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

CONTENTS

This Issue in the Journal

Editorial

Original Articles

Review Article

Viewpoint

Clinical Correspondence

Letters

100 Years Ago in the NZMJ

Medical History

Methuselah

Obituary

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

This Issue in the Journal

Abdominal aortic aneurysm disease in New Zealand: epidemiology and burden between 2002 and 2006
Nisha Nair, Caroline Shaw, Diana Sarfati, James Stanley

Abdominal Aortic Aneurysms (AAAs) are spontaneous dilatations of the abdominal aorta that are most common in older men. AAAs expand asymptomatically until rupture, unless the individual dies of another cause before this. Rupture carries a high mortality of 80-90% as patients often die before reaching hospital, and also because emergency repair carries high mortality. Detection of AAAs before rupture by abdominal ultrasound scans allows elective repair, which has a lower mortality.

There is international evidence that ultrasound screening at a population level reduces mortality from AAA. Little is known about AAA disease in New Zealand. This study has found that there were about 230 deaths annually in NZ from AAA disease between 2002 and 2006. There were 267 elective repairs and 87 emergency repairs annually. The standardised mortality rate in Māori was twice as high as New Zealand Europeans. This study provides essential information to evaluate the appropriateness and feasibility of AAA screening here.

Funding community medicines by exception: a descriptive epidemiological study from New Zealand
Dilky Rasiah, Richard Edwards, Peter Crampton

This study assessed rates of approval and tried to identify factors associated with successful applications for funding to the then current New Zealand Community Exceptional Circumstances (CEC) scheme. It found that there was no evidence that gender, ethnicity and socioeconomic status of patients were factors associated with successful applications. However, applications for younger patients, those made by specialists, and those made by applying clinicians from the Auckland District Health Board area were more likely to be successful. It is possible that this may to some degree be appropriate, but requires further research.

Blinded randomised controlled study of the effect of a discharge communication template on proton pump inhibitor prescribing
Alex Lampen-Smith, Janice Young, Mary-Anne O'Rourke, Astuti Balram, Stephen Inns

The use of proton pump inhibitors continues to increase with associated cost implications and increasing concerns regarding complications of long term use. The existing New Zealand guidelines for the use of proton pump inhibitors have been shown to be poorly adhered to, at least where patients are discharged from hospital on a proton pump inhibitor. This study attempted to use a strategy utilising discharge communication to GPs to increase adherence with the NZ guidelines in patients

discharged from hospital on proton pump inhibitors. This strategy was not shown to be more effective standard discharge information. Investigation into other strategies that might improve adherence with the NZ guidelines are warranted.

A review of interferon use in patients with relapsing remitting multiple sclerosis in the Canterbury region, New Zealand: 2000–2006
Susan Byrne, Deborah Mason

We report a retrospective medical chart review of 104 patients resident in Canterbury and surrounding districts with relapsing remitting multiple sclerosis (RRMS), who received funded interferon-beta between 2000 and 2006. The aim of the study was to review relapse rates, Expanded disability status scale (EDSS) scores and intravenous methylprednisolone (IVMP) use in the 2-year period before, and following, the initiation of interferon-beta therapy. Demographic analysis showed that the age at entry, duration of disease and EDSS at entry were each greater than in the landmark clinical trials. Relapse rates and usage of IVMP decreased when compared to the 2 years prior to treatment.

Incidental vertebral fractures on computed tomography
Pui Ling Chan, Taryn Reddy, David Milne, Mark J Bolland

Spinal fractures are common in elderly people and are a risk factor for subsequent fractures and mortality. We assessed whether routinely looking for spinal fractures on computed tomography (CT) scans of the chest/abdomen (performed for other reasons) would identify previously unrecognised spinal fractures. We found that 1 in 8 patients aged >65 years having a CT scan had a vertebral fracture, but the fracture was not mentioned in the discharge summary or clinic letter for the majority of people with fracture, and few were offered specific treatment to prevent future fractures. We concluded that looking for spinal fractures on CT images provides an opportunity to detect fractures that otherwise would be unrecognised and offer effective treatment to prevent further fractures.

Predictors of intent to vaccinate against HPV/cervical cancer: a multi-ethnic survey of 769 parents in New Zealand
Sally B Rose, Beverley A Lawton, Tolotea S Lanumata, Merilyn Hibma, Michael G Baker

Prior to the introduction of the school-based cervical cancer vaccination programme, we surveyed a multi-ethnic sample of parents in the Wellington area. The survey aimed to identify factors associated with parents intent to vaccinate their daughter(s). Views towards the new cervical cancer vaccine were generally positive, with two thirds of parents surveyed intending to have their daughter vaccinated. Findings were similar to those of studies conducted elsewhere to explore predictors of intent to vaccinate. Results suggested that provision of information about the widespread nature and consequences of HPV infection, and vaccine safety and efficacy will be important to help parents decide on vaccination.

Cases of cutaneous diphtheria in New Zealand: implications for surveillance and management

Ann Sears, Margot McLean, David Hingston, Barbara Eddie, Pat Short, Mark Jones

This paper describes two cases of skin infections caused by the diphtheria bacterium. 'Toxigenic' strains of this bacterium release a toxin that can cause serious disease (e.g. heart problems). Skin infections caused by this toxin-producing strain can spread from person-to-person. Immunisation is important to protect against the toxic effects of diphtheria.

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

Screening for aortic abdominal aneurysm in New Zealand

Ross Lawrenson

A ruptured abdominal aortic aneurysm (AAA) is a lethal condition with approximately 240 recorded deaths in New Zealand each year.[1] This number is proportionately much less than is seen in the United Kingdom (UK) where there are 6000 deaths per year.[2] Most deaths occur in men aged over 65 years.

Interestingly the age-standardised incidence in both New Zealand and the UK is falling steadily, presumably as a result of the medical and life style interventions that have caused a similar fall in cardiac events.[3] So although as the population ages we might expect an increase in the numbers of ruptured and fatal AAA, this increase is by no means certain if the age standardised incidence continues to fall. AAA can be diagnosed easily with ultrasound.

The number of elective repairs already being done in New Zealand would indicate that many patients are being diagnosed before becoming symptomatic and presumably in some patients their AAA has been an incidental finding of an ultrasound or CT investigation for another reason. AAA therefore seems to be a good candidate for an organised screening programme.

A number of randomised controlled trials have showed screening for AAA can save lives.[4] This has led to the institution of AAA screening in number of countries including the UK and the USA. Within New Zealand there has been increasing support for an organised program from a group of vascular surgeons.

Some private radiology clinics are already offering screening for AAA for both men and women and there are anecdotal reports that some GPs are screening opportunistically for AAA. As for any screening program there is a balance between risk and benefit. The authors of the two papers in this edition have provided an estimate of the proportion of people in the community with AAA and have appraised the suitability of an AAA screening program against the New Zealand Screening criteria. Their conclusions are that there is a good argument for considering an organised screening program for AAA in New Zealand men—although they note that there are some areas that do require further consideration and where additional information would be useful.

The discussion about a possible introduction of yet another screening program needs to be held in the context of the changing face of health practice within NZ. There is currently a global financial crisis and whilst New Zealand has been relatively sheltered from its impact, the devastating earthquakes in Christchurch and the subsequent need to protect and prioritise government funding to support the region, makes stark the need to be financially responsible in our planning.

We also look as though we are moving from the inefficient organisation of health services based around numerous PHOs and District Health Boards to a more rational, regionalised approach to the provision of health care. What is needed in this

environment is a transparent and publically acceptable way of deciding how to prioritise our spending.

We cannot afford unlimited health services and so the introduction of AAA screening needs to be considered against a range of existing or proposed new services. Currently it is unclear how such a decision is made. Another issue is that increasing technological demands have led to the centralisation of many health services and vascular surgery is now primarily offered in a limited number of hospitals within New Zealand.

With the increasing use of endovascular aortic repair (EVAR) as a treatment option for men with AAA it is likely that only centres who are expert in its use will be offering elective surgery. We do know that there are variations in the mortality rates from elective surgical repair—it has been shown that "incidental" elective repairs have a mortality rate of 6.1% but the rate in patients picked up from screening is 2.1%.[5] Nair et al have shown the mortality rate for elective procedures in New Zealand is 6.7%.[1] It maybe that the lower rate that is needed to make elective surgery acceptable can be achieved if only a limited number of centres are funded to deal with patients identified through a screening program. However this could mean that access to services for those in rural and provincial New Zealand would be problematic.

Those living in rural areas are proportionately more socially deprived and more likely to be Māori,[6] so it is important that any proposed program does not exacerbate the already known inequities that exist. The adoption of the principles of "Better, sooner, more convenient" and the development of integrated family health centres poses a question as to how we should be delivering new preventative health services. The implementation of any new screening program needs to ensure equal access for all at risk New Zealanders. Should we see screening as part of the role of integrated family health centres with delivery of the intervention being a regional responsibility? How should funding, quality assurance and patient acceptability be ensured in such a model?

Overall there is increasing consensus that AAA screening meets many of the criteria of the screening program and therefore policy advice in this area needs to be developed and adopted by the Ministry of Health. However the Ministry will have to prioritise AAA screening against other competing demands. It would appear timely for a consensus approach to be undertaken involving key stakeholders including the representatives of vascular surgeons, radiologists, primary health organisations and District Health Boards to come to an agreed position as to how we deal with this issue.

Competing interests: None declared.

Author information: Ross Lawrenson, Professor of Primary Care, Waikato Clinical School, University of Auckland

Correspondence: Ross Lawrenson, Waikato Clinical School, Peter Rothwell Academic Centre, Waikato Hospital, Private Bag 3200, Hamilton, New Zealand. Fax: +64 (0)7 8398712; email: LawrensR@waikatodhb.govt.nz

References:

1. Nair N, Shaw C, Sarfati D, Stanley J. Abdominal aortic aneurysm disease in New Zealand: epidemiology and burden between 2002 and 2006. N Z Med J. http://journal.nzma.org.nz/journal/125-1350/5074/content.pdf
2. Earnshaw JJ. Doubts and Dilemmas over abdominal aortic aneurysm. British Journal of Surgery 2011;98:607-8
3. Sandiford P, Mosquera D, Bramley D. Trends in incidence and mortality from abdominal aortic aneurysm in New Zealand. British Journal of Surgery 2011;98:645-651.
4. Cosford PA, Leng GC. Screening for abdominal aortic aneurysm. Cochrane Database Syst Rev. 2007;(2)CD002945.
5. Lindholt JS, Norman PE. Meta-analysis of post operative mortality after elective repair of abdominal aortic aneurysm detected by screening. British Journal of Surgery 2011;98;619-22.
6. Fraser J. Rural health; a literature review for the National Health Committee. Health Services Research Centre, Victoria University, Wellington, 2006.

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

Abdominal aortic aneurysm disease in New Zealand: epidemiology and burden between 2002 and 2006

Nisha Nair, Caroline Shaw, Diana Sarfati, James Stanley

Abstract

Background Abdominal aortic aneurysm (AAA) rupture has a high mortality. Four randomised controlled trials indicate significant mortality benefit from population screening for AAA. There is a lack of information on the epidemiology and burden of AAA disease in New Zealand, necessary to support policy in this area.

Methods A retrospective analysis was conducted on a dataset consisting of all AAA deaths and all hospital discharges with a AAA diagnosis between 2002 and 2006. Analysis by age, sex, ethnicity, and operative status was performed.

Results On average, there were 267 elective repairs and 87 emergency repairs annually between 2002 and 2006. The operative mortality rate was 35.2% for emergency repair, and 6.7% for elective repair.

There were about 236 known AAA-related deaths annually. Ninety-four percent of AAA deaths between 2002–2006 occurred in individuals >65 years. The case fatality for females was higher than males across every age group. The standardised mortality rate in Māori was twice as high as New Zealand Europeans.

Conclusions This study provides essential information to evaluate the appropriateness and feasibility of AAA screening here. A population-based prevalence study is recommended, along with further investigation of high case fatality in females and high mortality in Māori.

Abdominal aortic aneurysms (AAAs) are present in about 5 to 10% of men aged 65 to 79 years.[1] Generally, they expand without causing symptoms until they rupture, or, the individual dies of an unrelated cause. AAA rupture is a surgical emergency, and less than half of rupture patients reach the hospital alive. Emergency repair itself carries a high operative mortality of 30 to 65%,[2–4] attributable to haemodynamic compromise, advanced age, and medical comorbidities. Overall, AAA rupture carries a mortality rate as high as 80 to 90%.[3,5–8] In contrast, elective repair is associated with a considerably lower operative mortality, between 3 and 10%.[9–14]

Population-based AAA screening programmes use abdominal ultrasound scans to detect AAAs before they rupture. Four major randomised controlled trials evaluating AAA population screening have been performed to date.[9 15-17] Meta-analysis of these shows that AAA screening reduces AAA-related mortality by about 40% in males aged 65 to 79 years.[18] However, issues of concern include the risk of overtreatment, the benefit-harm balance of elective repair, and health system capacity. (see companion article in this NZMJ issue for further discussion on AAA screening).

The United Kingdom began gradually implementing population screening for AAA in 2009, screening males aged 65 years.[19] In the United States, Medicare has covered

AAA screening in male ever-smokers aged 65 to 75 and females with a family history of AAA since 2007.[20] There is currently no policy for AAA screening in New Zealand, although "awareness of the research evidence for screening is high."[21]

The evidence base for AAA screening draws heavily from international studies. The relatively small body of local research has been focused mainly on in-hospital mortality from rupture, selection criteria for emergency repair, clinical presentation of rupture, risk factors, and endovascular repair analysis. There is a lack of recent national-level information on overall epidemiology of AAA events and deaths, both in and out of hospital. This information is essential to inform any policy around AAA screening in New Zealand.

Accordingly, the objective of this study is to describe the burden of AAA disease in New Zealand by AAA events, AAA-related deaths, and vascular surgical workload. It also aims to describe AAA events and deaths by age, sex, ethnicity, and operative status. This is the first of two papers; the second evaluates the evidence for population screening for AAA in New Zealand against screening criteria.

Methodology

Study population—Records with ICD-10 codes for AAA [I71.3 'abdominal aortic aneurysm, ruptured' and I71.4 'abdominal aortic aneurysm, without mention of rupture'][22] were extracted from two national databases, the Mortality Collection and the National Minimum Dataset (NMDS).[23]

Collectively, these datasets contained all deaths between 2002 and 2006 for which the *underlying cause of death* was AAA, and all publicly funded hospital discharges from 2002 to 2006 with *any* diagnosis of AAA. From these datasets, three populations were defined: AAA Events, AAA Deaths, and AAA Alive Discharges (Figure 1).

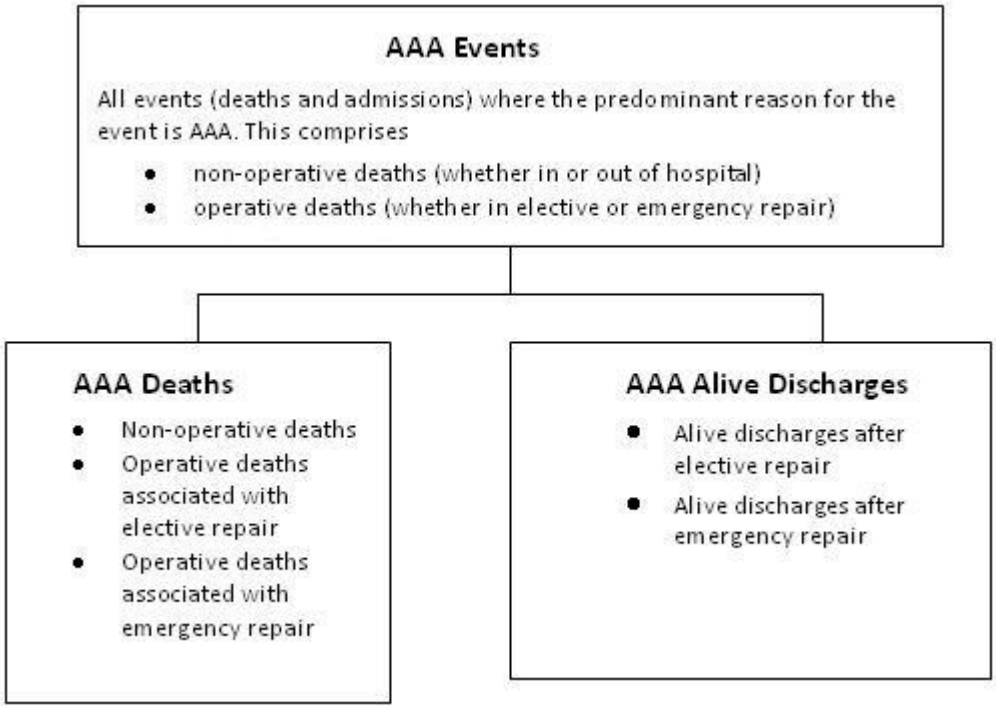
In order to identify these three populations, firstly, hospital discharges that involved a AAA operation were identified from the NMDS dataset (using ICD-10 operation codes for emergency and elective repair). These were then separated into AAA Operative Deaths (within 30 days of procedure) and AAA Alive Discharges using the event end type codes. All AAA Operative Deaths were then matched against the Mortality Collection, and duplicates identified.

The non-duplicates were assumed to be AAA Non-Operative Deaths, as AAA rupture without surgery carries a 100% mortality.[a]

Variables—The analysis was limited to the AAA Events and AAA Deaths populations. These were then analysed by age (<55 yrs; 55-64 yrs; 65-74 yrs; 75-84 yrs; 85+ yrs); sex; ethnicity (prioritised ethnicity fields were provided by the Ministry of Health Information Directorate as per Ministry of Health ethnicity data protocols and categorized as European, Māori, Pacific Island, Asian, and Other),[24,25] and operative status (elective repair, emergency repair after rupture, or no surgery after rupture).

[a] In a very small number of patients with AAA rupture, the surrounding tissue seals off the bleeding and the patient remains haemodynamically stable. This is termed chronic AAA rupture and patients can survive for a prolonged length of time. However, risk of free rupture is very high and prompt surgical repair is clinically indicated. For the purposes of this paper we have assumed a 100% mortality as this small group is unlikely to alter the findings.

Figure 1. Populations identified from datasets used



Statistical methods—The tables show frequency counts and proportions for AAA Events and AAA Deaths. Operative mortality (AAA operative deaths/AAA operative events x100), case fatality rates (AAA deaths/AAA events X 100), and age and sex standardised mortality and event ratios have been calculated. The reference population for standardised ratios was the 2006 Census Usually Resident Population (CURP),[26] apart from the prioritised ethnicity analysis (which utilised 2001 census data as prioritized ethnicity data by age and sex for the 2006 census were not available at the time of analysis).[27] Statistical analysis was performed using SAS version 9.1 software. Confidence intervals for case fatality rates were calculated using OpenEpi version 2.3 software.[28] Confidence intervals for indirectly standardised event and mortality ratios were calculated using the formulae from Rothman, Green & Lash.[29]

Prevalence and incidence of AAAs could not be calculated because it was not possible to identify individuals with AAAs too small for elective repair, those who do not qualify for/refuse elective repair, and those with intact but undiagnosed AAAs.

Ethical approval—Ethical approval was obtained from the Multi-Region Ethics Committee.[30] The Ngāi Tahu Research Consultation Committee was also consulted before project initiation.[31]

Results

Table 1 is an overview of AAA events and deaths, by operative status. There were 1182 AAA-related deaths between 2002 and 2006, equating to about 236 deaths per year. Almost 80% of these deaths were in patients after rupture who did not undergo surgery, and 13% and 7.5% in those not surviving emergency repair and elective repair, respectively.

There were 1774 AAA repairs between 2002 and 2006; about 25% of these were emergency repairs and 75% elective repairs. This equates to about 87 emergency

repairs and 267 elective repairs each year. The 30-day operative mortality rate was 35.2% for emergency repair, and 6.7% for elective repair.

Table 1. AAA events, AAA deaths, and operative mortality between 2002 and 2006

Operative status	AAA events Number (%)		AAA deaths Number (%)		Operative mortality
Rupture (No surgery)	926 †	(34.3%)	939 †	(79.4%)	Not applicable
Rupture (Emergency surgery)	438	(16.2%)	154	(13.0%)	35.2%
Elective repair	1336	(49.5%)	89	(7.5%)	6.7%
Total	2700	(100%)	1182	(100%)*	

* Due to rounding, percentages may not add up to exactly 100%.

† This table shows a discrepancy of 13 individuals between 'deaths' and 'events'. This is due to 13 people who underwent repair but died beyond the 30-day mark. From the AAA events perspective, they were counted as repairs. However, these 13 did not fulfil definition of an 'operative death' (i.e. within 30 days of operation) and so by default had to be included in the non-operative group.

Table 2 shows AAA events, deaths, case fatality, and operative mortality rates by age group. About 89% of all AAA events and almost 94% of all AAA deaths occurred in individuals aged ≥ 65 years.

The overall emergency repair operative mortality rate was 35.2%, and the elective repair mortality rate was 6.7%. Predictably, operative mortality rates increased with increasing age. Operative mortality in individuals aged > 85 years was about 58% for emergency repair, and almost 12% for elective repair.

Table 2. AAA events, deaths, case fatality and operative mortality by age group between 2002 and 2006

Age group (years)	AAA events Number (%)		AAA deaths Number (%)		Case fatality Percent (95% CI)		30-day operative mortality rate (%)	
							Emergency repair	Elective repair
≥85	350	(13.0%)	303	(25.6%)	86.6%	(82.6–90.0)	58.3%	11.6%
75–84	1180	(43.7%)	548	(46.4%)	46.5%	(43.6–49.3)	40.0%	9.3%
65–74	864	(32.0%)	255	(21.6%)	29.5%	(26.5–32.7)	28.8%	4.8%
55–64	278	(10.3%)	69	(5.8%)	24.8%	(19.9–30.3)	22.9%	2.2%
<55	28	(1.0%)	7	(0.6%)	25%	(10.7–44.9)	66.7%	9.1%
Total	2700		1182		43.8%	(41.9–45.7)	35.2%	6.7%

Table 3 shows AAA events by operative status in each age group. There is a pattern of reduced surgical intervention (both elective and emergency repair) with increasing age. Elective repairs predominated in younger age groups, and non-operative events predominated in older age groups. In individuals aged ≥85 years, non-operative events constituted almost 81% of all AAA events. Reduced surgical intervention at older ages is expected given that advanced age is a predictor of poor outcome.[32,33]

Table 3. AAA events by age group and operative status between 2002 and 2006

Age group	No surgery after rupture/ non-operative		Emergency repair after rupture		Elective repair		AAA events	
	Number (% of total events by age range)§							
>85 years	283	(80.9%)	24	(6.9%)	43	(12.3%)	350	(100%)
75–84 years	410	(34.8%)	200	(17.0%)	570	(48.3%)	1180	(100%)
65–74 years	179	(20.7%)	163	(18.9%)	522	(60.4%)	864	(100%)
55–64 years	51	(18.4%)	48	(17.3%)	179	(64.4%)	278	(100%)
<55 years*	3	(10.7%)	3	(10.7%)	22	(78.6%)	28	(100%)
Total	926		438		1336		2700	

* Small event numbers in this age group, should be interpreted with caution

§ Due to rounding, percentages may not add up to exactly 100%.

Table 4 shows AAA events and deaths by sex and ethnicity, along with age and sex standardised event and mortality ratios.

Table 4. AAA events and AAA deaths by sex and ethnicity between 2002 and 2006, with age and sex standardised event and mortality ratios

Sex	AAA events (n and %)		AAA deaths (n and %)		Standardised event ratio (indirect standardisation for age and sex)* † (ratio and 95%CI)		Standardised mortality ratio (indirect standardisation for age and sex)* † (ratio and 95%CI)		Case fatality rate (% and 95%CI)	
Male	1949	72.2%	760	64.3%	100	(ref)	100	(ref)	39.0%	(36.9–41.2)
Female	751	27.8%	422	35.7%	23.3	(21.7–25.0)	29.7	(27.0–32.7)	56.2%	(52.6–59.8)
Total	2700	100%	1182	100%						
Ethnicity:										
NZ European	2411	90.8%	1066	90.2%	100	(ref)	100	(ref)		
Māori	162	6.1%	82	6.9%	151.2	(129.6–176.4)	217.9	(175.5–270.6)		
Pacific	34	1.3%	20	1.7%	76.3	(54.5–106.7)	123.9	(79.9–192.0)		
Asian	27	1.0%	13	1.1%	46.3	(31.8–67.6)	61.4	(35.6–105.7)		
Other	20	0.8%	1	0.1%	412.5	(266.1–639.4)	53.2	(7.5–378.0)		
Total	2654#	100%	1182	100%						

* reference population for indirect standardisation in sex analysis was 2006 CURP males.

† reference population for indirect standardisation in ethnicity analysis was 2001 CURP for each ethnicity

46 events were missing ethnicity data.

About 72% of AAA events, and 64% of AAA deaths occurred in males. After indirect standardisation, the observed AAA event rate in females was about 23% that of males. The death rate in females was about 30% of that in males. The disparity between sexes in AAA death rates is narrower than in AAA event rates. One explanation for this is the higher case fatality in females (56%) compared to males (39%).

In other analyses not shown here, higher case fatality in females was evident in each age group, and females also presented at older ages for rupture and elective repair.

Almost 91% of AAA events between 2002 and 2006 occurred in New Zealand Europeans, 6% in Māori, and about 1% in each of Pacific, Asian and 'Other'. After age and sex standardisation, Māori had a AAA event rate about 1.5 times higher than New Zealand Europeans. However, the standardised mortality rate of Māori was about double that of New Zealand Europeans. In other analyses not shown here, Māori also presented at younger ages for rupture and elective repair.

The results suggest that Pacific people have somewhat lower event rates but higher mortality, although neither are statistically significant. Both event and mortality ratios suggest a lower disease burden among Asian people, but considerably higher burden among those in 'Other' ethnic groups.

Discussion

Between 2002 and 2006, there were on average 236 diagnosed AAA-related deaths per year. Almost 94% of these occurred in individuals aged ≥ 65 years. Almost 80% of AAA deaths occurred in a non-operative setting, 13% associated with emergency repair, and 7.5% associated with elective repair. There was an average of 267 elective repairs and 87 emergency repairs per year, with associated operative mortality rates of 6.7% and 35.2% respectively. Although over 70% of AAA events occurred in males, females had higher case fatality across every age group. Similarly, although over 90% of AAA events and deaths occurred in New Zealand Europeans, Māori had a standardised mortality rate twice as high as New Zealand Europeans.

The total number of AAA repairs here is similar to the 1868 repairs reported by Rossaak et al between 1993 and 1997. Any change in the relative proportions of elective and emergency repair between 1993-97 and 2002-2006 cannot be commented on, as Rossaak et al used three categories of AAA repair (emergency, urgent, and elective) as compared to the two categories used here.[34] The emergency repair operative mortality rate of 35.2% is similar to that reported by Grant et al (37.8%) and slightly lower than the 40% reported in a 2007 NZVASC audit.[35 36] It compares favourably with international estimates, which range from 30 to 65%.[2-4] The relatively low emergency repair mortality rate in New Zealand may reflect surgical expertise, good postoperative care, a stricter selection policy for emergency repair, or some combination thereof. The elective repair mortality rate of 6.7% is slightly higher than the 4% reported in the 2007 NZVASC audit,[36] and is in line with international estimates of 3 to 10%.[9-14] Based on this study, the risk of dying was five times higher with emergency repair than with elective repair.

This analysis identified three populations that appear to be particularly vulnerable. Firstly, individuals ≥ 65 years account for the vast majority of AAA deaths, and case fatality is particularly high in individuals ≥ 85 years. This is not surprising given AAA prevalence is estimated to increase by 6% per decade after 65 years.[3] Advanced age is also associated with lower rates of surgical intervention and significantly higher operative mortality rates from both elective and emergency repair.[37-40] However, less incidental/opportunistic detection of AAAs in this age group may also play a role, along with a higher likelihood of declining repair even when offered.

Secondly, although females have lower AAA prevalence and mortality than males, they have higher case fatality across every age group. This is consistent with both national and international evidence.[35 41 42] Possible reasons include higher risks of

rupture, lower rates of emergency repair being offered, and higher operative mortality from emergency repair. Internationally, concerns have been raised about possible gender bias in diagnosis of or selection for surgical treatment in AAA.[43]

Thirdly, Māori have higher AAA event and mortality rates as compared with New Zealand Europeans, and also present with the condition at a younger age. This is consistent with Rossaak et al's findings when analysing AAA admissions in New Zealand between 1993 and 1997. Additionally, more emergency procedures and a higher proportion of admissions for rupture was also reported.[34] The disproportionate burden of AAA disease in Māori is likely to be multifactorial. Higher prevalence of smoking in Māori is a risk factor for both AAA development and AAA rupture.[44] Higher prevalence of high blood pressure,[45] smoking,[44] diabetes, and obesity[46] may also increase mortality from emergency and elective repair. Māori also have poorer access to primary care, which may mean less opportunity for AAA detection. Additionally, there is increasing evidence (particularly from studies in cardiovascular disease management) that secondary and tertiary services may serve Māori less well than non- Māori.[47-49]

Strengths and limitations—The major strength of this study is that it combines mortality and hospital datasets to provide a more comprehensive picture of AAA burden. Previous studies have largely utilised hospital data, and this is a highly selected group given less than half of rupture patients reach the hospital alive. The wider view afforded by this study is essential in planning a population-based intervention.

Coding inaccuracies within the datasets used is a potential limitation of this study. This was minimized by using AAA operation codes to identify individuals with AAA-related diagnoses, rather than more subjective AAA diagnosis codes. Individuals admitted with AAA who did not undergo repair would not have had operation codes. However, these individuals would have been represented in the mortality dataset due to the fatal nature of this condition.

The analysis of AAA events and deaths by age, sex, and ethnicity provide valuable information on the demographics of individuals with AAA. However, in certain populations (< 55 years and some ethnicities), numbers were small and results should be interpreted with caution. This analysis also was not able to differentiate between endovascular and open repair. Trends in endovascular repair have significant implications for decisions relating to population-based screening. Finally, undercounting of Māori should always be considered. Studies have shown that there is no net undercount of Māori on mortality records from this period, but hospitalisation data may be less reliable.[50]

The study population was not able to include individuals with AAAs too small for elective repair, individuals who do not qualify for/refuse elective repair, and individuals with undiagnosed but intact AAAs. Thus, this study cannot reliably comment on AAA prevalence or incidence. It is also likely that the figure of 236 AAA-related deaths per year may be an underestimate. While deaths from elective or emergency repair are reliable, the same cannot be said for non-operative AAA deaths. Firstly, there are significant inaccuracies in death certification, particularly in the elderly. In particular, in an elderly individual with an undiagnosed AAA, there is a tendency for sudden death to be attributed to a more common condition like coronary

artery disease.[51 52] Secondly, low autopsy rates (particularly in the elderly) compound the risk of misclassifying the cause of death.[51 53 54] The only way of overcoming this knowledge gap is a population prevalence study.

Implications for policy—This study describes AAA events, deaths, and vascular surgical workload over a five-year period. Alongside other local studies, it provides a baseline for assessing the appropriateness and feasibility of a AAA screening programme in New Zealand. However, a population-based prevalence study would provide a more complete picture of AAA burden. Additionally, the drivers of high event and mortality rates in Māori, and high case fatality in females warrant further investigation. An understanding of existing inequalities in AAA disease is vital if a potential AAA screening programme is to avoid exacerbating them. Knowledge of vulnerable populations and existing service gaps is imperative in formulating AAA screening policy, identifying target areas for implementation, and guiding quality assurance measures.

Competing interests: Caroline Shaw is a member of the National Screening Advisory Committee which provides independent advice to the Director General of Health on screening issues.

Author information: Nisha Nair, Public Health Registrar, University of Otago Wellington School of Medicine & Health Sciences, Wellington; Caroline Shaw, HRC Clinical Training Research Fellow/Public Health Physician, Department of Public Health, University of Otago Wellington School of Medicine & Health Sciences, Wellington; Diana Sarfati, Senior Lecturer/Public Health Physician, Cancer Control and Screening Research Group, University of Otago Wellington School of Medicine & Health Sciences, Wellington; James Stanley, Biostatistician/Research Fellow, University of Otago Wellington School of Medicine & Health Sciences, Wellington

Correspondence: Nisha Nair, Public Health Registrar, c/o Cancer Control and Screening Research Group, University of Otago, Wellington, PO Box 7343, Wellington South. Phone (04)9186042, fax (04)3895319, email nisha.nair1004@gmail.com

References:

1. Vardulaki KA, Prevost TC, Walker NM, et al. Incidence among men of asymptomatic abdominal aortic aneurysms: estimates from 500 screen detected cases. Journal of Medical Screening 1999;6(1):50-4.
2. Basnyat PS., Biffin HB, Moseley LG, et al. Mortality from ruptured aortic aneurysm in Wales. British Journal of Surgery 1999;86(6):765-770.
3. Ginter JF, Linzmeyer J. Abdominal aortic aneurysm repair: matching patients with approaches. JAAPA;22(7):26.
4. Samy AK, Whyte B, McBain G. Abdominal aortic aneurysm in Scotland. British Journal of Surgery 1994;81(8):1104-6.
5. Fleming C, Whitlock EP, Bei TL, Lederle FA. Screening for abdominal aortic aneurysm: a best-evidence systematic review for the U.S. Preventive Services Task Force. Annals of Internal Medicine 2005;142(3):203-11.
6. Hirsch AT, Haskal ZJ, Hertzer NR, et al. ACC/AHA 2005 Practice Guidelines for the Management of Patients With Peripheral Arterial Disease (Lower Extremity, Renal, Mesenteric, and Abdominal Aortic): A Collaborative Report from the American Association for Vascular Surgery/Society for Vascular Surgery,* Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine and Biology, Society of Interventional Radiology, and the ACC/AHA Task Force on Practice Guidelines (Writing Committee to Develop Guidelines for the Management of Patients With Peripheral Arterial Disease):

Endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation; National Heart, Lung, and Blood Institute; Society for Vascular Nursing; TransAtlantic Inter-Society Consensus; and Vascular Disease Foundation. Circulation 2006;113(11):e463-465.

7. Lindholt JS. Screening for abdominal aortic aneurysms. European Journal of Vascular & Endovascular Surgery 2003;25(5):377-9.
8. Metcalfe D, Holt P, Thompson J. The management of abdominal aortic aneurysms. British Medical Journal 2011;342(d1384):644-649.
9. Ashton HA, Buxton MJ, Day NE, et al. The Multicentre Aneurysm Screening Study (MASS) into the effect of abdominal aortic aneurysm screening on mortality in men: a randomised controlled trial. Lancet 2002;360(9345):1531-9.
10. Cowan JA, Jr., Dimick JB, Henke PK, et al. Epidemiology of aortic aneurysm repair in the United States from 1993 to 2003. Annals of the New York Academy of Sciences 2006;1085:1-10.
11. Holt PJ, Poloniecki JD, Gerrard D, et al. Meta-analysis and systematic review of the relationship between volume and outcome in abdominal aortic aneurysm surgery. British Journal of Surgery 2007;94:395-403.
12. Lederle FA, Wilson SE, Johnson GR, et al. Immediate repair compared with surveillance of small abdominal aortic aneurysms. New England Journal of Medicine 2002;346(19):1437-44.
13. Powell JT, Brady AR, Brown LC, et al. Mortality results for randomised controlled trial of early elective surgery or ultrasonographic surveillance for small abdominal aortic aneurysms. Lancet 1998;352(9141):1649-55.
14. Swedvasc. Swedvasc database, 2005.
15. Lindholt JS, Juul S, Fasting H, Henneberg EW. Screening for abdominal aortic aneurysms: single centre randomised controlled trial.[Erratum appears in BMJ. 2005 Oct 15;331(7521):876]. BMJ 2005;330(7494):750.
16. Norman P, Jamrozik K, Lawrence-Brown M, et al. Population based randomised controlled trial on impact of screening on mortality from abdominal aortic aneurysm. British Medical Journal 2004;329(7477):1259.
17. Scott RA, Wilson NM, Ashton HA, Kay DN. Influence of screening on the incidence of ruptured abdominal aortic aneurysm: 5-year results of a randomized controlled study. British Journal of Surgery 1995;82(8):1066-70.
18. Cosford PA, Leng GC. Screening for abdominal aortic aneurysm. Cochrane Database of Systematic Reviews 2007(2):Art. No.: CD002945.
19. U.K. National Screening Committee. Abdominal Aortic Aneurysm: The UK NSC policy on Abdominal Aortic Aneurysm London, 2010.
20. Lee ES, Pickett E, Hedayati N, et al. Implementation of an aortic screening program in clinical practice: implications for the Screen For Abdominal Aortic Aneurysms Very Efficiently (SAAAVE) Act. Journal of Vascular Surgery 2009;49(5):1107-11.
21. National Screening Advisory Committee. Screening policy positions and practice in New Zealand: National Screening Advisory Committee, 2009.
22. World Health Organization. International Statistical Classification of Diseases and Related Health Problems, 10th Revision, Version for 2007, 2006.
23. New Zealand Health Information Service. Data and Services Available: Data Collections held by NZHIS. Wellington, 2009.
24. Ministry of Health. Ethnicity Data Protocols for the Health and Disability Sector. Wellington: Ministry of Health, 2004.
25. New Zealand Health Information Service. Ethnicity code table Wellington, 2009.
26. Statistics New Zealand. 2006 Census Population and dwellings tables
27. Statistics New Zealand. 2001 Census of Population and Dwellings: Maori. Wellington: Statistics New Zealand, 2002.
28. SAS [program]. 9.1 version. Cary, N.C.

