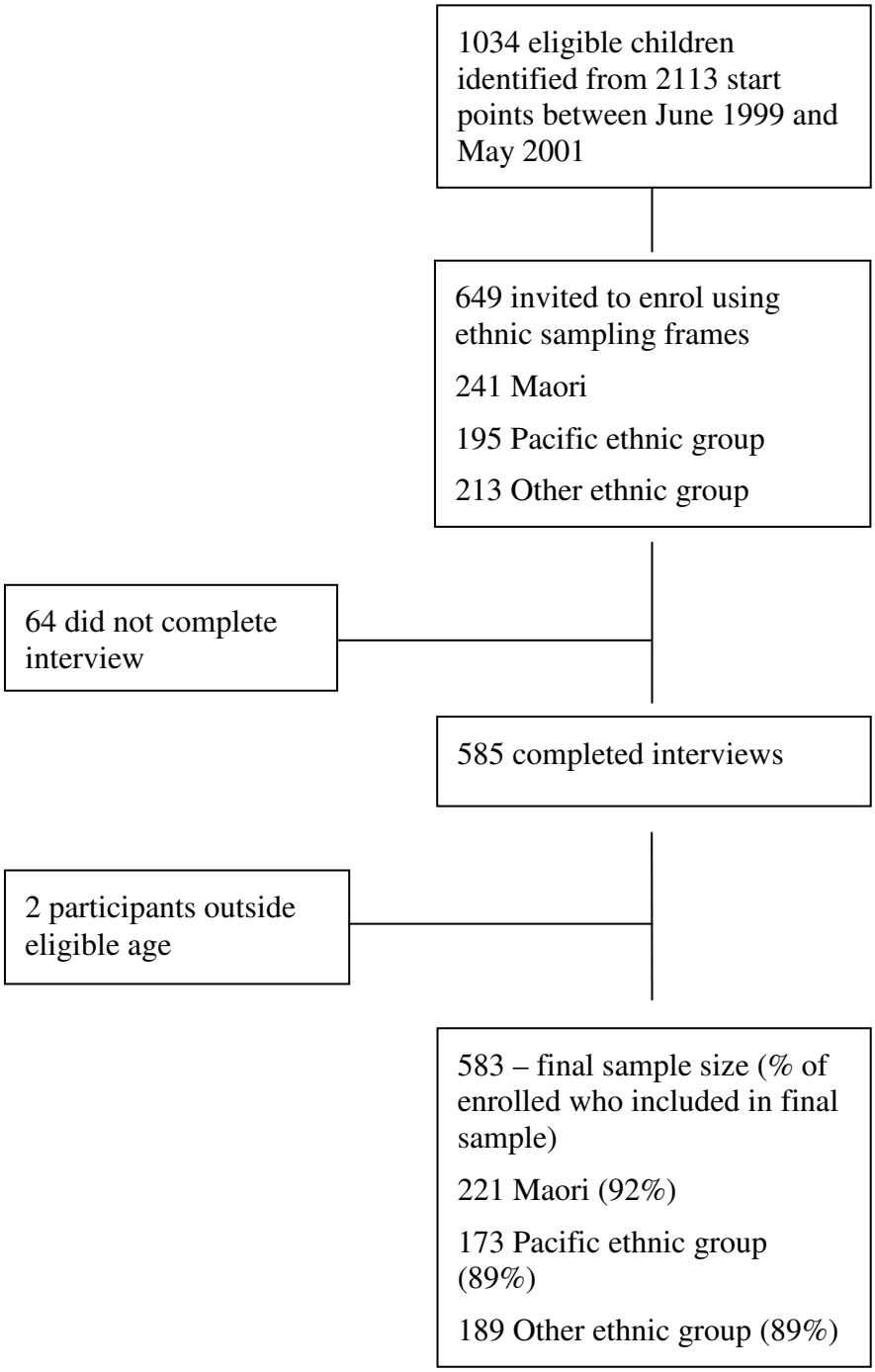

Table 1. Associations between ethnicity and sociodemographic variables

Variables	Māori		Pacific		European/other		Total	
	n	% (95%CI)	N	% (95%CI	n	% (95%CI)	n	% (95%CI)
Ethnicity (N=583)	221	38	173	30	189	32	583	100
Sex (N=583)								
Male	118	53 (46, 60)	92	53 (46, 61)	115	60 (53, 67)	325	55 (51, 60)
Female	103	47 (40, 54)	81	47 (39, 54)	74	40 (31, 47)	258	45 (40, 49)
NZDep96 decile (N=583) ***								
1-7	98	44 (37, 52)	71	42 (34, 50)	154	81 (75, 87)	323	55 (50, 61)
8-10	123	56 (48, 63)	102	58 (50, 66)	35	19 (13, 25)	260	45 (39, 50)
Total household income (N=510) ***								
≤ $40,000	124	63 (56, 70)	93	65 (57, 73)	50	32 (24, 39)	267	53 (48, 58)
> $ 40,000	71	37 (30, 44)	53	35 (28, 44)	119	69, (61, 76)	243	47 (42, 52)
Caregiver's education level (N=578) **								
No high school qualification	35	15 (10, 20)	29	17 (11, 23)	9	5 (2, 9)	73	12 (10, 15)
High school qualification	73	35 (28, 42)	74	43 (36, 51)	61	33 (26, 40)	208	37 (33, 41)
University or other tertiary institution	112	50 (43, 57)	68	40 (32, 48)	117	62 (55, 69)	297	51 (47, 55)
NZSEI occupational class (N=574) ***								
1 and 2	10	5 (2, 8)	11	7 (3, 11)	43	23 (17, 29)	64	11 (8, 14)
3	12	5 (2, 8)	14	9 (4, 14)	36	19 (13, 25)	62	11 (8, 13)
4	33	15 (10, 19)	27	15 (10, 21)	47	25 (19, 31)	107	18 (15, 21)
5 and 6	96	45 (38, 52)	79	46 (38, 54)	41	22 (16, 28)	216	38 (33, 42)
Not in the labour force	68	31 (24, 37)	36	23 (16, 30)	21	12 (7, 17)	125	22 (19, 26)
Parental history of asthma (N=582) **								
Yes	112	51 (44, 58)	56	33 (26, 40)	87	47 (40, 55)	255	44 (40, 48)
Sibling history of asthma (N=582) *								
Yes	92	45 (39, 52)	54	34 (27, 42)	53	30 (23, 37)	199	37 (33, 41)
Use of routine source of primary medical care (N=580)								
Always uses RSC	97	45 (38, 52)	92	54 (46, 61)	106	56 (48, 63)	295	51 (47, 56)
Has RSC and uses other GPs	105	47 (40, 55)	67	39 (32, 47)	77	42 (35, 49)	249	43 (39, 48)
No RSC	97	8 (4, 11)	13	7 (3, 11)	5	3 (0, 5)	36	6 (4, 8)

Morbidity in previous 12 months (N=577)****								
Very mild	57	25 (19, 31)	53	29 (22, 36)	67	35 (28, 42)	177	29 (26, 33)
Mild	55	25 (19, 31)	37	23 (16, 30)	60	32 (25, 40)	152	27 (23, 31)
Moderate	50	23 (17, 29)	42	24 (18, 31)	35	19 (13, 25)	127	22 (18, 26)
Severe	34	17 (12, 22)	25	15 (10, 21)	12	6 (3, 12)	71	13 (10, 16)
Very severe	23	10 (6, 14)	14	8 (4, 12)	13	8 (3, 12)	50	9 (6, 11)
Mean age at interview (years) (N=583)	221	7.4 (6.9, 7.8)	173	7.4 (6.9, 7.9)	189	7.9 (7.5, 8.4)	583	7.6 (7.3, 7.8)
Age (years)	221		173		189			
Median		7.0 (6.4, 7.5)		7.5 (6.8, 8.2)		8.0 (7.4, 8.6)		
Min, Max		2.0, 14.0		2.0, 13.9		2.0, 14.0		

* p<0.01; ** p=0.0002; *** p<0.0001; ****p=0.02.

Medication delivery systems used in the previous 12 months (Table 2)—The use of inhalers with or without spacer devices was reported by 95% of participants. There were no significant ethnic differences in the use of this device. Spacer devices were used by 80% of children ≤6 years of age and 34% of those aged ≥7 years of age.

Medication delivery using a nebuliser was reported by 53% of the total sample. Statistically significant ethnic differences ($p<0.0001$) were observed with more Māori (58%) and Pacific (65%) than European/other (34%) children received nebulised bronchodilators. Significant ethnic differences ($p<0.01$) in the delivery of medications in syrup form were also observed; (Māori 14%, Pacific 8%, European/other children 5%).

Table 2. Medication delivery systems used in previous 12 months by ethnicity

Variables	Māori		Pacific		European/other		Total	
	n	% 95% CI	n	% 95% CI	n	% 95% CI	n	% 95% CI
Had used an inhaler ± spacer (N=583)	211	95 92, 98	163	95 91, 98	179	95 92, 98	553	95 93, 97
Had used a spacer among children ≤6 years of age (N=265)	91	79 71, 87	59	76 66, 86	65	84 76, 93	215	80 75, 85
Had used a spacer among children ≥7 years of age (N=318)	30	30 21, 40	32	34 24, 43	43	38 29, 47	105	34 28, 40
Had used a nebuliser (N=583)*	124	58 52, 65	111	65 57, 73	63	34 27, 41	298	53 48, 57
Had used syrup medication (N=583)**	29	14 9, 19	14	8 4, 12	10	5 2, 8	53	9 7, 12

* $p<0.0001$; ** $p<0.01$.

Asthma medications used in the previous 12 months (Table 3)—The use of inhaled beta-agonists was almost universal with 96% of children receiving these types of medications. Sixty-nine percent of children had received an inhaled corticosteroid (ICS).

Logistic regression modelling identified significant interactions between ethnicity and morbidity for the outcomes 'inhaled beta-agonists in the previous 12 months' ($p<0.0001$) and 'inhaled corticosteroids in the previous 12 months' ($p<0.0001$). Consequently, morbidity stratified ethnic-specific prevalence estimates of having received these medication types were calculated. With regard to beta-agonists the pattern of use across morbidity levels varied slightly by ethnicity.

Among Māori, use of beta-agonists was lower at the extremes of morbidity than in the 'middle' morbidity levels. The very high overall use of these medications and the small size of the observed differences suggest that this finding is of limited clinical importance (data not shown). In relation to ICS, fewer Māori and Pacific children who had experienced severe morbidity in the previous 12 months had received ICS (Figure 2).

Figure 2. Percentage (and 95% confidence intervals) who had received ICS in the previous 12 months by morbidity and ethnicity

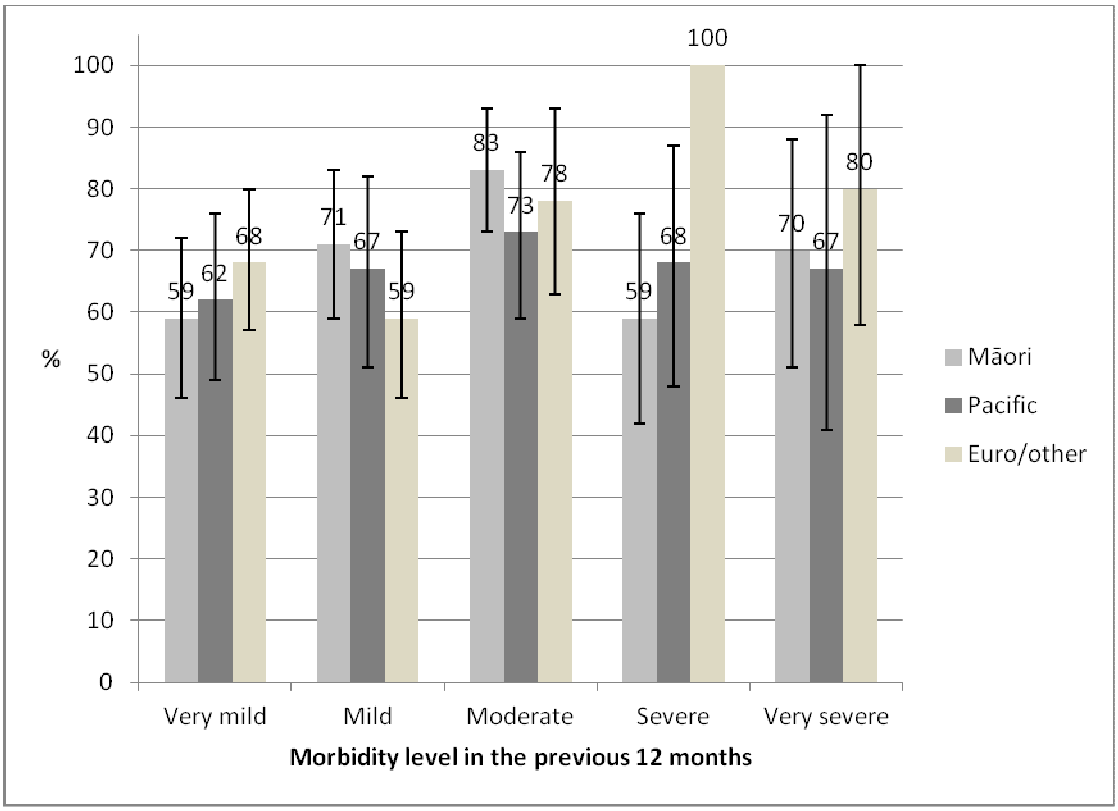

Table 3. Percent who had used medication in the previous year by ethnicity (N=583)

Variables	Māori		Pacific		European/other		Total	
	n	% 95% CI	n	% 95% CI	n	% 95% CI	n	% 95% CI
Inhaled beta- agonists	212	96 93, 99	168	97 95, 100	176	94 90, 97	556	96 94, 97
Inhaled anticholinergics	5	2 0, 4	4	2 0, 4	4	2 0, 4	13	2 1, 3
Inhaled corticosteroids	150	69 63, 75	114	67 60, 74	132	70 64, 77	396	69 65, 73
Cromoglycates	11	5 2, 7	5	3 0, 5	16	8 4, 12	32	5 4, 7
Oral steroids	32	15 10, 21	13	8 4, 13	29	16 10, 21	74	13 10, 16

Oral steroids had been given to 13% of children. Ethnic differences in the proportion receiving oral steroids approached statistical significance (p=0.06) (Māori 15%, European/other children 16%, Pacific 8%). Cromoglycates and inhaled anticholinergic medications were used by a small proportion and their use did not vary by ethnicity. Logistic regression analyses adjusting for age, sex, socioeconomic

position, and parental and sibling histories of asthma confirmed these findings for oral steroids, cromoglycates and anticholinergic medications (data not shown).

Discussion

In this study the use of inhaler devices with or without a spacer was almost universal and spacers were used with inhalers by the majority (≈ 80%) of children aged 6 years or less. The majority of children (96%) had received inhaled beta-agonists in the previous 12 months and 69% had received ICS. Consistent with the findings of Shaw et al,[11] there were no significant ethnic differences in the use of reliever or preventative asthma medications.

