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EDITORIALS

Words alone are not enough

"Words alone are not enough" said George Monbiot, author and Honorary Professor of Philosophy, University of Keele. Worried that the voices of concern regarding third world debt were being down-played, even disregarded by the industrial nations, and disturbed by the fighting in Genoa during World Trade Organisation talks, he stated: "I have simply stumbled once more upon the fundamental reality... that confrontation is an essential prerequisite for change... (t)hough I am scared to say it, it's now clear to me that we cannot win without raising the temperature... words alone are not enough".[1] Subsequent world events, in the last quarter of 2001, seem to bear this out.

What does all this have to do with the status of the public health in New Zealand? In common is rule by ideology unhindered by open debate or measurement of outcome. "There is only one way". The ideologically-based health reforms in this country, started under a Labour-led regime in the late 1980s, and carried on essentially unchanged under subsequent National and Labour-dominated coalitions, have patently failed to deliver health services to a standard acceptable to either the public or to health professionals. Medical education has been compromised, as has recruitment and retention of locally-trained medical, nursing and allied health professionals. Paradoxically, a fiscally-efficient health system may be further away than ever before. Throughout these "lost" fifteen years, many health professionals elected by their peers have been alienated from decision-making. Most of those with medical training in administration of Health have been selected by willingness to salute the ideological flag. Consultation has, with some exceptions, been sham.

High profile investigations such as the enquiries into Canterbury Health[2] and Gisborne Hospital[3] and onto cervical cancer,[4] carried out when sufficient disquiet was expressed, revealed that when the ideology had been enforced against the advice of health professionals, the outcomes have been "unfortunate". Not only were patient outcomes adverse, but costs to the taxpayer were likely to be considerably more than the implementation of sensible, sound health systems.

After so many high profile failures in the health system, one might logically hope that the prevailing ideology might change. This appears not to be the case as witness recent events in Auckland details of which will be discussed in a subsequent issue of the Journal. The parallels between events in Auckland and Christchurch or Gisborne are obvious. The only major difference is in timing.

Why was crisis-point reached later in Auckland than, for example, in Christchurch? A major contributing factor was the contrast in attitudes of senior management and health boards in the mid 1990s. The Crown Health Enterprise (CHE) Board and management at Canterbury Health proceeded forthwith to implement Treasury and the Crown Companies' Monitoring Advisory Unit (CCMAU) commands against the expressed concerns of their elected health professionals. By contrast, Brian Pankhurst, Chairman and Dennis Pickup, CEO at Auckland Healthcare saw clearly the problems and refused to compromise standards of patient care. Brian Pankhurst stated: "Treasury told us that, if we were hardnosed in their terms, confrontational, we'd just tell the docs that this is the way it's going to be. The outcome, we believe, would be telling the patients to go to blazes as well."[5] Pankhurst was asked by an official from CCMAU to resign.[5] Lin Stoddart, Chair of the Waitemata Health Board in Auckland did not renew his contract in 1996 noting that "when a succession of well-informed people told the Government of real problems in Auckland and what was needed to fix them, politicians had been extremely hard of hearing."[6] So, up to this point in the mid - 1990s, Auckland had senior managers and boards that listened to the voice of their elected professionals and their crisis was postponed until 2001/2.

Which brings us back to broader issues posed at the start of this article. Words alone over many years and from diverse sources have failed to alter the ideology of leaders in the industrial nations. That the situation is not sustainable becomes more obvious day by day. Regarding the state of public health in New Zealand, evidence that the current ideology is not delivering value for money cannot now be questioned. The problems resulting from implementation of the ideologically-based health reforms were never confined to one town or city. Rather, they were manifest at different times, to differing degrees and in slightly different forms in the different centres. What, alas, is now perfectly clear is that to alter the ideology thrust upon us by politicians and Treasury, words alone have proved insufficient.

The Editors

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2. A report by the Health and Disability Commissioner. Canterbury Health Limited. Auckland: 1998 April.
3. A report by the Health and Disability Commissioner. Gisborne Hospital 1999-2000. Auckland: 2000 March.
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6. Barber F. Health Board head bails out citing dearth of support. NZ Herald 1996 Jun 14.

PHARMACopsychiatry: problematic but promising

David B Menkes, ***Professor of Psychological Medicine, University of Wales Academic Unit, Wrecsam, Wales.***

Funding of drug treatment for mental illness is an important challenge in many countries, not least New Zealand. As Porter and Mulder argue in this issue's *Viewpoint*, some newer medicines available in other Western countries are not funded by PHARMAC, thus limiting treatment options, potentially comprising clinical care, and leading to a great deal of frustration among prescribers, patients, their carers and advocates.

Understanding the origins of this difficulty may help to identify solutions. Ours is an era of rapid development of new and promising pharmaceuticals. Applying these to patients in need is problematic for several reasons. Adequate clinical research often lags behind pharmaceutical development, and as Porter and Mulder point out, treatment-resistant psychiatric patients are a particularly difficult group to study, and the ethics and funding of such research also can be fraught. As a result, the true usefulness (and dangers) of a new drug may only become clear years after launch.