29. Rothman KJ, Greenland S, Lash TL. Modern Epidemiology: Lippincott, Williams & Wilkins, 2008.
30. Health and Disability Ethics Committees. New Zealand Health and Disability Ethics Committees. Wellington, 2010.
31. University of Otago. Research Consultation with Māori. Dunedin.
32. Biancari F, Heikkinen M, Lepantalo M, et al. Glasgow Aneurysm Score in Patients Undergoing Elective Open Repair of Abdominal Aortic Aneurysm: A Finnvasc Study. European Journal of Vascular & Endovascular Surgery 2003;26:612-7.
33. Hardman DT, Fisher CM, Patel MI, et al. Ruptured abdominal aortic aneurysms: who should be offered surgery? . Journal of Vascular Surgery 1996;23:123-9.
34. Rossaak JI, Sporle A, Birks CL, Van Rij AM. Abdominal aortic aneurysm in the New Zealand Maori population. British Journal of Surgery 2003;90(11):1361-6.
35. Grant M, Thomson I, Van Rij AM. In-hospital mortality of ruptured abdominal aortic aneurysm. ANZ Journal of Surgery 2008;78(8):698-704.
36. Otago Clinical Audit Research Group. 2007 Audit Report of Vascular Society of New Zealand: Vascular Society of New Zealand, 2007.
37. Kazmers A, Perkins AJ, Jacobs LA. Outcomes after abdominal aortic aneurysm repair in those > or = 80 years of age: recent Veterans Affairs experience. Annals of Vascular Surgery 1998;12(2):106-12.
38. O'Hara PJ, Hertzer NR, Krajewski LP, et al. Ten-year experience with abdominal aortic aneurysm repair in octogenarians: early results and late outcome. . Journal of Vascular Surgery 1995;21:830-7.
39. Heller JA, Weinberg A, Arons R, et al. Two decades of abdominal aortic aneurysm repair: have we made any progress? . Journal of Vascular Surgery 2000;32:1091-100.
40. Shackleton CR, Schechter MT, Bianco R, Hildebrand HD. Preoperative predictors of mortality risk in ruptured abdominal aortic aneurysm. Journal of Vascular Surgery 1987;6:583-9.
41. Norman PE, Powell JT. Abdominal aortic aneurysm: the prognosis in women is worse than men. Circulation 2007;2007(115):2865-9.
42. McPhee JT, Hill JS, Eslami MH. The impact of gender on presentation, therapy, and mortality of abdominal aortic aneurysm in the United States 2001-4. Journal of Vascular Surgery 2007;45:891-9.
43. Cina CS, Anand S. Applying the gender lens to abdominal aortic aneurysm screening. Vascular Medicine 2007;12(4):325-6.
44. Ministry of Health. Tobacco Trends 2006: Monitoring tobacco use in New Zealand. Wellington: Ministry of Health, 2006.
45. Ministry of Health. A Portrait of Health: Key Results of the 2002/03 New Zealand Health Survey. Wellington: Ministry of Health, 2004.
46. Ministry of Health. Maori Health Chart Book. Wellington: Ministry of Health, 2006.
47. Crengle S. Primary Care and Māori: Findings from the National Primary Medical Care Survey. In: Robson B, Harris R, editors. Hauora: Māori Standards of Health IV. A study of the years 2002-2005. Wellington: Te Ropu Rangahau Hauora a Eru Pomare, 2007.
48. Westbrooke I, Baxter J, Hohan J. Are Māori under-served for cardiac interventions? New Zealand Medical Journal 2001;114(1143):484-7.
49. Tukuitonga C, Bindman A. Ethnic and gender differences in the use of coronary artery revascularisation procedures in New Zealand. New Zealand Medical Journal 2002;115(1152):179-182.
50. Robson B, Purdie G. Appendix 1: Methods. In: Robson B, Harris R, editors. Hauora: Māori Standards of Health IV. A study of the years 2000-2005. Wellington: Te Ropu Rangahau Hauora a Eru Pomare, 2007.
51. Rose J, Civil I, Koelmeyer T, Haydock D, Adams D. Ruptured abdominal aortic aneurysms: clinical presentation in Auckland 1993-1997. ANZ Journal of Surgery 2001;71(6):341-344.

52. Brown SH, Frankovich M. How accurate are New Zealand death certificates? . New Zealand Medical Journal 1998;111(1072):321-2.
53. Cocchi A, Vecchio F, Pahor M, et al. Autopsy rate in younger and older hospitalized patients. European Journal of Epidemiology 1986;2(2):151-7.
54. Start RD, McCulloch TA, Benbow EW, et al. Clinical necropsy rates during the 1980s: the continued decline. Journal of Pathology 1993;171:63-66.

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

Funding community medicines by exception: a descriptive epidemiological study from New Zealand

Dilky Rasiah, Richard Edwards, Peter Crampton

Abstract

Aims To assess rates of approval and identify factors associated with successful applications for funding to the New Zealand Community Exceptional Circumstances (CEC) scheme.

Method Descriptive quantitative analysis of data in CEC applications database. The main outcome was initial application approval rate. Analysis included calculation of unadjusted and adjusted associations between potential determinants (for example patient age, gender) and outcomes using logistic regression analysis. All CEC applications with a decision about approval or decline 1 October 2001 to 30 September 2008 were included.

Results Application numbers were high, but had reduced since 2001. A small number of medicines (11) and indications comprised about a third of the applications to the scheme. While some common applications were clearly outside the remit of the scheme, many applications were for patients who fitted the scheme's eligibility criteria. The overall initial application approval rate was 16% and the renewal application approval rate was 88%. Approval rates varied widely by type of medicine, therapeutic group and indication.

After adjusting for other potential determinants there were no statistically significant differences in initial approval rates by gender, ethnicity or socioeconomic status of the patient. There were however, significant differences in initial application approval by age of the patient, type of applicant doctor and by geographical location of the applicant doctor.

Conclusions There was no evidence that gender, ethnicity and socioeconomic status of patients were factors associated with successful applications. However, applications for younger patients, those made by specialists, and those made by applying clinicians from the Auckland District Health Board area were more likely to be successful. It is possible that this may to some degree be appropriate, but requires further research.

Many countries face considerable challenges in allocating resources to non-mainstream use of medicines and there is growing interest in the funding of medicines for non-mainstream uses through exceptional circumstances-type schemes.[1–3] A literature review carried out as a preliminary investigation for this study indicated very little had been published internationally evaluating the operation of exceptions-type schemes.

The New Zealand scheme at the time this research was undertaken was similar to some in the United Kingdom (UK).[2] Mainstream pharmaceutical subsidies are

provided for patients in the community at a national population level through the New Zealand Pharmaceutical Management Agency (PHARMAC), via a national community formulary (called the Pharmaceutical Schedule).[4] There has been recent interest in the performance of the mainstream New Zealand scheme in relation to containing pharmaceutical costs.[5]

The Community Exceptional Circumstances (CEC) scheme until early 2012 is New Zealand's community medicines named-patients exceptions funding scheme. It provides access to non-mainstream community pharmaceutical funding for individual patients, and is one of PHARMAC's tools for fulfilling a legislated requirement: "...in exceptional circumstances providing for subsidies for the supply of pharmaceuticals not on the pharmaceutical schedule" (New Zealand Public Health & Disability Act 2000). A risk-pool, currently of up to NZ$3 million is available from within the community pharmaceutical budget to cover the funding of such treatments.

In June 2011 PHARMAC announced changes to the Exceptional Circumstances schemes following a two-stage consultation process that began in 2010. Under the new scheme, to be introduced early 2012, called Named Patient Pharmaceutical Assessment (NPPA), patients no longer need to have rare conditions to be considered for funding and there are a number of other changes. As a result the data presented in this study represents a useful historical analysis and stock-take of aspects of a scheme that has been in existence for approximately a decade. This study used national level data from the New Zealand CEC scheme. The study aimed to describe the extent and scope of the applications for funding to the CEC scheme; to analyse the PHARMAC database to assess the rates of approval/decline for CEC applications and to identify factors which are associated with successful applications.

Methods

All applications for CEC funding made from 1 October 2001 (when PHARMAC became responsible for administration of the scheme) to 30 September 2008 in which a decision about approval or decline available on the PHARMAC database were eligible for inclusion in the study. All other CEC application types, such as those awaiting further information or transferred to another scheme were excluded. Eighty-eight paper CEC applications not held on the database were added. The main outcome considered in the analysis was the initial application approval rate. The outcome of CEC renewal applications were not considered in detail because these applications had a very high approval rate.

There were three main components to the analysis:

- A descriptive analysis of distributions of key variables, of overall approval rates and approval rates in relation to potential determinants;
- Calculation of unadjusted estimates of association (odds ratios) between potential determinants and initial approval; and
- Calculation of adjusted estimates of association (using multivariate logistic regression) between potential determinants and initial approval.

The potential determinants of initial application outcome which were identified and included in the analysis were:

- Type of medicine applied for (medicine and therapeutic group);
- Clinical indication;
- Patient demographic factors including age, gender, ethnicity and socioeconomic status (SES);
- Type of applicant doctor classified by training and geographical location; and
- Application year.

We used multivariate logistic regression analysis to calculate odds ratios adjusted for the following: patient gender, age, SES (deprivation index of census area unit where patient lived), and ethnicity of patient; geographical location (in Auckland or outside Auckland District Health Board (DHB) area) of applicant doctor; nature of applicant doctor (specialist, GP, general registrant (including specialist trainees and those not vocationally registered or training)) and application year.

Due to the large number of indications and therapeutic groups, and the strong correlation between them it was not possible to enter these both into the logistic regression model as it would have created statistical instability. We therefore created a specialty group variable. This was a derived variable which was a combination of indication and therapeutic group grouped into categories according to the initial application approval rate. This variable was used to adjust for indication and therapeutic group within the multivariate model.

Results

Currently, to qualify for Community Exceptional Circumstances approval, one of the following criteria must be met: the condition must be rare; or the patient must have an unusual reaction to alternative funded treatments; or an unusual combination of circumstances applies. 'Rare' conditions and 'unusual' reactions are those which affect as a guide around 10 or fewer people nationally (New Zealand population approximately 4 million).

Supplementary eligibility criteria include suitability of the pharmaceutical, clinical benefit, the cost effectiveness of the treatment, and, although not considered in practice now, the patient's ability to pay for the treatment. In practice, applications are made for a wide range of medications and conditions; no pharmaceutical application is not considered.

Any medical practitioner can apply for CEC funding on behalf of their patients using a CEC application form or by writing to the CEC scheme. Applications are considered by a panel of six doctors which may: approve funding; decline funding; seek further information from the applicant before making a decision; or where the cost of treatment is more than $15,000 make a positive recommendation but refer the decision to PHARMAC . Applicants have the right of appeal following the CEC funding decision.

Number of applications and approval rates by year—Over the 7 years from October 2001 to September 2008 there were 3234 CEC applications that were either approved or declined (Table 1). Most (2564, 79.3%) were initial applications. Overall the initial application approval rate was 16% and the renewal application approval rate was 88%. This suggested that once an approval had been given it was likely to continue to be given via renewals.

The number of applications per year reduced by around two-thirds between 2001/2 and 2006/7, then increased slightly in 2007/8 (Table 1). The initial and renewal approval rates were lowest in 2001/2002 and then increased and fluctuated around the higher level. Initial approval rates were highest in 2007/8 at 34% and renewal approval rates approached 100% in 2006/7 and 2007/8.

Table 1. Outcome of initial and renewal applications by application year

Year	Initial			Renewal			Grand Total
	Approved	Declined	Proportion Approved (95%CI)	Approved	Declined	Proportion Approved (95%CI)	
2001/2002	72	756	0.09 (0.07-0.11)	53	36	0.60 (0.49-0.70)	917
2002/2003	90	323	0.22 (0.18-0.26)	86	12	0.88 (0.80-0.94)	511
2003/2004	57	346	0.14 (0.11-0.18)	62	14	0.82 (0.71-0.90)	479
2004/2005	49	242	0.17 (0.13-0.22)	80	7	0.92 (0.84-0.97)	378
2005/2006	39	198	0.16 (0.12-0.22	78	6	0.93 (0.85-0.97)	321
2006/2007	47	148	0.24 (0.18-0.31)	88	1	0.99 (0.94-1.00)	284
2007/2008	66	131	0.34 (0.27-0.41)	145	2	0.99 (0.95-1.00)	344
Grand Total	**420**	**2144**	**0.16 (0.15-0.18)**	**592**	**78**	**0.88 (0.86-0.91)**	**3234**

Common indications and medicines—The top 20 indications accounted for over 30% of the applications (initial and renewal) over the 7-year period (Table 2). The most common three indications were osteoarthritis, depression then hypertension. Other than four transplant-related indications (approval rate 58–71%), schizophrenia (7.4%) and epilepsy (21.9%), the initial approval rate for all these common indications was less than 3%.

There were 11 medicines with over 40 applications, which accounted for 32% of the initial & renewal applications over the 7 years. They were applied for under multiple indications. For six of these medicines—celecoxib, rofecoxib (both COX-2 inhibitors), venlafaxine, tramadol, clopidogrel and gabapentin—all initial applications were declined. Initial approval percents for the other five medicines most commonly applied for were cyclosporin (60%), sirolimus (48%), tacrolimus (84%) and mycophenolate (40%) (mostly for transplant indications) and fluoxetine (0.02%) (not including dispersible formulation).

Approval rates by therapeutic group—Initial approval rates varied widely by type of medicine and therapeutic groups. The highest initial approval rates were for agents to treat infections and oncology agents and immunosuppressants, at 0.41 (Table 3). The lowest initial approval rate was for musculoskeletal applications at 0.01. The largest number of applications (around a quarter of the total) was for nervous system medicines, which had one of the lowest approval rates.

Analysis of potential determinants of approval rates—Table 4 shows that there were significantly increased odds of initial approval among Asian, Pacific Island and Māori patients compared with European patients in the unadjusted analysis, but after adjustment for other potential confounders, all associations were non-significant except that unknown ethnicity patients had reduced odds of initial approval.

The unadjusted odds ratio for females suggested there was a lower odds of initial approval among females but once adjusted for potential confounders there was no statistically significant association between initial approval and gender. There was no significant association between deprivation and initial approval rate in the unadjusted or adjusted analyses.

Table 2. Twenty most common or applied for indications (initial & renewal applications) October 2001 to September 2008

Indication	Total (initial & renewal) applications	Percent of all (initial & renewal) applications	Percent of each indication's initial applications approved
Osteoarthritis	162	5.0	0.6
Depression	129	4.0	2.4
Hypertension	107	3.3	0.0
Pain	74	2.3	2.9
Transplantation of heart including failure/rejection	61	1.9	58.1
Transplantation of kidney including failure/rejection	58	1.8	61.3
Arthritis	57	1.8	0.0
Rheumatoid arthritis	52	1.6	0.0
Neuropathic pain	50	1.5	2.0
Back pain	49	1.5	2.0
Transplantation of lung including failure/rejection	45	1.4	71.4
Bipolar disorder	43	1.3	0.00
Epilepsy	40	1.2	21.9
Obesity	38	1.2	0.0
Unknown	36	1.1	2.8
Asthma	34	1.1	0.00
Dementia	33	1.0	0.00
Transplantation of liver including failure/rejection	31	1.0	61.1
Musculoskeletal pain including knee, neck, joints	30	0.9	0.0
Schizophrenia including psychosis	30	0.9	7.4
Total	**1159**	**35.8%**	**8.1**

There were however, strong associations between age group and initial application approval, with odds of approval much higher for patients aged 0–4 years (Table 5).

Table 6 shows that the odds of initial approval were over seven times higher among specialist applicants compared with GPs, even after adjusting for other potential determinants. Odds of approval were also increased to a lesser degree among applicants with unknown status or in the general registrant category.

Finally, rates of initial approval were much higher among applicant doctors from the Auckland area than elsewhere in New Zealand. The adjusted odds ratio of initial approval for applicant doctors from non-Auckland DHBs compared with Auckland DHB was 0.52 (95% CI 0.39 to 0.69).

Table 3. Approved and declined initial and renewal applications and proportion approved by Therapeutic Group

Therapeutic Group	Approved	Declined	Proportion Approved (95%CI)	Grand Total
Infections—agents for systemic use	59	86	0.41 (0.33-0.49)	167
Oncology agents and immunosuppressants	144	208	0.41 (0.36-0.46	549
Alimentary tract and metabolism	85	179	0.32 (0.27-0.38)	391
Sensory organs	13	30	0.30 (0.17-0.46)	72
Various	1	4	0.20 (0.01-0.72)	6
Hormone preparations-systemic excluding contraceptive hormones	29	131	0.18 (0.12-0.25)	198
Special foods	9	43	0.17 (0.08-0.30)	73
Blood and blood forming organs	19	125	0.13 (0.08-0.20)	180
Dermatologicals	4	34	0.11 (0.03-0.25)	73
Cardiovascular system	14	155	0.08 (0.05-0.14)	222
Genito-urinary system	4	50	0.07 (0.02-0.18)	64
Nervous system	33	677	0.05 (0.03-0.06)	777
Respiratory system and allergies	3	72	0.04 (0.01-0.11)	84
Musculoskeletal system	3	347	0.01 (0.00-0.02)	375
Grand Total	**420**	**2144**	**0.16 (0.15-0.18)**	**3234***

* Grand total is slightly higher than the sum of the individual therapeutic groups as three applications for which therapeutic group could not be determined have been excluded from the Table.

Table 4. Unadjusted and adjusted odds ratios for initial application approval by ethnicity, gender and deprivation

Variables	Unadjusted odds ratio (95%CI)	*Adjusted odds ratio (95%CI)
Ethnicity (number of initial applications)		
European (1400)	1.00	1.00
Asian (73)	2.48 (1.52-4.04)	1.40 (0.77-2.52)
Pacific Island people (40)	2.44 (1.27-4.70)	1.46 (0.68-3.12)
Māori (189)	1.74 (1.24-2.45)	1.04 (0.66-1.62)
Other including African, Hispanic, Middle Eastern (67)	1.08 (0.59-1.97)	1.30 (0.62-2.73)
Unknown (795)	0.21 (0.14-0.29)	0.26 (0.16-0.42)
Gender (number of initial applications)		
Male (1070)	1.00	1.00
Unknown (11)	2.67 (0.75-9.53)	1.65 (0.35-7.77)
Female (1483)	0.66 (0.53-0.81)	1.08 (0.83-1.41)
Deprivation (number of initial applications)		
Deprivation quintile 1 (365)	1.00	1.00
Deprivation quintile 2 (409)	0.85 (0.59-1.23)	0.99 (0.63-1.56)
Deprivation quintile 3 (484)	0.83 (0.58-1.19)	0.79 (0.51-1.23)
Deprivation quintile 4 (542)	0.97 (0.69-1.37)	1.11 (0.73-1.69)
Most deprived (466)	1.14 (0.81-1.61)	0.95 (0.61-1.48)
Unknown (298)	0.28 (0.16-0.48)	1.50 (0.71-3.15)

*Adjusted for gender, SES and ethnicity of patient (as applicable). All analyses adjusted for age of patient, Auckland/non-Auckland DHBs of applicant; specialty groups (a derived variable which was a combination of indication and therapeutic group, grouped by initial application approval rate); type of applicant; and application year.

Table 5. Unadjusted and adjusted odds ratios for initial application approval by age

Age (number of initial applications)	Unadjusted odds ratio (95%CI)	*Adjusted odds ratio (95%CI)
0 to 4 (143)	1.00	1.00
5 to 16 (210)	0.37 (0.24-0.58)	0.51 (0.30-0.87)
17 to 25 (139))	0.30 (0.18-0.50)	0.41 (0.23-0.75)
26 to 44 (568)	0.17 (0.12-0.26)	0.32 (0.20-0.51)
45 to 64 (735)	0.12 ().08-0.17)	0.25 (0.16-0.41)
65 to 80 (527)	0.06 (0.04-0.10)	0.23 (0.13-0.41)
over 80 (122)	0.09 (0.05-0.19)	0.31 (0.14-0.68)
Unknown (120)	0.04 (0.02-0.10)	0.29 (0.11-0.77)

*Adjusted for gender, SES and ethnicity of patient; Auckland/non-Auckland DHBs of applicant; specialty groups (a derived variable which was a combination of indication and therapeutic group, grouped by initial application approval rate); type of applicant; and application year.

Table 6. Unadjusted and adjusted odds ratios for initial application approval by nature of applicant doctor

Vocational Scope (number of initial applications	Unadjusted odds ratio (95%CI)	*Adjusted odds ratio (95%CI)
GPs (798)	1.00	1.00
Specialist (1353)	19.62 (11.61-33.15)	7.38 (4.24-12.83)
Unknown (214)	6.27 (3.21-12.25)	4.37 (2.13-8.99)
General registrant (199)	5.30 (2.62-10.71)	3.41 (1.59-7.28)

*Adjusted for age, gender, ethnicity and SES of patient; Auckland/non-Auckland DHBs of applicant; specialty groups (a derived variable which was a combination of indication and therapeutic group, grouped by initial application approval rate); and application year.

Discussion

Principal findings—We found that the New Zealand CEC scheme is well used, but the annual numbers of initial applications had declined since 2001. There was a low overall rate (16%) of initial approval, though this may have increased recently at 24% in 2006/7 and 34% in 2007/8.

The reason for the low rate would have been that the applications did not meet any of the entry criteria of the condition being rare or the patient having an unusual reaction to alternative funded treatments or an unusual combination of circumstances applying.

There was a very high rate of renewal approval. There was great variation in approval rates by indication, medicine and therapeutic group. Applications for a small number of medicines and indications comprised a large proportion of the applications to the scheme. Applications for some medicines and indications had very low initial approval rates and appeared to be routinely declined.

The analysis to investigate potential determinants of approval for initial CEC applications found no significant variation in initial approval rate by gender, SES or ethnicity after adjusting for other factors. The three main factors associated which were independently associated with greater approval were younger age of patient,

specialist applicants (as compared to other applicant doctors) and Auckland DHB applicant doctors (as compared to non-Auckland DHB applicants).

Strengths and limitations—The main strength of the study was the availability of a large and comprehensive dataset for a CEC type scheme. The dataset included information on a wide range of potential determinants. When Austin[8] outlined how to formulate a good CEC-type Individual Funding Request scheme, she included having a logging and tracking system as good practice. Because the New Zealand CEC scheme has a used and well-maintained logging and tracking system, we had access to good quality data. Most data was entered by a single person and the data was used to inform a decision so it was more likely to be of a high quality. The limited data to date available on exceptions funding suggests that having such a database is rare.[1]

A limitation of this study was that it only investigated factors associated with successful applications and did not assess whether the volume of applications in relation to need (prevalence of disease) was appropriate. Hence no conclusions can be reached about this aspect of performance of the CEC scheme. A weakness was the frequency of missing data. Of all the determinants considered in the analysis, this was greatest for ethnicity, with over 800 of the 3234 applications (25%) lacking ethnicity data. Furthermore the patients with unknown ethnicity had far lower initial approval rates (Table 4). Therefore, the analysis of initial approval in relation to ethnicity needs to be interpreted with caution. While there is no indication that the unknown group is more likely to come from particular ethnic groups, if they were, the low initial approval rate may mean that this would introduce a bias within the estimates of ethnicity-specific approval rates.

Implications for research and practice—The results show that there is a clear group of commoner indications (and medicines) that rarely meet CEC funding criteria. The PHARMAC information sheet and website provided some information about which indications and medicines are rarely funded. The results of this study suggest that more comprehensive information and communication to prescribers and patients about medicines and indications which are most and least likely to be approved would be helpful; this is likely to be the case for both the current (old) and any new scheme. This could facilitate setting realistic expectations about the likely outcomes of applications, and maximise appropriate applications, ensuring that patients who might meet the CEC eligibility criteria do not miss out because their doctor fails to apply for funding. A more in-depth case-based analysis of the complete process might also be informative in further research.

There are several possible explanations for the differences in initial application outcome by age group, type of doctor and geographical location of doctor. These could include variability in eligibility of applications (which may result in appropriate variations in approval), patient mix (Auckland having some supra-regional and national services especially for rarer diseases and more complex cases) and differences in the quality and completeness of applications. The great degree of variability suggests that further work should be carried out to assess the reasons for the differences in approval rate.

Conclusions—There was no evidence that gender, ethnicity and socioeconomic status of patients were factors associated with successful applications; further research is

required to explore the reasons for the association of applicant doctor type, DHB of applicant doctor and patient age with likelihood of initial approval.

Competing interests: None declared.

Sources of funding: The study was carried out as a dissertation for the Master of Public Health. University fees for the first author were paid by her employer, PHARMAC. The co-authors were involved via their role as university supervisors. The first author (but not the second and third author) and all additional contributors (acknowledged below) are PHARMAC staff members. Study and consultation with additional contributors was carried out during a mixture of personal and work time. There were no other sources of funding and no study sponsor. To the extent that there is a funder, researchers are independent of the funder. PHARMAC management were aware of the contents of the article and the proposal that it be submitted for publication.

Author information: Dilky Rasiah, Deputy Medical Director, PHARMAC, Wellington; Richard Edwards, Head of Department, Department of Public Health, University of Otago, Wellington; Peter Crampton, Pro-Vice-Chancellor, Division of Health Sciences, University of Otago, Dunedin

Acknowledgements: We thank Geoff Lawn and Jayne Watkins for assisting with data extraction; Jason Arnold for running the SAS statistical software analysis package; and Peter Moodie and Scott Metcalfe for reviewing manuscript drafts.

Correspondence: R D Rasiah. PHARMAC, PO Box 10-254, Wellington 6011, New Zealand. Email: dilky.rasiah@pharmac.govt.nz

References:

1. Rarer Cancers Forum. Taking Exception: An audit of the policies and processes used by PCTs to determine exceptional funding requests. Found on Rarer Cancers Forum webpage dated August 2008. Available from: http://www.rarercancers.org.uk/news/current/new_rcf_report_reveals_striking_postcode_lottery_in_the_chances_of_having_an__exceptional_request_approved [accessed September 2008].
2. Desai M, Nolte E, Mays N et al. International experience of paying for expensive medicines. BMJ May 2009;338:b1993.
3. NZ Government website. Panel to help improve access to high cost medicines. Wellington: NZ. Available from: http://www.beehive.govt.nz/release/panel+help+improve+access+high+cost+medicines [accessed May 2009].
4. PHARMAC website. Available from: http://www.pharmac.govt.nz [accessed January 2010].
5. Cumming J, Mays N, Daubé J. How New Zealand has contained expenditure on drugs. BMJ 2010;340:c2441.
6. PHARMAC website Exceptional Circumstances FAQs. Available from: http://www.pharmac.govt.nz/EC/ECFAQs [accessed February 2009].
7. Personal communication with a PHARMAC staff member, 2011.
8. Austin D. Priority setting: managing individual funding requests. The NHS Confederation, Primary Care Trust Network Supported by NHS Institute for Innovation and Improvement. Published by the NHS Confederation, 2008.

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

Blinded randomised controlled study of the effect of a discharge communication template on proton pump inhibitor prescribing

Alex Lampen-Smith, Janice Young, Mary-Anne O'Rourke, Astuti Balram, Stephen Inns

Abstract

Aim To evaluate whether the inclusion of advice in the hospital discharge letter regarding published guidelines for the review of PPI therapy can increase the number of patients that have documented PPI therapy review, consistent with the published guidelines, following hospital discharge.

Method Patients on PPIs at discharge from hospital were randomised to either have their hospital discharge letter completed as per usual practice or to have additional information on PPI review included that was aligned to published local guidelines. Patients' GP records were reviewed at 3 to 6 months post discharge to determine if a PPI review had occurred and if that review adhered to the guidelines.

Results Including specific, guideline based, PPI discharge instructions in the hospital discharge summary did not significantly increase the number of patients receiving post-discharge review consistent with the guidelines. Post discharge only 5/26 (19%) patients in the control group and 6/25 (24%) in the intervention group had their PPI therapy reviewed in accordance with the guidelines.

Conclusion We were not able to demonstrate a beneficial change in PPI prescribing practice from the inclusion of PPI prescribing advice in the discharge letter.

Proton pump inhibitors (PPIs) are widely used in New Zealand to treat acid-related gastrointestinal disorders and in those considered at high risk of a gastrointestinal (GI) bleed. They are generally considered to be safe and effective if used in accordance with published guidelines, although there is some evidence that long term use may be associated with increased risk of community-acquired respiratory infections and pneumonia,[1] vitamin B12 deficiency,[1,2] hypomagnesaemia and hypocalcaemia.[3,4]

The use of PPIs continues to grow in both primary and secondary care. In 2006 and 2007 omeprazole was the highest cost medicine in New Zealand with a rate of growth of approximately 16% per annun.[5] Increased usage of PPIs has also been recognised in Australia with a 1318% increase in prescribing in the primary care setting from 1995 to 2006.[6] This trend has been noted internationally with a concern that between 25-70% of patients are prescribed PPIs inappropriately.[7]

A number of studies have evaluated prescriber compliance with published guidelines.[8–16] A study set in Dunedin Hospital identified that 40% of patients who were initiated on a PPI had an inappropriate indication for use.[8] Of patients discharged on a PPI for an inappropriate indication, 71% remained on the PPI 6 months after discharge. An Australian study demonstrated that there was non-compliance with

prescribing guidelines in 21.6% of patients admitted to hospital on a PPI.[9] In particular there was failure to use step-down therapy in patients with gastro-oesophageal reflux disease (GORD). Other studies have identified that between 33-80.4% of patients are prescribed PPIs for unapproved or unknown indications.[13-16]

One strategy that could increase adherence to PPI prescribing guidelines is to improve the advice given to general practitioners (GPs) on the need for PPI review post discharge from hospital. The hospital discharge letter could be utilised for this. Several studies have identified that the quality of information concerning PPI review in the discharge letter is frequently inadequate.[8,10,17] The Dunedin study found that less than 25% of all patients started on PPI therapy in hospital had any discharge information recommending duration of therapy or review.[8]

Results from this study suggested that GPs were not provided with adequate guidance on reviewing PPI use in their patients post discharge from hospital, patients were not reviewed, and ongoing PPI treatment was continued, sometimes unnecessarily. A recent study set in Germany identified that inadequate recommendations for PPI review in discharge letters was common, with 54.5% of letters containing no information justifying the recommendation for continuous PPI medication. [17]

National guidelines for the management of patients with dyspepsia and heartburn have been published by the New Zealand Guidelines Group (NZGG).[18] Prescriber adherence to the NZGG guidelines could be increased by improving the advice given to GPs in the discharge letter. The aim of this study was to evaluate whether the use of an electronic tool with compulsory fields incorporated into an existing electronic discharge form could increase the number of patients that have PPI therapy stopped or reviewed following hospital discharge in accordance with the NZGG guidelines.

Methods

The study was set within the Hutt Valley District Health Board (HVDHB), Lower Hutt, New Zealand, with patients recruited whilst inpatients at Hutt Hospital, a 260-bed secondary-level care hospital. The study period was from February 2009 to February 2010.

Selection of patients—Hospital medical staff identified consecutive patients who had a PPI previously prescribed, or prescribed as an inpatient, and who were to be discharged on PPI. Enrolled patients were asked to consent to their GP medical notes being reviewed after discharge by a Kowhai Health Trust (KHT) pharmacist (study pharmacist). The following information was recorded at enrolment: gender, date of birth, place of initiation of PPI (during hospital admission or prior to hospital admission) and indication for PPI therapy. If therapy with a PPI was not indicated, this was also recorded.

Patients were excluded from the study if they did not provide consent for their medical notes to be reviewed after discharge, or if they died less than 3 months post discharge from hospital.

Intervention—Patients were randomised in blocks of four to either the control or intervention group. The control group had their discharge summary completed as per usual practice (no specific PPI template completed). The intervention group had a specific PPI template completed that allowed the discharge letter to be populated with instructions to the GP concerning the review of PPI therapy for that patient depending on PPI indication. These instructions were aligned to the NZGG guidelines[18] (Table 1).

Table 1: PPI review instructions populated on discharge letters of intervention group as per The New Zealand Guidelines for the Management of Dyspepsia and Heartburn

Indication identified by doctor	Review instructions on discharge summary
Dyspepsia	Treat 4–12 weeks and review
GORD	Treat 4 to 8 weeks and review then step down in 1 to 3 month
Gastric ulcer	Treat 8 to 12 weeks. Confirm healing with OGD & biopsy
Duodenal ulcer	Treat 4 to 8 weeks (Note: where H pylori has been treated, acid suppression is not essential)
Gastro-protection	Review patient risk. Consider using safer alternatives to NSAIDS & review need for ongoing gastro-protection
No clear indication	Please review in primary care
Other	Other instructions

GORD=gastro-oesophageal reflux disease.

Patient follow-up—GP consent was obtained for a study pharmacist to review the medical notes of all enrolled patients 3 to 6 months following discharge from hospital. Study pharmacists who reviewed patients' notes were blinded to allocation group and did not access information contained in the patient's discharge letter. Given the only method available for determining whether the discharge instructions (and thus the current NZ dyspepsia guidelines) had been followed was documentation of a review of the PPI prescription, patients' GP medical notes were reviewed to identify any such documentation.

The action taken by the GP was compared to the NZGG guidelines (Table 1). The primary outcome measure was the presence of a documented review that corresponded with practice consistent with the NZGG guidelines.

Ethical approval—The study was approved by the Upper South A Regional Ethics Committee.

Study size calculation and statistical methods—70% of patients remain on PPI 6 months after starting it in hospital whether or not the institution of therapy was appropriate.[8] We estimated that a significant contribution of an interventional tool would be to halve the proportion of patients not reviewed in accordance with the New Zealand guidelines (i.e. to 35% of patients). The sample size needed to show the above difference with alpha 0.05 and beta 0.8 is 65 patients.

A 2-sided Pearson Chi-squared test was used to compare the presence of a documented review, adhering to the New Zealand guidelines, between the control and intervention groups. Demographic variables were compared using a 2-sided Pearson chi-square test for categorical variables and the student t-test for parametric continuous variables.

Results

Sixty-five consecutive patients were enrolled in the study. Of these, 14 patients were excluded for the reasons outlined below (Table 2).

Table 2: Reasons for patient exclusion from the study

Reasons for exclusion from the study	Number of patients
Insufficient data recorded on enrolment form	3
Lost to follow-up, e.g. patient moved to another district health board area	3
Patient deceased <3 months post discharge from hospital	7
Duplicate enrolment	1
Total	**14**

Demographic information from patients enrolled in the control versus the intervention group is shown in Table 3. The two groups were similar in age, gender and ethnicity. With respect to indication for PPI therapy, the intervention group contained a higher percentage of patients receiving PPI for dyspepsia 8 (32%) compared to the control group 3 (12%).

Table 3. Characteristics of patients in control versus intervention groups

Variables	Control (n=26)	Intervention (n=25)	P value
Mean age	75 yrs (50-92)	77 yrs (57-93)	0.44
Male	8 (31%)	10 (40%)	0.49
Ethnicity			
NZ European	17 (65%)	16 (64%)	0.9
European – not defined	4 (15%)	6 (24%)	0.44
Pacific	1 (4%)	1 (4%)	0.97
Indian	-	1 (4%)	0.3
Māori	1 (4%)	1 (4%)	0.97
Unknown	3 (12%)	–	0.08
Indication for PPI			
Dyspepsia	3 (12%)	8 (32%)	0.08
GORD	6 (23%)	5 (20%)	0.79
Gastric ulcer	3 (12%)	–	0.08
Duodenal ulcer	–	1 (4%)	0.3
Gastrointestinal protection	9 (35%)	9 (36%)	0.92
No clear indication	4 (15%)	2 (8%)	0.41
Other	1 (4%)	–	0.32
PPI-initiated in hospital	5 (19%)	7 (28%)	0.46

Follow-up of patients in primary care post discharge—51 patients had their medical records reviewed at their GP practice (Table 4) by a study pharmacist to determine the presence of a documented review adhering to the New Zealand guidelines. At 3 to 6 months post discharge, 5 (19%) of patients in the control group and 6 (24%) of patients in the intervention group had had their PPI therapy reviewed in accordance with the guidelines.

Table 4. Follow-up of patients 3–6 months post discharge

Outcome 3–6 months post discharge	Control (n=26)	Intervention (n=25)
Documented review in accordance with NZGG guidelines	5 (19%)*	6 (24%)*
Reviewed – no change in PPI indicated	2	1
dose decreased	1	
PPI stopped then restarted		2
PPI stopped	2	3
No review or documented practice not consistent with NZGG guideline:	21 (81%)	19 (76%)
No evidence of a GP review or change in PPI prescribing	21	15
Evidence of review but no change in PPI		1
Reviewed PPI for side effects but not for appropriateness of use (PPI stopped then started again)		1
Dose increased		1
PPI stopped but was still indicated		1

*Pearson's Chi-squared: p=0.7.

Discussion

Inappropriate prescribing of PPI's in both primary and secondary care has been commented on in a number of studies.[8–16] Appropriateness of PPI prescribing in secondary care in New Zealand has been reported at 60%.[8] Our study is the first published investigation of the effectiveness of the discharge letter in promoting medication review through the provision of drug information or advice.

Our group shows poor compliance with New Zealand guidelines with only 5(19%) and 6(24%) of GP's within the control and intervention group respectively documenting that PPI therapy had been reviewed according to the NZGG guidelines. It may be that the number of patients who had a PPI review was underestimated by the methods used in our study, as reasons for continuation of therapy are not always documented in GP records even if a review has occurred.

In patients on a PPI for gastro-protection it was considered unlikely and impractical that the GP would actively document that they had reviewed the use of the PPI, unless the patient's NSAID was discontinued. It would appear however that this did not impact on the likelihood of a patient having a documented review, as the spread of indications for patients who had no evidence of a GP review appeared to be comparable to the spread of indications for the study population as a whole. However, it would be worth noting that 11/36 (31%) of patients who had no documentation of a PPI review were considered to be using a PPI for gastro-protection.