The results of this study suggest some aspects of the pharmacological management of asthma are more consistent with recommendations in evidence-based guidelines than previously reported in NZ. The proportion of children with asthma who were receiving beta-agonists and ICS were higher than that previously reported in NZ. Furthermore the low reported use of anticholinergics was consistent with recommendations for these drugs.

However, other findings suggested there is still room for further improvements to be made. Only 68–78% of children in the moderate, severe, and very severe morbidity groups reported ICS use in the previous 12 months, suggesting that this group is being under-treated. The use of nebulisers was no longer recommended except in extreme circumstances. However, one third of European/Other and over half of Māori and Pacific caregivers reported their child had received medications by nebuliser in the previous 12 months.

Spacer devices are recommended for the delivery of medication to children under 7 years and, ideally, for children up to 15 years of age.[16] In this study, about 80% of children under 7 years and 34% of the older age group reported use of spacer devices.

Some of the associations identified in this study suggest there may be ethnic differences in the quality of care including: the similarity in use of oral steroids in each ethnic group in the context of higher morbidity experience by Māori and Pacific children; the higher proportion of Māori and Pacific caregivers who report nebuliser use in the previous 12 months; and stratified analyses by morbidity suggesting Māori and Pacific children with severe morbidity may are less likely to receive preventative medications than Other ethnic group children.

Strengths and limitations of the study—This is the first study to have focused explicitly on whether there were ethnic differences in the management of children's asthma. Furthermore it is rigorously designed, and included sufficient numbers of Māori, Pacific and Other ethnic groups to examine the major outcomes for each group.

A very high proportion of participants completed the study and there were no ethnic differences in completion rates. Participants were recruited using a community-based sampling frame providing much greater representativeness than samples recruited from after-hours medical clinics, EDs and hospitals. As a result the findings are highly generalisable to non-participating children with asthma.

There are a number of limitations to the design of the study reported here. Firstly, the study is a cross-sectional survey and, therefore, cannot make inferences about causation. Participants were asked to recall information from the preceding 12 months, making the study vulnerable to recall bias. However, there is no evidence that recall bias would occur more frequently in any particular ethnic group so any recall bias should not affect the estimates of ethnic differences. Seasonal bias may also be found in studies of asthma but is unlikely in this study as recruitment occurred over a two year period, and the outcome variables used a 'last 12 months' timeframe.

We sought to identify what medications were provided by GPs. Participants may have reported what medications they had given to the child rather than those the doctor had provided (regardless of whether it had been given to the child or not) but we do not believe this is likely as participant information explicitly stated the focus was on the management of asthma by doctors, nurses and other health professionals in the community. As the study did not collect data about the dose of medications we are unable to assess whether medication doses were consistent with guideline recommendations.

Although the study had excellent completion rates in all ethnic groups, the mean age of non-completing children was lower than that of children who completed the interview. The impact of this is likely to be very small and will vary according to relationship between age and the specific outcome measure. Estimates of ethnic differences in outcomes will not be affected as there were no ethnic differences between the non-completing and completing groups, nor were there any differences in age across the three ethnic groups. Finally, the observed ethnic differences in preventive medication use were lower than those used for power calculations and this may have resulted in the current study being underpowered to identify ethnic differences in preventive medication use.

Implications for the health sector, health services and clinical practice—Asthma is a chronic condition that is associated with a high burden of disease and significant costs to the health sector and to the children and families who are affected by asthma. These are amenable to change through the provision of high quality primary care using readily available evidence based guidelines for managing asthma.

Reducing ambulatory sensitive hospitalisations is one of the Minister of Health's key targets for District Health Boards,[17] and improving access to and the effectiveness of 'mainstream' services is a key objective in the Māori Health Strategy.[18] The results of this study suggest there are opportunities for increased focus on the effective management of asthma as a means of reducing morbidity and the costs associated with this morbidity. At DHB and PHO levels asthma management should be explicitly incorporated into funding and service delivery strategies aimed at improving the outcomes of chronic diseases.

PHOs and individual providers should review their approaches to supporting and delivering high quality asthma care. Ensuring the care provided falls within the recommendations of evidence-based guidelines is important and has been shown to be beneficial.[19-21] The results of this study suggest that there is scope to improve practices associated with the provision of ICS, the use of spacer devices, and reducing the use of nebulisers. Clinical audit with feedback to individual clinicians is a useful tool for undertaking continuous quality improvement. Specific reporting of audit

findings by ethnicity will assist providers to reduce any identified ethnic differences in their practice.

Other tools, for example on-screen reminders for aspects of asthma care, continuing medical education workshops, and the provision of electronic access to information for health professionals,[22–25] have been shown to be effective strategies to assist clinical decision making and improve practice and these could be further implemented in individual practices or across PHOs. Computerised decision-support tools to assist practitioners to align their practice with evidence-based recommendations are also being implemented and evaluated.[26–30] This array of strategies should be considered when developing DHB or PHO-wide approaches to improving the management of asthma.

Improving the management of asthma in primary care requires a team of primary care professionals who are well informed about asthma; the provision of asthma care that is consistent with guidelines; and practitioners who are able to communicate with their patients in an acceptable, appropriate and effective manner. Providing culturally competent care is also important for ensuring that Māori and Pacific peoples access and receive the highest quality of care. PHOs and individual practitioners must take responsibility for increasing the cultural competence of, respectively, the primary care workforce and themselves.

The data presented in this study was collected between June 1999 and May 2001, raising the question of whether the data and study findings remain valid. Publicly available data about asthma management in the PHO environment is limited. Furthermore, there have been no publications addressing the questions raised in this study in the years since data collection was completed. Published data about asthma admissions over the years 2003–2006[31,32] do not provide convincing evidence of sustained reductions in asthma hospitalisations or in ethnic inequalities in children's asthma hospitalisations.

We believe that the data remains salient and provides useful information to guide primary care practitioners and organisations in their efforts to improve asthma care, reduce asthma morbidity and facilitate reductions in ethnic inequalities in asthma outcomes.

Competing interests: None.

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THE NEW ZEALAND MEDICAL JOURNAL
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Median sternotomy scar assessment

Hamesh Jina, Jeremy Simcock

Abstract

Introduction Median sternotomy wounds are formed following most cardiac surgery. These wounds may heal with problematic scars. We hypothesise that midline sternotomy scars will scar poorly in general and in comparison with control scarring from other sites.

Methods We evaluated 50 patients with mature median sternotomy scars using the Patient and Observer Scar Assessment Scale (POSAS), the Manchester Scar Scale (MSS) and photographs. Different scar features were assessed using these scales.

Results Patients were on average 65.9 years old, predominantly male (72%) and Caucasian (94%). Overall, 11 patients (22%) expressed concern over a symptomatic or poor scar with seven patients (14%) complaining of pruritis and three patients (6%) disappointed with the cosmesis of the scar. The clinician found five patients (10%) to have poor scarring defined as hypertrophic scarring. The predominant scarring characteristics assessed by the clinician were colouration, variable relief and increased contour which are the main areas of concern.

Discussion Our study shows that median sternotomy scarring can be problematic with 1 in 5 patients symptomatic and 1 in 10 patients developing hypertrophic scarring. Thus, this predominantly Caucasion population has a low but significant rate of scar problems in comparison to median sternotomy scarring in other populations. We could not identify patient factors which were predictive for poor scarring but anatomical location may be a key factor. Overall, we believe that median sternotomy patients should be offered preventative treatment to ensure the best scar outcome.

A median sternotomy wound is invariably formed following coronary artery bypass surgery (CABG) or heart valve replacement surgery (HVR). The scar typically takes 18 months to mature and represents the end-point of tissue repair. A hypertrophic scar is persistently red, raised and sometimes itchy.[1] Presternal wounds have been reported[2] to often scar poorly resulting in hypertrophic scar formation in comparison with scars formed in other anatomical locations.

Hypertrophic scarring can affect people aesthetically, symptomatically and psychologically. The purpose of this study is to evaluate scar formation following median sternotomy wounds using validated scoring tools.

Current wound management at Christchurch Hospital following CABG or HVR surgery is to apply a silver-based wound dressing for five days while the patient remains an inpatient. At discharge, the dressing is removed and an occlusive spray dressing is applied to the wound. No further dressings are applied in the community and no wound-care/scar management advice is given. Patients are followed up at six weeks post-surgery for clinical review.

In our study, we hypothesise that median sternotomy scars will scar poorly in general and in comparison with scarring from other sites (Bacillus Calmette-Guerin [BCG] vaccinations, open appendicectomy scars and ear piercings).

Methods

We examined the mature scar in patients who had median sternotomy scars from surgery 2 to 4 years previously. A database of patients existed who had CABG or HVR surgery during these years and every fifth patient was contacted and invited to participate in the trial. Invitations were sent until the study achieved 50 participants (20% of the eligible patient population). Exclusion criteria included those patients outside the Christchurch region. The patients were contacted by mail and telephone.

Sternotomy scars were assessed using the Manchester Scar Scale (MSS)[3] and the Patient and Observer Scar Assessment Scale (POSAS).[4] The MSS was used for the clinician evaluation of linear scars. This is a discontinuous scale which analyses the colour, contour, texture, margins and size of the scar. Part of the MSS includes assessment of control scars from other sites listed above. The POSAS is both patient and clinician-based using a continuous scale. The patient scale analyses variables such as pain, itch, colour, thickness and scar irregularity. These scar scales were used because they are reliable and valid measures of linear scarring.[5,6]

Patients also had their scars photographed. The same clinician scored all of the scars to eliminate interobserver differences.

Results

From a total of 84 patients who were invited to participate in this study we obtained our sample of 50 patients (response rate of 60%). Participants attended both a 15-minute outpatient consultation and photography under studio conditions. Baseline demographics were obtained as part of the MSS and shown in Table 1.

Table 1. Patient demographics

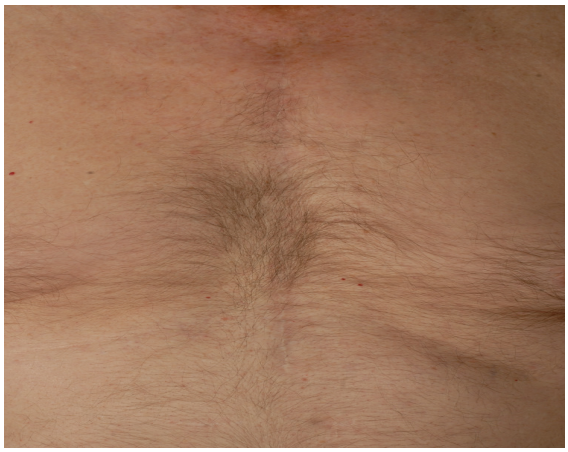
Gender	36 Males (72%) 14 Female (28%)
Ethnicity	47 White (94%) 2 Maori (4%) 1 Indian (2%)
Smoking status	15 Never (30%) 34 Ex (68%) 1 Current (2%)
Age (mean)	65.9 years
Diabetes	9 Patients (18%)

We found that patients report low rates of concerns about their scar. The most common complaints were pruritis in seven patients (14%), paraesthesia in three patients (6%) and one patient (2%) who experienced pain. Postoperative complications were noted in two patients (4%) with both patients having infection and one patient having wound dehiscence.

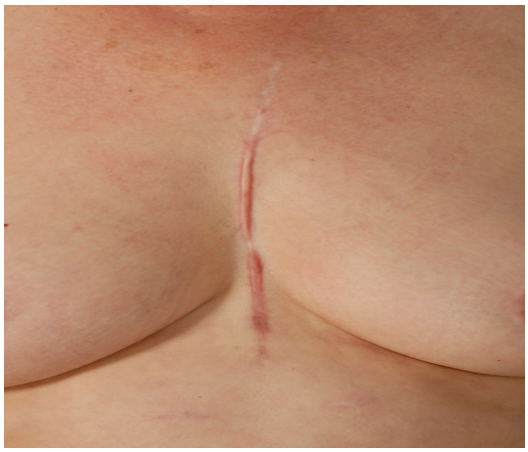
Patients were generally happy with the cosmesis of their scar with only three patients (6%) expressing concern.

Figure 1 demonstrates the variation in scarring within this patient group.

Figure 1. Images below demonstrate the difference in median sternotomy resultant scar



Sternotomy scar in a 65-year-old male with minimal scar formation. This was graded with a MSS of 9/20 and POSAS of 11/60



Sternotomy scar in a 54-year-old female with hypertrophic scar formation. This was graded with a MSS of 17/20 and a POSAS of 42/60

Total MMS scores ranged from 9–18 (maximum possible score of 20 for the worst scars) with a mean of 11.88. The highest score from a non-controllable variable was the colour of the scar at 2.18. Five patients (10%) had hypertrophic scarring with an overall average of 2.02. The sternotomy scar was also compared with scarring from previous BCG vaccination, appendectomy and piercing(s) and found to have a consistently higher score. These historic control scars scored from 7–13 with an average of 9.26. The appendicectomy scars were demonstrated in 24% of patients and accounted for 65% of all control scars. The overall MMS score for the open appendicectomy scar was 8.41 (7–10) which is 42% less than the sternotomy scar score.

The patient component of the POSAS ranged from 6–33 (maximum possible score of 60 for the worst scars) with a mean of 13.52. The highest score was colour (mean of 3.66). Pain and itch are two symptoms that patients did not score highly with average scores of 1.18 and 1.26 respectively. The clinician scale scores vascularisation, pigmentation, thickness, relief and pliability.

The total clinician scores ranged from 5–32 (maximum of 60) with an average of 16.08. The highest scored variable was relief at 4.22 followed by pigment at 3.58. All values from the MSS and POSAS can be seen in Table 2.

Table 2a–c. MSS and POSAS results

(a)

MSS	Average (range)
Size (maximum score 3)	3 (3)
Colour (4)	2.18 (1–4)
Contour (4)	1.98 (1–4)
Texture (4)	1.74 (1–4)
Matte/Shiny (2)	1.04 (1–2)
Margins (2)	1 (1)
Number (2)	1 (1)

(b)

POSAS – Observer	Average (range)
Relief (maximum score 10)	4.22 (1–7)
Pigmentation (10)	3.58 (1–7)
Pliability (10)	2.86 (1–6)
Thickness (10)	2.26 (1–8)
Vascularisation (10)	2.24 (1–6)

(c)

POSAS – Patient	Average (range)
Colour (maximum score 10)	3.66 (1–10)
Thickness (10)	3.18 (1–10)
Irregularity (10)	2.9 (1–10)
Stiffness (10)	1.32 (1–4)
Itch (10)	1.26 (1–4)
Pain (10)	1.18 (1–5)

MSS=Manchester Scar Scale; POSAS=Patient and Observer Scar Assessment Scale.

Discussion

Hypertrophic scarring has a number of causes including genetic factors, increased wound tension, delayed wound healing or location of the scar. In our study, the only identifiable cause of hypertrophic scar formation was the anatomical location. We found that the few patients who had postoperative complications did not have higher overall scores and patient demographics were not predictive for poor scarring.