There was a difference in documented PPI review of 10/25 (40%) in the intervention group versus 5/26 (19%) in the control group. This would suggest that our intervention made some difference to GP behaviour but did not lead to a significant difference in compliance with the local guidelines. It should be noted that unexpected patient exclusions post randomisation meant our final sample size did not meet that planned. In addition the rate of adherence with the guidelines in both groups was less than estimated. These factors reduced the power of our study and thus it's ability to detect a small difference between the groups.

A number of factors may have contributed to the ineffectiveness of the intervention. A GP survey performed following the study indicated that 66% of doctors in the intervention group did not see the additional PPI prescribing information. The length and layout of the discharge letter may have contributed to this. It has been identified that the perceived quality of a discharge letter decreases if it exceeds 2 pages in length.[20]

This study demonstrates that, according to documentation in the primary care record, adherence with the NZGG guidelines on PPI prescribing is poor post hospital discharge. We were not able to demonstrate a beneficial change in PPI prescribing practice from the inclusion of PPI prescribing advice in the discharge letter. This may relate to the fact that GPs did not notice the advice in the discharge letter.

Further research is needed to identify a strategy that could promote PPI review in primary care and beneficially affect PPI prescribing practice.

Competing interests: None declared.

Author information: Stephen Inns, Gastroenterologist, Gastroenterology Department, Hutt Valley DHB, Lower Hutt; Alex Lampen-Smith, Medical Registrar, Department of Internal Medicine, Hutt Valley DHB, Lower Hutt; Astuti Balram, Clinical Advisory Pharmacist, Kowhai Health Trust, Lower Hutt; Janice Young, Clinical Advisory Pharmacist, Kowhai Health Trust, Lower Hutt; Mary-Anne O'Rourke, Clinical Advisory Pharmacist, Kowhai Health Trust, Lower Hutt

Acknowledgements: The authors thank the patients and GPs who participated in this study as well as the hospital medical staff who assisted with enrolling patients (particularly Dr M Wolbinsky and Dr J Pigou). The authors also acknowledge PHARMAC (New Zealand's Pharmaceutical Management Agency) for its financial support in this study.

Correspondence: Stephen Inns, Gastroenterologist, Gastroenterology Department, Hutt Hospital, Private Bag 31-907, Lower Hutt 5010, New Zealand. Fax: +64 (0)4 5709526; email: stephen.inns@huttvalleydhb.org.nz

References:

1. Raghunath AS, O' Morain C, McLoughlin RC. Review article: the long-term use of proton-pump inhibitors. Aliment Pharmacol Ther. 2005;22(suppl.1):55–63.
2. Malaty W, Stigleman S, Mayer J. Clinical inquiries: Is the long-term use of proton pump inhibitors safe? The Journal of Family Practice. 2004;53(9):740–1.
3. Kuipers MT, Thang HD, Arntzenius AB Hypomagnesaemia due to use of proton pump inhibitors – a review. The Netherlands Journal of Medicine. 2009;67(5):169–172.
4. Omeprazole and risk of hypomagnesaemia. Prescriber Update. 2010;31(2):13.
5. PHARMAC Pharmaceutical Management Agency Annual Report 2007.
6. Hollingworth S, Duncan EL, Martin JH. Marked increase in proton pump inhibitors in Australia. Pharmacoepidemiology and Drug Safety. 2010;19:1019–1024.
7. Forgacs I, Loganayagam A. Overprescribing proton pump inhibitors. BMJ. 2008;336(7634):2–3.
8. Grant et al. Continuation of Proton Pump Inhibitors from Hospital to Community. Pharm Sci World. 2006;28:189–193.
9. Hughes JD, Tanpurekul W, Keen NC, Ee HC. Reducing the cost of proton pump inhibitors be adopting best practice. Quality in primary Care. 2009;17:15–21.
10. Chai M, Chiaroni ML, Li V, Marinkovich D, Woo T. A drug use evaluation of proton pump inhibitor prescribing at Middlemore Hospital (2007). School of Pharmacy, Faculty of Medical and Health Sciences, The University of Auckland. (unpublished).
11. Kirby CN, Piterman L, Nelson MR, Dent J. Gastro-oesophageal reflux disease: Impact of guidelines on GP management. Australian Family Physician. 2008;37(1/2):73–77.
12. Walker NM, McDonald J. An evaluation of the use of proton pump inhibitors. Pharmacy World and Science. 2001;23(3):116–117.
13. Mat Saad AZ, Collins N, Lobo MM, O'Connor HJ. Proton pump inhibitors: a survey of prescribing in an Irish general hospital. Int J Clin Pract. 2005;59(1):31–34.
14. Ramirez E, Lei SH, Borobia AM, et al. Overuse of PPIs in patients at admission, during hospitalisation, and at discharge in a tertiary Spanish hospital. Current Clinical Pharmacology. 2010;5:288–297.
15. Pillans PI, Kubler PA, Radford JM, Overland V. Concordance between use of proton pump inhibitors and prescribing guidelines. Med J Aust. 200;172(1):16–8.

16. Heidelbaugh JJ, Goldberg KL, Inadomi JM. Magnitude and economic effect of overuse of antisecretory therapy in the ambulatory care setting. American Journal of Managed Care. 2010;16(9):e228–34.
17. Ahrens D, Chenot JF, Behrens G, et al. Appropriateness of treatment recommendations for PPI in hospital discharge letters. Eur J Clin Pharmacol. 2010;6:1265–1271.
18. The New Zealand Guidelines for the Management of Dyspepsia and Heartburn. New Zealand Guidelines Group; 2004.
19. Bolton P, Mira M, Kennedy P, Moses Lahra M. The quality of communication between hospitals and general practitioners: An assessment. J Qual Clin Practice. 1998;18:241–247.
20. van Walraven C, Rokosh E. What is necessary for high quality discharge summaries? American Journal of Medical Quality. 1999;14:160–169.

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

A review of interferon use in patients with relapsing remitting multiple sclerosis in the Canterbury region, New Zealand: 2000–2006

Susan Byrne, Deborah Mason

Abstract

We report a retrospective medical chart review of 104 patients resident in Canterbury and surrounding districts with relapsing remitting multiple sclerosis (RRMS), who received funded interferon-beta between 2000 and 2006. The aim of the study was to review relapse rates, Expanded disability status scale (EDSS) scores and intravenous methylprednisolone (IVMP) use in the 2-year period before, and following, the initiation of interferon-beta therapy. Demographic analysis showed that the age at entry, duration of disease and EDSS at entry were each greater than in the landmark clinical trials. Relapse rates and usage of IVMP decreased when compared to the 2 years prior to treatment.

Multiple sclerosis (MS) is the most common debilitating neurological disease of young adults in Western countries including New Zealand. Historical treatments for MS were largely considered to be symptomatic. However, in 1993, based on evidence from several landmark clinical trials which showed benefit in reducing relapse rates, it was suggested that the accumulation of disability might be delayed, Interferon Beta (IFB)[1-3] was licensed by the Food and Drug Administration (FDA) authorities in the United States. Patients included in the pivotal trials[1-3] included those with: a diagnosis of relapsing remitting multiple sclerosis (RRMS); two relapses lasting 24 hours or longer, in the preceding 2 years and an EDSS between 0 (no disability) and 5.5 (able to walk 100 metres without support).

In 1999 the Pharmaceutical Management Agency of New Zealand (PHARMAC) agreed to fund IFB. The Multiple Sclerosis Treatments Assessments Committee (MSTAC) was formed to oversee the allocation of funding. Glatiramer acetate (Copaxone®),[4] a non-interferon, was added to the list in 2006. MSTAC established a unique set of eligibility criteria that required greater disease activity and disability than in the pivotal trials. These included, two relapses, each lasting longer than one week within the preceding 1 year, and an EDSS between 3.0 (moderate disability) and 6.5 (able to walk 20 metres with bilateral assistance).

The criteria were modified in December 2005, to include patients with a lower entry EDSS, (between 2.5 and 5.5 with two relapses in the previous year or between 2.0 and 5.5 with three or more relapses in the previous year). The brand of interferon was chosen by the neurologist in conjunction with the patient. Annual reassessment by a consultant neurologist/physician was required for continuation of funding. Exit criteria were also specified. These included the same or an increased annual relapse rate, a one-point worsening of the EDSS from entry, or worsening of EDSS to 7.0. In 2005, the exit EDSS was decreased from 7.0 to 6.0, or more.

Methods

A retrospective medical chart review of patients within the Canterbury region who received publicly funded interferon therapy was performed. Patients included in the review received funded Interferon between January 2000 and November 2006, 104 patients were identified from the MSTAC database. Complete ascertainment was confirmed by cross-referencing Christchurch Hospital Neurology Department's own database with the national MSTAC database. Local Ethics Committee approval was obtained.

Data was collected from medical records and from annual assessment records submitted by the neurologist to MSTAC. Data collected included: time since onset of first demyelinating symptom, time since diagnosis of MS; birth date; age at diagnosis; age at starting interferon therapy; type of interferon therapy; the number of relapses recorded by a doctor in the 2 years prior to initiating therapy; number of IVMP courses administrated in the 2 years prior to therapy and EDSS at entry. Post IFB relapse rates, IVMP usage and EDSS were analysed. Side effects and adverse reactions were also recorded. Reasons for discontinuation or switching of therapy were also noted.

Demographic data collected included age, gender, and duration of disease. Disease activity was assessed for the 2 years prior to the initiation of therapy by examining recorded relapse rates as well as intravenous methylprednisolone (IVMP) usage. Factors reflecting disease activity following the introduction of IFB including the annualised relapse rate, change in EDSS score and IVMP usage were also recorded. Adverse reactions were noted and details were obtained about patients who discontinued treatment or for whom funded treatment was withdrawn on the basis of reaching exit criteria.

Results

Of the 104 patients identified, 101 charts were available for review. Three of the 101 patients started self-funded interferon therapy prior to the introduction of government funding. The data for these three patients have been included. Seventy-five women and 26 men were started on funded interferon therapy during the period January 2000 to November 2006. Women on funded interferon therapy outnumbered men 2.9:1. Baseline characteristics of patients beginning therapy are given in Table 1. At audit date (November 2006), 72 patients (71%) were still on interferon therapy and 29 (29%) had withdrawn from treatment, 13 of whom were withdrawn because they reached exit criteria.

The average age for starting interferon therapy was 41.3±10.6 years. The average disease duration at initiation of therapy was 8.9±8.4 years. In 2002, two types of interferon were funded by PHARMAC. In 2005, Copaxone®(a non-interferon) was added. In 83 patients (82%) the initial treatment selection was Betaferon®,17 (16%) Avonex® and 1 Copaxone®. Of the 83 who started Betaferon®, 60 (72%) remained on it. Of the 23 no longer on Betaferon®, 5 fulfilled exit criteria, 5 could not tolerate side effects, 10 stopped for reasons discussed below and 3 switched to Avonex® and subsequently reached exit criteria. Of the 17 who started Avonex®, 5 (30%) remained on it, 8 fulfilled exit criteria, 1 planned pregnancy and 3 changed to Betaferon,® of which 1 subsequently fulfilled exit criteria. One patient remains on Copaxone®.

The annualised relapse rates for years 1 and 2 are given in Table 2. Relapse rates are presented by comparing year 1 (year +1) and year 2 (year +2) of therapy with year 1 (year -1) and year 2 (year -2) prior to treatment. Results are presented only for those patients who completed a full year.

Table 1. Baseline characteristics of patients beginning funded interferon therapy between 2000–2006, and comparison to baseline characteristics from pivotal interferon trials

Variables	Patients initiating treatment (M/F)	Type Interferon	EDSS at entry (mean±SD)	Age at entry (mean±SD)	Disease duration (yrs) (Mean±SD)
2000	42 (13/29)	Betaferon® 29 Avonex® 13	4.7±1.2	42.4±9.2	10.0±8.6
2001	4 (1/3)	Betaferon® 2 Avonex® 2	5.1±1.3	50.5±12.9	13.9±8.5
2002	16 (3/13)	Betaferon® 16 Avonex® 0	4.5±1.1	42.5±11.7	8.0±8.6
2003	15 (4/11)	Betaferon® 15 Avonex® 0	4.3±1.2	39.4±12.8	7.0±7.8
2004	10 (2/8)	Betaferon® 10 Avonex® 0	4.8±1.0	39.4±13.2	9.4±11.4
2005	8 (2/6)	Betaferon® 5 Avonex® 2 Copaxone® 1	4.1±1.0	38.6±7.8	9.6±6.8
2006	6 (1/5)	Betaferon® 6 Avonex®	3.6±0.7	37.3±9.2	5.3±4.7
All patients (2000–2006)	101 (26/75)	Betaferon® 83 Avonex® 17 Copaxone® 1	4.5±1.1	41.3±10.6	8.9±8.4
Current patients	72 (19/53)		4.5±1.1	41.5±10.7	8.6±8.7
Fulfilled exit criteria	13 (3/10)		4.8±1.2	43.5±11.7	10.5±7.3
MSCRG 1996 [7]		Avonex®	2.4	36.7	6.6
IFNB MS GROUP 1993 [7]		Betaferon®	2.9	35.2	4.7
PRISMS 1998 [7]		Rebif®	2.5	34.9	5.3

The average relapse rate for all patients in the year preceding therapy was 2.5 relapses±0.7; while the relapse rate for the penultimate year before therapy was 0.8±0.9. The relapse rate following the first year of therapy was 0.5±0.7. Ninety-four patients completed the first full year of therapy. Of the seven not included in the analysis of the first 12 months, 5 started treatment in the 12 months prior to census and two stopped therapy before completing 1 year because of side effects. One discontinued treatment as an alternate diagnosis to MS was made. Seventy-four patients received 2 full years of therapy and the annual relapse rate in the second year of therapy was 0.4±0.6.

Table 2. Annualised relapse rates for years 1 and 2 prior (year -1, -2) to therapy and for years 1 and 2 (year +1,+2) on therapy

Variables	Annual Relapse Rates			
	Year -2	Year -1	Year +1	Year +2
All patients	0.8±0.9 [101]	2.5±0.7 [101]	0.5±0.7 [94]	0.4 ±0.6 [74]
Patients currently on treatment	0.7±0.7 [72]	2.5±0.7 [72]	0.5±0.7 [66]	0.4±0.5 [56]
Patients who fulfilled exit criteria	1.2±1.5 [13]	2.5±0.7 [13]	1.1±1.0 [13]	1±0.8 [8]

Note: The numbers in square brackets represent the actual number of patients in each group.

The average EDSS at entry of all patients was 4.5±1.1. In the 72 patients still on Interferon therapy at audit date the EDSS was 4.5±1.1, while the entry EDSS for the patients withdrawn from therapy because they fulfilled exit criteria was 4.8±1.2 (Table 3). It should be noted that EDSS entry criteria were changed only at the end of 2005. The entry EDSS criterion before this time was greater than or equal to 3.0.

Table 3. Average EDSS scores on treatment

	EDSS Entry (average)	EDSS Year +1	EDSS Year +2	EDSS Current (Nov 2006)
All patients	4.5±1.1 [101]	4.3±1.5 [92]	4.3 ±1.4 [73]	n/a
Patients currently on treatment	4.5±1.1 [72]	4.1±1.4 [67]	4.2±1.4 [59]	4.0±1.5 [67]
Patients who fulfilled exit criteria	4.8±1.2 [13]	5.6 ±1.6 [11]	6.1±0.3 [4]	n/a

Note: The numbers in square brackets represent the actual number of patients in each group.

Annual IVMP treatment of relapse data for the 2 years before, and the 2 years following, treatment are summarised in Table 4.

Table 4. Annual IVMP use for years 1 and 2 prior to therapy and for years 1 and 2 on therapy

Variables	Annualised Use of IVMP			
	Year -2	Year -1	Year +1	Year +2
All patients	0.6±0.8 [101]	1.8±1.2 [101]	0.4±0.6 [94]	0.4±0.6 [74]
Patients currently on treatment	0.5±0.7 [72]	1.8±1.2 [72]	0.2±0.5 [66]	0.3±0.5 [56]
Patients who fulfilled exit criteria	0.8±1.4 [13]	1.9±1.3 [13]	1.1±1.0 [13]	0.9±0.9 [8]

Note: The numbers in square brackets represent the actual number of patients in each group

Nine of the 13 patients who reached funded exit criteria did so on the initially prescribed Interferon-beta (4 Betaferon®, 5 Avonex®), while 4 patients switched interferon brand and subsequently fulfilled exit criteria (1 Betaferon®, 3 Avonex®). Neutralising antibody status was not ascertained in any patient.

Of the 16 other patients who withdrew, the following reasons were recorded: 5 due to side effects (5 Betaferon®- not specified; pustular psoriatic flare; flu like symptoms; drug related hepatitis; mood disturbance; 3 planned pregnancy (2 Betaferon®, 1 Avonex®); 2 considered themselves to be too well to need treatment (2 Betaferon®); 2 moved away (2 Betaferon®); 1 person was non-compliant for reasons unrecorded (1 Betaferon®); 1 stopped for unrecorded reasons (1 Betaferon®); 1 died from deliberate self harm (1 Betaferon®) and 1 person was withdrawn due to an alternative diagnosis being made (1 Betaferon®). Withdrawal rates were similar for both men and women. Thirty-five side effects or adverse reactions from IFB were reported in the medical notes of 30 patients (Table 5).

Table 5. Reported side effects

Symptoms		Patients reporting this side effect
Flu-like symptoms	(1 withdrew)	8
Marked injection site reactions		7
Headache		3
Psoriatic flare	(1 withdrew)	2
Mood change	(1withdrew)	5
Hepatitis	(1 withdrew)	1
Itching		1
Menorrhagia		1
Fatigue		1
Arthralgia		1
Not specified	(1 withdrew)	1
Night sweats		1
Liver function abnormalities		2
Neutropenia		1

Discussion

Currently 520 Correct patients throughout New Zealand are receiving funded disease modifying drugs for RRMS (personal communication MSTAC). This audit of patients residing in Canterbury, details the clinical outcomes of 101 patients who received therapy between January 2000 and November 2006.

The PHARMAC funding eligibility criteria introduced in 2000 presumed that the therapeutic benefits of disease modifying drugs were likely to be greatest in those with a high relapse rate, 2 or more attacks in 12 months and those with more established disability (EDSS 3.0–6.5).

As a result the relapse rate and EDSS at entry is greater in our patient group as compared with the pivotal trials. This is the likely explanation also for the finding that the age at entry and the average duration of disease prior to treatment in this group of 8.9±8.6 years is longer than for patients in the pivotal trials (Table 1). In light of overseas experience suggesting benefit in treating people early in the disease[6], the entry criteria were revised in 2005 to include people with a lesser degree of disability (EDSS 2.0–2.5).

As a result, the trend over the 6 years is towards entering patients with a lower EDSS score and a shorter duration of disease (Table 1). This would seem to be appropriate given that 50% of patients will, within 10 years have converted to secondary progressive multiple sclerosis (SPMS).[5] Similarly the age at which patients first start treatment group has also decreased (Table 1).

Relapse rates decreased in the 2 years following treatment. The high relapse rate over the year prior to treatment (2.5±0.7) is not unexpected as the eligibility criteria required two or more relapses in the year before treatment. The relapse rate for all groups at 2 years prior to entry (year -2) was 0.8±0.9. The relapse rate for all groups at 1 year (year +1) and 2 years (year +2) post therapy was 0.5±0.7 and 0.4±0.6 respectively.

Comparing year -1 with year +1, the relapse rate decreased by 80%. Comparing year -2 with year +2, the relapse rate decreased by 50%. Although there may have been some under-reporting of relapses following the initiation of treatment (as patients whose relapse rate remained unchanged or increased were deemed ineligible for ongoing funding), the reduction in relapse rate recorded in this audit, when compared to trial relapse rates at 2 years, show a better outcome.[1–3] It is also possible that because these patients had MS longer than had participants in pivotal clinical trials they were more likely to show regression to the mean. It seems unlikely however that this would account for all the reduction seen in relapse rate.

Although the correlation between relapse rate and disease progression is still not clearly defined, the impact upon quality of life and the need for hospitalisation from relapses is important. IVMP usage decreased by 33% following treatment (Table 4).

Criteria were modified in December 2005 to include patients with an EDSS of 2.0 or 2.5 (depending on relapse frequency). Despite this the mean disability scores at initiation of therapy over the six year period of the audit remained significantly higher

than for those in the pivotal trials.[7] Of the patients on treatment at the time of audit, 45 patients had been on therapy for three or more years and 51% had had three consecutive years with no relapses and had a decreasing or static EDSS. Patients who fulfilled exit criteria had a slightly higher EDSS and disease duration at entry.

Adherence to therapy was excellent. This most likely reflects the high level of commitment in this particular patient group, together with measures in place that promote compliance. These include training and regular contact by MS nurses, the MS society and company representatives, through support programmes and yearly review by a neurologist or physician.

The rate of withdrawal from therapy was 29%. Of this group, 13 (45%) had funding withdrawn as they fulfilled exit criteria: 9 because of an increase in EDSS and four due to continuing relapses. Of the nine patients who lost funding, all did so because the EDSS score exceeded six. No one was withdrawn because their EDSS increased by 1.0 point, unless it then exceeded 6.0. Current immunodulatory therapies are not curative and it is therefore expected that the mean EDSS will increase over time.

There is currently no consensus among MS neurologists as to what constitutes "treatment failure". It has been shown that the mean change in EDSS over time is greater in those with an EDSS <3. This likely reflects the non-linear nature of the EDSS scale and the greater inter and intra-rater variability at low EDSS scores rather than reflecting greater disease activity. Changes to the entry criteria in 2005 were not adjusted to take this into account, so that this particular patient group may be expected to reach exit criteria earlier than those whose EDSS was greater than 3 at entry.

Limitations of this audit include the retrospective nature of the study in a single-region. However 13% of MSTAC approvals for IFB are from the Auckland region, 14% from Waikato, 26% from Canterbury and 38% from Otago, in part reflecting the latitudinal gradient one sees in the prevalence of MS in NZ. Therefore patients from Canterbury provide a reasonable sample of the overall use of IFB, particularly given that the criteria are centrally administered and universally applied throughout the country.

Another limitation is the possible bias introduced by the fact that data relevant to relapse rate was important for initiation and maintenance of therapy. Whilst this may have lead to some underreporting of relapses the inclusion of treatments with IVMP followed a similar trend. This audit provides only limited data for Copaxone which was not introduced until 2005. It would therefore be interesting to repeat this audit for the period 2006–2010 during which 35% of approvals were for Copaxone, 34% for Betaferon and 31% for Avonex.

This audit demonstrates that the safety profile and the adherence rate amongst patients using disease modifying treatments for MS has been excellent. More than half the patients who had been on therapy for 3 or more years have a stable EDSS and have been relapse free for 3 years or more. These benefits are present, despite entry criteria set to demand a higher level of disease activity and greater level of disability than those in published trials.

At present, less than 30% of all patients with RRMS are receiving funded treatment in New Zealand (Personal communication, MS Prevalence Study 2006,) By comparison

there are approximately 13,500 patients in Australia with relapsing remitting MS (Personal communication, Dr Bruce Taylor 2011of whom about 11,000 (80%) are receiving funded treatment.

It is our belief that similar benefits to those seen in MS patients in the Canterbury region could be achieved in a greater percentage of patients with relapsing remitting MS if the eligibility criteria were broadened.

Competing interests: None.

Author information: Susan Byrne, Neurology Fellow, Trinity College, Dublin, Ireland Deborah Mason, Consultant Neurologist, Neurology Department, Christchurch Hospital, Christchurch, New Zealand

Correspondence: Dr Susan Byrne. Email: suabyrne@gmail.com

References:

1. The IFNB Multiple Sclerosis Study Group. Interferon beta 1b is effective in relapsing-remitting multiple sclerosis. I. Clinical results of a multicenter, randomised, double-blind, placebo-controlled trial. Neurology 1993;43:655-661.
2. PRISMS (Prevention of Relapses and Disability by Interferon B-1a Subcutaneously in Multiple Sclerosis). Randomised double-blind placebo controlled study of interferon B-1a in relapsing/remitting multiple sclerosis. The Lancet 1998;352;1498-1504
3. Jacobs LD, Cookfair DL, Rudick RA, et al. Intramuscular interferon beta-1a for disease progression in relapsing multiple sclerosis. The Multiple Sclerosis Collaborative Research Group (MSCRG). Ann Neurol 1996:39(3):285-294.
4. Johnson KP, Brooks BR, Cohen JA, et al. Copolymer 1 reduces relapse rate and improves disability in relapsing-remitting multiple sclerosis: results of a phase III multicenter, double-blind placebo-controlled trial. The Copolymer 1 Multiple Sclerosis Study Group. Neurology 1995;45(7):1268-76
5. Jacobs LD, Beck RW, Simon JH, et al. Intramuscular interferon beta-1a therapy initiated during a first demyelinating event in multiple sclerosis. CHAMPS Study Group. N Engl J Med 2000;343:898-904.
6. Weinshenker BG, Bass B, Rice GP, et al. The natural history of multiple sclerosis: a geographically based study. 2. Predictive value of the early clinical course. Brain 1989;112:1419–28.
7. Rice G PA, Incorvaia B, Munari L, et al. Interferon in relapsing-remitting multiple sclerosis. Cochrane Database of Systematic Reviews 2001,Issue 4. Art. No.: CD002002. DOI: 10.1002/14651858.CD002002.

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

Incidental vertebral fractures on computed tomography

Pui Ling Chan, Taryn Reddy, David Milne, Mark J Bolland

Abstract

Vertebral fractures are the most common osteoporotic fracture and predict subsequent fracture and mortality. We undertook an audit (Auckland City Hospital, Auckland, New Zealand) to determine whether targeted assessment for incidental vertebral fractures on computed tomography (CT) examinations of the chest or abdomen in older people would detect previously unidentified vertebral fractures. In 175 consecutive patients aged >65 years, sagittal images of the spine were obtained by reformatting data from CT examinations of the chest or abdomen. Vertebral fractures were assessed using a semi-quantitative technique.

The prevalence of vertebral fractures was 13%, with 41 vertebral fractures identified in 22 patients; 12/22 (55%) had vertebral fracture mentioned in the formal CT report, and 2/12 patients with contemporaneous plain films had vertebral fracture mentioned in the X-ray report. The vertebral fracture was newly identified in 17 (77%) patients, but vertebral fracture and osteoporosis were each listed in the relevant discharge summary or clinic letter for only 14% of patients, and only 31% of patients with fracture subsequently received osteoporosis treatment.

In summary, assessing sagittal spine images reformatted from CT examinations of the chest or abdomen detects previously unidentified vertebral fractures, offering an undervalued opportunity to assess fracture risk and intervene with treatments that prevent fractures and reduce mortality.

Vertebral fractures are the most common osteoporotic fracture and frequently occur in older men and women. The incidence of radiological vertebral fractures is approximately 1% per year in older women and 0.5% per year in older men,[1] with a prevalence of 10–20% at age 65 years.[2] Radiological vertebral fractures are strong predictors of subsequent vertebral, hip and other osteoporotic fractures[3] and mortality.[4]

Vertebral fractures are usually diagnosed using lateral spine radiographs, although they are also commonly detected incidentally on chest radiographs. More recently, incidental vertebral fractures have been detected on multislice computed tomography (CT) examinations of the chest or abdomen.[5] Reformatting of the axially acquired dataset can be used to generate sagittal images of the spine, allowing ready detection of vertebral fractures.[5,6]

We undertook a simple audit to determine whether routine assessment for incidental vertebral fractures on CT examinations of the chest or abdomen in older people would detect previously unidentified vertebral fractures.

Methods

Sagittal reformatting was carried out on consecutive scans of patients aged >65 years who underwent CT examination of the chest and/or abdomen in Auckland City Hospital (Auckland, New Zealand) over 4 weeks in November 2009. All the CT scans were requested as part of routine clinical care, but we did not record the indications for each scan. All CT examinations were reported routinely by the duty radiologist.

For this audit, all images were subsequently assessed by one radiologist (TR) for vertebral fractures, using the semi-quantitative technique developed by Genant.[7] In brief, each vertebra is graded from 0 to 3: Grade 0 = normal, no fracture; Grade 1 = mildly deformed, approximately 20–25% reduction in anterior, middle, and/or posterior height and a reduction in vertebral area of 10–20%; Grade 2 = moderately deformed, approximately 25–40% reduction in any height and a reduction in area of 20-40%; Grade 3 = severely deformed, approximately >40% reduction in any height and area. It was also recorded whether any fractures identified on CT were noted in the formal CT report, and whether vertebral fractures were reported on plain films taken at the same visit or previously.

Finally, the relevant discharge summary or clinic letter was reviewed to determine whether the patient had pre-existing osteoporosis, whether the vertebral fracture was noted, and whether the patient was treated with osteoporosis medications.

Results

CT examinations from 175 patients were reviewed: 77 (44%) included the thoracic spine, 144 (82%) the lumbar spine, and 48 (27%) both the thoracic and lumbar spine. Eighty-two (47%) of the patients were male and 93 (53%) female; 80 (46%) were aged 65–74 years, and 95 (54%) were aged ≥75 years.

The prevalence of radiological vertebral fracture was 13%: 41 vertebral fractures were identified in 22 patients (Table 1).

Twenty-two fractures occurred in 14 women, and 19 fractures in 8 men; 11(50%) individuals with a vertebral fracture were aged 65–74 years, and 11 were aged ≥75 years.

Eighty-five percent of fractures were in the lower thoracic or lumbar region, and 15/22 (68%) patients had at least 1 fracture with severe deformity; 12/22 (55%) patients had vertebral fracture mentioned in the formal CT report.

In patients with vertebral fracture, 2 of 12 patients (17%) with contemporaneous plain films had vertebral fractures mentioned in the X-ray report. 4 of 12 patients (33%) with previous plain films had a previous report of a vertebral fracture: in all cases, this fracture was in the same location as the fracture identified on the current CT examination.

Of the 22 patients with vertebral fracture, 2 had pathological fractures, 8 (36%) had pre-existing osteoporosis, and 5 (23%) had a history of previous vertebral fracture. In the problem list or medication summary of the relevant discharge summary or clinic letter, 3 (14%) had vertebral fracture listed, 3 (14%) had osteoporosis listed, and 7 (31%) had treatment for osteoporosis listed.

Table 1. Characteristics of 22 patients with vertebral fractures identified on CT

Variables	n (%)
Gender	
Male	8 (36)
Female	14 (64)
Age (years)	
65–74	11 (50)
75+	11 (50)
Site of fractures	
Total fractures	41 (100)
Upper thoracic (T1–T6)	6 (15)
Lower thoracic (T7–T12)	14 (35)
Lumbar	21 (50)
Grade of fractures	
Grade 1	11 (27)
Grade 2	9 (22)
Grade 3	21 (51)

Discussion

The prevalence of incidental radiological vertebral fracture on sagittal spinal images reformatted from CT examination of the chest or abdomen was 13% in this audit of examinations performed on patients aged over 65 years. 77% of patients with a vertebral fracture identified had no previous history of vertebral fracture (thus a newly identified fracture), and in 83% of patients with contemporaneous plain films, no vertebral fracture was mentioned in the X-ray report. Thus, assessing sagittal spinal images from CT examinations of the chest or abdomen commonly detected otherwise unidentified vertebral fractures. Eight examinations were required to detect 1 patient with vertebral fracture, and 10 examinations to detect 1 patient with a newly identified vertebral fracture.

Vertebral fractures are the most common osteoporotic fracture with a prevalence of 10–20% at age 65 years,[2] although they are often asymptomatic. Studies have shown that vertebral fractures are under-reported on plain films and CT.[6,8] This may occur because the fracture was not seen on the radiology imaging. For example, many vertebral fractures cannot be diagnosed on chest films, or on spine axial or coronal CT images.[6,9]

Another possibility is that the reporting radiologists see the fractures but choose not to report them because they are perceived as common, unimportant, or perhaps not relevant to the patient because of co-existing pathology.[6,9] Regardless of the reason, this represents a lost opportunity to initiate a clinical review which may lead to intervention with osteoporosis treatments.

It is important to diagnose vertebral fractures because they are associated with increased risk of future fractures and mortality, whether diagnosed clinically or radiologically.[3,4]

The Study of Osteoporotic Fractures Group found that women >65 years with prevalent vertebral fracture had a 5.4, 2.3, and 1.8 fold increased risk of subsequent

vertebral, hip, and non-vertebral fracture respectively over 3.7 years,[3] and a 1.2-fold increased risk of mortality over 8.3 years.[4]

In the Dubbo Osteoporosis Study, men and women >60 years with an incident vertebral fracture had a 1.8–2.1-fold increased risk of subsequent mortality.[10] Treatment of patients with vertebral fractures effectively reduces further vertebral fractures by >50% and total non-vertebral fractures by 20–30%.[11,12]

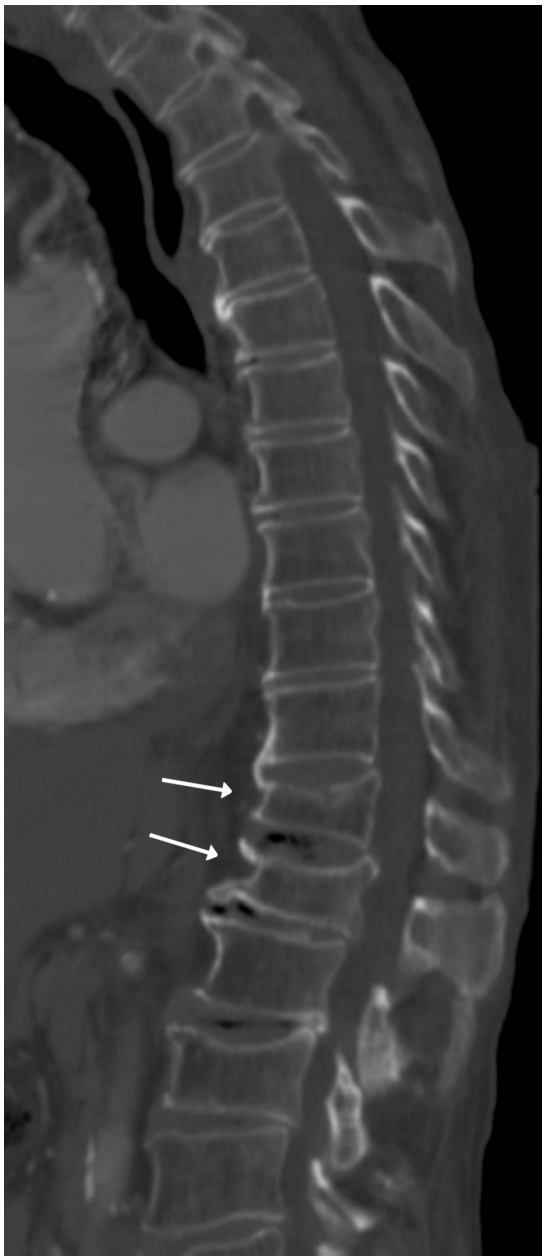
Effective treatment of patients with osteoporosis, of which vertebral fracture is often a hallmark, reduces mortality by approximately 10% over 3–4 years, particularly in the frail elderly.[13] Thus, identification of a vertebral fracture should prompt a clinical review of fracture risk, and in many cases, will lead to osteoporosis treatment.

There was evidence of underreporting of vertebral fractures in our current audit: vertebral fractures identified in our audit were not mentioned in 45% of CT reports and in 83% of plain film reports. Further, osteoporosis and vertebral fracture were each mentioned in only 14% of the relevant discharge summaries or clinic letters, and only 31% of patients with vertebral fracture were treated for osteoporosis. Thus, the significance of the vertebral fractures appears to have been overlooked by radiologists and clinicians, important information regarding fracture risk was not entered in the medical record, and osteoporosis treatment was underused.

It is possible that although the information regarding vertebral fracture and osteoporosis treatment did not appear in the medical record, nevertheless the fracture was recognised and appropriate treatment instigated but not recorded, but this seems unlikely.

There are several advantages to assessing vertebral fractures on sagittal spine images from CT examinations of the chest and abdomen. The sagittal reformatting is quick (<1 min) and does not require additional radiation exposure. CT overcomes some of the technical limitations for imaging the spine in chest and spine radiography, such as superposition of other structures. Finally, the image quality is high, allowing better interobserver agreement than for other methods (Figure 1).[6]

Figure 1. Reformatted sagittal image of the spine showing Grade 3 fractures of T12 and L1 vertebrae (arrows)



Taken together, the ability to accurately detect vertebral fractures, the high prevalence of vertebral fractures, and the changes in clinical management that should result from identification of a vertebral fracture strongly suggest that consideration should be given to routinely assessing reformatted sagittal spinal images for vertebral fractures in patients aged >65 years or at high risk of vertebral fractures undergoing CT examinations of the chest or abdomen.

Competing interests: None declared.

Author information: Pui Ling Chan, Endocrinology Registrar, Greenlane Clinical Centre, Auckland; Taryn Reddy, Radiologist, Vancouver General Hospital, Vancouver, BC, Canada; David G Milne, Radiologist, Auckland District Health Board, Auckland; Mark J Bolland, Senior Research Fellow, Department of Medicine, University of Auckland

Correspondence/reprints: Pui Ling Chan**,** Department of Endocrinology, Greenlane Clinical Centre**,** Private Bag 92 024, Auckland, New Zealand**.** Email: PuiLingC@adhb.govt.nz

References:

1. The European Prospective Osteoporosis Study (EPOS) Group. Incidence of vertebral fracture in europe: results from the European Prospective Osteoporosis Study (EPOS). J Bone Miner Res. 2002;17:716-24.
2. O'Neill TW, Felsenberg D, Varlow J, et al. The prevalence of vertebral deformity in european men and women: the European Vertebral Osteoporosis Study. J Bone Miner Res. 1996;11:1010-8.
3. Black DM, Arden NK, Palermo L, et al. Prevalent vertebral deformities predict hip fractures and new vertebral deformities but not wrist fractures. Study of Osteoporotic Fractures Research Group. J Bone Miner Res. 1999;14:821-8.
4. Kado DM, Browner WS, Palermo L, et al. Vertebral fractures and mortality in older women: a prospective study. Study of Osteoporotic Fractures Research Group. Arch Intern Med. 1999;159:1215-20.
5. Woo EK, Mansoubi H, Alyas F. Incidental vertebral fractures on multidetector CT images of the chest: prevalence and recognition. Clin Radiol. 2008;63:160-4.
6. Williams AL, Al-Busaidi A, Sparrow PJ, et al. Under-reporting of osteoporotic vertebral fractures on computed tomography. Eur J Radiol. 2009;69:179-83.
7. Genant HK, Wu CY, van Kuijk C, Nevitt MC. Vertebral fracture assessment using a semiquantitative technique. J Bone Miner Res. 1993;8:1137-48.
8. Majumdar SR, Kim N, Colman I, et al. Incidental vertebral fractures discovered with chest radiography in the emergency department: prevalence, recognition, and osteoporosis management in a cohort of elderly patients. Arch Intern Med. 2005;165:905-9.
9. Muller D, Bauer JS, Zeile M, et al. Significance of sagittal reformations in routine thoracic and abdominal multislice CT studies for detecting osteoporotic fractures and other spine abnormalities. Eur Radiol. 2008;18:1696-702.
10. Bliuc D, Nguyen ND, Milch VE, et al. Mortality risk associated with low-trauma osteoporotic fracture and subsequent fracture in men and women. JAMA. 2009;301:513-21.
11. Black DM, Cummings SR, Karpf DB, et al. Randomised trial of effect of alendronate on risk of fracture in women with existing vertebral fractures. Fracture Intervention Trial Research Group. Lancet. 1996;348:1535-41.
12. MacLean C, Newberry S, Maglione M, et al. Systematic review: comparative effectiveness of treatments to prevent fractures in men and women with low bone density or osteoporosis. Ann Intern Med. 2008;148:197-213.
13. Bolland MJ, Grey AB, Gamble GD, Reid IR. Effect of osteoporosis treatment on mortality: a meta-analysis. J Clin Endocrinol Metab. 2010;95:1174-81.

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

Predictors of intent to vaccinate against HPV/cervical cancer: a multi-ethnic survey of 769 parents in New Zealand

Sally B Rose, Beverley A Lawton, Tolotea S Lanumata, Merilyn Hibma, Michael G Baker

Abstract

Aim To identify factors predictive of parents' intent to have their daughters' receive the HPV/cervical cancer vaccine.

Methods 3123 questionnaires were distributed to parents recruited from 14 socioeconomically diverse schools in 2008. Survey questions were structured around the health beliefs model. The main outcome measure was intent to seek vaccination for daughter(s).

Results A quarter of parents completed questionnaires (769/3123). Two-thirds of respondents (67%) indicated they would want their daughter(s) to receive the vaccine, with no significant differences by ethnicity. Intent to vaccinate was significantly associated with having fewer negative views on vaccination (OR 0.47, 95%CI 0.37–0.59), having adequate information about the vaccine, perceiving HPV infection and cervical cancer as serious and likely to occur (OR 1.2, 95%CI 1.05–1.36), and considering efficacy and safety of the vaccine important (OR 1.17, 95%CI 1.06–1.28) ($p<0.01$). Awareness of HPV-related facts was lowest among Māori and Pacific parents ($p<0.001$). Pacific parents were more likely to have concerns about vaccination impacting negatively on girls' sexual behaviour.

Implications Strategies will be needed to provide detailed information outlining HPV prevalence and consequences, vaccine safety and efficacy to ensure all parents and their daughters are adequately informed when deciding on vaccination.

The human papillomavirus (HPV) is a common sexually transmitted virus that can cause cervical cancer and genital warts. Two vaccines are now available to protect against HPV. Gardasil® and Cervarix® both protect against two of the 'high-risk' HPV types (16 and 18) that are responsible for 70% of cervical cancer,[1] whereas Gardasil® also protects against two of the 'low-risk' HPV types (6 and 11) that cause about 90% of cases of genital warts.[2,3]

Gardasil® was chosen for the publically funded vaccination programme that began in September 2008 in primary care for girls born in 1990 or 1991. In February 2009, the vaccine was made available to girls aged 12–18 years through school-based programmes throughout New Zealand (with the exception of Canterbury and South Canterbury DHB areas).

Māori and Pacific women and those living in lower socioeconomic areas are disproportionately represented in cervical cancer incidence and mortality statistics.[4,5] Furthermore, marked disparities in access for Māori and Pacific women to screening (breast and cervical) and immunisation have been reported.[4–6]

Māori and Pacific have therefore been identified as priority groups for vaccination in the national HPV immunisation implementation plan,[7] with additional funding provided to district health boards to address coverage of priority groups.[7]

Research in New Zealand has been conducted to explore knowledge and attitudes of primary healthcare professionals,[8] and University students[9] towards the HPV vaccine. With the exception of an unpublished survey of parents commissioned by the Ministry of Health to gauge the success of the social marketing campaign to promote the vaccine;[10] parental attitudes have not yet been explored in New Zealand as they have elsewhere.[11]

The present paper describes the results of a multi-ethnic survey of the parents of intermediate and secondary school girls designed to identify predictors of intent to vaccinate.

Methods

Participants—The study was approved by the Central Region Ethics Committee in June 2008 (CEN/08/04/014). Eligibility criteria for schools included: located in the Wellington region; more than 100 pupils (with the exception of one Kura Kaupapa Māori language immersion school); attended by girls in year 8 and above (intermediate and secondary schools). Our recruitment strategy was based on school decile ratings (1 to 10) which are an indicator of socioeconomic status that takes into account household income and income support, occupation, household crowding, and the educational qualifications of the population within the school-defined area. Children attending a decile 1 school are likely to be from a lower socioeconomic background than those attending a decile 10 school.[12]

Schools were stratified by decile ratings into three groups: low (deciles 1 to 3), medium (deciles 4 to 7) and high (deciles 8 to 10). To target Māori and Pacific groups, we oversampled low and medium decile schools by inviting all those with decile ratings between 1 and 5. Schools with decile ratings of 6 and above were randomly chosen using the Excel RAND function. Twenty-two of 41 eligible schools (10 low, 6 medium and 6 high decile) were invited to participate by letter of invitation sent to the Principal, and arrangements for administering the survey made by phone, email or face-to-face meetings. A $50 book voucher was given to the school as koha (gift). Parents were eligible for participation if they had a daughter attending one of the participating schools.

Procedure—Surveys were distributed in term 4 of the 2008 school year (October-November), and completed surveys received up until the end of January 2009. Return of a completed survey signified parent's consent to participate. Surveys (with a Ministry of Health brochure about the vaccine)[13] were distributed in one of two ways as nominated by the school: girls took the survey home to their parents (10 schools), or the school posted the survey to parents (4 schools). Eight schools chose to have parents return surveys directly to the researchers (in a freepost envelope), and six had students return surveys to the school. These latter six schools offered small incentives (entry into a draw to win vouchers) to girls for returning the surveys in an attempt to increase response rates. All schools placed reminders about completion and return of surveys in school newsletters and/or daily notices. No contact details for parents were obtained by the research team due to privacy reasons, so direct contact was not made with parents.

Survey questions—Survey items were structured around the health beliefs model as the constructs of this model are important predictors of influenza vaccination,[14] and included: perceived likelihood and severity of illness (5 items); perceived attitudinal barriers to vaccination (negative views on vaccination) (4 items); perceived effectiveness and safety of the vaccine (7 items). Awareness of cervical cancer, HPV and the vaccine (6 items) was also explored. Intent to vaccinate daughter(s) was ascertained with the question "I intend to have my daughter(s) receive the HPV vaccination" with responses recorded on a 5-point Likert scale (strongly disagree, disagree, not sure, agree and strongly agree).

Demographic items included: gender, age, ethnicity (2001 New Zealand census question), education and employment status, religion, language if not English, number, age, sex and vaccination status of children. Data on parents' preferences for where their daughter(s) receive the HPV vaccine, at what age,

and their information needs were also collected in the present survey but have been published separately.[15]

Statistical analysis—Ethnicity was re-coded to the following four groups: Māori, Pacific, New Zealand European (NZEu) and 'Other' with assignment based on prioritised ethnicity.[16] Demographic data were collated, and response frequencies calculated for all yes/no and Likert scale questions and tabulated by ethnic group. 'Strongly agree' and 'agree' responses were pooled, as were 'strongly disagree' and 'disagree' responses. Chi-squared tests were performed to test for significant differences between categorical variables.

To determine whether responses to questions relating to constructs of the health beliefs model differed significantly between ethnic groups, a count of affirmative responses (yes or agree) to items in the construct was performed and scores compared using a Kruskal-Wallis test for overall significance followed by Wilcoxon pairwise comparisons (significance level set at 0.05/n comparisons). Logistic regression was used to build a model to predict intent to vaccinate. Analysis was conducted with SAS 9.1 (SAS Institute, Cary, N.C.) using a cumulative logit model across the three possible outcomes based on the assumption that the outcomes can be ordered from (a) intend to vaccinate, to (b) undecided, to (c) does not intend to vaccinate. Due to the large number of potential predictors available for the model, a backwards selection approach to modelling was used. In the first step, a number of possible explanatory variables were included in the model and non-significant predictors were removed until all remaining factors were either significant at $p<0.05$, or marginally significant at $0.05<p<0.1$.

Results

Table 1 presents the characteristics of schools recruited, with numbers of parents invited and returning surveys. Five low decile schools declined participation due to 'lack of time,' two schools were undecided after several weeks so were not further pursued, and a high decile girls' school was excluded to minimise over-representation of this demographic. Ethnicity data available on the Education Review Office's website[17] showed that participating schools were made up of approximately 44% NZEu students, 33% Māori, 11% Pacific and 13% 'Other' ethnicities.

Low decile schools were attended by a higher proportion of Māori and Pacific students. Non-participating schools had a similar overall proportion of Māori students (31%), a higher proportion of Pacific (32%) and lower proportion of NZEu students (29%).

Table 1. Characteristics of participating schools with numbers of surveys distributed and returned

School characteristics	Total invited	Total participating		Surveys distributed	Surveys returned	
	n	n	%	n	n	%
Type						
Secondary (Co-education)	10	6	60.0	1889	370	19.6
Secondary (Girls only)	3	2	66.7	520	182	35.0
Intermediate (Co-education)	6	5	83.3	704	215	30.5
Kura Kaupapa Māori (Co-education)	2	1	50.0	10	2	20.0
Decile band						
1–3 (Low socioeconomic communities)	10	4	40.0	838	157	18.7
4–6 (Medium)	6	6	100	1560	380	24.4
7–10 (High socioeconomic communities)	6	4	66.7	725	232	32.0
Totals	**22**	**14**	**63.6**	**3123**	**769**	**24.6**

Table 2. Characteristics of participating parents presented by ethnic group (n=769)

Characteristics	All parents (n=769)		Māori (n=126)		Pacific (n=57)		NZEu (n=477)		'Other' (n=109)		Chi-squared P-value
	n	%	n	%	n	%	n	%	n	%	
Gender											
Female	725	94.3	118	93.7	52	91.2	454	95.2	101	92.7	ns
Male	42	5.5	8	6.3	4	7.0	23	4.8	7	6.4	
Age-band											
20–29	27	3.5	7	5.6	2	3.5	13	2.7	5	4.6	<0.001
30–34	38	4.9	16	12.7	2	3.5	19	4.0	1	0.9	
35–39	146	19.0	33	26.2	18	31.6	70	14.7	25	22.9	
40–44	208	27.0	35	27.8	15	26.3	128	26.8	30	27.5	
45–49	229	29.8	19	15.1	8	14.0	166	34.8	36	33.0	
50–54	82	10.7	7	5.6	7	12.3	61	12.8	7	6.4	
55+	25	3.3	6	4.8	4	7.0	12	2.5	3	2.8	
Decile											
1–3 (Low)	157	20.4	42	33.3	21	36.8	80	16.8	14	12.8	<0.001
4–6 (Medium)	380	49.4	68	54.0	35	61.4	212	44.4	65	59.6	
7–10 (High)	232	30.2	16	12.7	1	1.8	185	38.8	30	27.5	
Education											ns
Tertiary	396	51.5	61	48.4	23	40.4	252	52.8	60	55.0	
English is first language											
Yes	660	85.8	121	96.0	18	31.6	472	99.0	49	45.0	<0.001
Employment											
Full-time	332	43.2	66	52.4	31	54.4	186	39.0	49	45.0	<0.001
Part-time	259	33.7	32	25.4	12	21.1	193	40.5	23	21.1	
Not employed	117	15.2	18	14.3	7	12.3	69	14.5	23	21.1	
Religious affiliation											
None	226	29.4	31	24.6	4	7.0	169	35.4	22	20.2	<0.001
Christian	347	45.1	36	28.6	38	66.7	224	47.0	49	45.0	
Other *	72	9.4	18	14.3	10	17.5	19	4.0	25	22.9	
**Number of children ** **											
1	54	7.0	11	8.7	5	8.8	30	6.3	8	7.3	<0.001
2	279	36.3	36	28.6	9	15.8	187	39.2	47	43.1	
3	213	27.7	25	19.8	8	14.0	150	31.4	30	27.5	
4 or more	207	26.9	48	38.1	33	57.9	105	22.0	21	19.3	
Children received childhood vaccinations											
All	686	89.2	112	88.9	49	86.0	435	91.2	90	82.6	<0.001
Partial***	50	6.5	8	6.3	4	7.0	33	6.9	5	4.6	
None	21	2.7	4	3.2	2	3.5	6	1.3	9	8.3	
Concern about child's reactions to past vaccinations											
Yes	82	10.7	6	4.8	2	3.5	61	12.8	13	11.9	0.019
No	647	84.1	112	88.9	51	89.5	400	83.9	84	77.1	
None	21	2.7	4	3.2	2	3.5	6	1.3	9	8.3	
Wants daughter(s) to have the HPV vaccine											
Agree	514	66.8	84	66.7	36	63.2	323	67.7	71	65.1	0.619
Disagree	71	9.2	11	8.7	4	7.0	40	8.4	16	14.7	
Not sure	154	20.0	25	19.8	13	22.8	95	19.9	21	19.3	

* Other religion includes: Buddhist, Hindu, Muslim, Jewish.

** Includes children in responders care (e.g. relatives' children, foster children).

*** All children had some vaccinations, or some children had all vaccinations.

Table 2 presents the characteristics of participating parents (n=769), with p-values denoting overall significant differences between ethnic groups on demographic variables. Over half (62%) of parents responding to the survey were NZEu, 16% were Māori and 7% Pacific. The majority of Pacific parents were Samoan (86%, 49/57). 'Other' ethnicities included 47 Asian, 14 African, 15 Middle Eastern, 27 Other European or British parents.

Pairwise comparisons revealed that Māori and Pacific parents were more likely to be younger ($p<0.0001$); have children attending lower decile schools ($p<0.0001$); and have more than four children than parents of NZEu and 'Other' ethnicities ($p<0.0001$). English was a second language for a significantly higher proportion of Pacific and 'Other' parents ($p<0.0001$).

Personal and family history of cancer, and vaccination status of children—Chi-squared testing showed an overall difference between ethnic groups in personal and family history of cancer ($p<0.0001$) and of cervical cancer ($p=0.019$). Pairwise comparisons showed that Māori and NZEu parents were most likely to report personal or family history of cervical cancer ($p=0.02$). Parents of 'Other' ethnicities were least likely to report personal or family history of any cancer ($p<0.001$) than all three comparison groups.

An overall difference was observed in the proportion women who had participated in cervical screening ($p<0.0001$). Fewer Pacific (36/52, 69%) and 'Other' women (77/101, 76%) had participated in screening than women of Māori (109/118, 92%) or NZEu (440/454, 97%) ethnicities. Thirty two percent of women (229/725) reported having had an abnormal smear in the past (chi square test for significance, $p=0.044$). Women of 'Other' ethnicities were less likely to report having had an abnormal smear (20.8%) than NZEu women (33.5%, $p=0.005$) and Maori women (31.4%, $p=0.04$).

Most parents (96%) reported that their children had received full or partial vaccinations in the past. Parents in the 'Other' ethnic group were significantly more likely to report having children who had received no vaccinations (8.0%) than NZEu parents (1.3%, $p=0.006$). An overall difference was observed between parents reporting concerns about reactions to past vaccinations ($p=0.019$), with a greater proportion of NZEu and 'Other' parents reporting concern than Māori or Pacific parents.

Table 3 presents the number (%) of participants in agreement with statements relating to awareness of cervical cancer and HPV and statements relating to constructs of the health beliefs model.

Table 3. Number (%) of parents agreeing to statements relating to awareness of cervical cancer, HPV and constructs of the health beliefs model presented by ethnic group

Constructs and statements	Total (n=769)		Māori (n=126)		Pacific (n=57)		NZEu (n=477)		'Other' (n=109)	
	n	%	n	%	n	%	n	%	n	%
Awareness of cervical cancer, HPV (6 items)[A]										
Had you heard of cervical cancer	726	94.4	119	94.4	50	87.7	468	98.1	89	81.7
Had you heard of the human papillomavirus (HPV)	454	59.0	66	52.4	19	33.3	320	67.1	49	45.0
Did you know that certain types of HPV cause cervical cancer	395	51.4	51	40.5	23	40.4	279	58.5	42	38.5
Did you know that the HPV virus is passed on during sexual contact	436	56.7	52	41.3	26	45.6	298	62.5	60	55.0
Did you know there is a vaccine against the virus that can cause cervical cancer	512	66.6	63	50.0	24	42.1	367	76.9	58	53.2
Did you know that the HPV vaccine will be offered to girls at school from 2009	449	58.4	61	48.4	19	33.3	322	67.5	47	43.1
Perceived likelihood and severity (5 items)[B]										
Cervical cancer is common in NZ	479	62.3	83	65.9	33	57.9	317	66.5	46	42.2
Cervical cancer is an illness with serious health effects	706	91.8	110	87.3	45	78.9	457	95.8	94	86.2
It is likely that someone I know will get cervical cancer in the future	460	59.8	82	65.1	29	50.9	309	64.8	40	36.7
HPV infections are common in New Zealand	359	46.7	49	38.9	21	36.8	256	53.7	33	30.3
HPV infections can cause serious illness	513	66.7	68	54.0	35	61.4	340	71.3	70	64.2
Potential attitudinal barriers to vaccination (4 items)[B]										
Vaccines are effective in stopping children from catching diseases	590	76.7	90	71.4	37	64.9	391	82.0	72	66.1
There is no need for immunisation if a child is healthy*	42	5.5	7	5.6	5	8.8	23	4.8	7	6.4
If vaccinated against HPV, girls might begin having sex younger	68	8.8	12	9.5	12	21.1	29	6.1	15	13.8
If vaccinated against HPV, girls might be more likely to have unprotected sex	93	12.1	18	14.3	15	26.3	44	9.2	16	14.7
Vaccine effectiveness and safety (7 items)[C]										
Scientific evidence to show that the vaccine is safe	692	90.0	112	88.9	46	80.7	444	93.1	90	82.6
A low risk of side effects following vaccination	651	84.7	100	79.4	35	61.4	434	91.0	82	75.2

Scientific evidence to show that the vaccine actually works	689	89.6	112	88.9	44	77.2	445	93.3	88	80.7
Protection against cervical cancer	712	92.6	116	92.1	47	82.5	455	95.4	94	86.2
The length of time the vaccine protects against disease	658	85.6	101	80.2	43	75.4	428	89.7	86	78.9
Protection against HPV infection	697	90.6	114	90.5	47	82.5	446	93.5	90	82.6
Protection against genital warts	588	76.5	98	77.8	42	73.7	371	77.8	77	70.6

Wording of questions preceding each set of statements listed above was as follows:

A. 'Before you received the enclosed cervical cancer vaccine brochure';

B. 'Do you agree or disagree with the following statements?';

C. 'When thinking about whether your daughter would have the HPV vaccine, what factors would be important to you? Tick whether you agree or disagree that the following factors are important';

* Scoring was reversed for this item. Respondents answering 'disagree' were included with the count of items answered in the affirmative.

Awareness of cervical cancer, HPV and the HPV vaccine (6 items)—'Yes' responses are presented in Table 3, 'don't know' responses made up less than 5% of answers to statements overall, while the remainder of parents responded 'no' to these statements. To gauge overall levels of awareness, a count of affirmative responses to the 6-items was performed. Kruskal-Wallis tests revealed an overall difference between groups ($p<0.001$), and Wilcoxin pairwise comparisons (significance level set at $0.05/6=0.0083$) indicated that NZEu parents appeared to have a higher overall level of awareness of HPV, cervical cancer and the vaccine than the other three groups of parents ($p<0.0001$ for all comparisons). No differences were observed between levels of awareness for Pacific, Māori and 'Other' parents ($p>0.1$ for all comparisons).

Perceived severity and likelihood of illness (5 items)—Thirty percent of parents were unsure whether cervical cancer was common in New Zealand (232/769). Similarly 33% were unsure whether someone known to them would get cervical cancer in the future (253/769), and 30% were unsure whether HPV can cause serious illness. Half the participants responded 'not sure' to the statement 'HPV infections are common in New Zealand' (382/769). 'Disagree' responses made up less than 7% of all responses to this set of statements. An overall difference was observed between ethnic groups in the count of affirmative responses to the 5-items ($p<0.001$). Pairwise comparisons showed that parents in the 'Other' ethnic group had lower overall scores than Māori and NZEu parents ($p<0.01$ for all comparisons).

Attitudinal barriers to vaccination (4 items)—Over three-quarters of parents agreed that childhood vaccines are important in prevention of disease (590/769, 77%), whereas 16% were unsure (122/769). Eighty percent of parents disagreed with the statement 'Immunisation is not needed if a child is healthy' (620/769), and 12% were not sure (90/769).

Twenty-three percent of parents indicated they were not sure in response to the statement 'if vaccinated for HPV, girls might be more likely to have unprotected sex'

(178/769), similarly 22% of parents were unsure if girls might be more likely to have sex younger if vaccinated (171/769).

Pacific parents were more likely to view the vaccine as having the potential to increase girls' likelihood of having unprotected sex or to be unsure (26% agreed, 30% unsure), compared to Māori (14% agreed, 26% unsure) and NZEu parents (9% agreed, 20% not sure). Likewise, Pacific parents were more likely to agree (or not sure) that vaccination might lead to earlier sex (21% agreed, 40% not sure) compared to Māori (10% agreed, 25% not sure) and NZEu parents (6% agreed, 16% not sure).

The count of affirmative responses to the 4-items differed significantly between ethnic groups ($p<0.001$). Pairwise comparisons revealed no differences between NZEu, Māori and 'Other' parents ($p>0.03$ for all comparisons), but Pacific parents had a significantly higher count than NZEu parents ($p<0.0001$).

Perceived effectiveness and safety of the vaccine (7 items)—Agreement was high for all statements relating to this construct, with less than 5% of all respondents disagreeing (the remainder were 'not sure'). An overall difference was observed between ethnic groups in the count of affirmative responses to the 7-items ($p<0.001$). A higher proportion of NZEu parents agreed with these statements than parents of 'Other' ethnicities ($p=0.005$), but no differences were observed between any other ethnic groups ($p>0.02$ for all comparisons).

Predictors of intent to vaccinate—Overall 66.8% of parents agreed with the statement 'I want my daughter(s) to receive the HPV vaccine', with no significant differences in responses by ethnic group ($p=0.62$). Thirty percent of parents (242/769) agreed that their daughter would decide for herself whether or not to have the vaccine, 40% disagreed with this statement (311/769) and 17% were unsure (132/769). Nine percent of parents indicated that at least one of their daughters had already received the vaccine (72/769), with no differences by ethnicity ($p>0.05$).

Table 4. Logistic regression analysis of factors associated with intent to vaccinate daughter(s) against HPV/cervical cancer

Factor	Odds ratio	Confidence limits		Factor P-value
		Lower	Upper	
Education				0.0156
Tertiary study	0.638	0.443	0.918	
No tertiary study	Reference			
Concern about child's reaction to past vaccine				<0.001
Yes	0.472	0.28	0.796	
Unsure	0.208	0.066	0.661	
No*	Reference			
Family or personal history of cervical cancer				0.0651
Yes	1.482	0.801	2.74	(ns)
Unsure	2.142	1.034	4.438	
No	Reference			
Would like additional information before deciding on vaccination for daughter**				<0.001
Yes	0.277	0.188	0.407	
Unsure	0.426	0.25	0.727	

No	Reference			
Perceived severity and likelihood of HPV and cervical cancer				0.0053
Ratio increase per question answered in affirmative	1.195	1.054	1.355	
Perceived attitudinal barriers to vaccination				<0.001
Ratio increase per question answered in affirmative	0.469	0.374	0.587	
Perceived effectiveness and safety of vaccine				<0.001
Ratio increase per question answered in affirmative	1.167	1.064	1.279	

* Includes by default those who answered that children had not received any immunisations or were unsure about child's immunisation status (n=26)

** Multinomial logistic regression indicated that those parents wanting more information (or who were unsure on this question) were more likely to be unsure about their intention to vaccinate than to report an agree/disagree opinion.

Logistic regression modelling—Odds ratios and 95% confidence limits for predictors of intent to vaccinate that were significant (or neared significance) are presented in Table 4. Non-significant predictors of intent to vaccinate were: Ethnicity, religious affiliation, school decile, child's vaccination status, awareness of HPV, cervical cancer and the vaccine. Personal or family history of cancer neared but did not reach significance (p=0.065). Odds ratios greater than one indicate a greater likelihood of intending to vaccinate, whereas odds ratios less than one indicate a greater likelihood of not intending to vaccinate.

Discussion

This is the first study to engage with a large number of New Zealand parents to identify predictors of intent to have their daughters receive the HPV/cervical cancer vaccine. Prior to the implementation of the school-based HPV/cervical cancer vaccination programme, two thirds (67%) of survey respondents agreed they would want their daughter(s) to receive the vaccine. Of interest, no difference was observed between parental intent to vaccinate between ethnic groups.

Intent to vaccinate was significantly associated with greater perceived effectiveness of the vaccine, greater perceived likelihood and severity of HPV infection and cervical cancer, and fewer perceived attitudinal barriers (or negative views on vaccination). This finding is consistent with past research on vaccine acceptability.[11 18 19]

Parents with a higher level of education were less likely to want their daughter to receive the vaccine primarily due to concerns about side effects, which has also been found in overseas research,[11] and in local reports on uptake of other vaccines (such as the measles, mumps, rubella – MMR vaccine).[20 21]

A strength of this research is the inclusion of groups most at-risk for cervical cancer (Māori, Pacific and lower socioeconomic groups). We aimed to oversample Māori and Pacific parents by targeting schools with a higher proportion of students in these groups. Six schools had over 30% Māori (ranging from 39-100%), and four had over 15% Pacific (ranging from 18-25%),[17] however response rates were generally lower from these schools.

An important limitation of the research is the overall response rate (25%), which is below the generally accepted level for generalisability of findings beyond the study participants. Due to ethical requirements for anonymity and privacy issues governing access to mailing addresses, we could not follow up non-responders. Although low, the return of surveys by 1 in 4 parents in this survey is similar to that of past studies in the area, for example Brabin et al achieved a 22% return rate from parents surveyed about HPV vaccination in UK secondary schools.[22]

Pacific parents most often responded in ways that differed from other groups, but these data need to be interpreted with caution due to the small sample size (n=57). Furthermore, Pacific parents differed from other groups on a number of demographic characteristics (as shown in Table 2).

At the time of the survey (prior to the nationwide publicity about the school-based vaccination programme) most participants had heard of cervical cancer and many were aware of HPV. Consistent with past (unpublished) research,[10] overall awareness of factors relating to cervical cancer and HPV was lower among parents of Māori, Pacific and 'Other' ethnicities than among NZ European.

Less than half of all parents agreed that HPV is common, reflecting a lack of detailed knowledge about HPV as a cause of genital warts which is one of the most prevalent STIs among young people.[23] Awareness of the link between HPV and cervical cancer was generally low, but lowest among Pacific and 'Other' participants. Around 10% of parents thought vaccination might lead to sexual risk-taking behaviour and Pacific parents were significantly more likely to hold this view. A high number of parents indicated they were unsure about the impact of vaccination on girls' sexual behaviour (23%). By comparison, only 5% of parents participating in a large cross-sectional phone survey in South Australia had concerns about use of the vaccine leading to sexual promiscuity.[24] A survey of primary care staff in New Zealand showed that 37% of practice nurses were concerned that vaccination against an STI might cause risky behaviour.[8]

Early vaccine coverage figures are lower than what might have been predicted from parental responses in the current survey. Ministry of Health data indicate that 95% of eligible schools are now participating in the school-vaccination programme and by March 2010 45% of young women born in 1990 and 1991 had begun the series of three injections, and 42% of younger girls born between 1992 and 1996 had begun vaccination.[25] It is possible that parents returning surveys in our study are those more likely to support the vaccine (the majority of parents reported all or partial vaccination of their children), thus skewing results in favour of vaccination.

To achieve higher uptake than is currently being achieved, a range of approaches will be needed. This study suggests that provision of adequate information to parents is vital to assist with decisions about vaccination. The widespread nature and consequences of HPV infection need to be highlighted in addition to cervical cancer incidence and mortality statistics. For example, each year 26,500 women are referred to colposcopy services following the report of an abnormal smear result,[26] and thousands of individuals are infected with genital warts annually.[23]

Information provided to parents and girls needs to highlight the efficacy and safety (low risk of side effects) of this vaccine. Furthermore, parents and healthcare

professionals need to be reassured that there is no evidence that educational or preventive measures around sexual health actually lead to an increase in risk-behaviours.[27 28]

Conclusions—Strategies to disseminate appropriately detailed information to parents need to be designed to reach Māori and Pacific parents. This will help to ensure they are well informed when making a decision about vaccination, and to minimise the risk of increasing health inequalities for these groups in New Zealand.

Competing interests: None declared.

Author information: Sally B Rose, Senior Research Fellow, Women's Health Research Centre, Department of Primary Health Care and General Practice, University of Otago, Wellington; Beverley A Lawton, Senior Research Fellow and Director, Women's Health Research Centre, Department of Primary Health Care and General Practice, University of Otago, Wellington; Tolotea S Lanumata, Research Fellow, Department of Public Health, University of Otago, Wellington; Merilyn Hibma, Senior Research Fellow, Department of Microbiology and Immunology, University of Otago, Dunedin; Michael G Baker, Associate Professor, Department of Public Health, University of Otago, Wellington

Acknowledgements: This study was funded by a grant from the Health Research Council Partnership Programme (08/602). The researchers also thank principals and their schools for consenting to take part (and for facilitating distribution and return of surveys); advisory group members for early advice on the study design, Selina Brown for assistance with survey distribution; and Dr James Stanley (Biostatistician, Department of Public Health) for statistical advice and help with analyses.

Correspondence: Sally B Rose, Women's Health Research Centre, Department of Primary Health Care & General Practice, University of Otago, Wellington, PO Box 7343, Wellington South, New Zealand. Fax: +64 (0)4 3855473; email: Sally.Rose@otago.ac.nz

References:

1. Muñoz N, Bosch FX, Castellsagué X, et al. Against which human papillomavirus types shall we vaccinate and screen? the international perspective. International Journal of Cancer 2004;111(2):278-85.
2. Mao C, Koutsky LA, Ault KA, et al. Efficacy of human papillomavirus-16 vaccine to prevent cervical intraepithelial neoplasia: a randomized controlled trial. Obstetrics & Gynecology 2006;107(1):18-27.
3. Schiller JT, Lowy DR. Prospects for cervical cancer prevention by human papillomavirus vaccination. Cancer Res 2006;66(21):10229-32.
4. Robson B, Purdie G, Cormack D. Unequal Impact: Maori and Non-Maori Cancer Statistics 1996-2001. Wellington: Ministry of Health Report 2006;Available at: http://www.moh.govt.nz/moh.nsf/pagesmh/4761/$File/unequal-impact-maori-nonmaori-cancer-statistics-96-01.pdf (Accessed Dec 9, 2009).
5. Centre for Public Health Research. Annual monitoring report 2004, National Cervical Screening Programme. Wellington: Massey University, 2007.
6. Ministry of Health. Immunisation Handbook 2006. Wellington: Ministry of Health, Wellington, New Zealand, 2006.
7. Ministry of Health HPV Project Team. The HPV (Human Papillomavirus) Immunisation Programme: National Implementation Strategic Overview. Population Health Directorate, Wellington: Ministry of Health. 2008; Available at:

http://www.moh.govt.nz/moh.nsf/pagesmh/7893/$File/hpv-national-implementation-strategic-overview.pdf (Accessed Aug 10, 2009).

8. Henninger J. Human papillomavirus and papillomavirus vaccines: knowledge, attitudes and intentions of general practitioners and practice nurses in Christchurch. Journal of Primary Health Care 2009;1(4):278-85.
9. Chelimo C, Wouldes TA. Human papillomavirus knowledge and awareness among undergraduates in healthcare training in New Zealand. N Z Med J 2009;122(1304). http://journal.nzma.org.nz/journal/122-1304/3829/content.pdf
10. Wyllie A, Brown R. HPV vaccine communications first tracking monitor. Research report for GSL network on behalf of the Ministry of Health. October 2009. Phoenix Research (Unpublished).
11. Brewer NT, Fazekas KI. Predictors of HPV vaccine acceptability: A theory-informed, systematic review. Preventive Medicine 2007;45(2-3):107-14.
12. Ministry of Education. Frequently asked questions about deciles. Wellington: Ministry of Education website 2007; Available at: http://www.minedu.govt.nz/index.cfm?layout=document&documentid=7696&data=l (Accessed Jun 26, 2009).
13. Ministry of Health. Cervical cancer vaccine brochure - Information for girls, young women and their families. Ministry of Health website: HPV Immunisation programme 2008;[Cited 2008 Aug 30]: Available from: http://www.moh.govt.nz/moh.nsf/indexmh/immunisation-diseasesandvaccines-hpv-programme#resources
14. Brewer NT, Chapman GB, Gibbons FX, et al. Meta-analysis of the relationship between risk perception and health behavior: the example of vaccination. Health Psychol 2007;26(2):136-45.
15. Rose SB, Lawton BA, Lanumata T, et al. HPV/cervical cancer vaccination: Parental preferences on age, place and information needs. Journal of Primary Health Care 2010;2(3):190-198.
16. Ministry of Health. Ethnicity Data Protocols for the Health and Disability Sector. Wellington: Ministry of Health 2004;[Cited 2010 Feb 24]:Available from: http://www.nzhis.govt.nz/moh.nsf/pagesns/228/$File/ethnicity-data-protocols.pdf
17. Education Review Office. Education Review Report. Wellington: Education Review Office 2008;[Cited 2008 Aug 27]: Available from: http://www.ero.govt.nz
18. Ogilvie GS, Remple VP, Marra F, et al. Parental intention to have daughters receive the human papillomavirus vaccine. Canadian Medical Association Journal 2007;177(12):1506-12.
19. Reiter PL, Brewer NT, Gottlieb SL, et al. Parents' health beliefs and HPV vaccination of their adolescent daughters. Social Science & Medicine 2009;69(3):475-80.
20. Gluckman P. How to improve completion rates of childhood immunisation. Briefing to Parliamentary Health Select Committee 2010;2 June 2010.
21. Hamilton M, Corwin P, Gower S, Rogers S. Why do parents choose not to immunise their children?[see comment]. N Z Med J 2004;117(1189):U768.
22. Brabin L, Roberts SA, Farzaneh F, Kitchener HC. Future acceptance of adolescent human papillomavirus vaccination: A survey of parental attitudes. Vaccine 2006;24(16):3087.
23. STI Surveillance Team, Population and Environmental Health Group, Institute of Environmental Science and Research Limited. Sexually Transmitted Infections in New Zealand. Annual Surveillance Report 2008. 2009. Available at: http://www.surv.esr.cri.nz/PDF_surveillance/STISurvRpt/2008_2nd/STIAnnual2008.pdf (Accessed Jul 30, 2009).
24. Marshall H, Ryan P, Roberton D, Baghurst P. A cross-sectional survey to assess community attitudes to introduction of Human Papillomavirus vaccine. Australian and New Zealand Journal of Public Health 2007;31(3):235-42.
25. Ministry of Health. Information about the HPV immunisation programme. How well is the programme going? Wellington, Ministry of Health 2010;Available at: http://www.cervicalcancervaccine.govt.nz/information-about-hpv-immunisation-programme (Accessed Jun 29, 2010).

26. National Screening Unit. Report on the findings of a review of District Health Board Colposcopy Services. Wellington, Ministry of Health 2006. Available at: http://www.nsu.govt.nz/Files/NCSP/DHB_Colposcopy_Services_review.pdf (Accessed Nov 16, 2009).
27. Kirby DB, Laris BA, Rolleri LA. Sex and HIV Education Programs: Their Impact on Sexual Behaviors of Young People Throughout the World. Journal of Adolescent Health 2007;40(3):206-17.
28. Monk BJ, Wiley DJ. Will Widespread Human Papillomavirus Prophylactic Vaccination Change Sexual Practices of Adolescent and Young Adult Women in America? Obstetrics & Gynecology 2006;108(2):420-24.

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

Cases of cutaneous diphtheria in New Zealand: implications for surveillance and management

Ann Sears, Margot McLean, David Hingston, Barbara Eddie, Pat Short, Mark Jones

Abstract

Aim Diphtheria is an acute bacterial illness caused by toxigenic strains of *Corynebacterium diphtheriae (C. diphtheriae)*. We describe two epidemiologically-linked cases of skin infections from which toxigenic *C. diphtheriae* was isolated, and discuss implications for diphtheria surveillance and management in New Zealand.