These results support our hypothesis that hypertrophic scar formation in median sternotomy wounds is a relatively frequent occurrence compared with scarring from other sites. In our predominantly Caucasian population, where scars were at least 2 years old (compared with other studies which have analysed scars of variable ages), we found a low but significant rate of scar problems. Specifically, we found that 22% of patients were symptomatic or noticed poor scarring and 10% of patients were assessed by the clinician as having hypertrophic scarring from the median sternotomy wound.

No patients who had appendicectomy scars were symptomatic or demonstrated hypertrophic scars. The scoring from the scars formed from the appendicectomy wound were lower than that of the median sternotomy wound which is a useful comparator given that both scars evolve from wounds formed in a controlled environment.

Truong et al[7] reviewed linear scarring in breast/chest wall and axillary wounds in women following breast surgery and, although different scoring tools were used, the scarring was poorer in breast/chest wall scars compared with axillary scars. This supports a predisposition to poorer scar formation across the chest wall rather than other regions.

It is clear from recent studies that ethnicity is a relevant factor in reported frequency of hypertrophic scar formation. Sproat found that the reported frequency of hypertrophic scar formation from median sternotomy scarring was 30% in Caucasian and 50% in Asian populations.[8]

Another recent paper looked at modifying the natural history of hypertrophic scar formation by utilising a topical silicone sheet in a population from Malaysia.[9] In this study the patients were of Malay, Chinese and Indian origin. The authors found a 94% rate of hypertrophic scarring overall, of which the majority were in the control group. Because of the different ethnic origin, and therefore skin type, of patients in this study the results cannot be generalised to our population.

In our study, the MSS and POSAS evaluated similar scar features and produced similar results. Patient self-evaluation of the scar was generally less critical than that of the clinician. It is interesting that in this population the predominant area of concern from the patients perspective was pruritis rather than poor appearance. This may be attributed to lower expectation and less overall concern about cosmesis with more interest in the functional benefit of the surgery, especially in this group of older males. It also demonstrates the importance of evaluating scars with a scoring tool which takes patient symptoms into consideration. This explains why the Vancouver Scar Scale has not shown correlation with patient scar satisfaction following breast surgery.[10]

Many authors feel scar management is best approached by prevention rather than treatment. Prevention refers to intervention that alters the natural history of scar maturation to minimise the chance of developing problematic scarring. Treatment occurs when the scar has transgressed to a hypertrophic or keloid scar. The consensus from the International Consensus on Scar Management[3] is that optimal treatment is managing the hypertrophic or keloid scar when the scar is immature but has an intact epithelium.

In summary, the majority of patients in our population have good median sternotomy scar scores. However, by using clinically relevant tools including patient symptoms, we have identified that at least one in five patients have a problematic scar and one in ten patients have hypertrophic scars. We found no patient factors which predict scar outcome and would recommend that all patients be offered preventative scar management

Competing interests: None.

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Academic performance and career choices of older medical students at the University of Otago

William Shelker, Alison Belton, Paul Glue

Abstract

Aims To compare the academic performance and postgraduate career choices of a cohort of medical students who are older and more life experienced at time of medical school entry ("Other Category" students) with students admitted through standard entry admission pathways.

Methods Examination performance, graduation rates, postgraduate specialisation and geographical location were compared between Other Category students and students entering via Standard Entry admission (including competitive first year entry and competitive graduate entry immediately after completing a Bachelor's degree).

Results Compared with Standard Entry students, Other Category students had equivalent examination pass rates, significantly higher rates of distinction passes in examinations in Year 2 (OR 1.86; 95% CI 1.05, 3.29; p=0.03) and Year 5 (OR 2.36; 95% CI 1.27, 4.37; p=0.005), and equivalent graduation rates. Retention of Other Category graduates in New Zealand was 14% higher than Standard Entry students over 10 years post-graduation (p<0.0001), and a higher proportion had specialised in General Practice (p=0.04).

Conclusions Compared with Standard Entry students, Other Category medical students had higher rates of distinction grades in examination results, higher rates of retention in NZ post-graduation, and a higher proportion taking up general practice as a specialty. These findings may be relevant in planning for recruitment and training of the future medical workforce in New Zealand.

There are three categories of student admission to medical school at the University of Otago. Approximately 70% of students gain entry via a competitive first year examination. Another 25% gain entry immediately after completion of a bachelor's degree (competitive graduate entry). For the purposes of this paper, students who enter via these pathways will be collectively termed as Standard Entry. The remaining 5% of students, termed "Other Category", comprise older applicants with a diverse range of backgrounds. These may include individuals who have completed a second or higher degree, or have completed a degree at an overseas university, in both cases at least three years prior to their application. Also included are graduates from any health-related profession (e.g. nursing, physiotherapy or pharmacy backgrounds), and who have at least five years of work experience.

Selection of Other Category students is by interview, and academic ability, interview performance and life experience are all considered in candidate selection. Successful candidates who have not completed courses equivalent to the first year medical school entrance examination may have their entry deferred until the first year medical school course is passed. Other Category entry has been in place for at least 24 years at Otago

Medical School and over 300 medical students admitted under this category have graduated.

Current research on the academic success of older medical students, or those with tertiary degrees, is rather limited. Older medical students have been shown to be academically more successful[1] or as successful[2-5] as younger entrants. However this research has generally reported on students who, at the Otago Medical School, would be classified as entering under the competitive graduate entry category. Therefore the purpose of this research was to evaluate the academic performance and postgraduate career choices of this older, more life-experienced group of medical students relative to their younger peers.

Methods

The objectives of this research were to compare the academic performance and postgraduate career choices of Other Category medical students relative to students admitted though Standard Entry pathways. Approval for this project was given by the Otago University Ethics Committee. The names of students admitted to Otago Medical School under the Other Entry category were identified through the Health Sciences Administration group and the Admissions Committee. Year of acceptance was recorded, along with any entry requirements (such as completion of a prescribed course of study, which was usually the first year medical course).

Anonymised academic data (examination performance in the two key examination years, Years 2 and 5 for 1996-2005, and year of graduation from 1992-2010) were obtained from the Otago University database under the supervision of an authorised staff member. Comparative data for all other medical students ("Standard Entry") over the same period were provided by the Faculty of Medicine Administration group.

Postgraduate information, including medical specialisation, geographical location (country, and for those in New Zealand, major city versus non-major city location), were gathered from medical registers in New Zealand, Australia, England, Ireland, USA and Canada. Comparative data for all New Zealand medical school graduates were obtained from the 2009 annual workforce report produced by the New Zealand Medical Council[6]. Summary statistical methods were used. Comparisons between groups used Chi-squared statistics, and Odds Ratios and Risk Differences were calculated using random effects Mantel-Haenszel methods (Review Manager 5.0).

Results

Between 1987 and 2010, a total of 347 students were offered a place at the University of Otago Medical School under the Other Entry category (approximately 5% of the total medical school enrolment over this time). Of these 347 students, 102 were required to complete a prescribed course of study (the first year medical course) before entry, compared with 245 students who were offered direct entry in Year 2 (Table 1). A greater proportion of students who had to complete a prescribed course of study did not enter Year 2 ((32/102) compared with students offered direct entry into Year 2 (46/245; OR=2.00; 95%CI 1.17–3.35; p=0.01).

Other Category students who completed Year 2 had an examination pass rate of 99% (237/239; 30 students still to sit exam), and a pass rate of 98% (193/196) in Year 5 exams. These rates are identical to those of Standard Entry students.

Examination distinction rates were significantly greater in Years 2 and 5 for Other Category students compared with Standard Entry students (Year 2: 16% vs 9%; OR=1.86, 95%CI 1.05–3.29; p=0.03; Year 5: 10% vs 6.8%; OR=2.36, 95%CI 1.27–4.37; p=0.005).

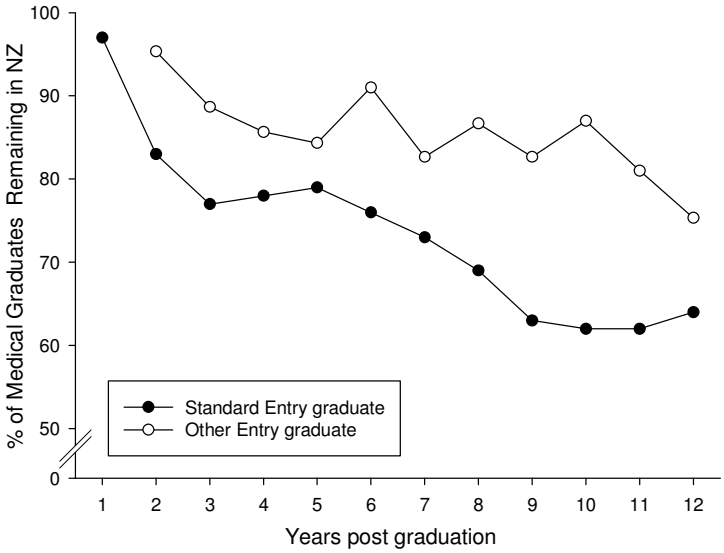
Table 1. Year 2 entry rates of Other Category students required to complete a prescribed study course or offered direct entry

	Did not enter Year 2	Entered Year 2	Total students
Prescribed course	32	70	102
Direct Entry into Y2	46	199	245

Graduation rates for Other Category students who entered Year 2 prior to 2005 (and were capable of graduating at the time of data collection) was 96% (187/194), identical to the graduation rate of 96% for Standard Entry students (2265/2363, Chi-squared=0.13, p=0.7).

A total of 7 Other Category graduates (4% of those who graduated) could not be located on any medical register, and in the following analyses were considered to be non-resident in New Zealand. The retention rate of Other Category graduates remaining in New Zealand over the 12 years post-graduation is shown in Figure 1.

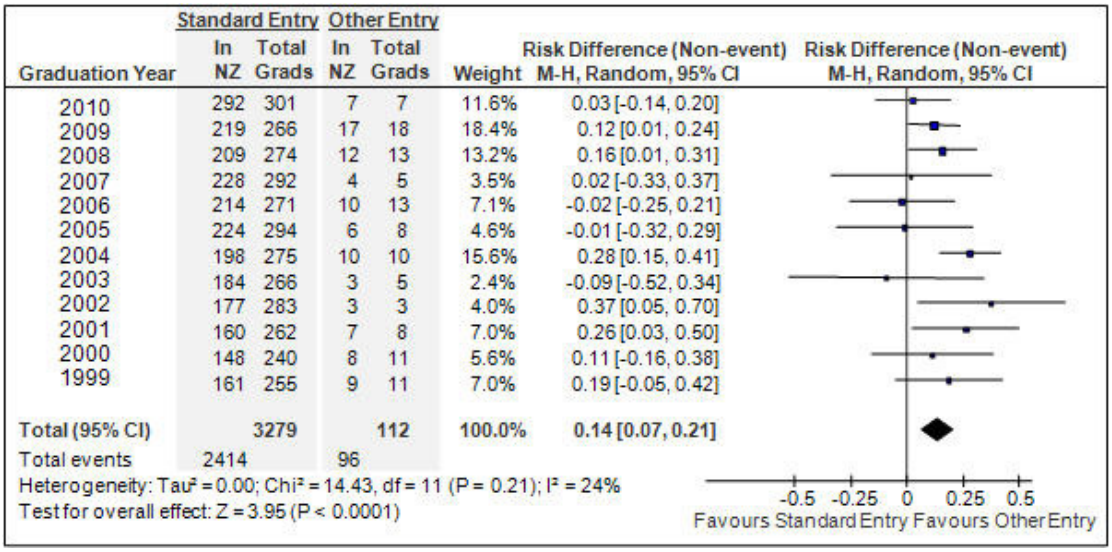
Figure 1. Retention rates over 12 years post-graduation for Standard Entry and Other Category medical graduates. Other Category data are a 3 year rolling average; Standard Entry data are from reference (6)



When compared with Standard Entry graduates, the decline in retention rates was less steep. Analysis of data from 1999–2010 showed a risk difference (RD) of 0.14 (95% CI 0.07, 0.21, p<0.0001) between the two populations (Figure 2). This corresponds to

a 14% increase in postgraduate retention in New Zealand of Other Category graduates compared with Standard Entry graduates.

Figure 2. Forest plot comparing retention of Other Category vs Standard Entry medical students in NZ from 1999–2010



The geographical location of Other Category graduates who remained in New Zealand was not significantly different from Standard Entry graduates in distribution between major urban centres and non-major centres (Other: 116:26; Standard: 8880:2284; Chi-squared=0.4, p=0.5). For graduates remaining in New Zealand and who had vocational (specialist) registration, a significantly larger number of Other Category graduates were General Practitioners (28/55 vs. 2573/6905; Chi-squared=4.34, p=0.04). The relative proportions of Other Category Graduates entering other specialties compared with Standard Entry graduates were too small to demonstrate meaningful differences.

Discussion

This study has identified a number of interesting findings. Academically, Other Category students who enter Year 2 of medical school perform as well or better than medical students entering via Standard Entry routes. This is demonstrated by equivalent examination pass rates, higher rates of distinction passes in examinations, and equivalent graduation rates. The retention rate of postgraduate Other Category students in New Zealand is significantly higher than Standard Entry students, and a higher proportion specialise in General Practice. This study also identifies a possible risk factor for Other Category students failing to enter Year 2.

These results agree with an earlier report[1] that older medical students achieve a higher percentage of honours degrees (equivalent to achieving distinction at the University of Otago). This study identified higher rates of distinctions in Year 2 and Year 5 for Other Category entrants compared with Standard Entry students. The overall pass rate

in Year 2 and Year 5, along with the graduation rate of Other Category students agrees with a body of literature[2–5] that older (or tertiary educated) medical students are as successful as younger medical students, who may be entering direct from high school or with one year of tertiary education.

Another important observation in this research is the higher retention rate of Other Category students in New Zealand post-graduation. Data from the New Zealand Medical Council[6] show a rapid decline in retention of doctors over the first three years after graduation, which continues to decrease steadily over the next six years, to stabilize at approximately 65% at nine years post-graduation (Figure 1).

In contrast, Other Category graduates show a much more gradual decline in retention, with a drop to 89% retention at three years post-graduation and 83% at nine years post-graduation. The overall difference represents a 14% increase in retention for Other Category Entrants, and may be an important consideration when addressing difficulties in retaining medical workforce in New Zealand[7] .

The reasons behind why Other Category graduates have a higher retention rate were not investigated in this research. Possible reasons might be that as older students, they have spent time overseas, are more settled in their lives, or have families, and thus the incentives to travel outside of New Zealand are diminished.

Other Category students also have a higher percentage of graduates specialising in General Practice (51%) compared to the overall General Practice rates (37%). The reason behind this preference for General Practice was also not investigated in this study, however may be relevant to consider when strategies are developed to increase GP numbers in the New Zealand Medical workforce[8].

Another finding was a possible risk factor for students who were selected not entering Year 2 of medical school. Students who were required to take a prescribed course (first year medical classes) were twice as likely not to enter Year 2. This may indicate a need for additional academic support for students required to take prescribed courses prior to medical school entry, to reduce the risk of non-entry.