Method A public health investigation was undertaken to identify and manage close contacts of the index case. National and international guidelines on the surveillance and management of cutaneous diphtheria were reviewed, and data on toxigenic *C. diphtheriae* isolates identified in New Zealand from 1987–2009 were examined.

Results The index case was an adult male who developed a cutaneous infection after being tattooed in Samoa. A wound swab taken from the infected tattoo grew a toxigenic strain of *C. diphtheriae (*var *gravis)*. A secondary case of toxigenic cutaneous diphtheria was identified in a household contact. Instances of respiratory diphtheria associated with toxigenic cutaneous lesions have been reported in the literature. The review of surveillance data revealed inconsistencies in the notification of toxigenic strains of *C. diphtheriae* isolated from cutaneous sites.

Conclusion These cases are an important reminder that diphtheria remains a threat in New Zealand. All cases with toxigenic *C. diphtheriae* isolated from a clinical specimen, regardless of the site of infection, should be notified to a Medical Officer of Health.

Diphtheria is an acute bacterial illness caused by infection with exotoxin-producing (toxigenic) strains of *C. diphtheriae* bacteria.[1] The most common sites of infection are the respiratory tract and the skin.[1-3]

Respiratory diphtheria is characterised by the development of a thick adherent greyish membrane on the pharynx.[1,4,5] Symptoms can include sore throat, enlarged cervical lymph nodes, severe neck swelling ('bull-neck'), dyspnoea, and progressive respiratory obstruction.[1] The case-fatality proportion from respiratory diphtheria is reported as being between 5 and 10% in developed countries.[1,6] Systemic toxic effects can occur due to the production of exotoxin.[2] These effects include myocarditis[7,8] and peripheral polyneuropathy.[9] Toxic effects can be reduced through prompt administration of diphtheria antitoxin.[2]

Diphtheria vaccination has been widely available since the 1940s.[10] The subsequent decades saw a marked decline in respiratory diphtheria incidence in New Zealand and other developed countries.[6,10] However, the 1990s saw a re-emergence of respiratory diphtheria in the former Soviet Union,[11–13] where more than 115,000 cases and 3,000 deaths occurred from 1990 to 1997.[13]

The last case of respiratory diphtheria notified in New Zealand occurred in 1998 in an unimmunised 32-month-old European male, and was the first case of respiratory diphtheria notified in New Zealand in over 19 years.[5] Notably, it was suggested that this case could have arisen through exposure to a family member's infected abrasion, which had been acquired during a trip to Indonesia.[5]

Skin infections caused by toxigenic *C. diphtheriae* have been implicated as a reservoir for the spread and transmission of respiratory diphtheria.[14-16] As well as being a reservoir for respiratory diphtheria, prolonged outbreaks of cutaneous diphtheria requiring public health intervention have been reported.[17] Transmission is thought to occur mainly via direct contact with exudate from skin infections or, more rarely, via items contaminated with discharges from an infected person.[2,14,18]

Toxigenic cutaneous diphtheria typically occurs in tropical areas where *C. diphtheriae* is endemic.[2,18] Classical features include punched out, well-circumscribed, non-healing ulcers with a grey membrane.[18,19] In developed countries cutaneous diphtheria more frequently presents as an infection of an existing skin condition or traumatic skin lesion, so-called secondary toxigenic cutaneous diphtheria.[18,20,21]

In these instances, the lesions are often indistinguishable from skin infections caused by other pathogens. In contrast to respiratory diphtheria, toxic sequelae rarely occur with cutaneous diphtheria, possibly due to a slower release of toxin across the skin barrier resulting in a more vigorous antitoxin immune response.[20]

We report a case of toxigenic cutaneous diphtheria notified in New Zealand and the subsequent public health response that was undertaken. We review the implications of this event for the response to toxigenic cutaneous diphtheria and for the notification of extra-respiratory toxigenic strains of *C. diphtheriae* in New Zealand.

Method

Following a report of a case of toxigenic cutaneous diphtheria to a Medical Officer of Health, a public health investigation was undertaken to identify close contacts with the aim of preventing spread of the toxigenic *C. diphtheriae* strain.

A literature review on the management of cutaneous diphtheria was undertaken, and national and international guidelines on the notification and management of diphtheria were reviewed. National surveillance data were obtained from the Institute of Environmental Science and Research Limited (ESR) on toxigenic *C. diphtheriae* isolates identified in New Zealand from 1987–2009. National surveillance reports and notification data were also reviewed to identify any reported cases of infection arising from toxigenic *C. diphtheriae*.

Results

Index case—The index case was an adult male who had recently travelled to Samoa. The case had been tattooed on his lower leg while in Samoa. There was uncertainty about whether traditional or machine-based tattooing methods were used.

On arrival back in New Zealand, the case presented to his Medical Centre complaining of swelling and pain in the lower leg associated with the tattoo. A course of oral flucloxacillin was prescribed, although it later became apparent that this prescription had not been dispensed. The case re-presented to the Medical Centre with worsening pain, ulceration and redness around the tattoo site.

A wound swab was taken from the ulcerated tattoo and clinical details, including the history of a tattoo acquired in Samoa were noted on the laboratory request form. A seven-day course of erythromycin was prescribed to cover the possibility of methicillin-resistant *Staphyloccocus aureus* (MRSA). It was uncertain whether the case had ever received a primary diphtheria immunisation course, but he had received a tetanus-diphtheria (Td) booster six years previously.

Laboratory staff noted the clinical history and added testing for *C. diphtheriae*. *C. diphtheriae (*var *gravis)* and *S. aureus* were isolated from the wound swab. The *C. diphtheriae* isolate was sent to ESR for urgent diphtheria toxin gene testing by polymerase chain reaction (PCR), and was confirmed to be a toxigenic strain.

Following the result of the wound swab, the case was reviewed again in primary care. Only six doses of the erythromycin course had been taken. The case was hospitalised with fever and worsening lower leg cellulitis, and was successfully treated with intravenous flucloxacillin and erythromycin. Nose and throat swabs were taken to test for nasopharyngeal *C. diphtheriae* carriage and were negative. Cardio-respiratory monitoring was undertaken during admission as a precaution but there were no signs of toxin-related effects or respiratory diphtheria.

To confirm bacteriological clearance, two sets of swabs (nose, throat and wound) were taken 24 hours after completion of antibiotic treatment, and more than 24 hours apart. Both sets of swabs were negative for toxigenic *C. diphtheriae*. Booster immunisation (Td) was given.

Contact tracing and management of contacts—All close contacts were screened for diphtheria symptoms (including cutaneous lesions) and were swabbed to test for nasopharyngeal *C. diphtheriae* carriage. Close contacts were also offered antimicrobial prophylaxis with either 10 days of oral erythromycin or a single dose of intramuscular (IM) benzathine penicillin. The diphtheria immunisation status of each contact was determined, and Td booster vaccination was offered if not received in the past five years (diphtheria-tetanus-pertussis (dTap) boosters were used in younger contacts). A total of 19 household and close family contacts were identified, as well as four health care workers who had examined the wound.

Verbal and written advice was given to all contacts outlining the symptoms of respiratory diphtheria, with instructions to seek urgent medical attention if any symptoms occurred. Due to the potential for environmental contamination arising from cutaneous lesions, the family was advised to clean all bedding, clothes and soft furnishings.

A secondary case of toxigenic cutaneous diphtheria was subsequently identified in a fully immunised 11-year-old household contact. The child had an existing traumatic laceration on the arm, and a wound swab grew toxigenic *C. diphtheriae (*var *gravis)* and *S. aureus*. This child had not travelled to Samoa. Nasopharyngeal screening swabs were negative, and the child was restricted from school and successfully treated with a 10-day course of oral erythromycin and flucloxacillin. Bacteriological clearance was confirmed with two sets of swabs (nose, throat and skin) taken more than 24 hours after the completion of antibiotics. There were no signs of respiratory disease or toxin-related symptoms.

School contacts of this case were provided with information on the signs and symptoms of diphtheria. Children from the same class had recently received their 11-year-old scheduled dTap boosters, and swabbing and antibiotic prophylaxis was deemed unnecessary due to minimal contact with the case (the wound had been well-covered). Staff members who had dressed the child's wound were offered Td boosters (as needed), swabbed for carriage and offered antibiotic prophylaxis.

In total, 27 close contacts of both cases were identified, including household contacts, close family members (who had slept in the same house as the index case), health care workers, and school contacts. All 27 contacts had nasal and throat swabs taken for *C. diphtheriae*, with no nasopharyngeal carriage detected, and were offered booster immunisation if not received in the past five years. Antibiotic prophylaxis was also offered.

During the course of the investigation, it was discovered that family members living in Samoa had been tattooed by the same tattooist. Attempts were made to identify the tattooist involved; however difficulties were encountered obtaining this information. The Ministry of Health liaised with Samoan health authorities to follow-up the tattooist and other family members who may have been tattooed in Samoa.

***C. diphtheriae* isolates in New Zealand—**The review of toxigenic *C. diphtheriae* isolates from 1987 to 2009 revealed that, in addition to the two cases described here (notified in 2009), there were five other toxigenic isolates detected by ESR (Table 1).

A review of surveillance and other reports was undertaken to determine whether these five cases had been notified. This revealed that two of these cases were notified: a respiratory case in 1998,[5] and a case in a four-year old with septic arthritis of the hip in 2002.[22,23] A cutaneous infection in a traveller in 1987 was also investigated.[22] However, for two of the toxigenic cutaneous isolates (one in 2008 and one in 2009), there was no evidence that they had been notified to a Medical Officer of Health.

Table 1. Toxigenic *Corynebacterium diphtheriae* isolates received at ESR's National Reference Laboratory, 1987–2009

Year*	Number of Isolates	Source and biovar (type)	
		Respiratory	Cutaneous and other extra-respiratory
1987	1		mitis
1998	1	intermedius	
2002	1		gravis (hip aspirate)
2008	1		gravis
2009	3		gravis

* No toxigenic isolates were identified in the intervening years.

Discussion

This report describes the first cases of toxigenic cutaneous diphtheria reported in New Zealand since 1987, and the first notifications of toxigenic *C. diphtheriae* isolates in New Zealand since 2002.

These two cases were diagnosed based on the isolation of toxigenic *C. diphtheriae* from infected skin lesions. The clinical features in both cases were consistent with cases of secondary toxigenic cutaneous diphtheria reported in the literature.[2,18,24] As occurred in this outbreak, secondary toxigenic cutaneous diphtheria is difficult to distinguish from skin infections caused by other pathogens.[18] Both cases were found to be co-infected with *S. aureus*, which has been frequently reported in cases of toxigenic cutaneous diphtheria in both developing and developed countries.[15,17,20,25] The isolation of *S. aureus* also raises the possibility that this bacterium may have been the primary pathogen for skin infection in these cases.

As illustrated by this event, most cases of toxigenic cutaneous diphtheria in developed countries occur in individuals returning or arriving from tropical areas where toxigenic *C. diphtheriae* remains endemic.[2,15,16,20,25] As such, toxigenic cutaneous diphtheria should be considered in any person with chronically or acutely infected skin lesions returning from disease-endemic regions, including the Pacific Islands.

In this outbreak, one of the cases had been tattooed in Samoa. In New Zealand, traditional tattooing has been recognised as a risk factor for serious skin infections, and the Ministry of Health has published guidelines around traditional tattooing.[26] While it was unclear in this case whether traditional or machine-based tattooing methods were used, the tattoo is likely to have been a risk factor for infection, and the possibility remains that contaminated tattooing tools may have been the mode of transmission in the index case.

Toxigenic cutaneous diphtheria infections have been implicated in cases of respiratory diphtheria, including in New Zealand, the United Kingdom (UK), Europe and North America.[5,15,16,20,27] Prolonged outbreaks of cutaneous diphtheria requiring public health intervention have also been reported, particularly within socioeconomically deprived communities.[17] Therefore, cases of toxigenic cutaneous diphtheria require public health action to help prevent the spread of both cutaneous and respiratory disease.

As seen in this outbreak, treatment of individual cases of toxigenic cutaneous diphtheria involves isolation, disinfection of potentially contaminated environments, and treatment with appropriate antibiotics.[2] While systemic toxic effects are less common than in respiratory diphtheria, antitoxin treatment should be considered, although lower doses may be recommended compared to those required for respiratory diphtheria.[2,17]

Close contacts should be screened for *C. diphtheriae* carriage by having nasal and pharyngeal swabs obtained for culture, and swabs should also be taken from any wounds or other skin lesions.[2-4] Close contacts should also be offered a 7-10-day course of oral erythromycin or a single dose of IM benzathine penicillin.[2,4]

Contacts at greatest risk include household contacts, and healthcare workers involved in dressing cutaneous infections.[2] Booster diphtheria immunisation should also be

offered to cases and contacts who have had a primary immunisation course, if no booster has been given in the preceding five years. Unimmunised contacts should be offered a complete immunisation course.[10] Unimmunised contacts and older immunised contacts (who may have waning immunity) are most at risk of developing infection.

As well as cutaneous diphtheria, other extra-respiratory presentations of toxigenic diphtheria have been described including septic arthritis, conjunctivitis, and genital and external auditory canal infections.[1,3] Such cases have been described in New Zealand, with a four-year-old with toxigenic *C. diphtheriae* isolated from a hip aspirate notified in 2002.[23] While there is minimal information on the infective potential of toxigenic *C. diphtheriae* isolated from these extra-respiratory sites, similar public health action to that required for respiratory and cutaneous infection may be appropriate. Notably, routine notification of extra-respiratory isolates of toxigenic *C. diphtheriae* (including cutaneous isolates) occurs in a number of countries, including the UK and the European Union (EU).[2,28]

Our review of surveillance reports and guidelines revealed some inconsistencies in the current notification of toxigenic *C. diphtheriae* isolates to Medical Officers of Health (and subsequent public health action) in New Zealand. Diphtheria has been a notifiable disease in New Zealand since 1901,[5] however, the current New Zealand case definition for diphtheria only refers to respiratory diphtheria and excludes cutaneous diphtheria from notification.[29] In contrast, the New Zealand *Direct Laboratory Notification* guidelines[30] require all toxigenic *C. diphtheriae* (and *C. ulcerans*) isolates to be reported to a Medical Officer of Health. Thus, cases of toxigenic cutaneous diphtheria are notifiable via this direct laboratory notification pathway.

Adopting a similar approach to the UK and the EU by including extra-respiratory presentations of toxigenic *C. diphtheriae* in the diphtheria case definition,[2,28] would help ensure that consideration is given to the level of public health action required for such cases, and improve consistency.

As observed in this event, primary care practitioners have key roles to play in identifying atypical skin infections and initiating treatment of toxigenic cutaneous diphtheria. Having a lower threshold for wound swabbing in the presence of risk factors for atypical skin infections (e.g. recent overseas travel and tattooing) is likely to bolster the early identification and management of toxigenic cutaneous diphtheria in New Zealand.

Culture for *C. diphtheriae* is not necessarily routine and providing complete clinical information on the laboratory request form is essential for alerting laboratories to the possibility of atypical organisms, such as toxigenic *C. diphtheriae*. *Corynebacterium* species are common skin commensals so identification of toxigenic *C.diphtheriae* relies on additional testing, including referring specimens to ESR for urgent toxigenicity testing.[10] In this case, if the specific diphtheria culture had not been performed, the diagnosis would have been delayed (or missed), risking further spread of this toxigenic strain.

Immunisation remains an important public health measure to prevent the development and spread of diphtheria. This outbreak is a timely reminder that toxigenic

C.diphtheriae strains continue to occur in New Zealand and that respiratory diphtheria remains a risk for susceptible individuals. Immunisation confers long but not lifelong immunity. National and international serological studies have highlighted waning immunity in adults.[31,32] The current New Zealand immunisation schedule includes booster Td vaccine doses at age 45 and 65 years.[10] However, more could be done to increase awareness of these booster vaccinations in adulthood.

These cases of toxigenic cutaneous diphtheria are an important reminder that diphtheria remains a threat in New Zealand, and that clinical suspicion for toxigenic *C. diphtheriae* infection is prudent medical practice, especially when a skin infection has been acquired in a disease-endemic area. Given ongoing transmission in Pacific countries, and the potential for missed diagnosis, there remains a small but real risk of an outbreak of diphtheria in New Zealand, particularly among groups with low immunisation coverage.

Competing interests: None declared.

Author information: Ann Sears, Public Health Medicine Registrar, Margot McLean, Medical Officer of Health, Barbara Eddie, Public Health Nurse, Regional Public Health, Hutt Valley District Health Board, Lower Hutt; David Hingston, General Practitioner, Wellington; Pat Short, Senior Scientist, Institute of Environmental Science and Research Ltd, Porirua; Mark Jones, Clinical Microbiologist, Aotea Pathology, Wellington.

Acknowledgements: We acknowledge and thank the general practitioners and practice nurses who assisted with the management of cases and contacts; Aotea Pathology staff, Wellington who assisted in the investigation; and the New Zealand Population Health Charitable Trust for providing a salary subsidy for AS.

Correspondence: Dr Margot McLean, Medical Officer of Health, Regional Public Health, Hutt Valley District Health Board. Email: margot.mclean@huttvalleydhb.org.nz

References:

1. Clements J. Diphtheria. In: Heymann D, editor. Control of Communicable Diseases Manual. 18th ed. Washington, DC: American Public Health Association; 2004. p. 171-6.
2. Bonnet J, Begg N. Control of diphtheria: guidance for consultants in communicable disease control. Commun Dis Public Health. 1999;2(4):242-9.
3. Tejpratap S, Tiwari M. Chapter 1: Diphtheria. In: Roush S, McIntyre L, Baldy L, editors. Manual for the Surveillance of Vaccine Preventable Diseases. 4th ed: Centers for Disease Control; 2008.
4. Farizo K, Strebel P, Chen R, et al. Fatal Respiratory Disease Due to *Corynebacterium diphtheriae*: Case Report and review of Guidelines for Management, Investigation, and Control. Clin Infect Dis. 1993;16:59-68.
5. Baker M, Taylor P, Wilson E, et al. A case of diphtheria in Auckland - implications for disease control. The New Zealand Public Health Report. 1998;5(10).
6. Bisgard KM, Hardy IR, Popovic T, et al. Respiratory diphtheria in the United States, 1980 through 1995. Am J Public Health. 1998;88(5):787-91.
7. Anima H, Malay M, Santanu H, et al. A study on determinants of occurrence of complications and fatality among diphtheria cases admitted to ID & BG Hospital of Kolkata. J Commun Dis. 2008;40(1):53-8.

8. Celik T, Selimov N, Vekilova A, et al. Prognostic significance of electrocardiographic abnormalities in diphtheritic myocarditis after hospital discharge: a long-term follow-up study. Ann Noninvasive Electrocardiol. 2006;11(1):28-33.
9. Logina I, Donaghy M. Diphtheritic polyneuropathy: a clinical study and comparison with Guillain-Barre syndrome. J Neurol Neurosurg Psychiatry. 1999;67(4):433-8.
10. Ministry of Health. Immunisation Handbook. Wellington: Ministry of Health; 2011.
11. Vitek CR, Wharton M. Diphtheria in the former Soviet Union: reemergence of a pandemic disease. Emerg Infect Dis. 1998;4(4):539-50.
12. Vitek CR, Brisgalov SP, Bragina VY, et al. Epidemiology of epidemic diphtheria in three regions, Russia, 1994-1996. Eur J Epidemiol. 1999;15(1):75-83.
13. Markina SS, Maksimova NM, Vitek CR, et al. Diphtheria in the Russian Federation in the 1990s. J Infect Dis. 2000;181 Suppl 1:S27-34.
14. Koopman J, Campbell J. The role of cutaneous diphtheria infections in a diphtheria epidemic. J Infect Dis. 1975;131:239-44.
15. Bowler I, Mandal B, Schlecht B, Riordan T. Diphtheria - the continuing hazard. Arch Dis Child. 1988;63:194-210.
16. Hart PE, Lee PY, Macallan DC, Wansbrough-Jones MH. Cutaneous and pharyngeal diphtheria imported from the Indian subcontinent. Postgrad Med J. 1996;72(852):619-20.
17. Harnisch J, Tronca E, Nolan C. Diphtheria among alcoholic urban adults: A decade of experience in Seattle. Ann Intern Med. 1989;111:71.
18. Hofler W. Cutaneous diphtheria. Int J Dermatol. 1991;30:845.
19. Wagner J, Ignatius R, Voss S, et al. Infection of the skin caused by *Corynebacterium ulcerans* and mimicking classical cutaneous diphtheria. Clin Infect Dis. 2001;33(9):1598-600.
20. de Benoist AC, White JM, Efstratiou A, et al. Imported cutaneous diphtheria, United Kingdom. Emerg Infect Dis. 2004;10(3):511-3.
21. Livingood C, Perry D, Forrester J. Cutaneous Diphtheria: A Report of 140 Cases. The Journal of Investigative Dermatology. 1946;7:341-64.
22. Sneyd E, Baker M. Infectious Diseases in New Zealand: 2002 Annual Surveillance Summary. Porirua: Institute of Environmental Science and Research Ltd; 2003.
23. Faraj S, French G, McAuslan A. Septic arthritis due to a toxigenic strain of *Corynebacterium diphtheriae gravis*. NZ Med J. 2003;116:1172.
24. Bacon DF, Marples MJ. Researches in Western Samoa II. Lesions of the skin and their bacteriology. Trans Roy Soc Trop Med and Hygiene. 1955;49(1):76-81.
25. Sing A, Heesemann J. Imported Cutaneous Diphtheria, Germany, 1997-2003. Emerg Infect Dis. 2005;11:343-4.
26. Ministry of Health. Customary Tattooing Guidelines for Operators. Wellington: Ministry of Health; 2010.
27. Bray J, Burt E, Potter E, et al. Epidemic Diphtheria and Skin Infections in Trinidad. J Infect Dis. 1972;126(1):34-40.
28. Efstratiou A, Crowcroft N, White J. EU Diphtheria Case Definition: Position Paper. London: DIPNET; 2002.
29. Ministry of Health. Communicable Disease Control Manual. Wellington: Ministry of Health; 1998.
30. Ministry of Health. Direct Laboratory Notification of Communicable Diseases - National Guidelines. Wellington: Ministry of Health; 2007.
31. Gidding HF, Backhouse JL, Burgess MA, Gilbert GL. Immunity to diphtheria and tetanus in Australia: a national serosurvey. Med J Aust. 2005;183(6):301-4.
32. Weir R, Jennings L, Young S, Brunton C, Murdoch D. National serosurvey of vaccine preventable diseases. Wellington: Ministry of Health; 2009; Available from: http://www.health.govt.nz/system/files/documents/publications/national-serosurvey-of-vaccine-preventable-diseases-may09.pdf

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

Population screening for abdominal aortic aneurysm: evaluating the evidence against screening criteria

Nisha Nair, Diana Sarfati, Caroline Shaw

Abstract

Screening for abdominal aortic aneurysm (AAA) has been initiated in the United Kingdom and United States. Screening using abdominal ultrasound scans allows AAAs to be detected and electively repaired before rupture. There is currently no policy for AAA screening in New Zealand (NZ). We reviewed literature to assess current evidence for AAA screening against standard criteria used to evaluate population-based screening programmes.

AAA rupture has high mortality, and people of Māori ethnicity are disproportionately affected. Abdominal ultrasound is a valid screening tool, and elective repair is an effective treatment. Screening reduces AAA-related mortality by about 40% in elderly men. However, the age and comorbidities of AAA patients means rupture risk has to be weighed against elective repair risk. Overtreatment is likely, given most individuals with AAA will not experience rupture in their lifetime. AAA screening appears to be cost-effective. It is unclear if the health system could support all the elements of a AAA screening pathway.

AAA appears to be an appropriate condition for which to consider population screening. We recommend research into the prevalence of AAA in NZ, the comorbidity profile of individuals with AAA, drivers of high mortality among Māori, and acceptability of AAA screening to the New Zealand public.

Abdominal aortic aneurysms (AAAs) are dilatations of the abdominal aorta, present in 5 to 10% of men aged 65 to 79 years.[1] AAAs expand asymptomatically until rupture, unless the individual dies of an unrelated cause before rupture occurs. Rupture carries a high mortality of 80 to 90%,[2–6] both due to individuals dying before emergency repair can be performed, and because emergency repair itself has a high mortality (30 to 65%).[3,7,8]

Detection of AAAs before rupture by abdominal ultrasound scans allows elective repair, which has a lower mortality (up to 10%).[9–14] Currently, detection of AAAs before rupture is largely incidental or opportunistic. Population-based AAA screening has been shown to reduce AAA-related mortality in older men,[15] with acceptable cost-effectiveness in international studies.[16]

In the United Kingdom, the National Screening Committee approved AAA screening in men aged 65 in 2007, and screening began in 2009.[17,18] In the United States, the United States Preventive Services Task Force (USPSTF) recommended AAA screening in male ever-smokers aged 65 to 75 in 2005. Since 2007, Medicare has covered one-time ultrasound screening in this group (and in women with a family history of AAA).[19,20]

Currently, there is no policy for AAA screening in New Zealand, although "awareness of the research evidence for screening is high".[21] The National Health Committee (NHC) has developed eight screening assessment criteria by which potential screening programmes can be evaluated.[22]

The purpose of this paper is to examine how contemporary knowledge about AAA stands in relation to these criteria, within a New Zealand context. It also identifies critical areas where knowledge is lacking or uncertainty remains. This is the second of two articles relating to AAA, the first article describes the epidemiology and burden of AAA in New Zealand between 2002–2006.

Criterion 1: The condition is a suitable candidate for screening

The NHC considers a condition to be suitable for screening if it is important in terms of mortality and morbidity, if there is adequate understanding of the natural history of the condition, and if there is a detectable disease marker and pre-symptomatic stage.[22]

AAA prevalence ranges from 4.5 to 7.7% in men aged 65 to 73 years in developed countries.[9,23–26] There are no population-based studies of AAA prevalence in New Zealand.

AAA is a cause of death in 1 to 3% of men aged over 65 years old in industrialised countries.[27,28] In New Zealand, there were approximately 236 AAA-related deaths per year between 2002 and 2006. However, this is likely to represent an underestimate. About 90% of these deaths were in New Zealand Europeans, and 7% in Māori.

Although absolute numbers were low, AAA event rates were 1.5 times higher in Māori than in New Zealand Europeans between 2002 and 2006. AAA mortality was twice as high, and Māori also presented at younger ages.

Similar to other countries, in New Zealand, rates of AAA events in women are considerably lower (about 23% of male rates between 2002 and 2006). Because AAA is more common among males, the bulk of AAA research is focused on males. However, females appear to have a higher rupture rate, higher case fatality in general, and higher mortality from emergency repair specifically than males.[6,29–31] Despite this, due to a dearth of AAA research in females, this review is limited to AAA screening in males.

The pathophysiology of AAA disease is well understood. It is usually related to atherosclerosis, and shares a similar pool of risk factors: age, male sex, smoking, and family history.[3,4,6,27,32,33] Aneurysmal size predicts likelihood of rupture.[34,35] For example, a AAA measuring between 5.1 and 5.9 cm has a rupture risk of 4% in the subsequent year, compared to 20% for a AAA measuring between 6.0 and 7.0 cm.[4,36]

If rupture does occur, overall mortality can be as high as 80 to 90%.[2–5] This is because less than half of rupture patients reach the hospital alive,[37] diagnosis is difficult,[38,39] fitness for surgery is often problematic,[4,40] and mortality from emergency repair is high.[3,7,8] However, a significant proportion of individuals with AAAs may never experience any problems from them during their lifetimes.

AAA is asymptomatic until rupture, and so a pre-symptomatic stage is clearly present. The 'disease marker' is an infrarenal aortic diameter of ≥3 cm on abdominal ultrasound, diagnostic of a AAA.[4]

Criterion 2: There is a suitable test

The abdominal ultrasound scan is non-invasive, and poses no physical risk to the patient. The test usually takes no longer than 10 minutes.[41,42] It is relatively inexpensive compared to other imaging modalities such as computed tomography (CT) and magnetic resonance imaging (MRI). CT and/or MRI are usually performed for anatomic mapping if aneurysm repair is clinically indicated.

The sensitivity of abdominal ultrasound scans in detecting AAAs is high, ranging from 92 to 99%. Its specificity is almost 100%.[43–45] The positive predictive value has been estimated at 97% and the negative predictive value at 99.9%,[43] which means that false positive rates are minimal. These are extremely high values, compared to screening tools used in other programmes.[46–48]

Scanning technique is susceptible to both intra and inter-observer variability, both reported as less than 4 mm in several studies. Intra-observer variability has been shown to change with scanning personnel, with less intra-observer variability reported in radiologists as compared to sonographers. [43,49,50]

Criterion 3: There is an effective and accessible treatment or intervention for the condition identified through early detection

The mainstay of effective treatment for screen-detected AAAs is elective repair. However, the majority of screen-detected AAAs will be of a size that does not warrant immediate elective repair. These individuals will require ultrasound surveillance. The frequency of surveillance is dependent on aneurysmal diameter and there is significant variation in recommended protocols.[9,12,13,23,24,51,52]

Overall mortality for AAA rupture is very high, and among those that undergo emergency repair, the 30-day operative mortality is 30 to 65%.[3,7,8] In contrast, the 30-day mortality from elective repair of an intact AAA is much smaller, between 3 and 10%.[9–14] Framed differently, for an individual with AAA, the risk of dying once AAA rupture has occurred is eight times higher than the risk of dying from elective repair. If an individual with AAA rupture makes it to surgery, the risk of dying during or after emergency repair is between three and six times higher than the risk of from elective repair.

This ‘better outcome’ from elective repair needs to be considered alongside the fact that a proportion of AAAs will never rupture, that is, people die with them instead of them. Estimating this proportion is problematic as there are very few population-based autopsy studies available. From our interpretation of a Finnish autopsy study conducted between 1959–1979[53] (which has the most comprehensive data on this issue) with about 400 cases, the ‘natural’ lifetime rupture rate was at least 30% and possibly up to 50%.

Using these estimates, about 50% to almost 70% of AAAs may not be problematic during an individual’s lifetime. It is clear that AAA screening has the potential to result in overtreatment in a cohort where AAA rupture would never have occurred.

Determining when the risk of rupture outweighs the risk of elective repair is thus a key issue in AAA management.[6] There is good consensus that elective repair should

be considered at an aneurysmal diameter of ≥5.5 cm.[4,6] As important as *when* to offer elective repair is the question of to *whom* it should be offered.

Older age and the presence of comorbidities are directly related to higher elective repair risk.[54–57] For example, between 2002 and 2006, elective repair mortality in New Zealand was almost 12% for individuals aged ≥85 years (compared to the national average of 6.7%). This means more than 2 deaths for every 20 individuals aged ≥85 years undergoing elective repair. Procedural factors such as type of approach (open or endovascular) as well as hospital volumes also affect elective repair mortality rates.[6,11,58–60]

Criterion 4: There is high quality evidence, ideally from randomised controlled trials, that a screening programme is effective in reducing morbidity and mortality

Four large population-based screening randomised controlled trials (RCTs) have been conducted: two in the UK (the MASS[9,61,62] and Chichester studies),[23,63,64] 1 in Denmark (the Viborg study),[24,65] and one in Australia (the Western Australia study).[25] All four studies primarily assessed the effect of invitation to AAA screening on all-cause mortality and AAA-related mortality, among other outcomes. (The details of the study design and results of each of these studies are available in a web appendix). Meta-analyses of these results have been conducted by the Cochrane Collaboration,[15] the USPSTF,[2] and Lindholt and Norman.[66] In each of these, the MASS study contributed the most weight to the pooled results, being the largest study.

There was no significant reduction in all-cause mortality. This is unsurprising as the contribution of AAA to all-cause mortality is small. There was a 40% reduction in AAA-related mortality at 3 to 5 years, and sustained up to 15 years. The Cochrane meta-analysis concluded that this benefit applied to males aged 65 to 79 years.[15] The USPSTF concluded benefit in males aged 65 to 74 years.[2] In terms of surgical workload, the Lindholt and Norman meta-analysis reported two to three-fold increases in elective repair rates in the short and long term. A decrease in emergency repair rates by about 50% was also noted.[66]

Each of the four screening RCTs also highlighted the variables upon which the benefits of AAA screening depend. One of these is overall AAA prevalence. The prevalence of AAAs in the Western Australia study population was relatively high at 7.2%.[25] New Zealand may have similar prevalence, although no data exist on this. Other variables include the background level of incidental detection and treatment, the exclusion of 'ineligible' individuals from screening, adequate screening uptake, minimising delays in the screening pathway, and maintaining low operative mortality from elective repair.

Criterion 5: The potential benefit from the screening programme should outweigh the potential physical and psychological harm (caused by the test, diagnostic procedures, and treatment)

AAA screening refers to not just a test but a pathway: from the invitation and ultrasound, through to surveillance and/or elective repair. The potential physical and psychological benefits and harms at each stage should be considered.

The main physical benefit of AAA screening at a population level is the reduction in rupture-related mortality. The screening process also presents opportunities for medical optimisation, in particular cardiovascular risk management.[6] The MASS study found a possible small reduction in deaths from ischaemic heart disease among those screened for AAA.[62]

As the abdominal ultrasound scan is non-invasive, the main physical harm from AAA screening lies in elective repair. Advanced age and the presence of comorbidities mean that the majority of AAA patients are high-risk for adverse postoperative events. Cardiac complications are the most common, occurring in approximately 11% of elective repair patients. Others include respiratory and renal failure, ischaemic colitis, spinal cord ischaemia, and prosthetic graft infections. Mortality from elective repair has already been discussed under Criterion 3.[67]

The psychological benefits of AAA screening may be in the form of reassurance after a negative scan. Individuals with a family history of AAA may derive significant benefit from having a feared condition confirmed/refuted, and from accessing elective repair if appropriate.

Four main studies considered psychological harms associated with AAA screening.[9,68–70] There appears to be some distress associated with attending a scan. This is transient if the scan is negative, but may not be so if the test is positive. After this point, there is conflicting evidence as to whether surgery or surveillance (or both) is associated with psychological distress. Reassuringly, the MASS study found that all scores were within population norms at all times.[9]

Overall, the majority of individuals screened by a screening programme will not have a AAA and can be 'reassured and discharged'. For those diagnosed with AAA, the benefit-harm balance requires clarification. Firstly, it is unclear how 'acceptable' the not insubstantial risk of elective repair is to the New Zealand public. Secondly, there is insufficient information on the comorbidity profile of AAA patients in New Zealand, and how this translates into fitness for surgery. There is also lack of research on the psychological impact of not being fit for surgery despite having a AAA of operable size.

Criterion 6: The health care system will be capable of supporting all necessary elements of the screening pathway, including diagnosis, follow-up and programme evaluation

A major practical issue in implementing AAA screening will be in identifying an eligible population. In New Zealand, the likely best source for recruitment is primary care registers. This is associated with good uptake and the ability to exclude genuinely ineligible candidates.[9,25,71] Adequate uptake of AAA screening in Māori will be vital given their disproportionate burden from AAA. Other key issues include where scans should be done (hospital or community) and who does them (ultrasonographers or other trained personnel). Alongside this is the need to consider who holds responsibility for explaining results to patients, and for arranging surgical referral or surveillance.

Identifying potential 'bottlenecks' in health services is dependent on scoping existing services and estimating the projected burden of AAA screening on these services. For

example, a national screening programme will increase elective and decrease emergency vascular surgical workload. Two meta-analyses estimate an approximate doubling in elective repairs,[15,66] which by 2002–2006 data would equate to a total of 534 elective repairs annually (based on an annual average of 267 elective repairs).

Estimates of vascular surgical workload, ultrasound surveillance, and other health service requirements as a result of population screening are highly dependent on AAA prevalence, the proportion of AAAs that are of operable size, the proportion of individuals with operable AAAs that are fit for surgery, and the levels of incidental detection.

There is lack of local data in each of these areas. Using MASS study figures and treatment protocols,[9] if 10,000 men aged 65 to 74 years were scanned, a AAA would be detected in about 490 men. Of these, about 431 men would require further surveillance at intervals ranging from 3 months to yearly depending on aneurysmal diameter (348 men would have AAAs between 3 and 4.4 cm, 83 men would have AAAs between 4.5 and 5.4 cm). About 59 would have AAAs ≥5.5 cm, thereby requiring referral for elective repair.

AAA screening will impact on a wide range of health services. These include radiological services, vascular outpatient and pre-assessment clinics, theatres, intensive care units, surgical and medical wards, rehabilitation and allied health services, nursing homes and community support services. Ability to screen will depend on workforce capacity and infrastructure in all these areas.

Coordination, monitoring, and evaluation is mandatory for a screening programme to be both efficient and effective. A central agency with mandate and oversight will be required,[72] along with appropriate information systems. A quality assurance framework will need to be established from the outset in order to deliver promised benefits and minimise harms. An important component of this will be to ensure that operative mortality and morbidity rates are consistently low, and there is a pre-determined system for managing surgical outliers.[6,73]

Criterion 7: There is consideration of social and ethical issues

There is an ethical obligation to convey potential harms and benefits to the individual, to allow them to make an informed decision about whether screening is right for them. Critical to the informed consent process is how evidence is framed, as it determines how harms and benefits are perceived.[74] For example, the reduction in rupture-related mortality could be presented as a relative risk reduction, an absolute risk reduction, or as numbers needed to screen (NNS).