There are a number of possible shortcomings related to the findings of this study. The Other Category student population was relatively small (~5%) and highly selected compared with total medical student enrolment, and these factors may reduce the ability to generalise these findings. As there are no directly comparable publications or reports on a similarly selected medical student cohort, it would be important to independently confirm these findings.

This research cannot address whether the academic and retention advantages noted for Other Category students would also be seen in graduate entry students at Otago Medical School (i.e. those who enter medical school after completion of a Bachelors degree, but who are younger than, and lack the life experience of Other Category students).

This research draws attention to possible advantages for medical school enrolment of older students, graduates or health professionals with considerable life experience. These students demonstrate high levels of academic performance, and after graduation, are more likely to remain in New Zealand and to be working in General Practice when compared with colleagues who entered medical school via Standard

Entry pathways. These findings may be relevant in planning for recruitment and training of the New Zealand medical workforce in the future.

Competing interests: None.

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THE NEW ZEALAND MEDICAL JOURNAL
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Do pharmaceutical score cards give us the answers we seek?

(Commentary on Wonder and Milne in the same issue of the *Journal*
Wonder M, Milne R. Access to new medicines in New Zealand and Australia. N Z Med J. 2011;124(1346). http://journal.nzma.org.nz/journal/124-1346/4966)

Peter Moodie, Scott Metcalfe, Matthew Poynton

Abstract

Few countries can afford to fund all pharmaceuticals for all of their people all of the time, and the current international economic climate brings this into clearer focus. Various agencies have tried to solve the problem in different ways, varying from funding a restricted list that applies to the whole population, to funding most medicines but with a significant part charge, or as in the United States, funding for only selected groups and leaving others to fend for themselves other than in an emergency.

For countries like New Zealand and Australia who have universal health coverage but restricted (and different) lists of funded pharmaceuticals, comparisons of those lists can occur, but are problematic.

Comparisons need to be interpreted with caution as systems and policies vary between countries.

That one country funds more new medicines than the other is one thing, but the more important questions are whether one country gets more health gains and more value for precious health dollars than the other.

Difficulties with international comparisons

There are many reasons why health costs in general, and pharmaceutical expenditure in particular, are rising and at a rate where many countries now recognise they are unsustainable.[1] In terms of managing pharmaceutical expenditure over the last 18 years, New Zealand's Pharmaceutical Management Agency (PHARMAC) has by international comparisons been successful.[2,3] However, that success has not come without criticisms from both within and outside the country.

It is therefore very important to ensure that the financial success of PHARMAC has not been at the expense of health gain, and one way to do this is by way of inter-country comparisons.[4,5] An apparent natural comparator for New Zealand is Australia, as both countries have universal health care systems with roughly similar types of populations. Both have well-developed pharmaceutical regulatory systems, and funding systems which appear similar but have fundamental differences.

In particular, New Zealand has a budget which is set annually by the Minister of Health on the advice of PHARMAC, district health boards (DHBs) and the Ministry of Health.[6] Decisions about such resource allocation are appropriately made by the Government of the day. By comparison Australia has the ability to seek more funding when it sees fit—a difference that should not be underestimated. The two countries

also have very different co-payment systems, where in New Zealand the cost per item is much less than Australia.[7] *

Making comparisons appears simple, but they can come up with results that appear valid but tell us little. For example, an audit undertaken by the Karolinska Institute on the use of oncology therapies in various countries (and sometimes quoted when looking at New Zealand's funding[8]) was quickly discredited for both its methodological flaws and inappropriate conclusions.[9,10] (See endnote †.)

A new comparison of New Zealand and Australia

To make useful comparisons, we need to ask a number of more detailed questions about the reasons for funding or not funding a particular medicine, including:

- What framework was used for making the funding decision?
- Was there any harm done by taking longer to fund a particular medicine in one country rather than another? Indeed was it ultimately an advantage to take the extra time?
- Was the particular medicine good value for money compared with other options?
- Were there alternative therapies available which were more cost effective?

With these sorts of questions in mind, Michael Wonder and Richard Milne in this issue of the *Journal* (http://www.nzma.org.nz/journal/124-1346/4966 [8]) have undertaken a detailed and systematic analysis comparing the extent and timing of new pharmaceutical funding decisions between Australia and New Zealand. They make a number of good points, particularly highlighting the fact that many patients cannot afford to pay for medicines out of their own pockets and that therefore both countries have comprehensive and universal pharmaceutical benefits schemes.

Accounting for differences?

However, while the lists in the Wonder and Milne article[8] are comprehensive, there are differences in the way some medicines are funded in the two countries, and other issues, that have not been addressed.

Different systems—In the first instance, apart from pharmaceutical cancer treatments (PCTs), therapies in New Zealand used in a hospital setting are funded at the discretion of the individual DHB hospital and not PHARMAC. This particularly applies to infusion therapies. It therefore follows that some of the hospital medicines on the Australian list will not be found on the NZ Pharmaceutical Schedule, including bivalirudin for anticoagulation prior to surgery.

Secondly there are some minor errors including levetiracetam (for refractory epilepsy), which was funded in New Zealand on the Pharmaceutical Schedule through a Special Access scheme before it came off-patent.

Different time periods, metrics and opportunities to fund—Any number of comparisons can be done, and some will favour different views.

For instance, Wonder and Milne have used a long time period to gather their data. However (and if we suspend issues of validity, see below), this was also a time of

significant fiscal constraint for New Zealand. Had they reviewed the last 2 years, where the Government has invested significant new money in pharmaceuticals, the lists would have looked significantly different with some 59 new medicines funded in New Zealand during that period.

Likewise, New Zealand has fewer restrictions and lists more treatments overall than Australia.[7] (See endnotes ‡,§.)

There are also differences between the two countries in opportunities for funding. Pharmaceutical suppliers decide when they will bring products to market in each country, which means Australia and New Zealand may not have the opportunity to fund them at the same time.

The effect of a budget cap and cost effectiveness—Although New Zealand may in some cases be slower to fund a drug than Australia, the reality of a budgetary cap means that extra care must be taken to forecast expenditure and ensure that we are getting true value for money. In fact New Zealand spends half as much per person than Australia does on medicines in the community, and the direct patient costs are less than a quarter.[7] (See endnote *.)

Talk about PHARMAC declining to list "highly cost effective pharmaceuticals" because of a pharmaceuticals budget cap[8] needs some thought. This is not so much because it implies opportunity costs managed by budgeting (which is true[11,12]) but that somehow Australia is funding highly cost-effective medicines that New Zealand is not. The article's Table 3[8] does not state what these medicines are, particularly when many have NZ-funded alternatives, no cost-effectiveness information is provided, and some cost over $100,000 per quality adjusted life year (QALY) in the New Zealand setting.

We well understand the authors' frustration at the lack of available cost-effectiveness information; this is not entirely of PHARMAC's making.[13] ††

Is the size of the list important?—Notwithstanding some data inconsistencies in the article, the more important question relates to the usefulness of the, "my list is bigger than your list" approach for inter-country comparison without a lot more supporting information. For instance in New Zealand there is a reticence to fund "me too" medicines unless there is a financial or other obvious clinical advantage.**

As an example, rosiglitazone (now withdrawn from the market due to safety concerns) was funded in Australia but not in New Zealand; however a similar medicine, pioglitazone, was. Likewise we have two angiotensin II receptor antagonists on the New Zealand Pharmaceutical Schedule (PS) and we can see little extra benefit from the other four funded in Australia.

What really matters?

From an international perspective, the realities of burgeoning health expenditure are beginning to sink in. Many affluent countries are more closely examining ways to not only reduce the growth of expenditure but also to seek ways to identify the best value for money.

The paper by Wonder and Milne[8] adds to the debate.[14] Ultimately however the question is about the quality of health care and the quantity of health gain, rather than

numerical item counts and timecourses. We all agree that trans-Tasman comparisons of health gains from pharmaceutical expenditure invested and forgone may be valuable.[4,5,8,15-19] ‡‡

Competing interests: None.

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Endnotes:

* Standard prescription fees are higher in Australia (up to A$34.20) compared with NZ$3 here for publicly-funded patients—so that Australians pay on average 4½ times the prescription fees of New Zealanders.[7] In addition, proportionately many more prescriptions in Australia will be paid for in full by the patient as they fall under the cost of A$34.20 (note that charge is per dispensing so usually this will provide one month's supply only). Hence Australia's actual prescriptions fees will be likely be much higher than reported.

† Although inter-country assessments sound straightforward, the analysis is in fact complex and results must be interpreted carefully. As has been seen in other settings (e.g. the Karolinska Institute report on the uptake of new cancer drugs and cancer survival, cited by the authors), such comparisons can be fraught (the devil being in the detail).

Detailed criticisms of the Karolinska report included incorrect outcome statistics (using not survival but a medley of prevalence and incidence data), incorrect drug usage data, incomparable time periods, reporting bias with mortality, and confounding (e.g. tobacco use).[9,10]

In addition, New Zealand's expenditure on cancer medicines as recorded by that report was undercounted compared with other countries, as DHB hospital pharmaceutical cancer spend was poorly captured at the time.

As was stated by Michel Coleman:

> "In short, the new Karolinska report uses flawed methods to reach flawed conclusions about the link between cancer drug 'vintage' and cancer survival in European countries. …It is neither premature nor petulant to criticize a 75-page report that invents an incorrect method of estimating cancer survival in a single short sentence, gets the wrong answer, models the incorrect results with drug data for a period some 10 years after the patients were diagnosed, and then concludes that low national survival rates are due to poor access to cancer drugs and slow national drug licensing."[10]

‡ The debate about access to pharmaceuticals often focuses around access to the very newest medicines; however, for health outcomes, it is more important that the population at large has access to the entire pharmaceutical armamentarium on affordable and equitable terms. In this respect, New Zealanders enjoy superior access than our neighbours. Any number of comparisons can be done, and some will favour different views. For example New Zealand spends, in total, half as much per person on pharmaceuticals, has direct patient costs of less than a quarter, fewer restrictions, and lists more treatments than Australia.[7]

§ In the 2 years 2009/10[15] and 2010/11[17] PHARMAC funded 59 new medicines and widened access to a further 68, benefitting an average of 180,000 additional patients each year. This level of investment was aided by government injecting a further $100 million (over 2008/09 baseline) into community and cancer pharmaceuticals, with a further $80 million invested in 2011/12 likely to lead to further increases in the number of medicines funded.

** Often new treatments provide little or no health gains over existing funded treatments, and are relatively poor investments compared with other options in the health sector. There are me-toos of little advantage, and others proposals give relatively little added-value for their added costs.

†† The authors mention the availability of cost-effectiveness results for public scrutiny.[8] In fact withholding of such information has been at the request of the industry itself.[13]

‡‡ During 2010/11 PHARMAC funded 39 new medicines for an estimated 176,000 new patients by the end of 12 months' funding, and widened access to 43 listed medicines for 264,000 additional patients.[17]

QALY data are available for 28 of these 82 new and widened access medicines during that year; in the first year these medicines were (or will likely be) used by 174,000 patients (i.e. actual or estimates for 12 months' use following implementation). Taken over their remaining treatment time spans, with consequent probable improvements in quality of life and/or increased life-expectancy, the new medicines for these patients alone will likely give approximately 4800 QALYs over remaining treatment time spans more than from standard current treatments (ranging between 3,800 and 10,700 QALYs, given uncertainties with the estimates of individuals' time span gains and other assumptions). These QALY estimates are discounted at 3.5% per annum.[17]

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Positive provider interventions for enhancing influenza vaccination uptake among Pacific Peoples in New Zealand

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Abstract

Despite having reported influenza vaccination rates similar to New Zealand Europeans, Pacific peoples have significantly higher rates of infection, hospitalisation and intensive care unit admission than any other group in New Zealand. Much of this may be due to the presence of comorbidities. However, it is in the interest of Pacific health to promote vaccination widely within this group. Little has been written about what prevents and encourages positive vaccination amongst Pacific peoples. This article reviews current themes about vaccination practices amongst ethnic minorities with a view to identifying positive vaccination strategies for Pacific peoples living in New Zealand.

In the 2009 H1N1 pandemic in New Zealand, Pacific peoples had the highest infection rates of any ethnic group within New Zealand with seroprevalence of 49.5% (CI: 35.1-64.0). Hospitalisation and intensive care unit admission rates also surpassed those of other groups.[1] Further, those long-term conditions which are thought to make the consequences of influenza more severe (diabetes, hypertension, asthma and obesity) are rife amongst Pacific Island peoples in New Zealand.[2]

This increased vulnerability to influenza reflects patterns observed in aboriginal and indigenous peoples in other parts of the word. Indigenous peoples in first-world countries consistently have much higher incidence of vaccination-preventable infectious disease than non-indigenous peoples in the same countries as well as worse outcomes.[3]

American Indian and Alaska Native populations had a mortality rate ratio of 4.0 in a group of 12 US states.[4] Similarly, Canadian Inuit had significantly higher rates of both hospital admissions and death from H1N1 infection.[5] Seventy-four percent of those children hospitalised with H1N1 infection in New Caledonia were Melanesian, despite comprising only 57% of the population.[5]

The high susceptibility to influenza is not driven by lack of vaccination alone. Pacific peoples had similar reported vaccination rates to European New Zealanders during the 2009 pandemic.[1] Whilst New Zealand does not have vaccination targets as part of its influenza prevention strategy, it is clear that Pacific peoples would benefit from increased vaccine coverage in order to circumvent the high infection and complication rates experienced by this group.

The fact that Pacific peoples are amongst the better vaccinated of the general population suggests that there is potential to recruit higher participation in a vaccination programme, an option that this manuscript explores.

Little research has been undertaken on Pacific Island populations in New Zealand to understand their attitudes towards vaccinations, and identify both barriers and facilitators of vaccination. This essay uses a traditional narrative approach to the literature to locate a range of themes which NZ health providers might consider to enhance immunisation amongst Pacific peoples.

Our initial step was to search the PubMed and CINAHL databases using the terms vaccination, vaccine coverage, immunization; AND, Pacific, Polynesian and island and their derivatives. As is often the case with understudied populations, this search availed no results, and compelled us to expand our search to include other indigenous peoples, and ethnic minorities.

We hand searched to extend the thematic areas that our initial search revealed, and explored literatures which describe barriers to vaccination, and health promoting practices in other indigenous and minority ethnic groups. We also looked at local publications to contextualise these findings.

From this and from our experience with this population (our first author is a Samoan-born registered nurse), we make recommendations health practitioners in New Zealand might consider in relation to improving vaccination rates amongst Pacific island peoples.

Ethnic minorities and vaccination

Poor vaccination rates have been observed in minorities peoples in other nations, despite, like Pacific peoples in New Zealand, often being more frequently burdened with chronic illnesses that make influenza infection more likely to incur complications. Studies in the US show that white [sic] Americans have an adjusted odds ratio of influenza vaccination of 1.52 (95%CI=1.35–1.71) for influenza vaccination relative to African-Americans.[6] Similar discrepancies are observed amongst Hispanic Americans.

In Australia, influenza vaccination coverage amongst indigenous adults is higher than in non-indigenous. Vaccination is, however, completely funded for indigenous peoples, and only for those 65 years of age and older in non-indigenous. This funding initiative was developed in response to the observation that indigenous peoples were seven times more likely to be hospitalised than their non-indigenous counterparts.[7]

Less has been written about Polynesian peoples. Whilst Pacific peoples in Hawai'i aged 50-64 had similar rates of vaccination to Caucasians (OR 1.1, 95% CI=0.8-1.5); those with chronic disease, on the other hand, had the lowest rates of vaccination of any ethnic group (OR: 0.7, 95%CI: 0.4–1.2).[8]

Vaccination rates in the Pacific Islands may be higher than for Pacific Islanders living in New Zealand. The Cook Island achieved a H1N1 vaccination rate of approximately 98% during in 2010, with those declining due reportedly to religious reasons, or allergy to the vaccine.[9] The H1N1 team made signed editorial newspaper appeals for the public to be vaccinated, reassuring them about the safety of the vaccination and its origins. Vaccination was free, and was delivered in schools, in drop-in clinics and to each of the outer islands.[9]

In Australia, a similar pattern is noted in Aboriginal settings. Influenza vaccination rates, as well as pneumonia vaccinations were significantly higher in National Aboriginal and Torres Strait Islanders if they lived in remote, as opposed to non-remote areas (80% for remote and 52% for non-remote).[10] This speaks to better vaccination practices in more homogenous and less marginalised population settings.

By way of comparison, in May 2010, Samoa received 28,000 doses of HINI vaccine and as of November 2010, 22,489 people had received the vaccination. Whilst this does not constitute a high percentage of the population (total population 180,000), it makes very full use of the limited vaccination which was made available to the country by the World Health Organization, which only provided 10% population vaccination coverage to developing countries.

The priority groups identified by the Samoan Ministry of Health were health workers, pregnant mothers, adolescent and people with chronic illnesses. The vaccination was delivered free by community nurses (outreach nurses) both in the city and rural area. Private clinic/medical centres also immunised clients who requested the HINI vaccine.[11]

Understanding vaccination practices

Lay-professional relationships have been identified as pivotal to vaccine coverage in minority groups. Health professionals have been shown to fall short in providing adequate information about vaccinations to ethnic minorities; in establishing a trusting relationship which could enhance vaccination practices; and in adjusting their communication style to the ethnic group.

Herbert et al reported "missed vaccination opportunities" among ethnic minorities in the United States. African-American and Hispanic patients who visited a primary care service during vaccination weeks for a reason other than vaccination were twice as likely to remain unvaccinated than their white counterparts, even if they did not have "resistant" beliefs about vaccination.[12] The authors describe this as a health care provider failure to provide information to minority groups, and propose that its rectification would result in significant gains in vaccine coverage. This lack of information is accentuated in groups who have English as a second language. Indeed, poor language proficiency was positively associated with lack of vaccination in older adults in the United States.[13]

In New Zealand, the problem of "missed opportunities" has also been noted with childhood, as opposed to influenza, vaccinations, across many groups.[14] Thirty-one percent of a cohort of Tongan children had missed vaccination opportunities (an office visit at which a scheduled immunisation was due but not given).[15]

Speaking the same language, however, does not mean that health belief systems are aligned or that indigenous people and health professionals will understand one another's position. Gruen and colleagues pointed out that not only were concepts of health, illness and medicine unfamiliar to Australian Aboriginal peoples, hospital staff had poor understanding and appreciation of the needs of indigenous people and communities.[16] As Ngata and Pomare have written about Māori people, "For Maori people health & sickness are inseparable from social encounter, economic

endeavours, recreation pursuit, respect for the environment and the maintenance of traditional cultural beliefs and healing practices" (p. 50).

The relationship between providers and patients is linked to vaccination rate. The information-giving skills and accessibility of the general practitioner were positively associated with vaccination.[6] Trust in the GP has featured as contributing to accessing other preventive services by low-income African-American women, emphasising the importance of the health care relationship.[17] However, the time required to build these relationships and provide information is often lacking in high deprivation practices, which may also help explain poor vaccination practices amongst under-privileged ethnic minorities.[6]

African American and Latino adults participating in a focus group echoed the fact that information from their GP was important to their decision to be vaccinated. They described inadequate information about vaccination, and reported insufficient direction from their primary health provider.[18] This is borne out by Lindley et al's study demonstrating that provider recommendation resulted in higher vaccination rates among patients with a negative attitude towards vaccination.[19] African Americans were more likely to have a negative attitude to influenza vaccination. This point is also evident in studies which don't consider ethnicity in particular, but which identify physician recommendation as the most important factor in patient choice to vaccinate,[20] and in parental choice to vaccinate their children.[21]

Vaccination rates are affected by deprivation. If individuals are not included in targeted groups, the cost of vaccination itself may be prohibitive. However, deprivation has effects which go beyond the cost of vaccination itself. Even when services are free, the expense and availability of transportation contributes to poor use of medical services in Australian Aboriginal communities.[16]

Encouraging vaccination

These limited studies do raise issues which should resonate with health care providers in New Zealand who seek to improve vaccination rates among Pacific peoples. They also align with findings about Pacific peoples which have been associated with health matters other than vaccination.

Whilst the systemic barriers to vaccination present in the mainly North American contexts are different than in New Zealand, important factors are nonetheless similar. This brief review clearly highlights the role of the patient-health care provider relationship as it contributes to immunisation disparities with African-American and Hispanic peoples in America.

Improving the vaccination of minority group members involves optimising the opportunities to discuss the benefits of flu vaccine. As we have observed in our own primary practice and position in the Samoan community, personal beliefs of Pacific peoples may be based on misinformation, and may give rise to vaccination avoidance. For example, we have had patients report that the vaccine would result in more and worse complications in case of infection, and that friends and family members had suffered from side-effects.

Countering lay beliefs about the risk of vaccination can arise from better circulation of information between primary care providers, Pacific peoples, and the wider

community. However providers must take the opportunities when they present to discuss flu vaccination with their clients. These are the opportunistic moments when patients visit their providers for other concerns. Waiting for fortuitous encounters alone is not adequate, particularly as Pacific peoples may not receive public health messages as effectively as the wider population.[22] Sending reminder letters in the patient's native language may encourage vaccination requests.

Language has been shown to impact Pacific people's access to and use of health care services for other health concerns. Follow-up phone calls (from a Pacific nurse when possible) should optimise the potential for vaccination requests. Linked with this is the imperative that providers be aware of minority groups enrolled in their medical centre so they can recommend the flu vaccine, as patients are unlikely to ask for it.[21]

Yet, we cannot separate the issues of information from those of trust and suitable communication style. Community leaders are a valuable asset to health prevention strategies in general, and vaccination drives in particular.[23] Faith based leadership is particularly important within Pacific populations, and could increase trust in the vaccination message as has been demonstrated in Hispanic populations.[24, 25] Within the primary practice, attempting to greet Pacific patients in their own language can enhance the patient-health care worker relationship.[25]

Casting vaccination as a community responsibility with flow-on benefits to children and grand-children may be effective in vaccine acceptance. This has been acknowledged as a motivator amongst Pacific Peoples in New Zealand for other health-related decision-making. Keeping the children healthy was touted as a reason for adult smoking cessation by Pacific peoples.[26] This has been seen in other close-knit ethnic communities; concern for families and community was part of the moral code for elderly Chinese people to vaccinate during the SARS epidemic, in adherence to principles of filial piety.[27]

An additional advantage of using external community organisations in vaccination education delivery is that it circumvents practical barriers like transportation, language and family support. The church serves as a community hub; attendance at Sunday and other services is a social expectation to which a large number of the community adhere. If language presents a barrier for some individuals, making contact with them, or even offering vaccinations, in the church or in church-related activities ensures the presence of family members with better English proficiency.

However, community contact must extend to the other health professionals with whom Pacific peoples have regular interaction. Providers might consider working in collaboration with their local pharmacists and other health care workers already established in the community to ensure that the educational messages about the benefit of influenza vaccination are consistent and reinforced with clients not only at the medical centres, but in other health encounters.

Avoiding the missed opportunities highlighted by Herbert and colleagues involves not only educating Pacific peoples about the benefits of influenza vaccination, but educating health care providers about both the frequency and the manner in which they present this information to patients. Messages from health providers to minority peoples may not be tailored to their needs.[12]

Reminder messages and post cards, for example, which are a common means of communicating health reminders within a practice, may not work effectively in a population which does not necessary have English as a first language, and which may not have a strong level of trust in their non-Pacific health provider. With this in mind, the exploration of how we might expand effective message delivery in ways more suitable to this particular population. Using local knowledge provides a powerful support to primary care providers to ensure access to improve the number of vaccinated clients.

Such local knowledge may include understanding practices surprising for main stream health providers such as praying, eating particular foods and employing traditional health practices. Caribbean islanders, for example, see Western medicine as a second, rather than first-tier approach to influenza prevention and treatment.[28] The advice of elders (for example, the Cook Island tūpuna and the Samoan matai) may carry more weight than that of the health professional; enlisting their support would be useful.

Finally, recognising that deprivation may be a barrier to vaccination in Pacific Peoples, as it is to other forms of health care, must be considered.[22] Influenza vaccination is only subsidized for targeted group including pregnant women, the morbidly obesity, those with some chronic diseases, aged over 65 or under 5 in high risk groups. Ensuring that every opportunity for subsidization is explored within this group may increase vaccination requests.

Actions which improve vaccination rates have the potential to provide significant health gains to the Pacific community. The unequal impact of the recent H1N1 pandemic on Pacific peoples punctuates the importance of vaccination in this vulnerable group.

Possible strategies for enhancing influenza vaccination for Pacific Peoples in New Zealand

- Increase opportunistic vaccination opportunities
- Target Pacific Peoples in their own language with reminders and telephone follow-up
- Work with community leaders—including faith-based local pharmacies and other trusted health care providers
- Provide vaccination opportunities in the community: outside of the health care setting
- Stress the community benefit of individual vaccination
- Maximise subsidization opportunities

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THE NEW ZEALAND MEDICAL JOURNAL
Journal of the New Zealand Medical Association

Difficulties in diagnosing soft-tissue sarcomas: a case of synovial sarcoma of the foot

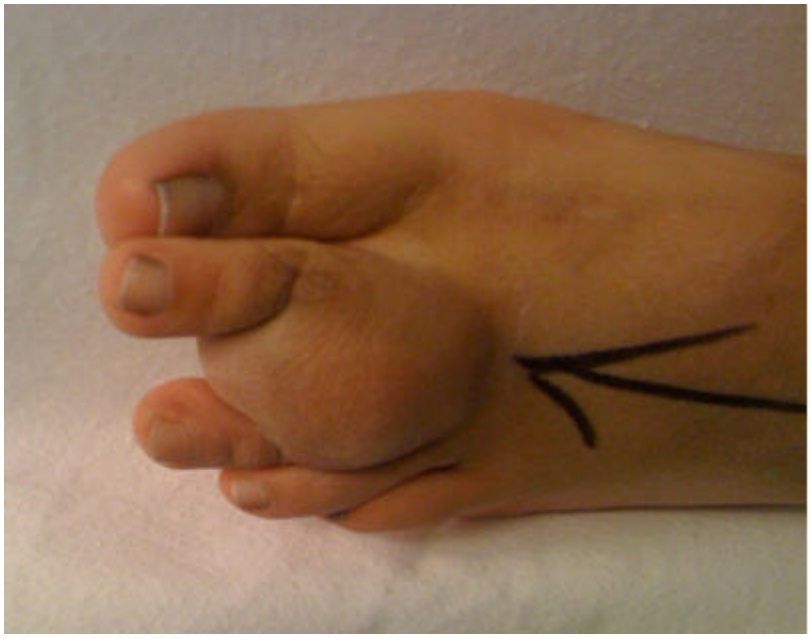
James Blackett

Soft-tissue sarcomas can be difficult to diagnose in the primary care setting, with around 87% of all tumours found in the foot being benign.[1] History and clinical findings can make them difficult to distinguish from benign tumours. Kirby et al found that ganglions make up to one-third of benign tumours of the foot.[1] Synovial sarcoma is the most common malignant tumour of the foot.[1,2]

Case report

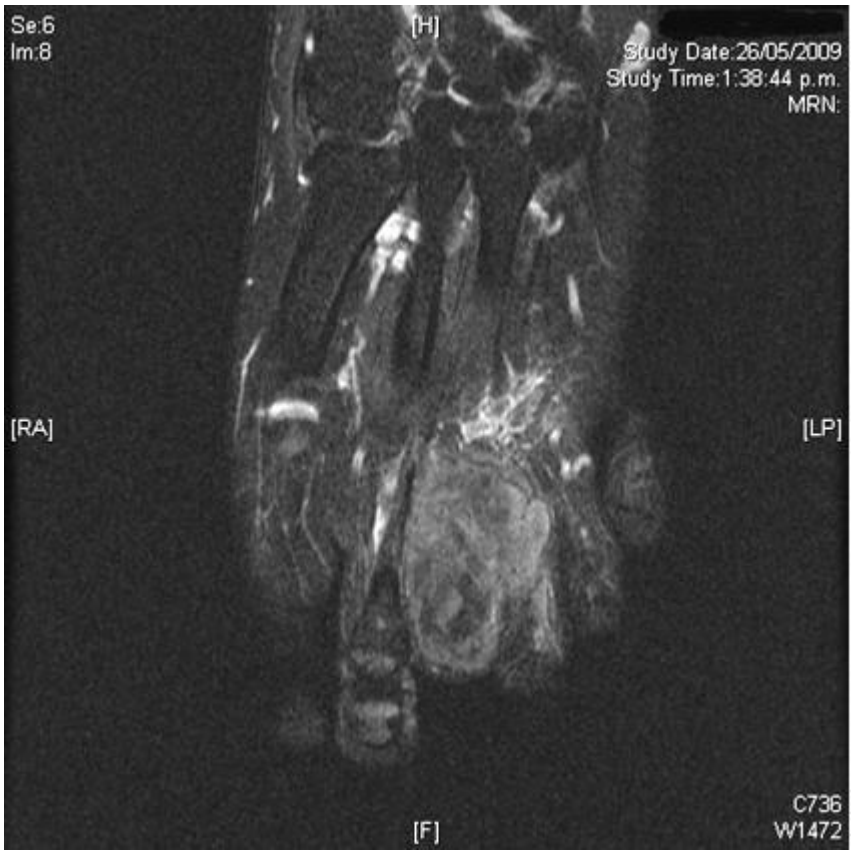
A 39-year-old woman, with a past history of traumatic brain injury and cervical cancer, presented to her general practitioner with a 2-year history of a mass between her second and third toes (Figure 1). It had accelerated in growth over the last 4 months, and on examination was firm and mobile with normal neurovascular findings.