MASS study figures for these are 42% (the risk of dying from a AAA is 42% lower in a group invited to be screened), 0.14% (the risk of death from a AAA drops from 0.33% in a group not invited to screening to 0.19% in an invited group, a 0.14% reduction), and 714 (714 men need to be screened in order to avoid one death from AAA) respectively. The expression of benefits and harms in a variety of forms allows for a more balanced informed consent process.[74 75]

The limitations of AAA screening should be made evident. The chances of falsely negative or positive scans are small but not negligible. The potential participant should understand that a positive scan is by no means a guarantee of elective repair, as

the latter is dependent on both aneurysmal size and fitness for surgery. An individual who normally considers himself healthy could then be in a situation where he knows he harbours a potentially dangerous disease but cannot access definitive treatment.

Offering population screening when a significant proportion of individuals with AAA (10 to 25% by some estimates) will be considered unfit for elective repair is a major ethical issue.[42] Additionally, the majority of AAAs may not rupture within the individual's lifetime. There is a significant probability of overtreatment for a condition that may never have manifested. This is especially important when the treatment in question has a mortality rate of up to 10%.

An equity focus is important if a screening programme is to avoid exacerbating existing inequalities. It is appropriate for AAA screening to be targeted to males in view of their higher prevalence. However, concerns have been raised about a possible gender bias (against females) in AAA diagnosis and selection for surgical treatment.[76] It is also worth noting that existing screening programmes do not appear to serve Māori particularly well,[77,78] and AAA disease has a higher mortality for Māori. Specific strategies to ensure high uptake and good access to treatment will be vital.

Criterion 8: There is consideration of cost-benefit issues

The cost of a population-based AAA screening programme is clearly far greater than the cost of the screening tool alone. Cost components include the invitation to screening process, ultrasonography, hospital costs (from pre-assessment to rehabilitation after surgery), community care, and costs to the patient and family. There is also significant cost associated with coordinating, monitoring, and evaluating a screening programme.

A systematic review considered the results of 16 cost-effectiveness studies, a mixture of decision analytic modelling as well as those 'piggybacked' to clinical trials.[79] Comparison was limited due to different methodology (types of models, time frames, screening strategies) as well as different assumptions (cost assumptions and discounting rates).

The highest quality trial, the MASS trial,[61,80] had an incremental cost-effectiveness ratio (ICER) of £36,000 per gained quality-adjusted life year (QALY) at four years. The National Institute for Health and Clinical Evidence (NICE) uses a threshold of below £25,000 to £30,000 per QALY to determine if an intervention is cost-effective.[81,82] By this measure, the MASS trial was on the margin of cost-effectiveness at 4 years, and improved over time.

There was wide discrepancy in ICERs , but in general, AAA screening appears to be cost-effective. Extrapolation to the New Zealand setting is limited due to large variations in cost assumptions. There are no local cost-effectiveness studies to date. Additionally, uncertainty about AAA prevalence in New Zealand limits the cost assumptions that can be made.

Conclusion

On the whole, AAA screening appears to be an appropriate condition for which to *consider* population screening. AAA screening fulfils five out of the eight NHC screening criteria. The remaining three criteria (benefit-harm balance, health system

capacity, and cost-effectiveness) are areas which lack New Zealand data, and where extrapolation from international studies is of limited value. Four core recommendations are proposed, arising from these gaps in knowledge.

Firstly, it is recommended that a population-based prevalence study be undertaken in New Zealand. Findings from this study will be essential in assessing true burden of disease, evaluating benefit-harm balance, forecasting health system requirements, and assessing cost-effectiveness.

Secondly, further research should be done on the comorbidity profile of individuals with AAA, particularly in terms of fitness for elective repair. This has significant implications for benefit-harm balance, and is also an ethical issue.

Thirdly, it is recommended that the drivers of high mortality in Māori be investigated further. This will be important in ensuring the benefits of AAA screening are evenly distributed between population groups.

Finally, it is recommended that further research be done on the acceptability of AAA screening to the New Zealand public. The perceived acceptability of AAA screening will influence uptake of both the screening test and any consequent treatment.

Competing interests: None declared.

Disclosure statement: Caroline Shaw is a member of the National Screening Advisory Committee which provides independent advice to the Director General of Health on screening issues.

Author information: Nisha Nair, Public Health Registrar, University of Otago Wellington School of Medicine & Health Sciences; Caroline Shaw, HRC Clinical Training Research Fellow/Public Health Physician, Department of Public Health, University of Otago Wellington School of Medicine & Health Sciences, Wellington; Diana Sarfati, Senior Lecturer/Public Health Physician, Cancer Control and Screening Research Group, University of Otago Wellington School of Medicine & Health Sciences, Wellington; James Stanley, Biostatistician/Research Fellow, University of Otago Wellington School of Medicine & Health Sciences, Wellington

Correspondence: Nisha Nair, Public Health Registrar, c/o Cancer Control and Screening Research Group, University of Otago, Wellington, PO Box 7343, Wellington South, New Zealand. Fax: +64 (0)4 3895319; email nisha.nair1004@gmail.com

References:

1. Vardulaki KA, Prevost TC, Walker NM, et al. Incidence among men of asymptomatic abdominal aortic aneurysms: estimates from 500 screen detected cases. Journal of Medical Screening 1999;6(1):50-4.
2. Fleming C, Whitlock EP, Beil TL, Lederle FA. Screening for abdominal aortic aneurysm: a best-evidence systematic review for the U.S. Preventive Services Task Force. Annals of Internal Medicine 2005;142(3):203-11.
3. Ginter JF, Linzmeyer J. Abdominal aortic aneurysm repair: matching patients with approaches. JAAPA;22(7):26.
4. Hirsch AT, Haskal ZJ, Hertzer NR, et al. ACC/AHA 2005 Practice Guidelines for the Management of Patients With Peripheral Arterial Disease (Lower Extremity, Renal, Mesenteric, and Abdominal Aortic): A Collaborative Report from the American Association for Vascular Surgery/Society for Vascular Surgery,* Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine and Biology, Society of Interventional Radiology, and the ACC/AHA Task Force on Practice Guidelines (Writing Committee to

Develop Guidelines for the Management of Patients With Peripheral Arterial Disease): Endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation; National Heart, Lung, and Blood Institute; Society for Vascular Nursing; TransAtlantic Inter-Society Consensus; and Vascular Disease Foundation. Circulation 2006;113(11):e463-65.

5. Lindholt JS. Screening for abdominal aortic aneurysms. European Journal of Vascular & Endovascular Surgery 2003;25(5):377-9.
6. Metcalfe D, Holt P, Thompson J. The management of abdominal aortic aneurysms. British Medical Journal 2011;342(d1384):644-49.
7. Basnyat PS., Biffin HB, Moseley LG, et al. Mortality from ruptured aortic aneurysm in Wales. British Journal of Surgery 1999;86(6):765-70.
8. Samy AK, Whyte B, McBain G. Abdominal aortic aneurysm in Scotland. British Journal of Surgery 1994;81(8):1104-6.
9. Ashton HA, Buxton MJ, Day NE, et al. The Multicentre Aneurysm Screening Study (MASS) into the effect of abdominal aortic aneurysm screening on mortality in men: a randomised controlled trial. Lancet 2002;360(9345):1531-9.
10. Cowan JA, Jr., Dimick JB, Henke PK, et al. Epidemiology of aortic aneurysm repair in the United States from 1993 to 2003. Annals of the New York Academy of Sciences 2006;1085:1-10.
11. Holt PJ, Poloniecki JD, Gerrard D, et al. Meta-analysis and systematic review of the relationship between volume and outcome in abdominal aortic aneurysm surgery. British Journal of Surgery 2007;94:395-403.
12. Lederle FA, Wilson SE, Johnson GR, et al. Immediate repair compared with surveillance of small abdominal aortic aneurysms. New England Journal of Medicine 2002;346(19):1437-44.
13. Powell JT, Brady AR, Brown LC, et al. Mortality results for randomised controlled trial of early elective surgery or ultrasonographic surveillance for small abdominal aortic aneurysms. Lancet 1998;352(9141):1649-55.
14. Swedvasc. Swedvasc database, 2005.
15. Cosford PA, Leng GC. Screening for abdominal aortic aneurysm. Cochrane Database of Systematic Reviews 2007(2):Art. No.: CD002945.
16. Kim LG, Thompson SG, Briggs AH, et al. How cost-effective is screening for abdominal aortic aneurysms? Journal of Medical Screening 2007;14(1):46-52.
17. U.K. National Screening Committee. Abdominal Aortic Aneurysm: The UK NSC policy on Abdominal Aortic Aneurysm London, 2010.
18. U.K. National Screening Committee. Essential elements in developing an abdominal aortic aneurysm (AAA) screening and surveillance programme. London: National Health Service, 2010.
19. U.S. Preventive Services Task Force. Screening for abdominal aortic aneurysm: recommendation statement. Annals of Internal Medicine 2005;142(3):198-202.
20. Lee ES, Pickett E, Hedayati N, et al. Implementation of an aortic screening program in clinical practice: implications for the Screen For Abdominal Aortic Aneurysms Very Efficiently (SAAAVE) Act. Journal of Vascular Surgery 2009;49(5):1107-11.
21. National Screening Advisory Committee. Screening policy positions and practice in New Zealand: National Screening Advisory Committee, 2009.
22. National Health Committee. Screening to improve health Wellington: National Health Committee, 2003.
23. Scott RA, Wilson NM, Ashton HA, Kay DN. Influence of screening on the incidence of ruptured abdominal aortic aneurysm: 5-year results of a randomized controlled study. British Journal of Surgery 1995;82(8):1066-70.
24. Lindholt JS, Juul S, Fasting H, Henneberg EW. Screening for abdominal aortic aneurysms: single centre randomised controlled trial.[Erratum appears in BMJ. 2005 Oct 15;331(7521):876]. BMJ 2005;330(7494):750.

25. Norman P, Jamrozik K, Lawrence-Brown M, et al. Population based randomised controlled trial on impact of screening on mortality from abdominal aortic aneurysm. British Medical Journal 2004;329(7477):1259.
26. Chichester Aneurysm Screening Group, Viborg Aneurysm Screening Study, Western Australian Abdominal Aortic Aneurysm Program, Multicentre Aneurysm Screening Study Group. A comparative study of the prevalence of abdominal aortic aneurysms in the United Kingdom, Denmark, and Australia. Journal of Medical Screening 2001;8(1):46-50.
27. Tiefenbacher CP. Abdominal aortic aneurysm repair in cardiac high risk patients--medication, surgery or stent? Clinical Research in Cardiology 2008;97(4):215-21.
28. Wilmink ABM, Quick CRG, Hubbard CS, Day NE. Effectiveness and cost of screening for abdominal aortic aneurysm: results of a population screening program. Journal of Vascular Surgery 2003;38:72-7.
29. Santilli SM, Littooy FN, Cambria RA, et al. Expansion rates and outcomes for the 3.0-cm to the 3.9-cm infrarenal abdominal aortic aneurysm. Journal of Vascular Surgery 2002;35(4):666-71.
30. Wanhainen A, Lundkvist J, Bergqvist D, Bjorck M. Cost-effectiveness of screening women for abdominal aortic aneurysm. Journal of Vascular Surgery 2006;43(5):908-14; discussion 14.
31. Brewster DC, Cronenwett JL, Hallett JWJ, et al. Guidelines for the treatment of abdominal aortic aneurysms: report of a subcommittee of the Joint Council of the American Association for Vascular Surgery and Society for Vascular Surgery. Journal of Vascular Surgery 2003;37:1106-17.
32. Singh K, Bonaa KH, Jacobsen BK, et al. Prevalence of and risk factors for abdominal aortic aneurysms in a population-based study: the Tromso study. American Journal of Epidemiology 2001;154(3):236-44.
33. Wilmink TB, Quick CR, Day NE. The association between cigarette smoking and abdominal aortic aneurysms. Journal of Vascular Surgery 1999;30(6):1099-105.
34. Englund R, Hudson P, Hamel K, et al. Expansion rates of small abdominal aortic aneurysms. ANZ Journal of Surgery 1998;68(1):21-4.
35. Conway KP, Byrne J, Townsend M, et al. Prognosis of patients turned down for conventional abdominal aortic aneurysm repair in the endovascular and sonographic era: Szilagyi revisited? Journal of Vascular Surgery 2001;1(33):752-7.
36. Taylor LMJ, Porter JM. Basic data related to clinical decision-making in abdominal aortic aneurysms. Annals of Vascular Surgery 1987;I:502-4.
37. Bengtsson H, Bergqvist D. Ruptured abdominal aortic aneurysm: a population-based study. Journal of Vascular Surgery 1993;18(1):74-80.
38. Kiell CS, Ernst CB. Advances in the management of abdominal aortic aneurysm. Advances in Surgery 1993;26:73-98.
39. Rose J, Civil I, Koelmeyer T, Haydock D, Adams D. Ruptured abdominal aortic aneurysms: clinical presentation in Auckland 1993-1997. ANZ Journal of Surgery 2001;71(6):341-44.
40. Schouten O, van Waning V, Kertai M , et al. Perioperative and long-term cardiovascular outcomes in patients undergoing endovascular treatment compared with open vascular surgery for abdominal aortic aneurysm or iliaco-femoral popliteal bypass. American Journal of Cardiology 2005;96(6):861-66.
41. NHS Abdominal Aortic Aneurysm Screening Programme. Abdominal Aortic Aneurysm (AAA) Screening: Information for men invited for screening by the NHS Abdominal Aortic Aneurysm Screening Programme. In: Programmes NS, editor. London, 2009.
42. Bergqvist D, Bjorck M, Wanhainen A. Abdominal aortic aneurysm--to screen or not to screen. European Journal of Vascular & Endovascular Surgery 2008;35(1):13-8.
43. Lindholt JS, Vammen S, Juul S, et al. The validity of ultrasonographic scanning as screening method for abdominal aortic aneurysm. European Journal of Vascular & Endovascular Surgery 1999;17(6):472-5.

44. Ebaugh JL, Garcia ND, Matsumura JS. Screening and surveillance for abdominal aortic aneurysms: who needs it and when. Seminars in Vascular Surgery 2001;14:193-9.
45. Vazquez C, Sakalihasan N, D'Harcour JB, et al. Routine ultrasound screening for abdominal aortic aneurysm in a primary care screening programme. British Journal of Surgery 1998;12:544-9.
46. Fahey MT, Irwig L, Macaskill P. Meta-analysis of Pap test accuracy. American Journal of Epidemiology 1995;141(7):680-89.
47. Colorectal Cancer Screening Advisory Group. Report of the Colorectal Cancer Screening Advisory Group. Wellington: Ministry of Health 2006.
48. Baines CJ, Miller AB, Wall C, et al. Sensitivity and specificity of first screen mammography in the Canadian National Breast Screening Study: a preliminary report from five centres. Radiology 1986;160:295-98.
49. Singh K, Bonaa KH, Solberg S, et al. Intra- and interobserver variability in ultrasound measurements of abdominal aortic diameter. The Tromso Study. European Journal of Vascular & Endovascular Surgery 1998;15(6):497-504.
50. Jaakkola P, Hippelainen M, Farin P, et al. Interobserver variability in measuring the dimensions of the abdominal aorta: comparison of ultrasound and computed tomography. European Journal of Vascular & Endovascular Surgery 1996;12:230-37.
51. McCarthy RJ, Shaw E, Whyman MR, et al. Recommendations for screening intervals for small aortic aneurysms. British Journal of Surgery 2003;90(7):821-6.
52. Lindholt JS, Vammen S, Juul S, et al. Optimal interval screening and surveillance of abdominal aortic aneurysms. European Journal of Vascular & Endovascular Surgery 2000;20:369-73.
53. Rantakokko V, Havia T, Inberg MV, Vanttinen E. Abdominal aortic aneurysms: a clinical and autopsy study of 408 patients. . Acta Chirurgica Scandinavica 1983;149(2):151-5.
54. Huber TS, Wang JG, Derrow AE, et al. Experience in the United States with intact abdominal aortic aneurysm repair. Journal of Vascular Surgery 2001;33:304-10;discussion 10-1.
55. Kazmers A, Perkins AJ, Jacobs LA. Outcomes after abdominal aortic aneurysm repair in those > or = 80 years of age: recent Veterans Affairs experience. Annals of Vascular Surgery 1998;12(2):106-12.
56. O'Hara PJ, Hertzer NR, Krajewski LP, et al. Ten-year experience with abdominal aortic aneurysm repair in octogenarians: early results and late outcome. . Journal of Vascular Surgery 1995;21:830-7.
57. Heller JA, Weinberg A, Arons R, et al. Two decades of abdominal aortic aneurysm repair: have we made any progress? . Journal of Vascular Surgery 2000;32:1091-100.
58. EVAR trial participants. Endovascular aneurysm repair versus open repair in patients with abdominal aortic aneurysm (EVAR trial 1): randomised controlled trial. Lancet 2005;365:2179-86.
59. Prinssen M, Verhoeven EL, Buth J, et al. A randomized trial comparing conventional and endovascular repair of abdominal aortic aneurysms. New England Journal of Medicine 2004;351:1607-18.
60. Jibawi A, Hanafy M, Guy A. Is there a minimum caseload that achieves acceptable operative mortality in abdominal aortic aneurysm operations? European Journal of Vascular & Endovascular Surgery 2006;32(3):273-76.
61. Thompson SG, Ashton HA, Gao L, Scott RAP, Multicentre Aneurysm Screening Study G. Screening men for abdominal aortic aneurysm: 10 year mortality and cost effectiveness results from the randomised Multicentre Aneurysm Screening Study.[see comment]. BMJ 2009;338:b2307.
62. Kim LG, P Scott RA, Ashton HA, Thompson SG, Multicentre Aneurysm Screening Study G. A sustained mortality benefit from screening for abdominal aortic aneurysm.[Erratum appears in Ann Intern Med. 2007 Aug 7;147(3):216]. Annals of Internal Medicine 2007;146(10):699-706.

63. Vardulaki KA, Walker NM, Couto E, et al. Late results concerning feasibility and compliance from a randomized trial of ultrasonographic screening for abdominal aortic aneurysm. British Journal of Surgery 2002;89(7):861-4.
64. Ashton HA, Gao L, Kim LG, et al. Fifteen-year follow-up of a randomized clinical trial of ultrasonographic screening for abdominal aortic aneurysms. British Journal of Surgery 2007;94(6):696-701.
65. Lindholt JS, Juul S, Fasting H, Henneberg EW. Preliminary ten year results from a randomised single centre mass screening trial for abdominal aortic aneurysm. European Journal of Vascular & Endovascular Surgery 2006;32:608-14.
66. Lindholt JS, Norman P. Screening for abdominal aortic aneurysm reduces overall mortality in men. A meta-analysis of the mid- and long-term effects of screening for abdominal aortic aneurysms.[see comment]. European Journal of Vascular & Endovascular Surgery 2008;36(2):167-71.
67. Blankensteijn JD, Lindenburg FP, Van der Graaf Y, Eikelboom BC. Influence of study design on reported mortality and morbidity rates after abdominal aortic aneurysm repair. British Journal of Surgery 1998;85:1624-30.
68. Spencer CA, Norman PE, Jamrozik K, et al. Is screening for abdominal aortic aneurysm bad for your health and well-being? ANZ Journal of Surgery 2004;74(12):1069-75.
69. Lindholt JS, Vammen S, Fasting H, Henneberg EW. Psychological consequences of screening for abdominal aortic aneurysm and conservative treatment of small abdominal aortic aneurysms. European Journal of Vascular & Endovascular Surgery 2000;20(1):79-83.
70. Lucarotti ME, Heather BP, Shaw E, Poskitt KR. Psychological morbidity associated with abdominal aortic aneurysm screening. European Journal of Vascular & Endovascular Surgery 1997;14(6):499-501.
71. O'Kelly TJ, Heather BP. General practice-based population screening for abdominal aortic aneurysms: a pilot study. British Journal of Surgery 1989;76:479-80.
72. Duffy AP, Barrett DK, Duggan MA. Report of the Ministerial Inquiry into the Under-reporting of Cervical Smear Abnormalities in the Gisborne Region. Wellington: Ministry of Health, 2001.
73. Scott RAP. Priorities in the management of abdominal aortic aneurysm. British Journal of Surgery 2007;94:653-4.
74. Sarfati D, Howden-Chapman P, Woodward A, Salmond C. Does the frame affect the picture? A study into how attitudes to screening for cancer are affected by the way benefits are expressed. . Journal of Medical Screening 1998;5(3).
75. Gigerenzer G, Gaissmaier W, Kurz-Milcke E, et al. Helping doctors and patients make sense of health statistics. Association for Psychological Science 2008;8:53-96.
76. Cina CS, Anand S. Applying the gender lens to abdominal aortic aneurysm screening. Vascular Medicine 2007;12(4):325-6.
77. Holsted I. Review of targeted policies and programmes: Ministry of Health Review of the National Screening Unit targeted contracts. Wellington: Ministry of Health, 2005.
78. National Screening Unit. Cervical Campaign Media Release. Wellington, 2007.
79. Ehlers L, Sorensen J, Jensen LG, Bech M, Kjolby M. Is population screening for abdominal aortic aneurysm cost-effective? BMC Cardiovascular Disorders 2008;8:32.
80. Multicentre Aneurysm Screening Study Group. Multicentre Aneurysm Screening Study (MASS): cost effectiveness analysis of screening for abdominal aortic aneurysms based on four year results from randomised controlled trial. BMJ 2002;325(7373):1135.
81. Raftery J. NICE: faster access to modern treatments? Analysis of guidance on health technologies. BMJ 2001;323(7324):1300-3.
82. Rawlins MD, Culyer AJ. National Institute for Clinical Excellence and its value judgements. British Medical Journal 2004;329(7459):224-7.

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

The NEEDNT Food List: non-essential, energy-dense, nutritionally-deficient foods

Jane L Elmslie, J Douglas Sellman, Ria N Schroder, Frances A Carter

Abstract

Aim To provide a list of non-essential, energy-dense, nutritionally-deficient foods in New Zealand (NEEDNT foods) which are usually high in calories and either bereft of nutritional benefits or easily replaced with lower calorie, more nutritious alternatives.

Methods The List was compiled using the National Heart Foundation and Diabetes New Zealand "Foods to Avoid", "Stop Eating" and "Optional Foods" lists and the Canterbury District Health Board "Supermarket Shopping Guide". Foods and beverages were included if they contained alcohol, saturated fat, added sugar, were prepared using a high fat cooking method or contained a large amount of energy relative to their essential nutrient value. As it has no energy value, salt was not a criterion for inclusion on the List.

Results Over 50 potential foods or groups of foods were identified that contained alcohol, saturated fat, added sugar, were prepared using a high fat cooking method or contained a large amount of energy relative to their essential nutrient value. Forty-nine foods/groups of foods were included on the final list (Table 1).

Conclusions The NEEDNT Food List will be a useful tool for medical practitioners and other health professionals working with people wanting to lose weight.

Obesity results when energy intake exceeds expenditure. However, the relative importance of the many factors that contribute to energy balance continues to be the subject of considerable debate.[1,2] Most researchers and clinicians agree, however, that reduction of energy intake (eating fewer calories/kilojoules) is a vital component of weight management.[2,3] Furthermore, humans did not evolve to eat a highly processed diet[4] and the benefits of consuming less processed diets, high in naturally occurring micronutrients, such as the Mediterranean diet or that used in the Diabetes Prevention Programme, are very clear.[5,6]

Advising obese patients to "eat moderately," "eat a balanced diet," "reduce fat and sugar" or "eat fewer calories" seems sensible. However, the complexity of the modern food supply and the widespread availability of various types of energy-dense (high calorie) foods, low in essential nutrients, makes it difficult to provide simple, clear information about what and how much to eat. Excessive consumption of such foods reduces overall diet quality, and frequently results in inadequate intakes of essential nutrients, while adding considerably to energy intake.[7–10]

Many processed foods, for example muesli/granola bars, are marketed as 'healthy', but while they may contain fruit and nuts, they are also high in fat and sugar, and are essentially just another form of biscuit/cookie. However, in the public mind, 'healthy' is often equated with 'not fattening.'

In practice, patients frequently believe they will lose weight by replacing a biscuit with a muesli bar or soft [soda, fizzy, carbonated] drink with fruit juice, in effect substituting one energy-dense food for another. They are usually surprised to learn that 'healthy' muesli bars can contain almost twice as many calories as one Toffee Pop® [chocolate coated] biscuit.[11]

Misleading or irrelevant nutritional claims further blur the distinction between healthy and energy-dense, nutritionally-deficient foods. Examples include labelling high sugar foods 'low fat' or implying that a food is 'healthy' merely because it has some 'natural' or 'organic' ingredients. Even foods that have received nutritional endorsements such as the Heart Foundation Tick may just be the best options in a category of typically high calorie food products such as oven chips, pies or ice cream. Consumers often do not understand these subtleties.[12]

Various countries have attempted to make the distinction between nutrient rich, and energy-dense, nutritionally-deficient foods clearer to consumers. The United States (US) Dietary Guidelines distinguish between "discretionary calories" (from saturated fat, added sugars and alcohol) and calories found in foods rich in essential nutrients.[13] However, US food manufacturers are not currently required to clearly stipulate the proportion of discretionary calories on food labels, although consumers can derive this information from the food label provided if they are sufficiently numerate and motivated to do so.[14,15]

Both Food Standards Australia and New Zealand[16] and the United Kingdom (UK) Food Standards Agency[17] have recommended "Traffic Light", front of pack labelling for foods to provide clarity over which foods form the basis of a healthy diet. This system uses red, amber or green, front of pack colour coding (traffic lights) to indicate, whether levels of total and saturated fat, sugar and salt are high, medium or low per 100 g/ml. This allows consumers to judge at a glance, the relative dietary merits of the foods they are considering purchasing. Perhaps not surprisingly, the food industry has reacted negatively to this system and is vigorously lobbying governments to prevent its mandatory introduction.[18]

Currently, New Zealand does not require food to be labelled using this system, although its voluntary introduction has been recommended by a joint Australian and New Zealand review of food labelling law and policy.[16] Instead consumers are required to make complex decisions, often requiring a sophisticated understanding of nutrition and food composition to eat healthily. In such a complex landscape, clinicians may struggle to provide patients with meaningful weight control advice and support.

The need for disease-specific dietary education materials for patients with comorbidities such as diabetes and cardiovascular disease can make this task even more difficult. Simple, unambiguous patient education materials may make it easier to provide nutritional messages while at the same time maintaining patients' motivation to change.

The present paper aims to provide a list of non-essential, energy-dense, nutritionally-deficient foods (NEEDNT foods). This is not simply another list of high calorie foods. This is a list of foods which are usually high in calories and either bereft of nutritional benefits or easily replaced with a lower calorie, more nutritious alternative. It is hoped

that this list will be a simple tool to help adult patients differentiate foods required for good health, from those that are non-essential, energy-dense, and nutritionally deficient. It is intended that this list will be used by medical practitioners and other health professionals working with adults who are overweight or obese, who want to lose weight.

Methods

The NEEDNT Food List was compiled using the National Heart Foundation and Diabetes New Zealand "Foods to Avoid", "Stop Eating" and "Optional Foods" lists,[19–21] the Canterbury District Health Board "Supermarket Shopping Guide" [22] and the USDA population guidance on discretionary calories.[13] Foods and beverages were included if they contained alcohol, saturated fat, added sugar, were prepared using a high fat cooking method or contained a large amount of energy relative to their essential nutrient value. As it has no energy value, salt was not a criterion for inclusion on the List.

Results

More than 50 potential foods or groups of foods, such as desserts and takeaway foods were identified that contained alcohol, saturated fat, added sugar, were prepared using a high fat cooking method or contained a large amount of energy relative to their essential nutrient value. Following discussions with current research patients undergoing obesity treatment and obesity treatment colleagues, the List was finalised as an arrangement of 49 foods/groups of foods. Many of the identified foods are high in salt as well as energy. Tables 1 and 2 show the NEEDNT Food List organised alphabetically and for easy reference, in groups according to potential uses. Suitable alternative foods are provided where possible.

Discussion

The present paper aims to provide clinicians and patients with a clear unambiguous list of non-essential energy-dense, nutritionally-deficient foods. This is not simply another list of high calorie foods. This is a list of foods that are usually high in calories and either bereft of nutritional benefits or easily replaced with lower calorie, more nutritious alternatives. The List is intended as a simple tool to help medical practitioners and other health professionals initiate conversations about food consumption patterns which may promote and maintain obesity and to increase patients' awareness of the relative energy and nutrient densities of many commonly consumed foods.

The purpose of the NEEDNT Food List is to clearly distinguish empty calorie, nutrient poor foods from which it is possible to safely abstain without adverse nutritional consequences. All foods with high energy density relative to essential nutrient content are included on the NEEDNT Food List. For the most part distinctions between foods that require users to read food labels are avoided but this was not possible in some cases, such as breakfast cereals and crackers. To avoid confusion, the List does not distinguish between "red" and "amber" foods.

Many amber foods are energy-dense and relatively low in essential nutrients, just not to quite the same degree as "red" foods. For example, fruit juice is on the NEEDNT Food List because while it contains more essential nutrients than soft drink, its sugar content is similar; it is easily consumed in large amounts and it is much higher in energy and lower in essential nutrients than whole fruit.

Table 1. Non-essential energy-dense nutritionally-deficient (NEEDNT) foods and their healthy replacement choices

NEEDNT food	Replace with
Alcoholic drinks	Water/diet soft drinks
Biscuits	*
Butter, lard, dripping or similar fat (used as a spread or in baking/cooking etc.)	Lite margarine or similar spread or omit
Cakes	*
Chocolate	*
Coconut cream	Lite coconut milk/coconut-flavoured lite evaporated milk
Condensed milk	*
Cordial	Water/sugar-free cordial
Corn chips	*
Cream (including crème fraiche)	Natural yoghurt (or flavoured yoghurt depending on use)
Crisps (including vegetable crisps)	*
Desserts/puddings	*
Doughnuts	*
Drinking chocolate, Milo® etc.	Cocoa plus artificial sweetener
Energy drinks	Water
Flavoured milk/milkshakes	Trim, calci-trim or lite blue [cap] milk
Fruit tinned in syrup (even lite syrup!)	Fruit tinned in juice/artificially sweetened
Fried food	Boiled, grilled or baked food
Frozen yoghurt	Ordinary yoghurt
Fruit juice (except tomato juice and unsweetened blackcurrant juice)	Fresh fruit (apple, orange, pear etc. + a drink of water)
Glucose	Artificial sweetener
High fat crackers (≥10g fat per 100g)	Lower fat crackers (≤ 10g fat per 110g)
Honey	*
Hot chips	*
Ice cream	*
Jam	*
Marmalade	*
Mayonnaise	Lite dressings/lite mayonnaise
Muesli/granola bars	*
Muffins	*
Nuts roasted in fat or oil	Dry roasted or raw nuts (≤1 handful per day)
Pastries	*
Pies	*
Popcorn with butter or oil	Air popped popcorn
Quiches	Crust-less quiches
Reduced cream	Natural yoghurt
Regular luncheon sausage	Low fat luncheon sausage
Regular powdered drinks (e.g. Raro®)	Water/diet/sugar-free powdered drinks
Regular salami	Low fat salami
Regular sausages	Low fat sausages
Regular soft drinks	Water/diet soft drinks
Rollups	Fresh fruit
Sour cream	Natural yoghurt
Sugar (added to anything including drinks, baking, cooking etc.)	Artificial sweetener

Sweets/lollies	*
Syrups such as golden syrup, treacle, maple syrup	Artificial sweetener
Toasted muesli/granola and any other breakfast cereal with ≥15g sugar per 100g cereal	Breakfast cereal with <15g sugar per 100g cereal, >6g fibre per 100g cereal and <5g fat per 100g cereal (or <10g fat per 100g cereal if cereal contains nuts and seeds)
Whole milk	Trim, calci-trim or Lite Blue [cap] milk
Yoghurt-type products with ≥10g sugar per 100g yoghurt	Yoghurt (not more than one a day)

* No suitable alternative.

Whole milk is on the List because while it is a valuable source of essential nutrients (such as calcium and protein) it is also a significant source of energy and saturated fat. It can be easily replaced by low fat milk, which is higher in calcium and protein, without any detrimental effect on overall nutrition, except in the very young. However high calorie unprocessed foods such as plant oils, avocadoes, hard cheeses and dry roasted or unroasted nuts were categorised as nutritious because these foods are valuable sources of essential nutrients despite their relatively high energy content. This categorisation is deliberately different from most "traffic light systems" intended for population dietary guidance, which place nutrient-dense, energy-dense foods such as cheese and plant oil spreads in the amber category because of their high energy and/or saturated fat content.[12,23]

The NEEDNT Food List is similar to proposed Front of Pack Traffic Light Labelling schemes in that it clearly identifies foods that are high in empty calories and low in essential nutrients. However the List is not intended to give consumers specific information about the relative fat, sugar and salt content of different products in the same way as Front of Pack Traffic Light Labelling or programmes such as 'Pick the Tick'.[24] Instead it provides a clear framework for conversations about eating for weight control that does not require a sophisticated knowledge of nutrition or food composition.

To discourage patients from thinking about their eating in morally judgemental terms such "good" and "bad" or "naughty" without understanding the reasons for these distinctions, categorising foods as healthy or unhealthy has been deliberately avoided and the more accurate and objective terms, energy-dense and non-essential have been used instead to highlight the fact that these foods can be safely avoided without compromising nutritional status, while promoting weight loss.

While we are conscious that simply advising avoidance of NEEDNT foods is unlikely to be an effective obesity treatment strategy on its own, it is increasingly clear that in most western countries such foods constitute a large proportion of the total foods consumed and play an increasingly important role in the maintenance of dietary energy surpluses.[25,26] Major social change will be required to reduce the prevalence of obesity at a population level. In the meantime we need to ensure that the available treatment options meet the needs of individual patients.[27]

We are currently evaluating the utility of the NEEDNT Food List for weight control. The List can help patients become aware of their unnecessary or recreational energy consumption and enable them to prioritise dietary changes accordingly. Recognising the distinction between NEEDNT and nutritious foods can help patients to think about

their eating differently. It is envisaged that the List will be given to adults who are obese or overweight, who want to lose weight, and who do not have a current or past history of eating disorders involving restriction and/or binge eating.

Table 2. Non-essential energy-dense nutritionally-deficient foods by group

Foods by group/use	Replace with:
Beverages	
Alcoholic drinks	Water/diet soft drinks
Cordial	Water/Sugar-free cordial
Drinking chocolate, Milo® etc.	Cocoa plus low fat milk and artificial sweetener/Lite drinking chocolate
Energy drinks	Water
Flavoured milk/milkshakes	Trim, calci-trim or Lite Blue [cap] milk
Fruit juice (except tomato juice and unsweetened blackcurrant juice)	Fresh fruit (apple, orange, pear etc. + a drink!)
Regular powdered drinks (e.g. Raro®)	Water/Diet/Sugar-free powdered drinks
Regular soft drinks	Water/Diet soft drinks
Whole Milk	Trim, calci-trim or Lite Blue [cap] milk
Biscuits/cakes	*
Muffins	*
Muesli bars	*
Breakfast cereals	Any breakfast cereal with ≤15g sugar per 100g cereal, ≥ 6g fibre per 100g cereal and ≤5g fat per 100g cereal (or ≤10g fat per 100g cereal if cereal contains nuts and seeds)
Toasted muesli and any other breakfast cereal with ≥15g sugar per 100g cereal	
Dairy products	
Yoghurt type products with ≥10g sugar per 100g yoghurt	Yoghurt (not more than one a day)
Whole Milk	Trim, calci-trim or Lite Blue [cap] milk
Desserts/puddings	*
Ice cream	*
Frozen yoghurt	Ordinary yoghurt
Fats	
Butter, lard, dripping or similar hard fat (used as a spread or in baking/cooking etc.)	Lite margarine or similar spread or omit
Coconut cream	Lite coconut milk/coconut flavoured lite evaporated milk
Cream (including crème fraiche)	Natural yoghurt (or flavoured yoghurt depending on use)
Mayonnaise	Lite dressings/lite mayonnaise
Reduced cream	Natural yoghurt
Sour Cream	Natural yoghurt
Fried foods	Boiled, grilled or baked food
Doughnuts	*
Hot chips	*
Fruit	
Fruit tinned in syrup (even lite syrup!)	Fruit tinned in juice/artificially sweetened
Roll-Ups®	Fresh fruit
Meats	
Regular luncheon sausage (or other processed meat)	Low fat luncheon sausage (or other processed meat)
Regular salami	Low fat salami
Regular sausages	Low fat sausages
Pastries	*
Pies	*

Quiches	Crust-less quiches
Snacks	
Corn chips	*
Crisps (including vegetable crisps)	*
High fat crackers (≥ 10g fat per 100g)	Lower fat crackers (≤ 10g fat per 100g)
Nuts roasted in fat or oil	Dry roasted or raw nuts (≤ 1 handful per day)
Popcorn with butter or oil	Air popped popcorn
Sugars/sweets	
Chocolate	*
Condensed milk	*
Glucose	Artificial sweetener
Honey	*
Jam	*
Marmalade	*
Sugar (added to anything including drinks, baking, cooking etc.)	Artificial sweetener
Sweets/lollies	*
Syrups such as golden syrup, treacle, maple syrup	*
Takeaways	*

*No suitable alternative.

The List is also suitable for use in patients with cardiovascular disease and diabetes in conjunction with other disease-specific nutrition education information.

Conclusion

Consumption of non-essential energy-dense, nutritionally-deficient foods (NEEDNT foods) undermines patients' attempts at weight loss, while contributing little in terms of nutrients. Many foods which are marketed as "healthy" are NEEDNT foods. The NEEDNT Food List makes the distinction between nutritious foods and empty calorie foods clear. It is hoped that this List will be a useful tool for medical practitioners and other health professionals working with people wanting to lose weight.

Competing interests: None declared.