Figure 1. Clinical photograph taken preoperatively. Note the large size of the tumour



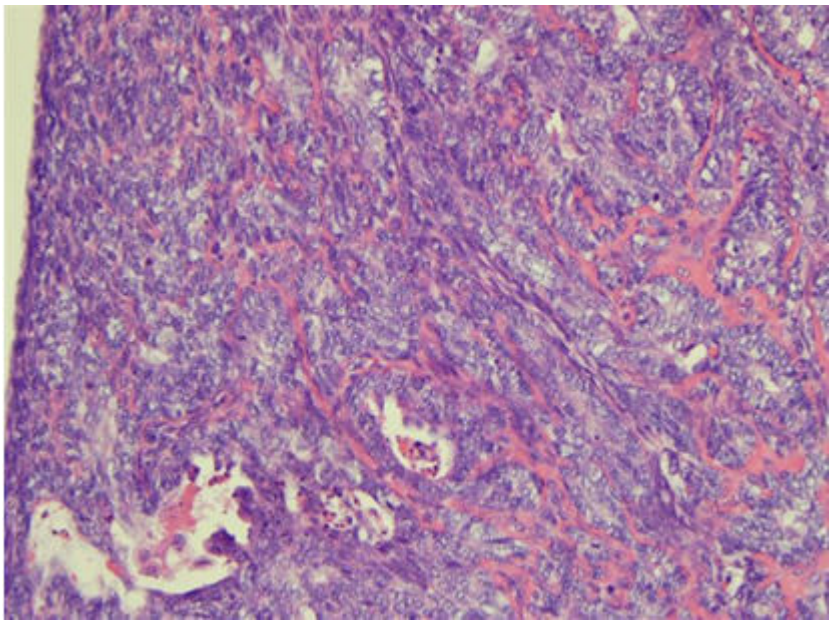
Plain X-rays were normal. Magnetic resonance imaging (MRI) showed a soft-tissue mass measuring 3.1 × 3.3 × 4.1 cm with no bony involvement or apparent association with neurovascular structures. Post contrast there was inhomogenous enhancement (Figure 2).

Figure 2. T2 weighted image showing a well circumscribed lesion between the second and third toes. Note the inhomogenous enhancement of the tumour



The patient went on to have an excision biopsy of a well circumscribed tumour. There was a close association with the digital nerves. Histology revealed biphasic synovial cell sarcoma with spindle cell element (Figure 3). Atypical 18q11.2 SS18 gene rearrangement was detected.

Figure 3. Histological slide showing biphasic cells with spindle cells present



The patient went on to have a normal staging computed tomography scan (CT) of the chest and MRI of the lower limb and was referred to a tertiary tumour centre. She proceeded to amputation of the second and third rays with an uneventful postoperative course. She received a course of adjuvant radiotherapy and is doing well 8 months postoperatively.

Discussion

Soft-tissue sarcomas classically present as a painless enlarging mass.[3,4] Growth can be fast or slow and is often associated with the grade of the tumour, with higher grades tending to be faster growing.[5] Sarcomas are usually non-tender, firm and well circumscribed. They have a tendency to be large in size (>5 cm) and fixed to local tissues.[2,4]

Imaging consists of plain X-rays followed by advanced imaging for local and systemic staging. Plain X-rays can show spotty calcification however this finding is not limited to synovial sarcoma.[3,4] MRI is the best available imaging modality for local staging with low signal intensity on T1 weighted images and high signal on T2 weighted.[2] A CT scan of the chest should be performed to rule out distant metastases.

Biopsy is then performed and should involve consultation with a musculoskeletal oncologist to ensure incisions avoid contamination and allow for adequate limb salvage if required.[2,3,8]

Synovial sarcoma is the third most common soft-tissue sarcoma of the extremity. It accounts for 6–9% of all adult soft-tissue sarcomas.[3,6] Synovial sarcoma is most commonly seen in the extremity (80%) and despite its name is not associated with normal synovial cells.[5,6] Incidence is similar between males and females.[9]

Synovial sarcoma commonly presents as a mass that has been present for months or years that has had recent rapid growth.[2] Common metastatic sights are the lung and peripheral lymph nodes with reported rates over 50% and 10–12% respectively.[5]

Histologically synovial sarcoma presents as one of two subtypes; monophasic or biphasic. Monophasic consists of ovoid spindle cell elements, while biphasic has both spindle cell and epithelial cell components. Over 90% of cases show a characteristic translocation between chromosomes X and 18.

Management is largely surgical with the focus on en bloc excisions through normal tissues planes. This should be performed with either primary excision or include an incisional biopsy site if present. Surgery in the main is limb sparing but amputations are considered, especially in the setting of local recurrence. Surgery has a very limited role in metastatic disease.[5]

Radiotherapy has a role when tumour size is greater than 5 cm and is shown to improve local recurrence rates. Ideally this should be started post operatively to reduce the risk of wound complications. [9]

Survival rates for synovial cell sarcoma vary with 65–75% 5-year survival in those with no metastatic disease on presentation.[2,6,10] This drops to 10–22 months if metastatic disease is present at presentation.

Other negative prognostic factors for survival include tumour size greater than 5 cm and invasion of bone, nerve or vascular structures.[6–8,10] Negative prognostic factors for local recurrence include proximal location and positive margins.[8,10]

This case illustrates the difficulties of distinguishing benign from malignant soft-tissue tumours. The New Zealand Guidelines Group recommends patients with an unexplained mass associated with increasing size or that is hard or tethered to surrounding tissues should have advanced imaging and referral to specialist prior to any biopsy.[11]

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Urinary incontinence in a young girl due to ectopic ureter: the importance of history in a diagnostic challenge

Fatih Hizli, Engin Yilmaz, M Cemil Uygur

Abstract

In girls who are otherwise well and whose history is that of continuous wetting day and night, despite successful toilet training, for a lifelong history, an extravesical infrasphincteric ectopic ureteral orifice should be strongly suspected and imaging should be vigorously pursued. Here, delayed diagnosis of vaginal ectopic ureter in a young girl with a lifelong history of urinary incontinence is presented. The importance of history and imaging procedures are also discussed.

Wetting is a common problem during childhood which includes majority of patients who have no underlying abnormality of the urinary tract. A minority of children are incontinent secondary to structural abnormalities. It is important to recognise these cases which will not improve spontaneously.

Ectopic duplex ureter is a rare cause of urinary incontinence in girls. A constant dribble of urine, every day and every night in a girl who has been successfully toilet-trained is the characteristic story of a young girl who has a ureter that drains ectopically outside the bladder and below the sphincter. This ectopic ureter usually carries urine from upper pole of a duplex kidney.

In this report we present 20-year-old girl with a lifelong history of urinary incontinence due to left duplicated ectopic ureter opening to the vagina. Also, imaging findings of intravenous urography (IVU), ultrasonography (USG) and computerised tomography (CT) are described.

Case report

A 20-year-old girl presented with a lifelong history of urinary incontinence. There were no other associated urinary symptoms and bowel control was normal. She received medical therapy including imipramine, anticholinergics, desmopressin and used alarm devices for diagnosis of enuresis nocturna but, could not be cured. There was no history of trauma or pelvic operation.

Physical examination didn't reveal any evidence of neurological deficit of the lower limbs and perianal region, the anal tone was normal. There was no expressible or distented urinary bladder. Her chief complaint was wetting at night, however, it was detected in detailed anamnesis that she had wetting not only at night but also during the day, the amount of wetting declined through years but not ceased completely. IVU demonstrated left kidney with a missing of upper pole calices (Figure 1).

USG examination showed a cystic mass at the upper pole of the left kidney (Figure 2). Especially in the light of history and IVU findings ectopia of the ureteral orifice draining the upper moiety of a duplex kidney was strongly suspected and CT imaging was performed to confirm this and to determine the side of abnormality. CT scan

revealed a dysplastic duplex kidney located at left upper pole unit and drained by a dilated ureter extending to the vagina (Figure 3-a and 3-b).

Figure 1. IVU demonstrating missing upper pole calices at the left kidney (arrows)

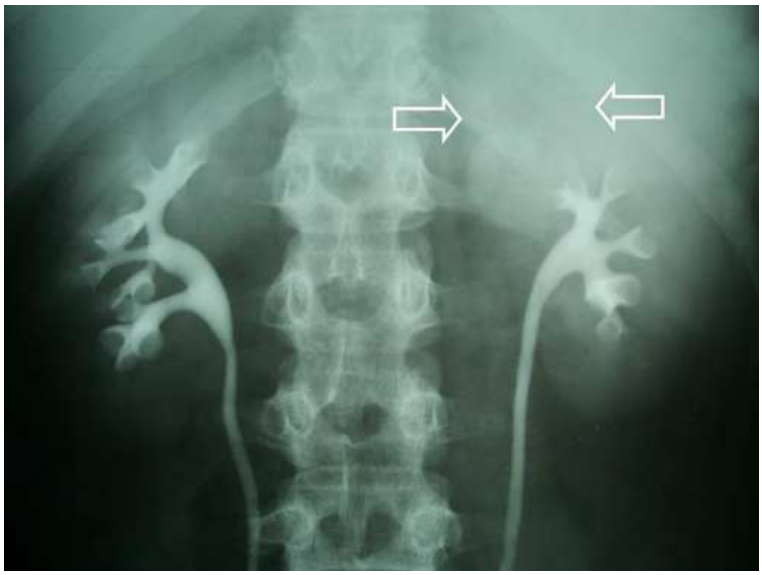


Figure 2. USG demonstrating left kidney with normal lower pole (solid arrow) and dilated dysplastic upper pole (curved arrow).

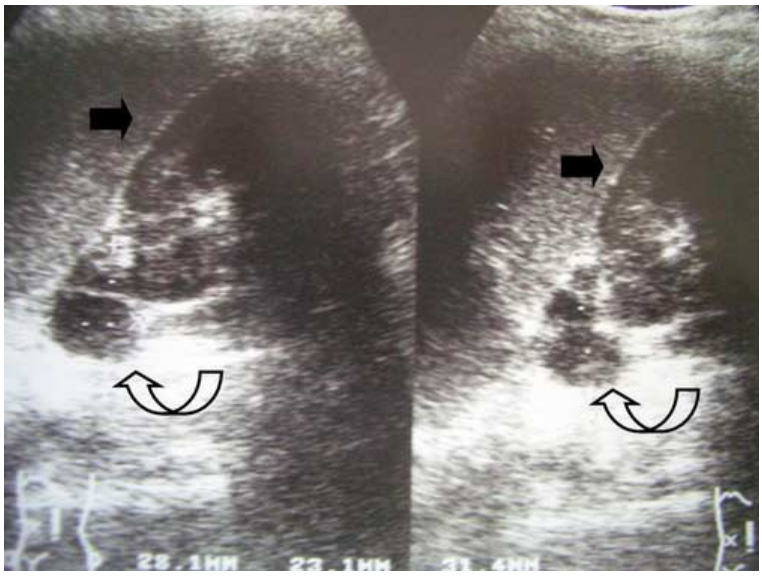


Figure 3-a. CT scan shows dilated dysplastic upper pole segment (left duplicated kidney)

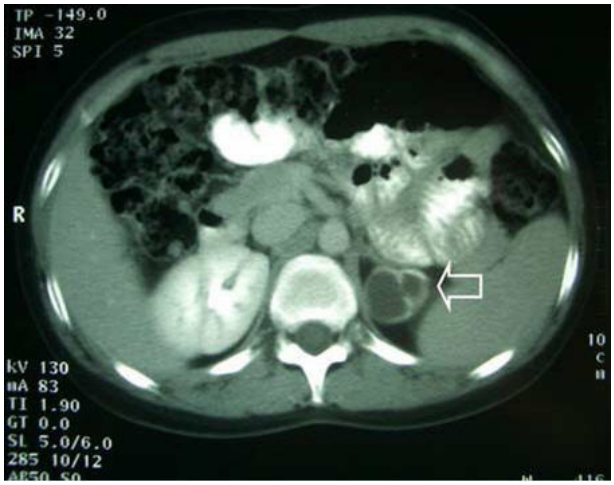
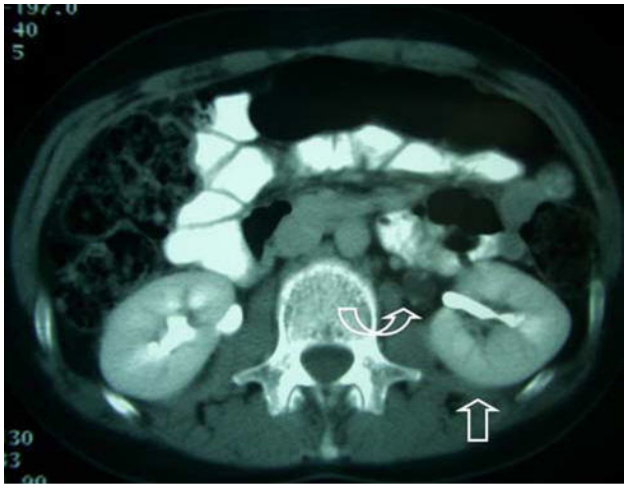


Figure 3-b. CT scan shows normal left lower pole kidney (solid arrow) and dilated ureter of the left dysplastic upper pole moiety (curved arrow)



Exploration of the left kidney demonstrated a dysplastic upper pole segment with a draining dilated ureter. Partial nephrectomy (upper pole heminephrectomy) was performed and the dilated ureter was excised as far as possible with an extensive care not to compromising the blood supply to the ureter of normal lower pole segment. Postoperative recovery was uneventful and the patient was cured of her wetting.

Discussion

Wetting is a common symptom in children and may occur at night, during the day or at both times. Those who wet during the day or both day and night are the ones that need to be investigated. The majority of cases have functional causes. Organic causes are much less common but important because it will not improve spontaneously and may be curable with surgical intervention. Anatomic abnormalities causing incontinence of urine include spinal dysraphism, sacral agenesis and epispadias. Such conditions are usually evident on careful physical examination of the back, perineum, and lower extremities.

In girls who are otherwise well and whose history is that of continuous wetting day and night, despite successful toilet training, for a lifelong history, an extravesical infrasphincteric ectopic ureteral orifice should be strongly suspected and imaging should be vigorously pursued.

An ectopic ureter as a cause of wetting is well documented [1]. Ureteral ectopia with incontinence is uniquely female, because the most caudal location for an ectopic ureteral orifice in a male is always above the urethral sphincter [2]. Its diagnosis may be delayed due to inadequate medical history but often may be suspected from detailed medical history and the clinical presentation with a characteristic pattern of wetting, as exemplified in the present case.

As a result, a detailed history, including the pattern of wetting, and a thorough physical examination supplemented with appropriate investigations usually lead to a diagnosis [3]. In the majority of cases the ectopic ureters are derived from the upper moiety of duplex kidneys. Ectopia of the ureteral orifice is often associated with dysplasia of the kidney or of that portion of the kidney drained by the ectopic ureter. As a rule, the more ectopic the orifice the worse will be the dysplasia [4].

The majority of ectopic ureters associated with renal duplication can be diagnosed by clinical history, renal and bladder USG or IVU. USG often shows evidence of a duplicated collecting system with hydronephrosis of the upper pole of the collecting system. A dilated ureter is often visualized posterior to the bladder.

Findings on IVU vary based on amount of renal function present, and range from functioning upper pole moieties associated with hydroureteronephrosis to poorly functioning upper moieties with downward and lateral displacement of the lower pole collecting system (The "drooping lily" sign). However, when the upper pole ectopic ureter is not dilated and the kidney is small, dysplastic, poorly functioning, findings on USG and IVU are often inconclusive. Therefore, additional diagnostic procedures including, renal scintigraphy [5], CT [6, 7] and MR [8, 9] are recommended. In our patient IVU suggested poorly functioning segment at the upper pole of left kidney, USG revealed a cystic mass in the upper pole. To maximize our diagnostic sensitivity we performed CT and detected a left duplex kidney located at left upper pole unit and drained by a dilated ureter extending to the vagina.

In conclusion, girls with continuous wetting should be considered to have an ectopic ureteral orifice until proved otherwise. IVU with CT is indicated to confirm the suspicion and to show the side or sides of involvement. In most cases IVU will be diagnostic. However, when the history is highly suggestive and the urographic findings seem normal, enhanced CT may show the abnormality, which is almost certainly present.

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THE NEW ZEALAND MEDICAL JOURNAL
Journal of the New Zealand Medical Association

Primary oral tuberculosis

Tapan D Bairagya, Sibes K Das, Dilip C Barman, Somnath Bhattacharya

A 46-year-old non smoker, non-diabetic man presented to us complaining of an ulcer in the mouth which had been present for the last 6 months and was gradually increasing in size. Oral cavity examination revealed a single discrete ulcer of less than 1 cm in diameter present on the left buccal mucosa. The ulcer was bordered by ill-defined margins around which were several small ridges like swellings. On palpation, the ulcer was tender with indurated margins (Figure1). There was no cervical lymphadenopathy.

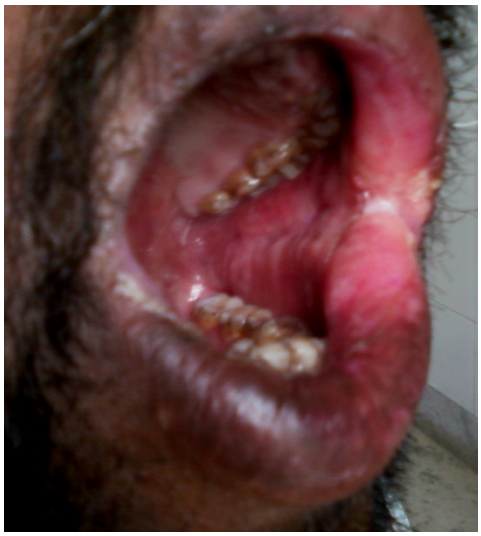
Systemic examination was unremarkable. His serology for HIV was negative. Incisional biopsy was taken from the edge of the ulcer. The histopathology showed multiple confluent and discrete granulomas composed of epithelioid histiocytes and Langhans giant cells and having no evidence of malignancy (Figure 2).

Mantoux test was positive (23 mm × 20 mm) with 1TU PPD. Sputum smear for acid-fast bacilli was negative. Chest X-ray (PA View) was normal. We started anti-tuberculous therapy with WHO Category – I regimen.

Six months later at follow up, the oral ulcer had healed with some fibrosis.

Figure 1. Oral cavity showing ulcer over the left buccal mucosa (A), before treatment; (B), after 6 months of antituberculous drug intake

(A)



(B)

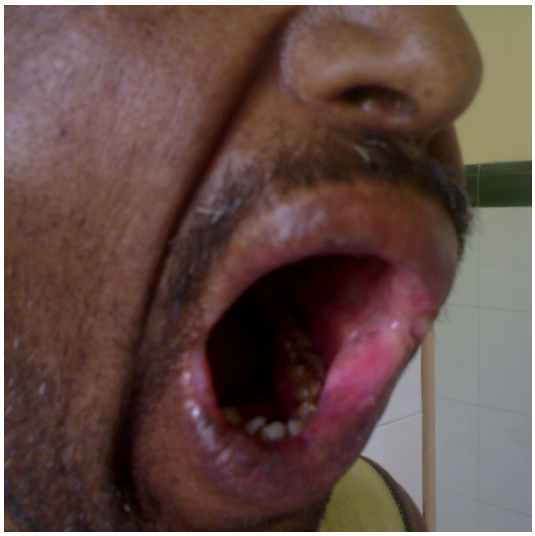
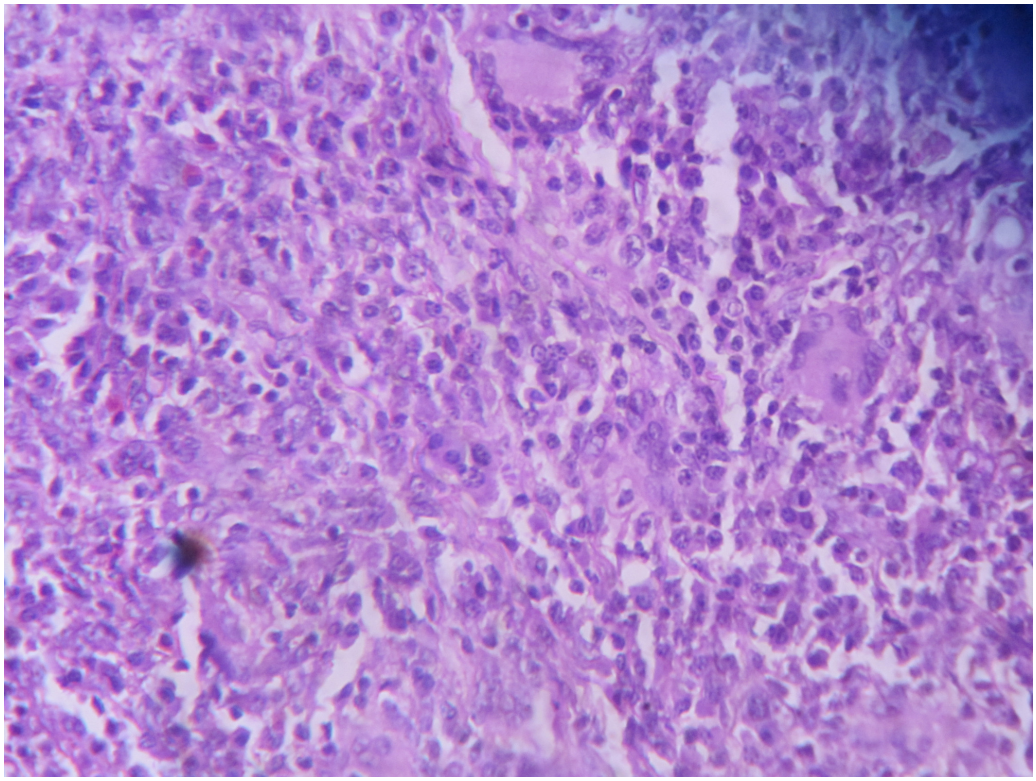


Figure 2. Histopathology of the biopsy material showing multiple confluent and discrete granulomas composed of epithelioid histiocytes and Langhans giant cells (H&E stain, ×100)



Discussion

Differential diagnosis of granulomatous ulcer of the oral mucosa are tuberculosis, sarcoidosis, fungal infection, Wegener's granulomatosis, foreign body granuloma etc. The primary occurrence of oral tuberculosis is very uncommon. The presenting symptoms of oral tuberculosis are ulceration, swelling, cervical lymphadenitis, fever, focal pain, nonhealing extraction wound. Most common presentation is ulceration.[1]

Oral tuberculosis usually coexists with pulmonary disease. Primary oral tuberculosis can occur in any age group. It usually involves the gingiva, mucobuccal folds, inflammatory foci adjacent to teeth or extraction sites, and it often is associated with enlarged cervical lymph nodes.[2]

Whether primary or secondary oral tuberculosis, early detection, diagnosis, and treatment are the utmost importance.

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Journal of the New Zealand Medical Association

Pulmonary popcorn

Prem P Gupta, Krishan B Gupta, Dipti Agarwal

Clinical

A 38-year-male with no clinical symptoms underwent chest radiology for an employment-related assessment (Figure 1). A CT was also performed (Figure 2).

Figure 1. Chest radiograph postero-anterior view, showing a 3.8 cm × 3.0 cm sized solitary pulmonary nodule with areas of calcification and fat density, classically described as popcorn calcification

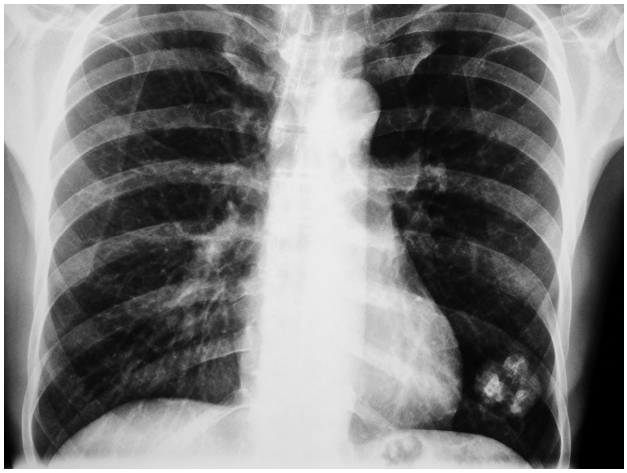
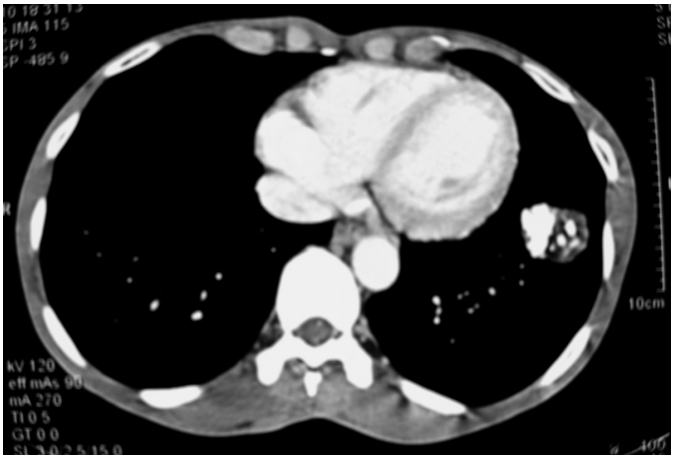


Figure 2. CT scan



What is the diagnosis?

Answer

The CT thorax, axial view, shows a solitary pulmonary nodule with smooth margins, irregular (popcorn) calcification, and areas with intermingled fat density—all characteristics of *pulmonary hamartoma*.

Bronchoscopic examination revealed no endobronchial lesion with a non-contributory bronchoalveolar lavage fluid. He was advised for fine needle aspiration cytology of the pulmonary nodule to rule out alternative diagnoses but he did not consent. He has been on regular follow up for last 18 months and has no change in the opacity.

Discussion

A hamartoma is a solid tumour of the bronchus which consists of benign mesodermal and epithelial elements.[1] Hamartomas are believed to arise from embryologic rests that are present since fetal life but manifest usually during adulthood. It is composed of tissue elements normally found at that site, but which are growing to a disorganised mass. Hamartomas may be chondromatous or leiomyomatous or a mixture. They are unencapsulated, lobulated tumours with connective tissue septa.

The prevalence of hamartomas varies from 0.025%[2] to 0.32%[3] across various large studies. They typically manifest between 40 and 60 years of age, with a ratio of 3 men to 1 woman. They may occur at various sites, the most frequent being in the lungs. Endobronchial hamartomas comprise only 1%–19.5% of cases. Hamartomas can cause problems due to their location. They may obstruct practically any organ in the body, such as the eye, the colon, etc.

Intrapulmonary chondromatous hamartoma is the most common variant. The majority of intrapulmonary hamartomas is solitary, less than 4 cm, peripheral in position and produces no symptoms. A few central hamartomas may obstruct a bronchus with progressive atelectasis, pneumonitis, fever, cough, expectoration, and chest pain. Hemoptysis is rare.

On a chest radiograph, a pulmonary hamartoma usually appears as a sharply demarcated solitary pulmonary nodule with a typical volume doubling time of over 400 days. Computed tomography is far superior in detecting intra-lesional fat and calcification. The calcification in hamartomas on CT can be seen in 5% to 50% while fat may be identified in up to 50% of hamartomas. Calcification is typically dispersed in the form of multiple clumps throughout the lesion in a *popcorn configuration*. Presence of fat in a well circumscribed solitary pulmonary nodule which does not demonstrate significant growth is pathognomonic of a pulmonary hamartoma.[4]

Malignant transformation of a hamartoma is exceedingly rare. Isolated reports of squamous cell carcinoma, adenocarcinoma and sarcoma developing from hamartomas have been described[5,6] and due to this reason, surgical removal of pulmonary hamartoma is often recommended.[7] The recurrence of a hamartoma is highly improbable.

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THE NEW ZEALAND MEDICAL JOURNAL
Journal of the New Zealand Medical Association

Screening for prostate cancer is not recommended

Lamb et al argue for population-wide testing with the PSA test for prostate cancer.[1] Their argument is that screening saves lives. However, they ignore the complexities of screening for prostate cancer, and the large potential for doing harm.

Firstly, the evidence for a mortality benefit is weak. It is true that the US PLCO trial was heavily contaminated, possibly beyond repair.[2,3] Lamb et al therefore prefer to rely on the European ERSPC and Swedish Gotenburg trials, that both showed a statistically significant mortality benefit.[4,5] What they do not mention is that the Gotenburg trial is part of the ERSPC, and when its results are removed from the analysis, the ERSPC mortality benefit is no longer statistically significant.[6] So in the end the argument of Lamb et al is based on results from a single trial, that happens to be one with a design that makes it vulnerable to selection bias.[6]

In addition to this single positive trial result there is some observational evidence that the prostate cancer mortality decline in US and UK may be due to screening, but of course this evidence comes with all the caveats about the confounding that observational studies are subject to.[7–9] In all, not a strong case.

Secondly, even if we accept the case for a mortality benefit, Lamb et al completely ignore the elephant in the room. That elephant is called overdiagnosis and overtreatment. Screening leads to overdiagnosis because many tumours detected by screening would never become clinically apparent within the lifetime of the patient, and for prostate cancer the risk of overdiagnosis is clearly large.[5,9,10] And overdiagnosis leads to overtreatment because we cannot reliably predict which cancers will progress and which will stay indolent. The side-effects of treatment for prostate cancer are severe.[11]

Therefore the decision to screen or not cannot be based on the simple argument that it saves lives (even if we accept it does), but it must make the difficult balance between reduced mortality and increased morbidity.

For the Assessing Cost-Effectiveness of Prevention study we did an analysis using the results from the ERSPC trial on mortality reduction and incidence increase.[12] We used disability-adjusted life years (DALYs), an outcome measure that combines mortality and morbidity, to evaluate prostate cancer screening. Our results show that screening does indeed decrease prostate cancer mortality, but that in a screened population more disability adjusted life years are lost than in an unscreened one. We therefore concluded that prostate cancer screening is not recommended.