Author information: Jane L Elmslie, Research Fellow/Dietitian[1]; J Douglas Sellman, Professor of Psychiatry and Addiction Medicine and Director[1]; Ria N Schroder, Research Fellow[1]; Frances A Carter, Research Fellow[2]

1. National Addiction Centre, Department of Psychological Medicine, University of Otago, Christchurch
2. Department of Psychological Medicine, University of Otago, Christchurch

Correspondence: Dr Jane Elmslie, Research Fellow/Dietitian, Department of Psychological Medicine, University of Otago – Christchurch, PO Box 4345, Christchurch, New Zealand. Fax: +64 (0)3 3720407; email: jane.elmslie@otago.ac.nz or jane.elmslie@cdhb.govt.nz

References:

1. Galgani J, Ravussin E. Energy metabolism, fuel selection and body weight regulation. Int J Obes (Lond). 2008;32:S109-19.

2. Foster-Schubert KE, Alfano CM, Duggan, CR, et al. Effect of Diet and Exercise, Alone or Combined, on Weight and Body Composition in Overweight-to-Obese Postmenopausal Women. Obesity (Silver Spring). doi:10.1038/oby.2011.76
3. Ministry of Health, Clinical Trials Research Unit. Clinical Guidelines for Weight Management in New Zealand Adults. Ministry of Health: Wellington. 2009.
4. McGill AT. Malnutritive obesity ('malnubesity'): is it driven by human brain evolution? Metab Syndr Relat Disord. 2008 Dec;6(4):241-6.
5. Hill AM, Kris-Etherton PM. Contemporary strategies for weight loss and cardiovascular disease risk factor modification. Curr Atheroscler Rep. 2008;10(6):486-96.
6. Brown T, Avenell A, Edmunds LD, et al. Systematic review of long-term lifestyle interventions to prevent weight gain and morbidity in adults. Obes Rev. 2009;10(6):627-38.
7. Bowman SA, Vinyard BT. Fast food consumption of U.S. adults: impact on energy and nutrient intakes and overweight status. J Am Coll Nutr. 2004;23:163-8.
8. Guo X, Warden BA, Paeratakul S, et al. Healthy Eating Index and obesity. Eur J Clin Nutr. 2004;58:1580-6.
9. Ovaskainen ML Reinivuo H, Tapanainen H, et al. Snacks as an element of energy intake and food consumption. Eur J Clin Nutr. 2006;60:494-501.
10. Sacks G, Veerman JL, Moodie M, Swinburn B. 'Traffic-light' nutrition labelling and 'junk-food' tax: a modelled comparison of cost-effectiveness for obesity prevention. Int J Obes (Lond). doi:10.1038/ijo.2010.228.
11. Lesperance L, Clarke Z, Sivakumaran S, Sharp K. The Concise New Zealand Food Composition Tables. The New Zealand Institute for Plant & Food Research Limited and Ministry of Health New Zealand; 2009.
12. Lobstein T, Davies S. Defining and labelling 'healthy' and 'unhealthy' food. Public Health Nutr. 2009;12:331-40.
13. United States Department of Agriculture and United States Department of Human Services, Dietary Guidelines for Americans. 7th Edition, Washington, DC: U.S. Government Printing Office; 2010.
14. U.S. Department of Health and Human Services and Food and Drug Administration, Eating healthier and feeling better using the Nutrition Facts Label; 2006.
15. U.S. Department of Health and Human Services. Food Labeling Guide. 2009 [cited 2011 27/05/2011]; Available from: http://www.fda.gov/Food/GuidanceCompliance RegulatoryInformation/GuidanceDocuments/Food Labeling Nutrition/Food Labeling Guide/default.htm
16. Blewett NC, Goddard N, Pettigrew S, et al. Labelling logic. Review of food labelling law and policy. Department of Health and Ageing, Canberra; 2011.
17. Food Standards Agency. Food Standards Agency Board Agrees Principles for Front of Pack Labelling. [Front of Pack Labelling. Press Release March 9] 2006 May 2011]; Available from: http://www.food.gov.uk/news/newsarchive/2006/mar/signpostnewsmarch
18. Fight the Obesity Epidemic. UK Food Standards Agency backs down on traffic light food labelling. 2010 May 2011]; Press release]. Available from: http://foe.org.nz/2010/03/12/uk-food-standards-agency-backs-down-on-traffic-light-food-labelling/
19. National Heart Foundation of New Zealand. Heart Healthy Dietary Pattern. National Heart Foundation. Auckland; 2008.
20. National Heart Foundation of New Zealand. A Guide to Heart Healthy Eating. National Heart Foundation. Auckland; 2009.
21. Diabetes New Zealand. Diabetes and Healthy Food Choices. Diabetes New Zealand. Wellington; 2007.
22. CDHB Community and Public Health Division. Supercard. Make healthy choices super fast. Canterbury District Health Board, Christchurch. New Zealand; 2006.

23. Queensland Government, Smart Choices. Healthy Food and Drink Supply Strategy for Queensland Schools. Department of Education and the Arts Queensland Health, Brisbane; 2007.
24. National Heart Foundation of New Zealand, Tick Shopping Guide. National Heart Foundation. Auckland; 2011.
25. Lindstrom J, Peltonen M, Tuomilehto J. Lifestyle strategies for weight control: experience from the Finnish Diabetes Prevention Study. Proc Nutr Soc. 2005;64:81-8.
26. Cohen DA, Sturm R, Scott M, et al. Not enough fruit and vegetables or too many cookies, candies, salty snacks, and soft drinks? Public Health Rep. 2010;125:88-95.
27. Brownell KD. The humbling experience of treating obesity: Should we persist or desist? Behav Res Ther. 2010;48:717-719.

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

A case of cutaneous diptheria in New Zealand

David C R McGouran, Stanley K F Ng, Mark R Jones, David Hingston

Abstract

We report the case of an adult male who contracted cutaneous diphtheria after receiving a tattoo in Samoa. The infection required hospital admission. The Regional Public Health Service conducted urgent contact tracing. We review the techniques employed in traditional tattooing and highlight the importance of considering *C. diphtheriae* as a causative organism in cutaneous infection acquired in the tropics.

Diphtheria is an acute bacterial disease caused by infection with toxin-producing strains of *Corynebacterium diphtheriae* (*C. diphtheriae*). Upper respiratory tract infection is the most common presentation[1] with a fatality rate of 5–10%.[2]

Sore throat, cervical lymphadenopathy ("bull neck"), a grey membrane obstructing the airway and respiratory distress predominate in severe infection. Other systemic consequences are well recognised.

The prevalence of diphtheria has changed over the last three decades. Having almost disappeared completely by the 1980s,[2] a serious outbreak in the Newly Independent States of the former Soviet Union in the 1990s required a mass immunisation campaign to stem the outbreak.[3] Cutaneous *C. diphtheriae* infection is less common but acts as a potential source of respiratory *C. diphtheriae* infection.

We report the case of an adult male who presented to Wellington Hospital's Emergency Department having contracted cutaneous toxigenic *C. diphtheriae* whilst visiting Samoa where he acquired a tattoo.

Case report

Within days of acquiring the tattoo, the man noticed redness and swelling overlying the tattoo, spreading to his mid-calf. A week later after returning to New Zealand he presented to his medical centre with an infected lesion. Flucloxacillin was prescribed but he was non-compliant with his medication. Four days later he returned to hospital.

The doctor attending noted a coin-sized erythematous lesion discharging pus was present within the tattoo on the leg, with peau d'orange surrounds. Swabs were taken and erythromycin was prescribed. The patient was again non-compliant. One week later he again presented, with fevers and rigors where examination of his leg also showed cellulitis. Cultures had grown *Staphylococcus aureus* and toxigenic *Corynebacterium diphtheriae var gravis*. The patient was referred to our Emergency Department. He had taken only four doses of erythromycin.

He was admitted to a single negative-pressure room and nursed with "droplet" precautions. Intravenous erythromycin and high-dose flucloxacillin were commenced. Within 4 days he was well enough to be discharged on oral antibiotics. . A

Diphtheria-Tetanus booster was given post discharge. Contact tracing was conducted by the Public Health Service.

Discussion

Cutaneous *C. diphtheriae* infection is common in developing countries where chronic carriage has long been recognised.[4] It should be considered in any case of tropical ulcer.

Primary cutaneous diphtheria often begins as an acutely tender pustule which breaks down and enlarges to form an oval, punched-out ulcer. This often becomes secondarily infected leading to surrounding cellulitis.[5] Septicaemia and septic arthritis can occur. Myocarditis is relatively rare. Neurological complications including Guillain-Barre syndrome have been reported in 3–5% of ulcerated lesions.[6]

The performance of a traditional Samoan tattoo is of great cultural significance. The techniques involved have their origins dating back thousands of years. Typically the penetrating implement is made from a pig's tooth, sliced and fashioned into a series of sharp spikes. This is bound with nylon fishing line, for example, to a larger piece of bone or plastic, which, in turn, is bound to a wooden handle. The implement is difficult to adequately clean and, as a consequence, sterilisation cannot be achieved. Heat sterilisation using an autoclave is not performed, as the instruments would break down. At best, the "chemical" treatment of such implements can only achieve a moderate level of disinfection.

In Samoa, each tattooing session is followed by bathing in seawater, a procedure that is believed to account for the purportedly low rates of post-tattoo infections. In New Zealand the rate of post-traditional tattoo infection is unknown however cases of severe infection have been reported in the past.[7]

Learning points:

- It is important to consider *C. diphtheriae* in any patient with a recent tattoo who presents with a wound infection.
- *C. diphtheriae* should also be considered for all cases of tropical ulcer or skin infections acquired in disease-endemic areas.
- Provision of appropriate clinical description information to the laboratory is necessary to trigger non-routine culture techniques allowing identification of uncommon organisms such as *C. diphtheriae*.

Author information: David C R McGouran, Gastroenterology Registrar, Wellington Hospital, Wellington; Stanley K F Ng, Paediatric SHO, Wellington Hospital, Wellington; Mark R Jones, Lead Pathologist in Microbiology, Aotea Pathology, Wellington; David Hingston, General Practitioner, Wellington

Correspondence: David C R McGouran, Gastroenterology Registrar, Wellington Hospital, Private Bag 7902, Wellington South, New Zealand. Email: d.mcgouran@googlemail.com

References

1. Clements J. Diphtheria. In: Heymann D, editor. Control of Communicable Diseases Manual. 18th ed. Washington, DC: American Public Health Association; 2004:171-6.

2. Bisgard KM, Hardy IR, Popovic T, et al. Respiratory diphtheria in the United States, 1980 through 1995. Am J Public Health 1998;88 (5):787-91.
3. Vitek CR, Bogatyreva EY, Wharton M. Diphtheria surveillance and control in the Former Soviet Union and the Newly Independent States. J Infect Dis 2000;181 Suppl 1:S23-6.
4. Hofler W. Cutaneous diphtheria. Int J Dermatol 1991;30:845.
5. Belsey MA, LeBlanc DR. Skin infections and the epidemiology of diphtheria; acquisitions and persistence of C. diphtheriae. Am J Epidemiol 1975;102:179-84.
6. Vetrichevvel TP, Gajanan AP, Kishan KA, et al. Cutaneous diphtheria masquerading as a sexually transmitted disease. Indian J Dermatol Venereol Leprol. 2008;74:187-187.
7. Porter CJ, Simock JW, Mackinnon CA. Necrotising fasciitis and cellulitis after traditional Samoan tattooing: case report. J Infect 2005;50:149-52.

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

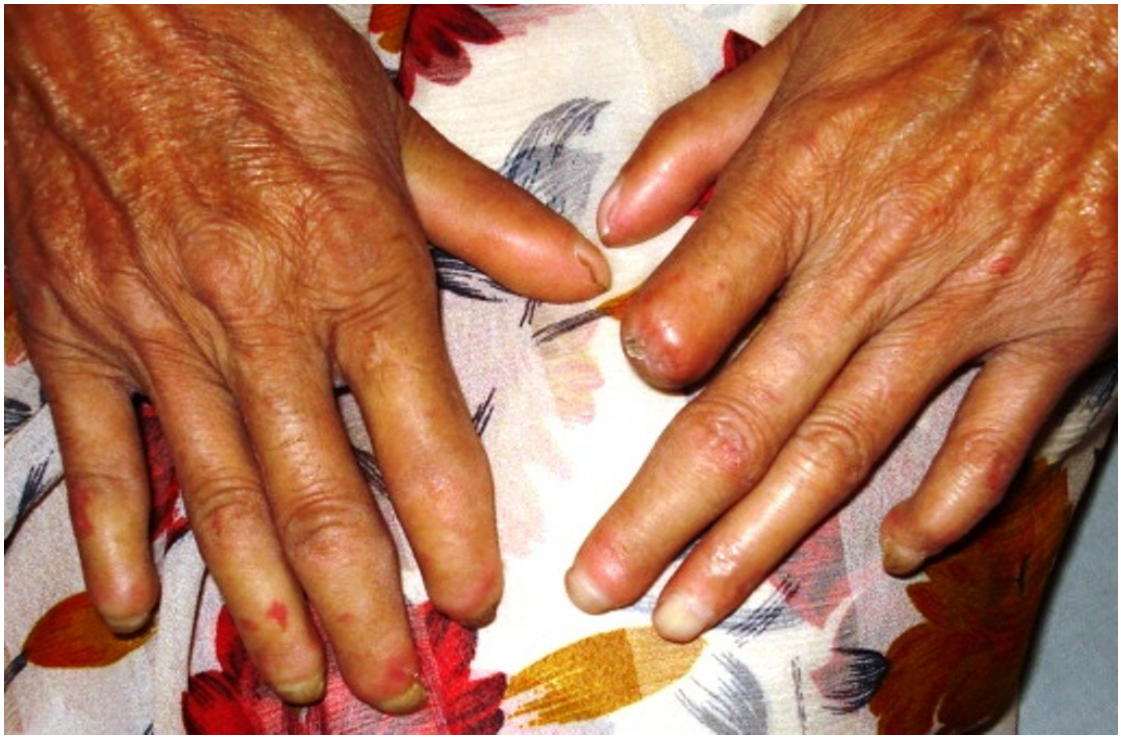
A case of acro-osteolysis

Alka Sharma, Vishal Sharma

Clinical—A 42-year-old lady presented with a history of bluish discoloration of her fingers and toes for the past 2 years. This especially occurred during the winter months. The skin discoloration improved with warming of the extremities. She also complained of tightening of the skin on her fingers and toes.

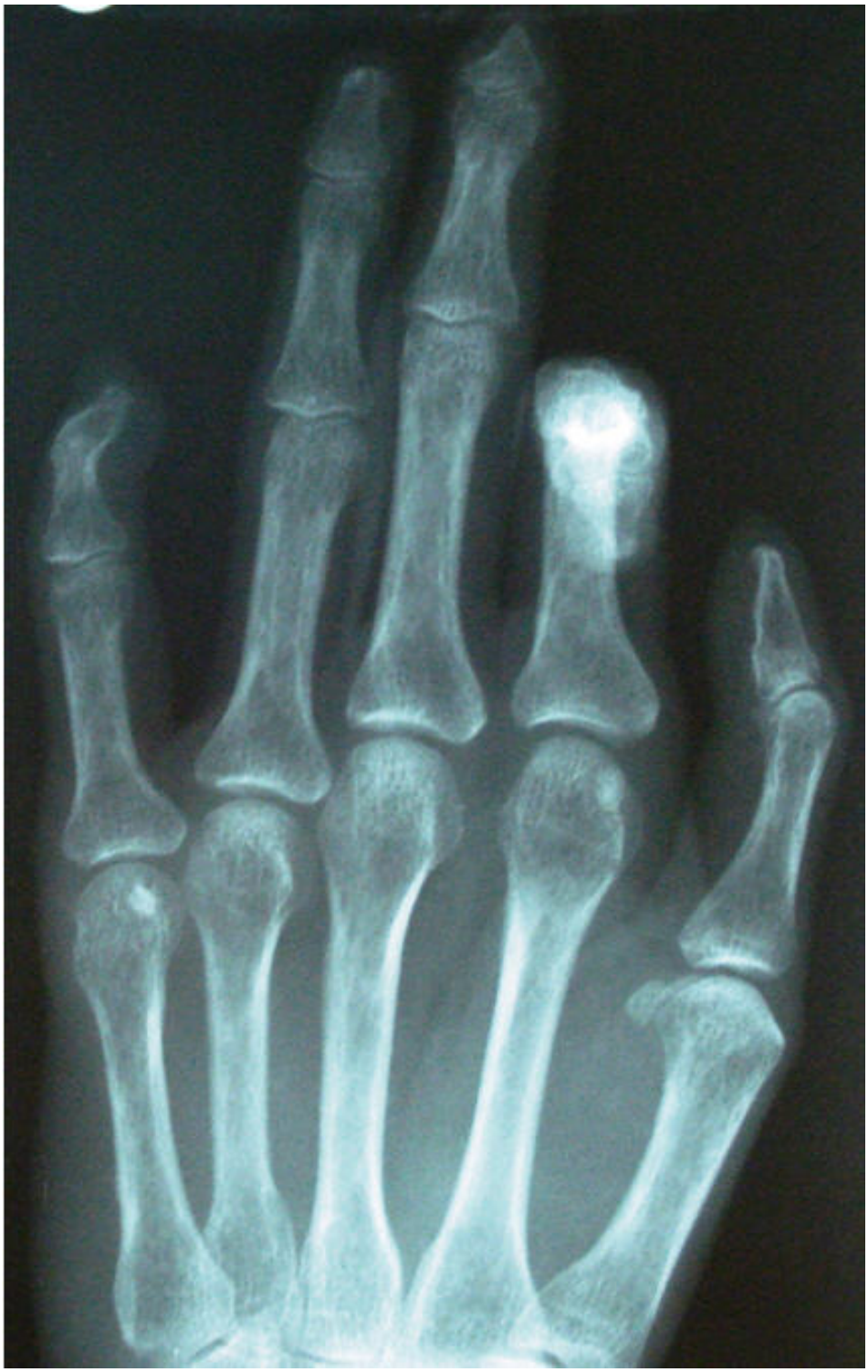
On examination, the skin on her hands was tightly tethered to the underlying tissue. A contracture was present in the index finger of the left hand. The terminal parts of fingers revealed loss of soft tissue (Figure 1).

Figure 1



The X-ray of the hand revealed evidence of acro-osteolysis of terminal phalanges (Figure 2). Her antinuclear antibodies were positive. Anticentomere antibodies were also positive.

Figure 2



What is the diagnosis?

Answer—A diagnosis of *limited systemic sclerosis* was made.

Acro-osteolysis results from ischemic destruction of the terminal phalanges. This usually occurs in association with various diseases which may include vasculitides (like scleroderma, psoriasis, rheumatoid arthritis), exposure to vinyl chloride, neuropathic (diabetes mellitus, tabes dorsalis, leprosy), following trauma or in association with hyperparathyroidism.[1] However this finding is usually characteristic for systemic sclerosis. The frequency has been variably reported from one-fifth to four-fifths of the cases studied.[2]

Author information: Alka Sharma, Senior Resident, Department of Medicine, Government Medical College and Hospital, Chandigarh, India; Vishal Sharma, Senior Resident, Department of Gastroenterology, Postgraduate Institute of Medical Education and Research, Chandigarh, India

Correspondence: Vishal Sharma, 1819 Gobind Nagar, Subhash Road, Chheharta, Amritsar, India. Email: docvishalsharma@gmail.com

References:

1. Kemp SS, Dalinka MK, Schumacher HR. Acro-osteolysis. Etiologic and radiological considerations. JAMA 1986;255:2058-61.
2. Avouac J, Guerini H, Wipff J, et al. Radiological hand involvement in systemic sclerosis. Ann Rheum Dis 2006;65:1088-92.

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

PHARMAC has no cost-effectiveness threshold

Regarding recent discussion in the *Journal* about treatments for insomnia,[1] we clarify that PHARMAC has no cost-effectiveness threshold for the funding of medicines.

PHARMAC funds medicines within a fixed budget, and as cost-effectiveness is only one of its nine decision criteria used to inform decisions,[2] thresholds cannot be inferred or calculated. Thresholds also inadequately account for opportunity cost and affordability, and are incompatible with budgets and maximising health gains. PHARMAC's medicines investments can only be considered 'cost-effective' when prioritised against other proposals at the time; imputed threshold levels must inevitably vary with available funds and the other decision criteria.[3,4]

The authors of the article refer to an historical weighted-average imputed cost per QALY of $6,865 (for the 1999 to 2005 financial years), stating this to be a cost-effectiveness threshold for PHARMAC's funding decisions for new medicines over that time.[1] However, this $6,865/QALY value is an average, which spans a range of investments that were funded—including investments that were more cost-effective (and even cost-saving to the health sector) and investments that were less cost-effective.[5] PHARMAC has never had cost-effectiveness thresholds.

PHARMAC's 'Prescription for Pharmacoeconomic Analysis' (http://www.pharmac.govt.nz/2007/06/19/PFPAFinal.pdf),[5] the source of the cited average cost-effectiveness figure,[1] stresses that the cost-effectiveness of new investments varies widely each year, reflecting both the mix of investment opportunities and the funding available at any one time.

For example, between the 1999 and 2007 financial years,[6] individual new investments made by PHARMAC varied between 25 QALYs gained for every $1 million ($1M) saved by the New Zealand health sector (i.e. cost savings with health gains) and less than 5 QALYs gained for every $1 million spent. Expressed as costs per QALYs, these investments varied between saving $40,000 per QALY gained ($-40,000/QALY) and spending over $+200,000 per QALY. Investments also varied widely each year.

How budgets can relate to health gains and affect the overall cost-effectiveness of funding decisions can be seen in the following diagram:

Example budget	Investment 1: $1M, 100 QALYS (i.e. $10k/QALY)	Investment 2: $1M, 50 QALYS (i.e. $20k/QALY)	Investment 3: $1M, 20 QALYS (i.e. $50k/QALY)	Cumulative total QALYs	Cumulative average QALYs gained per $1M
	Invest?				
$1M	√ - Yes	X - No	X - No	100	100
$2M	√ - Yes	√ - Yes	X - No	150	75
$3M	√ - Yes	√ - Yes	√ - Yes	170	57

We note that the QALYs per $1M measure (i.e. the incremental QALY gains per $1 million net expenditure to the health sector, when compared with the comparator) is interchangeable with cost per QALYs.[7] The QALYs per $1M measure better expresses opportunity cost within funding, and has mathematical advantages over cost per QALYs.[8]

We found the article[1] overall to be informative; our observations relate to one particular aspect of the article and we are not commenting on the article in full.

Scott Metcalfe (scott.metcalfe@pharmac.govt.nz)
Chief Advisor Population Medicine

Alexander Rodgers
Health Economist

Rachel Werner
Health Economist

Carsten Schousboe
Health Economist

PHARMAC, Wellington

References:

1. O'Keeffe KM, Gander PH, Scott WG, Scott HM. Insomnia treatment in New Zealand. N Z J Med 2012;125(1349):U5051. http://journal.nzma.org.nz/journal/125-1349/5051/
2. PHARMAC. Operating policies and procedures of the Pharmaceutical Management Agency ("PHARMAC"), Third Edition, January 2006. http://www.pharmac.govt.nz/2005/12/22/231205.pdf

3. Metcalfe S, Grocott R. Comments on "Simoens, S. Health economic assessment: a methodological primer. Int. J. Environ. Res. Public Health 2009, 6,2950-2966"—New Zealand in fact has no cost-effectiveness threshold. Int J Environ Res Public Health. 2010 Apr;7(4):1831-4. http://www.mdpi.com/1660-4601/7/4/1831/
4. Grocott R. Applying Programme Budgeting Marginal Analysis in the health sector: 12 years of experience. Exp Rev Pharmacoecon 2009;9:181-7 http://www.expert-reviews.com/doi/abs/10.1586/erp.09.2
5. Prescription for Pharmacoeconomic Analysis: methods for cost-utility analysis, Version 2. PHARMAC: Wellington, New Zealand, 2007. http://www.pharmac.govt.nz/2007/06/19/PFPAFinal.pdf
6. Data derived from PHARMAC's Annual Reports to Parliament at http://www.pharmac.govt.nz/AnnualReport .
7. PHARMAC. Operating policies and procedures of the Pharmaceutical Management Agency ("PHARMAC"), Third Edition, January 2006. http://www.pharmac.govt.nz/2005/12/22/231205.pdf
8. Metcalfe S, Grocott R. Comments on "Simoens, S. Health economic assessment: a methodological primer. Int. J. Environ. Res. Public Health 2009, 6,2950-2966" - New Zealand in fact has no cost-effectiveness threshold. Int J Environ Res Public Health. 2010 Apr;7(4):1831-4. http://www.mdpi.com/1660-4601/7/4/1831/
9. Grocott R. Applying Programme Budgeting Marginal Analysis in the health sector: 12 years of experience. Exp Rev Pharmacoecon 2009;9:181-7 http://www.expert-reviews.com/doi/abs/10.1586/erp.09.2
10. Craig BA, Black MA. Incremental cost-effectiveness ratio and incremental net-health benefit: two sides of the same coin. Expert Rev Pharmacoecon Outcomes Res. 2001 Oct;1(1):37-46. http://www.expert-reviews.com/doi/pdf/10.1586/14737167.1.1.37
11. Zethraeus N, Johannesson M, Jönsson B, Löthgren M, Tambour M. Advantages of using the net-benefit approach for analysing uncertainty in economic evaluation studies. Pharmacoeconomics. 2003;21(1):39-48. http://adisonline.com/pharmacoeconomics/Fulltext/2003/21010/Advantages_of_Using_the_Net_Benefit_Approach_for.3.aspx

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

The importance of vitamin D: a response to the article by Bolland and colleagues

Bolland et al (*NZMJ* 10 Feb 2012)[1] have sounded a note of caution in rushing to over interpret the wave of epidemiological data linking vitamin D deficiency and insufficiency with a wide range of diseases, and appropriately pointed out that there is evidence that there may be harm in excessive supplementation. Further to their list of concerns it can now be added that vitamin D, whilst being anti inflammatory when supplemented in the context of a deficiency, appears to switch to be pro-inflammatory when given in excess.[2] Bolland et al conclude " a policy of widespread use of vitamin D supplements should only be implemented in the context of rigorous evidence of the benefits and safety of vitamin D supplements in populations with vitamin D insufficiency."

However an alternative view is that a policy of widespread neglect of a vitamin deficiency regarded by many as pandemic, associated with such a wide array of chronic diseases and in the context of an established Public Health policy of lifelong sun avoidance should also only be implemented in the context of rigorous evidence for its safety.

Vitamin D deserves a bit of respect. Although so many questions are unanswered, when I am confronted with an obese Maori patient with treatment resistant mental illness and type 2 diabetes who is doing very poorly, I have opted for assessment, treatment and follow up of her vitamin D levels along with the standard management of her conditions.

We should not really be surprised that vitamin D appears to have such pleiomorphic effects in health and disease. In an evolutionary sense it has been described as the oldest hormone associated with life on earth.[3] Most cells in the body have a nuclear vitamin D receptor, and it regulates the expression of some 229 genes via 2776 different genomic positions,[4] furthermore the expression of vitamin D-related genes are themselves influenced by DNA methylation.[5] Many of these genes are involved in cell growth, proliferation, apoptosis, inflammation and immune system functioning. Vitamin D also modulates the activity of many transcription factors such as the potent mediator of inflammatory signalling, Nuclear Factor-kB (NF-kB).[6] These factors all contribute to the plethora of associated disease and the individuality of possible clinical response to correction of deficiency.

All of this does not fit at all well with standard models of medical research that focus on a single determinant, or the dysregulation of a single molecular target in investigating the aetiology or the treatment of a specific disease process. Historically vitamin D adequacy was judged to be the dose required to prevent Rickets. This is akin to how much iodine might be required to prevent the birth of a cretin in the family, or how little vitamin C is required to prevent scurvy, but it may not tell us how much of any of these nutrients is required for optimum health. It also does not tell us about optimum doses for other target organs in the body, such as the central nervous system.[7]

Vitamin D receptors are widely expressed in neurons and glial cells. Vitamin D induces Nerve Growth Factor (NGF) and Brain Derived Neurotrophic Factor (BNDF), inhibits Inducible Nitric Oxide Synthase (iNOS) and influences Glucocorticoid receptor function. Epidemiological studies link vitamin D insufficiency with mood disorders, Multiple Sclerosis , brain tumours and schizophrenia. The latter is a prenatal association, underscoring the importance of adequate vitamin D status in pregnancy and making vitamin D yet another piece of the fabric that determines the fetal origins of adult disease.

Bolland et al rightly point out the pitfalls of interpreting observational studies and confusing correlation with causality. However the same epidemiological observations made between various diseases and vitamin D status have also been made in populations according to their distribution in latitude from the equator. In the case of cancer the observation that rates of cancer increased with distance from the equator was made nearly 100 years ago, long before vitamin D was considered to be the link . The point being that such data provides an additional cross check on disease associations with vitamin D levels that further controls for many of the confounding variables listed in Bolland et al's discussion.

The patient in question had serum 25OHD levels of 12 nmol/L and required very significant amounts of vitamin D in order to correct her deficiency. Both her physical and mental health have improved substantially since then.

William Ferguson
General Practitioner
Kumeu

References:

1. Bolland MJ, Grey A, Davidson JS, Cundy T, Reid IR. Should measurement of vitamin D and treatment of vitamin D insufficiency be routine in New Zealand? N Z Med J 10 Feb 2012;125(1349). http://journal.nzma.org.nz:8080/journal/125-1349/5045/content.pdf
2. Amer M, Qayyam R Relation Between serum 25-HydroxyvitaminD and C-Reactive Protein in asymptomatic adults (from the Continuous National Health and Nutrition Examination Survey 2001 to 2006). Am J Cardiology 2012;109(2):226-230.
3. Holick MF Vitamin D: Evolutionary, Physiological and Health Perspectives. Current Drug Targets 2011;12:4-18.
4. Ramagopalan SV, Heger A, Berlanga AJ, et al. A ChIP-seq defined genome – wide map of vitamin D receptor binding: Associations with disease and evolution. Genome Research 2010;20:1352-1360.
5. De Borst MH, deBoer RA, Stolk RP, et al. Vitamin D Deficiency: Universal Risk Factor for Multifactorial Diseases? Current Drug Targets 2011;12:97-106.
6. Kiraly SJ, Kiraly MA, Hawe RD, Makhani N. Vitamin D as a Neuroactive Substance: Review. The Scientific World Journal 2006;6:125-139.
7. Hoffman FL, The mortality of cancer throughout the world. Appendix E Prudential Press 1915.

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

BPAC recertification plan and the Medical Council

Having had more time to try to make sense of the Medical Council's plan for us doctors practising in "a general scope of practice in a collegial relationship", it is clear more questions need answers before those affected can feel the changes are justified.

Council should first tell us what is wrong with the present collegial relationship. There is no argument doctors need continuing education, but surely not all need the same degree of supervision. The juggernaut proposed is a one-size-fits-all attempt to cover all eventualities.

Just take the following examples. A retired surgeon may agree to help an under-doctored general practice with holiday and weekend cover. Or a recently retired principal of the same practice may agree to offer the same services. Then a recently qualified overseas graduate, on his or her medical OE (overseas experience trip), may wish to join the practice as a locum.

I would need a lot of convincing that each of these doctors requires the same supervision outlined in this blunderbuss approach. They can all be in a collegial relationship; each needs an individual assessment, with the supervisor giving an opinion of the competency of the doctor, without the need for the $1200 annual fee for a warrant of fitness.

Presumably, although we're not told, this has all to do with protecting the public. Yet to many generalists it's all a bit draconian, a view supported by the editorial in the latest Medical Protection Society's *Casebook*: …… "In New Zealand, of course, MPS's experience of complaints against our members is relatively benign, especially when contrasted with experiences in our other territories, such as South Africa, the UK and Ireland."

Humphrey B Rainey
Upper Hutt

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

The ethics of care

Ethical care of patients includes, doing good, not doing harm, respect for autonomy, justice, confidentiality and truth telling. It certainly includes the sharing of all relevant information when patients are referred on to other specialists or institutions or back to their General Practitioner.[1 (Sections 39,44, 50, 52, 53)]

Twenty years ago I worked for the Canterbury Area Health Board as the liaison Assistant Medical Superintendant in Chief with General Practitioners (GPs) and community services. One of the tasks I was given was to design and distribute admission forms for the hospital to ensure that all essential information—the diagnoses, investigations, treatment and medications were included in the referral from GPs to the hospital clinics and Emergency Department (ED).

It seems ironical that I am now complaining that many letters from hospital clinics, wards and EDs are severely lacking in clear and essential clinical information. As a GP and working in a hospice I have frequently received discharge letters from hospital admissions, the ED, and hospital clinics with serious omissions.

Discharge summaries from hospital and ED usually include a diagnosis, occasionally include a drug list (frequently inaccurate) but very seldom have information about what medications have actually been administered to the patient during their stay in hospital or in ED. More often than not the drugs at discharge are recorded as “none entered”. ED discharges frequently do not have the investigations done and the results of these.

Letters from hospital clinics usually fail to have any list of medications. Occasionally they do include medication changes.

The Medical Council specifies that accurate information should be given when transferring patients so why is this not done? It puts patients at risk and is negligent not to inform GPs and those caring for patients in other institutions what drugs the patient is taking and what have been administered on the day of discharge.

It would be good to see consultants leading the way and always including a list of current medications in any letter they send. Since they are also responsible for the training of junior staff it would also be good to see them ensuring that their junior staff observe this practice.

Maybe a discharge form with all the appropriate topics listed might be the way to go. This would be distributed centrally to all departments of the hospital and audited regularly, to ensure the safe and smooth transfer of patient care. It would be quite simple to design an IT system that refused to send incomplete letters.

Anna Holmes
Clinical Senior Lecturer, ELM, Department of General Practice, Dunedin School of Medicine
Medical Officer, Otago Community Hospice
Dunedin

Reference:

1. Good Medical Practice: A Guide for Doctors. Medical Council of NZ; 2008. http://www.mcnz.org.nz/portals/0/guidance/goodmedpractice.pdf

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

Relative risk according to the proportion of a population deemed to be at high risk after risk factor analysis: a correction

I have discovered errors in my earlier letter[1] on this topic and wish to correct these and withdraw the previous letter.

The question under discussion is the relative risk of a sub-population of patients, said to be at "high" risk, defined according to the presence of a combination of recognized disease risk factors. For example, when medical patients are deemed to be eligible for thromboprophylaxis according to standard guidelines,[2] up to 82% are found to be at high risk.[3] In this context, the precise quantitative meaning of "high-risk" is uncertain, as the risk of disease in the population as a whole must be the weighted average of the contributions from the low- and high risk-groups.

Previously, I expressed this relationship[1] as

$$\text{Population risk} = 1 = P.R_H + (1-P).R_L$$

where P is the proportion deemed to be at high risk and R_H and R_L are the relative risks in the high risk and low risk populations. This equation is flawed in two respects:

- Assigning a standardized risk of 1 is incorrect. The dependent variable should be the absolute risk of the whole population, which I shall denote as R_T.
- The values R_H and R_L should be absolute risk, not relative risk. Relative risk in the two sub-populations is given as R_H/R_T and R_L/R_T respectively.

Thus the correct equation is $R_T = P.R_H + (1-P).R_L$ (Eq. 1) where the meaning of R has changed from relative to absolute risk.

Thereafter, the logic is similar to before. R_L has a limiting minimum value of zero so the maximum value of R_H ($R_H^{\max}$) is reached as $R_L \rightarrow 0$. Thus, from Eq. 1, $R_H^{\max} = R_T.\frac{1}{P}$ (Eq. 2; the previous result[1] was $R_H^{\max} = \frac{1}{P}$). R_H must be less than $R_H^{\max}$, because in practice $R_L > 0$, i.e. $R_H = k.R_H^{\max}$ where k is unknown but has a value between 0 and 1. Thus $R_H = R_T.\frac{k}{P}$. As before, we find that R_H is proportional to $\frac{1}{P}$. Note that if $k < P$ then $R_H < R_T$ which is not possible, hence $k > P$.

These equations are useful in studying the relationships between dichotomous low- and high-risk groups in a population and in calculations of cost-effectiveness of treatment. These aspects will be reported separately, using medical thromboprophylaxis as an example, in due course.

J Alasdair Millar
Physician and Clinical Pharmacologist
Consultant Director, Acute Care Services
Albany Regional Hospital
Albany, Western Australia 6330
Australia

References:

1. Millar JA. Relative risk according to the proportion of a population deemed to be at high risk after risk factor analysis. NZ Med J 2011 (25 March). http://journal.nzma.org.nz/journal/124-1331/4597/content.pdf
2. The Australia and New Zealand Working Party on the Management and Prevention of Venous Thromboembolism. Prevention of venous thromboembolism (4th Edition). Best Practice Guidelines for Australia and New Zealand. Health Education & Management Innovations Pty Ltd, 2007.
3. Gibbs H, Fletcher J, Blombery P, Collins R, Wheatley D. Venous thromboembolism prophylaxis guideline implementation is improved by nurse directed feedback and audit. Thrombosis Journal 2011, 9:7 (5 April). http://www.thrombosisjournal.com/content/9/1/7

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

Comment on "ACC response on rotator cuff tears"

I refer to the letter published in the 11 February 2011 issue of the *NZMJ* titled *ACC response on rotator cuff tears*.

I write to you as someone who represents ACC claimant in both the review and appeal process and have successful overturned a number of decisions by ACC declining to fund shoulder surgery and have a sound knowledge of the legislative requirements in issues of causation, including leading case law.

I take issue with the following statement (paragraph 2): " New Zealand is unique, although there is a similar discussion in Germany, in **that the ability to attribute a substantial or wholly traumatic contribution to pathology requiring treatment determines the funding stream** and the waiting time for the appropriate operation."

The highlight part of that sentence is grossly incorrect and misleading to your members and really gets to the heart of the issue/problem.