We are not alone. The U.S. Preventive Services Task Force is in the process of revising its previous recommendation for screening of men under 75 years of age to one of not screening at all, based on a similar line of reasoning outlined above: the evidence for mortality benefit is weak, and for harm is strong.[13]

One would wish the New Zealand men a more serious discussion than the simplistic statement that screening saves lives.

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THE NEW ZEALAND MEDICAL JOURNAL
Journal of the New Zealand Medical Association

A regional non-melanoma skin cancer (NMSC) collection as part of the National Cancer Registry

We support the view of Brougham et al that monitoring the control of non-melanoma skin cancer (NMSC) in New Zealand has not been given enough emphasis.[1] NMSC is an important cancer in New Zealand, as the high NMSC incidence rate and high volume of patients create considerable annual cost to the health service. In addition, NMSC was the cause of 122 deaths in New Zealand in 2007. A minimum data set should be established to monitor this cancer.

We suggest that a regional collection of NMSC be part of the New Zealand Cancer Registry, with the aim of monitoring NMSC and facilitating evaluation and research into reducing the burden of this disease.

A region with the following characteristics would be appropriate:

- **A population size just large enough to obtain a useful annual number of registrations.** A manageable data collection is required with up to 2000 new cases of NMSC per year. Collection of data for new diagnoses of NMSC for the whole country would swamp the Cancer Registry.
- **A relatively contained geographical region.** A population with an easily defined geographical and health service region with sparsely populated borders.
- **Low external migration, particularly among those 60 or more years of age.** A place considered a retirement area would be appropriate.
- **Relatively high sunshine hours.** This would facilitate assessment of the short-term effects of sun exposure, a major causative agent.
- **A single pathology reporting laboratory** for ease of data collection.

In addition, there are likely to be advantages from using a defined DHB region regarding data collection and linkage to treatment or other data. An area of New Zealand that would appear to meet most of these requirements is the Nelson-Marlborough DHB region with a population of about 130,000 people. A published estimate of NSMC incidence[2] suggests that about 750 new diagnoses of NMSC are likely in the Nelson-Marlborough region each year.

We suggest that the feasibility of establishing a complete, timely, and accurate NMSC collection for the Nelson-Marlborough DHB as part of the New Zealand Cancer Registry be assessed. The scope of the Cancer Registry Act to cover such a data collection also needs to be examined.

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THE NEW ZEALAND MEDICAL JOURNAL
Journal of the New Zealand Medical Association

Valuation of lives 'saved' via control of urban air pollution

Since per capita health costs rise steeply towards the end of life, the problems referred to by Dr Victor Fuchs[1] mainly relate to care of elderly people. Developed countries currently spend about 50% of their health budget on people aged over 65 comprising about 13% of their populations.[2]

Considerable incentive for preserving life via control of urban air pollution undoubtedly is provided by the availability of established, fixed, values for a statistical life (VOSL) put typically at around US$2–3M.[3] When combined with statistically-derived numbers of potentially avoided/delayed deaths this can lead to the calculation of highly favourable, but nonetheless conjectural, benefit/cost ratios.[4]

However, if instead of reduced numbers of deaths, increased life expectancy results[5] as an altogether more credible consequence of air pollution control, what then? Is it not likely that, with this point accepted as valid, the alleged positive dollar benefits conferred, based on the value of an average life saved, will turn out to be imaginary? If so, an adjustment of priorities here, too, may well be overdue.

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THE NEW ZEALAND MEDICAL JOURNAL
Journal of the New Zealand Medical Association

Waikato DHB website and Thames Hospital: a response to Dr Ridley-Smith's letter

I'm astonished you allowed Dr Roger Ridley-Smith's letter (http://journal.nzma.org.nz:8080/journal/124-1345/4951/content.pdf) to be published without referring it to us here at Waikato District Health Board so that we could at least have the right of reply and the opportunity to correct the mistakes in it.

There are many photographs of individual doctors in the employ of the Waikato DHB—they appear on department-specific pages, so e.g. cardiothoracic http://www.waikatodhb.govt.nz/page/pageid/2145839481 and also here http://www.waikatodhb.govt.nz/page/pageid/2145864357/Our_medical_team where we've profiled some of our doctors and nurses.

I'd be keen to have pictures of every single doctor working for Waikato DHB on our website. Having features on all the senior doctors is a particular aim of mine but not all senior doctors want their pictures and profile on our website.

We have about 300,000 hits a month to our website—up from 26,000 4 years ago. Eighty percent of those who visit the site are looking for a job/career at Waikato DHB. The focus of our website therefore must be on the people who visit it and the information they require.

If the point of Dr Ridley-Smith's letter was that he wanted to find a GP in Thames then we have a heading primary health care http://www.waikatodhb.govt.nz/page/pageid/2145868508/Primary_Health_Care which lists all the primary health care organisations in the Waikato DHB area.

If his point was that our website is muddled then I'm happy to take that on board and review it.

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THE NEW ZEALAND MEDICAL JOURNAL
Journal of the New Zealand Medical Association

Quackery and Proprietary Medicines: Part 1

Published in Dominion Notes section of NZMJ May 1912:11(42):136–138.

The two following excerpts from the recent numbers of the *Chemist and Druggist of Australasia* exemplify the general tone of this the official organ of the Trade towards the medical profession in general while dealing with the question of Quackery and Proprietary Medicines. The first article is a review of a booklet by Henry Sewill, and the second is an Editorial on several subjects. We are of opinion that these views should be better known by members of our profession, and we can see that we are plainly not both working for the same object in regard to repressing the sale of Proprietary Drugs as a whole.

It is admitted that much cruel quackery exists, but it is not recognised that a great cruelty exists in the criminal charges that are made for valueless drugs. We recently ordered some P.D and Co. pills, which are listed at 1/6 per hundred, when our patient said he could not continue with them on account of the price, and I found he was being charged at the rate of 2/-.per dozen.

We are also aware that even reputable chemists tend to make capital on prescriptions, especially if any maker of drug is specified, whether the individual drug adds to the cost or not, and we have long been of the opinion (and on reading this C. and D. A. are more firmly convinced) that it would be to our patients' and our own interests if we established a dispensary where only our own prescriptions could be made up, and where we could guarantee our drugs, and control their price to our patients, it being optional to the patient whether he went to a trading chemist or the dispensary. We append the two articles in question:-

Part 2 (the two articles) will appear in the next issue: 16 December.

THE NEW ZEALAND MEDICAL JOURNAL
Journal of the New Zealand Medical Association

Proceedings of the 210th Scientific Meeting of the Otago Medical School Research Society: Wednesday 9 November 2011

THE NEW ZEALAND MEDICAL JOURNAL
Journal of the New Zealand Medical Association

Do hormones protect women from ischaemic heat disease?

Although heart disease mortality increases with age, it was thought to be lower in women than in men because of the protective effects of premenopausal hormone levels. This proposition is examined in this paper which reviews three birth cohorts in England and Wales and the US and their subsequent incidence of death from ischaemic heart disease. They regarded 45 years of age to be the average age of menopause and their findings were that heart disease mortality in women increased exponentially with age, with no acceleration after age 45 years.

On the other hand they report that in men there was a rapid increase during young adulthood followed by a deceleration in mortality rates after age 45 years. They suggest that the early rapid acceleration seen in male heart disease mortality could explain these sex differences rather than menopausal changes in women.

BMJ 2011;343:5170.

Can the anticoagulant effects of rivaroxaban and dabigatran be reversed by prothrombin complex concentrate (PCC)?

Currently dabigatran (a direct thrombin inhibitor) and rivaroxaban (a direct factor Xa inhibitor) are the most extensively evaluated novel anticoagulant agents. Neither of these drugs require monitoring blood tests and neither have significant interactions with other drugs. Their anticoagulant effects are comparable with warfarin. However, to date, no method of reversing their effects has been demonstrated. In this randomised, double-blind, placebo-controlled study, 12 healthy male volunteers received ribaroxaban 20mg twice daily (n=6) or dabigatran 150mg twice daily (n=6) for 2½ days. This was followed by a single bolus of PCC (50 IU/kg) or a similar volume of saline. They report that PCC immediately and completely reverses the anticoagulant effect of rivaroxaban in healthy subjects but has no influence on the anticoagulant action of dabigatran at the PCC dose used in this study. Encouraging.

An editorial writer notes these results but points out that they need to be confirmed in the real life setting—viz will the PCC reverse the bleeding as well as the blood tests? She also points out that there is some variability in different PCC formulations.

Circulation 2011;124:1573-9 & 1508-9.

New guidelines for hypertension management in UK

The recent updated guidelines from the National Institute for Health and Clinical Excellence (NICE) on the management of hypertension in adults are not without interest and are relevant to our situation. They recommend ambulatory or home blood pressure monitoring to avoid the over treatment of people with “white coat” hypertension.

For the first time, targets have been partially relaxed. Admittedly this applies only to people aged 80 or more, in whom a target blood pressure lower than 150/90mmHg is recommended. The previous target of 140/90mmHg is retained for everyone else. Thiazides are no longer recommended as first line drugs unless other indications exist. Calcium channel blockers are preferred first drugs for patients over 55 years and angiotensin converting enzyme inhibitors or angiotensin receptor blockers are recommended for younger patients. It is acknowledged that many patients will need a combination of drugs for optimal management.

BMJ 2011;343:5644.

Chronic obstructive pulmonary disease (COPD) – lifetime risk

This paper from Canada sets the scene by noting that the World Health Organisation has declared chronic obstructive pulmonary disease the fourth most common cause of death worldwide and estimates that it will be the third by 2030. They performed a retrospective longitudinal cohort study from health records in Ontario (population roughly 13 million).

All individuals free of COPD in 1996 were monitored for up to 14 years for three possible outcomes; diagnosis of COPD by a physician, reached 80 years of age, or death. Well over half a million individuals were diagnosed as having COPD over the study period. The precise figure was 27.6% lifetime risk by the age of 80 years. It was higher in men (29.7%) than in women (25.6%). They advocate a more aggressive approach to detection, prevention and management.

Lancet 2011;378:991-6.

Oral teriflunomide for relapsing multiple sclerosis

Teriflunomide, the active metabolite of leflunomide, has been shown in phase 1 and 2 trials to possibly be useful in the management of relapsing multiple sclerosis. This report concerns a phase 3 randomised trial comparing two dosages of teriflunomide with a placebo. 1008 patients with multiple sclerosis who had previously suffered at least one relapse in the previous year or at least two relapses in the previous two years were entered in the trial. They were randomly assigned (in a 1:1:1 ratio) to placebo, 7mg of teriflunomide, or 14mg of teriflunomide once daily for 108 weeks. The primary end point was the annual relapse rate and the secondary end point was disability progression.

Their conclusions were that teriflunomide significantly reduced relapse rates, disability progression (at the higher dose), and MRI evidence of disease activity, as compared with placebo. Diarrhoea, nausea, and hair thinning were more common with teriflunomide than with placebo. However, these events rarely lead to discontinuation of treatment.

N Engl J Med 2011;365:1293-303.

THE NEW ZEALAND MEDICAL JOURNAL
Journal of the New Zealand Medical Association

Grants Awarded November 2011

At the November meeting of the Scientific Advisory Group of the National Heart Foundation, a total of 19 grants were awarded. The awards included 9 Small Project Grants, 1 Grant-in-Aid and 9 Travel Grants.

SMALL PROJECT GRANTS

Dr Alexandra Chisholm

Department of Human Nutrition, University of Otago, Dunedin

The Nuts2 Study

$14,807 for 1 year

Dr Scott Harding

Department of Cardiology, Wellington Hospital

High on treatment platelet reactivity in acute coronary syndromes.

$14,000 for 30 months

Dr Regis Lamberts

Department of Physiology, University of Otago, Dunedin

Effect of β_2-adrenoceptor function in the human diabetic myocardium.

$14,655 for 1 year

Assoc Professor Welma Stonehouse

Institute of Food, Nutrition & Human Health, Massey University (Auckland)

Fruit and vegetables and cardiovascular disease risk.

$14,886 for 1 year

Dr Anna Rolleston

The Cardiac Clinic, Mt Maunganui

A Kaupapa Maori exercise and education based programme for cardiovascular risk education.

$13,294 for 1 year

Dr Jun Lu

Faculty of Health & Environmental Sciences, AUT University

SSAT in human heart.

$15,000 for 1 year

Ms Susan Waterworth

School of Nursing, University of Auckland

'It's just not about heart failure': optimising the primary health care (practice nurse) role as a navigator in supporting patients with multiple long term conditions, and their family/whanau.

$14,975 for 9 months

Dr Arlo Upton

Microbiology Department, Labtests, Auckland

Throat swabs for diagnosis of group A streptococcus (GAS) pharyngitis: comparison of rapid antigen diagnostic test (RADT) using flocked swabs to conventional swabs in a high risk population of children.

$8,786 for 18 months

GRANT-IN-AID

Mr Jesse Ashton

Auckland Bioengineering Institute, University of Auckland

Research internship for study titled 'Influence of autonomic stimulation on the genesis of atrial arrhythmias in heart failure'.

$3,222 for 1 year

TRAVEL GRANTS

Mr Nathan Cowie

Centre for Tobacco Control Research, Social & Community Health, University of Auckland

15th World Conference on Tobacco or Health, Singapore.

Assoc Professor Nick Wilson

Department of Public Health, Te Tari Hauora Tumatanui, University of Otago, Wellington

Studying cigarette butt littering to inform smokefree street policies: A new methodology and results.

$3,619 for 4 months

Ms Christina Ergler

School of Environment, University of Auckland

32nd International Geographical Congress - Down to Earth, Cologne, Germany.

Mr Anjeela Kumar

National Addiction Centre, Department of Psychological Medicine, University of Otago, Christchurch

15th World Conference on Tobacco or Health, Singapore.

Ms Catherine Lizamore

Department of Social Science, Parks, Recreation, Tourism & Sport, Lincoln University

American College of Sports Medicine: 59th Annual Meeting and 3rd World Congress on Exercise is Medicine, California, USA.

Dr Jun Lu

Faculty of Health & Environmental Sciences, AUT University

20th Annual Scientific Meeting of International Society for Magnetic Resonance in Medicine, Melbourne, Australia.

Ms Suzanne Mavoa

SHORE & Whariki Research Centre, School of Public Health, Massey University

Geographic Information Systems Research UK Conference, Lancaster, & SenseCam Symposium, Oxford, UK.

Ms Karen Peebles

Department of Surgery & Anaesthesia, University of Otago, Wellington

17th Meeting of the European Society for Neurosonography and Cerebral Haemodynamics, Venice, Italy.

Dr Anna Pilbrow

Department of Medicine, University of Otago, Christchurch

American Heart Association Scientific Sessions, Orlando, USA.

Dr John Thompson

Department of Paediatrics: Child & Youth Health, University of Auckland

1st International Conference of Nutrition and Growth, Paris, France.