The ACC legislation excludes a personal injury if the physical injury has been caused wholly or substantially by an underlying degenerative condition.

The above statement gives the reader the impression that the physical injury has to be caused "wholly or substantially" by an accident, which is not true. I refer you to Section 26, subsection 2 & 4 of the Accident Compensation Act 2001, link here: Section 26 of the ACA 2001

The term "wholly or substantially" is regarded by the ACC Appeal Courts as "largely" or "closer to 100% than 50%". In other words, a degenerative process can be more than a 50% contribution to the cause of a physical injury and that injury still covered as a personal injury caused by an accident. This is a typical scenario for shoulder injuries where it seems likely, based on my experience as an ACC advocate, that there is usually some degree of degenerative process present within the shoulder, which may or may not be relevant to the actual physical injury e.g. a tendon tear.

It is very frustrating to see ACC's medical advisors confuse the legislative criteria, which discourage your members, and claimants, from pursuing funding from ACC because they do not understand the actual criteria for a personal injury, as defined in the legislation. It seems that decisions on causation are being made by medical people when it is a matter for those with a sound understanding of the legislative criteria, where ACC internal medical advice is but one opinion to be considered by the decision-maker, the treating surgeon another, when weighting up the evidence and making a decision based on the balance of probability.

I would like the NZ Medical Association to challenge ACC on this point and a correction to the statement made.

David Wadsworth
Access Support Services Ltd, Motueka

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

Comment on "Under-use of secondary prevention medication" article by Looi and colleagues

The figures quoted by Khang L Looi et al for secondary prevention medication in patients who have had coronary artery bypass graft surgery do indeed look unnecessarily low. From a general practice point of view there are many reasons why patients may not be on long-term medication as recommended by a specialist, including intolerance, problems of polypharmacy and patient preference. However it is certainly possible to achieve better results with a close attention to chronic disease management in primary care.

For comparison, we undertook an audit last year in our Very Low Cost Access practice, which serves a relatively deprived population in East Christchurch. Of 185 patients with a recorded diagnosis of ischaemic heart disease,153 (83%) were taking both aspirin and a statin.

Ten patients (5.4%) were not taking aspirin and adequate clinical reasons for this were recorded for seven, one patient had declined and no reason was found for two patients.

Twenty-three patients (12.4%) were not taking a statin of which ten patients were recorded as intolerant, ten had significant co-morbidities or other clinical reasons and two had declined. Only in one patient could no reason be found.

Thus there were only three patients out of 185 where the lack of aspirin or statin prescription may have resulted from accidental omission, the failure for some reason to follow best practice or failure to record appropriate decisions.

This demonstrates that whatever the situation as regards hospital prescribing, it is possible to achieve good results through attention in primary care. We do not know whether the Auckland results indicate that patients are being discharged without having a GP to follow them up—this may explain some of the low figures. However it is also important to point out that a proportion of patients (in our practice 18%) will have good reasons for not taking their long-term prophylactic medication as recommended.

Pat McIntosh
General Practitioner
Christchurch

Reference:

1. Looi KJ, Chow KL, Looi JL et al. Under-use of secondary prevention medication in acute coronary syndrome patients treated with in-hospital coronary artery bypass graft surgery. N Z Med J. 2011Sep 23;124(1343):27-30. http://journal.nzma.org.nz:8080/journal/124-1343/4883/content.pdf

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

Hands-only CPR

As retired cardiologists we are concerned that instruction to the public on hands-only cardiac resuscitation (CPR) may not being promulgated sufficiently in New Zealand.

Citizen-initiated CPR has long been known to improve the chance of successful defibrillation by paramedics.[1] Most cases of ventricular fibrillation happen outside hospital and most are witnessed by relatives or bystanders. Despite recent advances, defibrillation can still prevent more deaths from heart attack than any other treatment.[2]

A recent meta-analysis of three randomised trials of dispatcher-assisted CPR has shown that hands-only CPR for victims of cardiac arrest gives more successful results than CPR with mouth to mouth respiration.[3] (This of course does not apply to victims of respiratory arrest or drowning where artificial respiration should be given.)

The fact that mouth-to-mouth respiration is unnecessary for heart attack victims, clearly makes CPR easier to learn and more likely to be aesthetically acceptable for many people. We are concerned that free information and free opportunities for training in hands-only CPR are insufficiently available in New Zealand.

This contrasts with the situation in the United Kingdom[4] where television advertising using the popular song "Stayin' alive", free training courses in localities and schools, and a free mobile application for Android and iPhones are all available. TV advertising in New Zealand would seem particularly likely to have an impact.

Robin M Norris

Kevin P O'Brien (k.p.obrien@xtra.co.nz}

Retired cardiologists
Auckland

References:

1. Thompson RG, Hallstrom AP, Cobb LA. Bystander-initiated cardiopulmonary resuscitation in the management of ventricular fibrillation. Ann Intern Med 1979;90:737.
2. Julian DG, Norris RM. Myocardial infarction: is evidence-based medicine the best? Lancet 2002;359:1515-6.
3. Hupfl M, Selig HF, Nagele P. Chest compression only versus standard cardiopulmonary resuscitation: a meta-analysis. Lancet 2010;376:1552-7.
4. www.bhf.org.uk (accessed 13/2/12).

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

Perioperative results in the Canterbury pilot programme of public-funded weight loss surgery

In 2010 the Associate Minister of Health Tariana Turia announced a funding package that guaranteed 300 weight loss operations across New Zealand over 4 years.[1] In response to this the Canterbury District Health Board committed to the development of a public-funded weight loss surgical service. Here we describe the initial perioperative results the pilot programme of a small cohort of patients undergoing laparoscopic adjustable gastric banding.

Methods—Patients were sourced from the Department of Endocrinology, Christchurch Hospital and selected by an independent committee that included a surgeon, a diabetologist, a GP liaison, and a hospital manager.

The pre-surgical work-up consisted of a surgical, psychological and a dietician assessment before commencing a 2-week very-low-calorie diet (VLCD; up to 800 calories a day). All patients had a fitness plan designed in conjunction with an exercise specialist.

Laparoscopic adjustable gastric bands (LapBand AP, Allergan Inc., CA) were used for all patients and placed by a local surgeon (GC, RF, SK, RR) using a standard pars flaccida technique.[2]

Perioperative complications were categorised as per the Clavien-Dindo classification system.[3] Weight loss was expressed as mean total weight loss and percentage of excess body weight lost (using ideal body weight as per the Deitel & Greenstein formula).[4] Glycaemic control was measured by the number of units of insulin used per 24 hour, HbA1c, C-peptide, and insulin resistance (using HOMA2 IR). The expenditure of insulin was used as a surrogate of potential health cost benefits of the programme. The cost of insulin usage was determined from PHARMAC Pharmaceutical Schedule September 2011.

All statistical analysis was performed by InStat version 3.0 (GraphPad Software Inc., San Diego, USA). All descriptive data is expressed as mean ± standard deviation.

This study was reviewed and approved by the New Zealand Health and Disability Ethics Committee (Upper South A Region/11/EXP/047).

Results—There were 13 patients (7 female; mean age was 39±6 years) that entered the pilot programme. The initial mean body weight was 131.0±15.0 kg, and initial mean body mass index was 43.3±2.3 kg/m^2.

Comorbidities are detailed in Table 1. There were nine patients (69%) taking regular insulin (mean total 70.1±38.5 units / 24 hour). Insulin was not used in the remaining four patients because of patient refusal (two patients), dangerous levels of non-compliance (one), and not clinically indicated (one). All but two patients were taking metformin. Only one patient was taking a thiazolidinedione preoperatively. The initial mean HbA1c was 7.9±1.7 %, mean C-peptide 1007.0±505.9 ng/mL, mean HOMA2 IR 2.8±1.8.

Table 1 Comorbidities in 13 patients in the pilot programme

Comorbidities	n	Percentage
Diabetes	13	100
Retinopathy Nephropathy Neuropathy	4 3 1	
Hypertension	9	69%
Polycystic ovary syndrome	5	71%*
Gastroesophageal reflux disease	4	31%
Hyperlipidaemia	4	31%
Depression	2	15%
Obstructive sleep apnoea	0	0

Percentage of females.

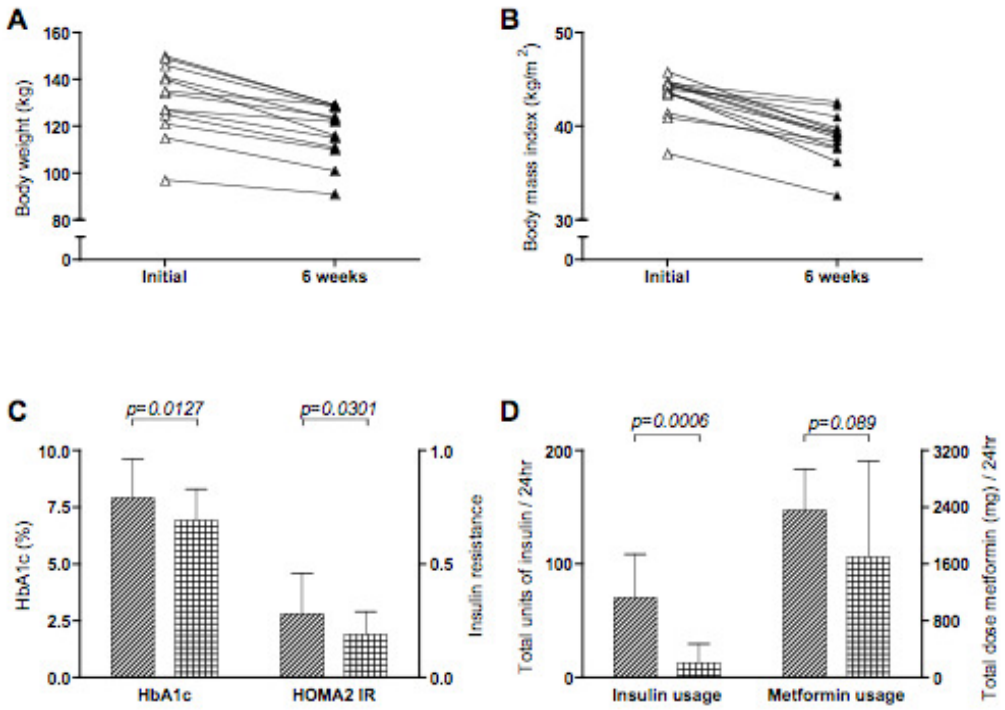
All but one patient was compliant with the preoperative VLCD. Surgery was successfully completed in all 13 patients with no conversion to laparotomy. All patients were discharged to home the next morning.

Follow-up was complete for all patients at 6 weeks postoperative. There were no deaths during the study period, nor were there any grades 1 to 4 complications. There were no emergency department visits or any readmissions to hospital.

At 6 weeks all patients had experienced significant weight loss (Figure 1A and B) with a mean loss of 13.8±6.2 kg (mean 21±8 % excess body weight loss; $p < 0.0001$). The mean BMI at 6 weeks was 38.8 ± 2.6 kg/m^2.

Glycaemic control had significantly improved at 6 weeks (Figure 1C and D). Insulin usage decreased (70.1±38.5 units / 24 hour decreased to 12.7±16.9 units / 24 hour; p=0.0006) with five patients (55%) no longer taking insulin. There was no attempt to stop oral hypoglycaemics but the dosages were reduced; metformin usage was down from mean 2347±585 mg to 1694±1348 mg and glipizide usage had decreased from mean 20±17 mg to 2.5±5 mg. However neither of these reductions reached statistical significance (p=0.089 and p=0.0605 respectively). The HbA1c at 6 weeks had reduced by 1.0 % (down to 6.9±1.4 %; p=0.0127), insulin resistance had fallen by 32% (HOMA2 IR down to 1.9±1.0; p=0.0301). C-peptide remained relatively unchanged at 1091.5±397.4 (p=0.2647).

Figure 1. Weight loss and glycaemic control in 13 diabetic patients undergoing adjustable gastric banding



(A) Change in body weight for each patient.

(B) Change in body mass index for each patient.

(C) Change in HbA1c and insulin resistance for the entire cohort (mean + SD; initial = diagonal shading, 6 weeks postoperative = hatched shading).

(D) Change in insulin usage and metformin usage in the entire cohort (legend as per the previous graph).

The expenditure of insulin for the entire cohort of patients before surgery was $51.47 per day. At 6 weeks this had reduced to $14.28 a day. This equates to an ongoing saving of $1152.86 per month in insulin costs for this cohort of patients.

Discussion—This paper reports the initial perioperative findings of the Canterbury pilot programme of weight-loss surgery. The use of adjustable gastric bands resulted in no perioperative complications or deaths and induced significant early weight loss and diabetes control.

Our findings of good early results with no complications may be viewed with some incredulity but are consistent with published literature. In the Longitudinal Assessment of Bariatric Surgery study (LABS; a prospective, multi-centre observational study of 30-day outcomes following weight-loss surgery) there were no

deaths amongst 1198 patients having adjustable gastric bands. Only nine patients required re-operation and the rate of adverse events within 30 days was only 1%. [5] The Michigan Bariatric Surgery Collaborative 2006–9 reports similar results with only 2 deaths amongst 5380 patients having laparoscopic adjustable gastric bands. In that series only 3% of patients visited the emergency department after their surgery; readmission rate was only 2% and re-operation rate just 0.63%.[6] Similar results are described in European centres.[7, 8] However, it must be emphasised that some of the complications following adjustable gastric bands tend to occur several months after the surgery and can affect a significant proportion of patients.[9] These will not be accounted for in this early report of perioperative results.

In conclusion the initial results of this pilot study are encouraging but are at a very early stage. Obesity surgery can be performed safely in the public setting but ongoing follow-up is needed to determine the long-term efficacy of this programme.

Richard Flint (richard.flint@otago.ac.nz)
Senior Lecturer, Christchurch School of Medicine, University of Otago
Consultant General Surgeon, Christchurch Hospital
Christchurch

Debbie Osborn
Practice Nurse
Southern Obesity Surgery
Christchurch

Grant Coulter
Consultant General Surgeon, Christchurch Hospital
Christchurch

Steven Kelly
Consultant General Surgeon, Christchurch Hospital
Christchurch

Ross Roberts
Consultant General Surgeon, Christchurch Hospital
Christchurch

Acknowledgements: The authors would like to acknowledge Dr Helen Lunt and members of the Christchurch Hospital Diabetes Clinic who were instrumental in the success of this current study.

References:

1. www.beehive.govt.nz/release/ Turia delighted with funding for life-saving weight-loss operations. 2010.
2. O'Brien P, Dixon J, Laurie C, Anderson M. A prospective randomized trial of placement of the laparoscopic adjustable gastric band: comparison of the perigastric and pars frlaccida pathways. Obes Surg. 2005;15:820-6.
3. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg. 2004;240:205-13.
4. Deitel M, Greenstein RJ. Recommendations for reporting weight loss. Obes Surg. 2003;13:159-60.

5. Flum DR, Belle SH, King WC, et al. Perioperative safety in the longitudinal assessment of bariatric surgery. N Engl J Med. 2009;361:445-54.
6. Birkmeyer NJ, Dimick JB, Share D, et al. Hospital complication rates with bariatric surgery in Michigan. JAMA. 2010;304:435-42.
7. Morino M, Toppino M, Forestieri P, et al. Mortality after bariatric surgery: analysis of 13,871 morbidly obese patients from a national registry. Ann Surg. 2007;246:1002-7; discussion 7-9.
8. Burns EM, Naseem H, Bottle A, et al. Introduction of laparoscopic bariatric surgery in England: observational population cohort study. BMJ. 2010;341:c4296.
9. Suter M, Giusti V, Worreth M, et al. Laparoscopic gastric banding: a prospective, randomized study comparing the Lapband and the SAGB: early results. Ann Surg. 2005;241:55-62.

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

A case of rupture of the liver

By Ivan Wilson, M.D., M.R.C.S., Eng. Read before the Hawke's Bay Division.

Published in NZMJ 1911 May;10(38):8–9.

On November 5th last at 5.30 p.m., a man aged 35 years was admitted into the Napier Hospital suffering from a kick on the abdomen from a horse. On admission he was in a state of collapse, showing signs of severe shock and haemorrhage. His skin was blanched and cold, his pulse imperceptible, and his respirations rapid and shallow. He was very restless and complained of great pain in the right side of the chest on inspiration. On examining the abdomen, I found two red marks, one in the epigastrium and the other in the right hypochondrium just above the costal margin, corresponding to the kicks from the two hind hoofs. The abdomen was fixed on respiration, somewhat distended, and soon showed signs of fluid in both flanks.

On passing a catheter, I obtained several ounces of pure blood, and on passing a measured amount of saline into the bladder and receiving most of it back I concluded that the bladder wall was intact, and that the haemorrhage was renal. He was then given two pints of saline slowly per rectum, and the pulse steadily improved. About 8 p.m. his bowels acted twice, and each time he had a large amount of melaena, the stools being dark and tarry. About this time he also coughed up some bright red blood. No fracture of the ribs could be discovered. After consultation with the staff, I decided to perform laparotomy, as although the intra-peritoneal haemorrhage had apparently ceased as indicated by the improving pulse, the melaena pointed to a, probable injury to the bowel.

Dr. Henley assisted at the operation. Open ether was administered, and the patient stood the operation well except at one stage, when the pulse became very feeble but quickly responded to saline intravenously with Pituitary Extract minims XX. On opening the abdomen I found the peritoneal cavity full of blood and blood clot, and on passing my hand round the liver found a huge laceration towards the posterior part of the right lateral surface. It was large enough to admit the whole hand. The right kidney did not feel damaged, although it must have had some injury from the blow to cause the rather sharp haematuria which occurred. The blood was turned out from the peritoneal pouches, and the whole abdomen then flushed out clean with normal saline. A rapid examination of the intestines revealed no injury. As the tear in the liver was too far back and too lacerated to suture, I packed it with plain sterilized gauze, the latter acting as a drain through the incision in the right rectus muscle.

After History.—The patient had slight melaena, blood in the urine and rusty-coloured sputum for a few days after the operation, but these all cleared up. Later he had a thin layer of fluid over the base of the right lung, but this absorbed in about a week. The packing I removed for the first time four clays after the operation. The sinus rapidly filled in, and the wound was completely healed and the patient up and convalescent four weeks after the operation.

Apart from the severe injuries this patient sustained, and the bad prognosis one-could not help giving on his admission, I think the interesting point about the case is the melaena. No injury to the, intestine could be found at the operation, nor did the subsequent history of the case point to any involvement of the bowel, and yet at the time one felt that it was a symptom of bad omen. I think the explanation for the melaena lies in the severe injury to the liver, that organ probably being infiltrated with blood which passed along the bile capillaries to the hepatic ducts, and thus to the intestine.

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

The Cockroft and Gault formula for estimation of creatinine clearance: a friendly deconstruction

J Alasdair Millar

Abstract

Aims To review the derivation of the Cockroft and Gault formula for estimating creatinine clearance from serum creatinine in a historical context.

Method The derivation described by Cockroft and Gault was reviewed, and an alternative formula was sought using the data reported in the paper.

Results Cockroft and Gault used 24 hour urine creatinine data expressed as mg/kg body weight and mathematical manipulation of a linear regression equation which introduced body weight as an independent variable into the formula. This involved a circular logic and may have been mathematically invalid. A more logical equation not containing body weight was derived from the data.

Conclusion The Cockcroft and Gault formula has been validated by long usage but the derivation appears logically insecure. Nevertheless, its role in estimating renal function at the bedside is established.

The Cockroft and Gault formula for estimating creatinine clearance (C_{Cr}) as a proxy for glomerular filtration rate (GFR) has been in use for clinical and research purposes since its derivation in 1976.[1] Recently it has been largely superceded by the eGFR, based on the MDRD formula [$C_{Cr}\ (\mathrm{ml/min/1.73\,m^2}) = 175 \times Cr^{-1.154} \times age^{-0.203}$, (omitting factors for sex and race)] but remains a valuable bedside tool for estimating the need to adjust the doses of drugs that are cleared by the kidney in patients with renal dysfunction.[2]

In this paper I review the derivation of the Cockroft and Gault formula from a historical perspective and comment on its use at the bedside.

Methods

This work is based on an analysis of the paper by Donald W Cockroft and M Henry Gault in Nephron (1976)[1] and some extrapolations therefrom. The formula as published was

$$C_{Cr} = \frac{(140 - age)(wt\ kg)}{72 \times S_{Cr}(mg/100ml)} \quad \text{or using molar units,} \quad C_{Cr} = \frac{1.23 \times (140 - age)(wt\ kg)}{S_{Cr}(\mu mol/L)}$$

(Equation 1). An alternative formula without weight as a dependent variable was derived from the paper after calculating total 24 hr creatinine excretion, following the method described by Cockroft and Gault.

Derivation of the formula:

Cockroft and Gault studied 534 consecutive patients in whom creatinine clearance was measured on 2 or more occasions using serum and 24-hour urine creatinine concentrations. Ninety six percent of the patients were male. Patients (n = 29) were excluded if not in steady state (blood creatinine values differed by > 20%). A sub-group ("Group II") used for the derivation of the formula (n = 236) was formed from "Group I" by further excluding patients whose 24-hr urine creatinine values differed by

more than 20% (n = 173) or was < 10 mg/Kg (n = 31) or where the records were inadequate (n = 65). Group II was augmented by re-inclusion of 23 patients who satisfied the second criteria but whose 24-hr urine volume was > 500 ml (final n = 249).

The steps in deriving the formula were:

Step 1. The relationship between creatinine excretion expressed as mg/kg/24h (as the dependent variable) (CrUV24/kg) was plotted against age (independent variable) after aggregating data into age bands of 10 years (data given as table II in their paper).

Step 2. The equation for the curve was obtained by linear regression:

$$CrUV24/kg\ (\text{mg/kg}) = 28 - (0.2 \times age) \quad \text{(Equation 2)}$$

Step 3. Both sides of the equation were multiplied by weight, to give

$$CrUV24\ (\text{mg}) = 28 - (0.2 \times age)(wt\ kg) \quad \text{(Equation 3)}$$

Step 4. Equation 3 for CrUV24 (mg) was inserted into the expression for creatinine clearance and hence the final equation was derived:

$$C_{Cr}\ 24\ (\text{ml/min}) = \frac{CrUV24 \times 100}{1440 \times S_{Cr}} = \frac{(28 - 0.2age)(wt\ \text{kg})}{72 S_{Cr}\ mg/100ml} = \frac{(140 - age)(wt\ \text{kg})}{72 S_{Cr}\ \text{mg/100ml}}$$

Cockcroft and Gault validated their formula by comparing it to three other formulae[3-5] for creatinine clearance and against a nomogram published from Denmark,[6] which contained body weight. Cockroft and Gault noted that as the average weight in their Group II was 72 kg, their formula simplified to

$C_{Cr} = \frac{(140 - age)}{Cr}$ for patients of average weight.

Comment and discussion

From a modern perspective, several aspects of the derivation of the Cockroft and Gault formula require comment.

- The total number of patients studied (n= 249) was low by modern standards, though it represents a prodigious amount of clinical and laboratory work. By comparison, the derivation of the MDRD equation used data from 1070 patients[7] from the Modification of Diet in Renal Disease Study.[8]
- A modern analysis (of which the derivation of the MDRD equation is an example) would not have aggregated data into bands of age. This is statistically suspect since it decreases the degrees of freedom in the regression analysis. I believe the reason was the absence of computing power using statistical software packages that we now take for granted.
- In order to express urine creatinine data as mg/kg, Cockroft and Gault must have taken the measured 24 hour creatinine and divided by body weight. Thus the development of the formula uses circular logic because in Step 3 the regression equation is multiplied throughout by weight to re-express the dependent variable as 24 hr creatinine (mg) and thereby create a variable for weight on the right side of the equation and hence in the final formula. Furthermore, it is not clear whether the multiplication is by body weight as a measured variable or by ‘weight” (mass) as a dimension; either is mathematically suspect in this context.
- Note that the weight used throughout is the actual body weight, not some other measure of weight such as lean body mass.

It is possible to derive a valid equation from the Cockroft and Gault data that does not depend on weight, by calculation of the 24 hr urine creatinine according to each age group assuming that the average weight applies throughout, and using these data to follow the stepwise procedure used by the authors.

The new data are:

Age	CrUV (mg/kg/24 h)	Wt (kg)	CrUV (mg/24 h)
24.6	23.6	72	1699
34.6	20.4	72	1469
46.2	19.2	72	1382
54.4	16.9	72	1217
64.6	15.2	72	1094
74.4	12.6	72	907
85.1	12.1	72	871

Regressing CrUV (mg/24 h) on weight gives the linear equation

$CrUV\,24(mg) = -13.9 \times age + 1997$ (Compare with equation 2 above). When this equation is substituted into the equation for creatinine clearance, the result after collection of terms becomes $C_{Cr} = \frac{144 - age}{S_{cr}}$, or in SI units, $C_{Cr} = \frac{85 \times (144 - age)}{S_{Cr}}$ (Equation 4). This is almost identical to the Cockroft and Gault formula when it is applied to patients of average weight, but this is to be expected since the derivation involved using the constant factor, equal to average weight, of 72. I did not study the performance of this formula in detail and mention it here only to emphasize the circumstances surrounding the inclusion of body weight in the Cockroft and Gault formula. However, it is of interest that body weight was not a significant independent variable in the derivation of eGFR using the MDRD Study patients.

Because 96% of Cockroft and Gault's patients were male, the original formula applies only to male patients. The creatinine clearance in females is about 85% of males. Hence the use of the formula at the bedside is greatly simplified if the factor of 1.23 in equation 1 is ignored and the result is regarded as the value of CL_{Cr} in females. For a male patient, simply add 20%.

Conclusion

The Cockroft and Gault formula has stood the test of time and hence may be said to have been validated by usage. However, its derivation was unusual and involved circular logic. The introduction of the weight variable appears to have come from an arbitrary regression of 24 hr creatinine excretion (as mg/kg) on age, with a subsequent manipulation that caused body weight to appear as an independent variable in the published formula.

With the possible exception of formula III,[5] all the pre-existing formulae for creatinine clearance listed by Cockroft and Gault gave usable values, as does Equation 4 above (results not shown). Thus it appears that there are a range of potentially usable formulae for CCr that are reciprocal functions of serum creatinine

but vary in the other dependent variables and scaling factors. This is confirmed by the example of the eGFR equation in which the term $Cr^{-1.154} = \frac{1}{Cr^{1.154}} \approx \frac{1}{Cr}$.

Historical note

Professor Cockroft graduated in medicine at the University of British Columbia in 1950. He now works as a researcher in asthma at the Department of Medicine, University of Saskatchewan in Saskatoon. His career has taken him there via San Jose, Montreal, Vancouver and Hamilton (Ontario).

This author approached Professor Cockcroft at his place of work and requested clarification on the reason for including weight in the regression equation. Professor Cockcroft replied that the primary interest of the work was effectively to validate the values for CL_{Cr} obtained from the Danish nomogram,[6] which contains weight, but he could not recall the specific reason for the choice of regression. In the event, his objective was secured (see Cockroft and Gault, Table III).

Professor Gault died in May 2003. His obituary from the University of Newfoundland[9] describes him as a pioneer in the field of nephrology. As a young man he survived 31 wartime bombing missions over Germany with the Royal Canadian Air Force. His subsequent nephrology career was in Montreal and Newfoundland.

Competing interests: None declared.

Author information: J Alasdair Millar, Consultant Physician and Clinical Director, Medical Department, Southland Hospital, Invercargill.

Correspondence: J Alasdair Millar, Consultant Director Acute Care Services, Albany Regional Hospital, Warden Ave, Albany, WA 6330, Australia. Email Alasdair.millar@health.wa.gov.au

References:

1. Cockroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. Nephron 1976; 16: 31-41.
2. McNeill GBS, Martin JH. How reliable is eGFR when calculating drug dosage in acute medical admissions? Internal Medicine Journal 2011;41:327-331.
3. Jelliffe RW. Estimation of creatinine clearance when urine cannot be collected. Lancet 1971;i:975-976.
4. Jelliffe RW. Creatinine clearance. Bedside estimate. Ann Int Med 1973;79:604-605.
5. Edwards KDG, Whyte HM. Plasma creatinine level and creatinine clearance as tests of renal function. Aust Ann Med 1959;8:218-233.
6. Siersbæk-Nielsen K, Hansen JM, Kampmann J, Kristensen M. Rapid evaluation of creatinine clearance. Lancet 1971;i:1133-1134..
7. Levey AS, Coresh J, Greene T, Stevens LA, Yaping Z, Hendrikson S, Kusek JW, van Lente F for the Chronic Kidney Disease Epidemiology Collaboration. Ann Int Med 2006;145:247-254.
8. Klahr S, Levey AS, Beck GJ, Caggiula AW, Hunsicker L, Kusek JW, et al. The effects of dietary protein restriction and blood-pressure control on the progression of chronic renal disease. Modification of Diet in Renal Disease Study Group. N Engl J Med. 1994;330:877-84..
9. In Memory: Dr Henry Gault. University of Newfoundland Faculty of Medicine Newsletter (Munmed), 2003; 2 (1). http://www.med.mun.ca/munmednews/201/gault.htm (accessed 4 Aug 2011).

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

Fish oil for secondary prevention of atrial fibrillation

Atrial fibrillation (AF) is the most common sustained arrhythmia and represents a growing burden on healthcare systems. It is responsible for considerable morbidity and mortality because of its association with thromboembolism and worsening heart failure. Although rhythm control and rate control strategies seem to provide comparable results the restoration and maintenance of sinus rhythm remains the preferred therapy for a large number of patients. Electrical cardioversion is very useful in restoring sinus rhythm but often its effects are temporary. A recent meta-analysis suggests that renin-angiotensin system blockade therapy in combination with amiodarone may have more efficacy in preventing AF than amiodarone alone.

As n-3 polyunsaturated fatty acids (n-3 PUFAs) are reputed to have antiarrhythmic effects this study attempts to clarify this issue. 199 patients with persistent atrial fibrillation, with at least 1 relapse after cardioversion, and treated with amiodarone and a renin-angiotensin-aldosterone system inhibitor were assigned to placebo or n-3 PUFAs 2g/d and then underwent direct current cardioversion 4 weeks later. At 1 year follow-up the probability of maintenance of sinus rhythm was significantly higher in the n-3 PUFAs treated patients. Very good. The authors conclude that “further studies are needed to confirm our findings and to determine whether treatment with n-3 PUFAs may prevent AF recurrence independently of antiarrhythmic therapy”

Circulation 2011;124:1100-1106.

Frequency of bone mineral density (BMD) testing in older women

Osteopenia and osteoporosis are significant problems in the elderly, particularly in the elderly female. BMD testing is a valuable tool in detecting and predicting bone loss thus facilitating prophylactic and therapeutic measures. This study attempts to define the timing of BMD testing in the elderly female. They studied nearly 5000 women 67 years or older with a normal BMD or some evidence of osteopenia, but no history of fracture or treatment for osteoporosis for up to 15 years. Their data indicated that osteoporosis would develop in less than 10% of their subjects during rescreening intervals of 15 years for those with normal BMD or mild osteopenia, 5 years for those with moderate osteopenia and 1 year for women with advanced osteopenia.

N Eng J Med 2012;366:225-33.

Do statins reduce the risk of infection?

Statins have a well established role in the treatment of hyperlipidaemia and in the prevention of cardiovascular problems. Several observational studies have noted that those treated with statins have less infections. This meta-analysis seeks to elucidate. Data was culled from 11 trials involving 30,947 patients; 14,103 received statins and 16,844 received placebo. 4655 participants experienced an infection during treatment as an adverse event or cause of death. 2368 were on statins and 2287 on placebo.

These results showed no benefit of statins on the occurrence of infection (relative risk 1.0) or death as a result of infection. Obviously evidence from prospective randomised trials is more reliable than observational data.

BMJ 2011;343:d7281.

Delayed versus early umbilical cord clamping on neonatal outcomes and iron status at 4 months

Apparently in developing countries it is common practice to delay cord clamping as this increases the infant's blood volume by about 30% which is beneficial in an environment where iron deficiency is common. However, early clamping is the pattern in Western countries on the grounds that this prevents polycythaemia and hyperviscosity in the infant. This randomised trial from Sweden involved 400 full-term low risk pregnancies.The intervention consisted of delayed clamping of the umbilical cord (≥180 s after delivery) or early clamping of the umbilical cord (≤10 s). The primary outcome was haemoglobin and iron status at 4 months of age. And the results were that delayed cord clamping improved all measures of iron status and reduced the prevalence of iron deficiency but had no effect on haemoglobin at 4 months of age. An editorial commentary is enthusiastic and suggests that the results of the study are convincing enough to encourage a change of practice.

BMJ 2011;343:157 & 2011;343:d7127.

Treatment of pulmonary embolism with enoxaparin followed by once-weekly idrabiotaparinux

Currently the standard treatment of pulmonary embolism is subcutaneous enoxaparin followed by the vitamin K antagonist, warfarin. This is effective but somewhat tedious and careful monitoring is required to maintain anticoagulation without haemorrhage. Idraparinux, a synthetic pentasaccharide with a specific inhibitory effect on factor Xa activity that is mediated through plasma antithrombin, has proven to be efficacious and safe without the need for frequent monitoring with blood tests. The addition of a biotin moiety to idraparinux (i.e. idrabiotaparinux) allows rapid reversal of the anticoagulant effect through infusion of avidin which makes it more attractive than its parent drug.

This report concerns a trial involving 3202 patients with pulmonary embolism. The researchers randomly allocated patients to receive 5–10 days enoxaparin 1.0 mg/kg twice daily followed by subcutaneous idrabiotaparinux (starting dose 3.0 mg) or adjusted-dose warfarin (target international normalised ratio 2.0–3.0). The primary efficacy outcome was recurrent thromboembolism at 99 days and the enoxaparin-idrabiotaparinux treatment was shown to be non-inferior to enoxaparin-warfarin. Clinically relevant bleeding occurred in 5% of the enoxaparin-idrabiotaparinux patients and in 7% of the enoxaparin-warfarin patients.

Lancet 2012:379:123-29.

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

Alan Bernard Howard Howes

MBE, MBChB, FRCGP (10 July 1922 – 26 November 2011)

Dr Alan Howes spent most of his professional life in Pukekohe.

Alan was born in Whakatane and spent his primary school years at various schools in the North Island. He won a scholarship to New Plymouth Boys High School where he took up many of the sports that would become life-long interests and that he found himself excelling at, including rugby, cricket, badminton and surf lifesaving. His initial tertiary education was at Auckland University and Auckland Teachers College. After graduating, he taught for 2 years, and then accepted a medical bursary to study at Auckland and Otago Medical Schools.

Upon qualifying in 1948 he married Marjorie and this began a wonderful partnership of 54 years. Alan's first position was as a house surgeon at Waikato Hospital, followed by a position in a three-man general practice in Te Kuiti. He owed the government 18 months of 'tied service' so accepted a position in Tokanui, Southland. Alan and Marjorie and their two young daughters then moved to Pukekohe in December 1952 where Alan began a long and dedicated service to the Franklin community.

From this time Alan and his family became part of the Pukekohe community. Throughout the 1950s, 1960s and 1970s the general practice grew bigger and bigger and developed into the first group practice in the area. The new Pukekohe Maternity Hospital was built in 1954, and trained its own midwives. Here Alan lectured the Obstetrics Nurses.

Obstetrics was a major part of a GP's life and Alan recalled delivering five babies in a 24-hour period as well as carrying out his general practice duties. As one of only a few GPs in the area Alan was always in high demand. Over the years he did endless house visits, covering as far as Mangatawhiri, Glen Murray, Tuakau and Patumahoe and he also delivered hundreds of future residents.

Alan was an inaugural member of the Royal College of General Practitioners and his efforts towards medicine and community health were acknowledged when he was presented with a Fellowship of the Royal College of General Practitioners in 1981. His sporting interest influenced his medical practice and he was also involved at the forefront of sports medicine, including the establishment of what is now Sports Medicine NZ.

Alan had an association with Peter Snell and proudly took some of the credit for having him fit enough to perform at the Rome Olympics. The 1990 Commonwealth Games in Auckland saw Alan as the medical officer for cycling and he assisted in the creation of the Manukau Velodrome. He was responsible for helping to set up the drug testing procedures and protocols for the competing cyclists.

Alan assisted in the development of Age Care and the Pukekohe Geriatric Hospital and the establishment of Counties Home Care. He was a member of the Auckland Hospital Board for two terms. Alan and Marjorie also completed two exchanges to the UK, working in general practice, for 6 months each.

During his 59 years living in Pukekohe Alan was involved in many other pursuits. He was a life member of Counties Racing Club and a life member of Counties Rugby Club having been the medical officer for both for many years. He was a life member of the Auckland Polo Club and was the medical officer for Prince Charles during his two visits to NZ. Alan also became a life member of the Pukekohe Fire Brigade after serving as their honorary surgeon, and a Life member of Counties Rugby Club.

One of Alan's passions was Contract Bridge. He was instrumental in setting up the Franklin Bridge Club where he had a regular commitment for many years playing and directing, teaching bridge lessons, serving as president, and patron and he also was a life member of both the Franklin Bridge Club and the Papakura Bridge Club. His finest bridge achievement was winning the North Island pairs championship in 1976 with Marjorie.

Alan was also heavily involved in netball both as an umpire and coach, and later an avid spectator and supporter of his daughters, granddaughters and more recently his great granddaughter. He spent many hours with coaching, advising and assisting netball players and was a life member of Counties Netball.

In 1991 Alan was awarded an MBE for services to primary health care, sports and sports medicine.

Alan's personal qualities earned him the deepest of respect of his friends, patients and colleagues. His enthusiasm for life and true community spirit saw him become a part of the fabric of the Franklin community. He will be sadly missed.

Alan is survived by his two daughters and their families.

Denise Edwards (a daughter) wrote this obituary.