A second problem, rather avoided by Porter and Mulder, relates to the often high cost of new, patented medicines. It may take ten years or more for a new drug to reach the market, and to survive the company's need to recoup development costs, fund advertising, and make a profit. There is, of course, nothing intrinsically wrong with this, and for many years pharmacotherapeutic progress across medical disciplines has depended on such entrepreneurial activity. A problem arises, however, when the financial cost of new medicines must be reckoned against their evident clinical worth, as must occur in the setting of a limited health budget like New Zealand's. The situation is complicated by incomplete evidence (above), and by competing priorities in psychiatry and elsewhere to fund other new treatments. PHARMAC was constituted eight years ago to contain unsustainable growth in the drugs budget and to maximize health gains.[1]

If funding decisions must reflect the cost-effectiveness of new treatments across a range of disorders, then a standard way of reckoning this is essential. PHARMAC and a number of drug purchasers overseas use 'quality adjusted life years' (QALYs) as a means of doing this and thereby setting priorities for funding. While this model is fair, it is often difficult to implement, and neglects the cost savings which might accrue from, for instance, reduced hospital bed occupancy.

Other sources of frustration with PHARMAC arise from the widespread perception among prescribers that purchasing decisions appear based on price more than clinical utility.

Examples include

1. Reference pricing of drug sub-groupings which have been inappropriately lumped together. For example nefazodone was lumped with the SSRIs, which made very little pharmacological sense.[2] Similarly, statins of differing efficacy were lumped together with unfortunate consequences.[3] ACE inhibitor funding may be unfolding in a similar way. Unfortunately, reference pricing appears, in many cases, to restrict the range of pharmaceuticals available.[1]
2. Illogical restrictions are perceived by many specialists and general practitioners. For example, parenteral bisphosphonates are only available in cancer and in advanced osteoporsis with two or more fractures, not in early osteoporosis where prevention might be feasible. Oral bisphosphonates are available, but poorly tolerated and less effective. Similarly, the expensive calcitriol is funded, while equally efficacious vitamin D capsules are not. In rheumatology, a number of patients unable to tolerate NSAIDs would benefit from COX-2 selective agents, but these simply are not funded, even on a restricted basis. Similarly, new treatments of rheumatoid arthritis (eg leflunomide) could be of substantial use in a small number of patients who fail to benefit from conventional treatment. Finally, uricosuric agents, although low volume and effective are not funded, which is particularly unfortunate given the high rates of gout in Polynesian populations and PHARMACs explicit inclusion of "Maori and Pacific peoples" in its decision criteria.[4]
3. Some PHARMAC pricing decisions appear to deviate from the cost-effectiveness model because of 'deals' made with pharmaceutical companies, which yield rather inconsistent effects or prescribing quality. Apart from the reference pricing approach (above), tendering also generates controversy. For example, many familiar formulations of common medicines (Ritalin, Augmentin, Renitec etc.) have been replaced by cheaper alternatives, sometimes generic equivalents, other times not. This has been confusing for doctors and patients alike, and PHARMAC has struggled to keep everyone informed of the many changes. Some patients have not coped well with such changes.

Few doctors would contest the assertion that good prescribing requires continuing dedication and effort, and most of us fall short of our target. This is little wonder, given the time required to attend to good clinical practice, careful audit, and study of the evolving evidence on drug treatment. It is regrettable that many doctors in New Zealand view PHARMAC as compromising rather than fostering quality care, but in theory restrictions on drug access are part of a package which could (and should) improve cost-effective prescribing.[4,5] Doctors may also benefit from 'counter-detailing' and promotion of best practice standards which, rather surprisingly, often are cheaper than conventional practice. This may arise from the fact that prescribers can be influenced in unhelpful ways by pharmaceutical promotion.[5,6]

Porter and Mulder are critical of PHARMAC's apparent reluctance to admit company-sponsored trial data, making the point that no challenge to the data *per se* was provided and often no other data are available. However, some of PHARMAC's scepticism may be justified, based on a number of careful studies which conclude that sponsorship may affect not only prescribing attitudes and interpretations of drug treatment data in peer-reviewed publications[7,8] but also, in some cases, the actual data.[9] This appears to be a pervasive problem and it is notable that the Vancouver group are continuing to refine and strengthen their approach to managing conflict of interest.

I agree with Porter and Mulder that psychiatrists in New Zealand do need more prescribing choice, particularly when faced with treatment-resistant patients. In their example, venlafaxine would certainly be a useful option, and it seems extraordinary that it is not yet available in New Zealand, given its wide availability in the UK, Europe, North America and Australia. On the other hand, the evidence cited by Porter and Mulder to demonstrate the usefulness of venlafaxine in treatment resistance comes from a sponsored French study[10] which unfortunately does not specify what proportion of patients failed to respond to SSRIs during the index episode. If this proportion is high, as seems likely, then the study shows

rather unsurprisingly that SSRI non-responders tend not to respond when re-challenged with another SSRI. To fairly judge the clinical utility and cost-effectiveness of venlafaxine, one would need a better idea of the size of the target population (SSRI non-responders) and, ideally, a comparison with an alternate strategy (eg augmentation of SSRI with reboxetine).

Bill Cosby observed that he didn't know the secret of success, but the secret of failure must surely be trying to please everyone. By adopting a systematic, unbiased approach to reckoning cost-effectiveness of pharmaceuticals, PHARMAC can ensure that it will never please everyone. But the purchaser's job is not to be popular, but rather to be fair, and to get the best health outcomes for the money available. Unfortunately, life is seldom that simple, and PHARMAC's other policies appear to have led to much disappointment. Although complex to develop, implement and enforce, restricted prescribing of expensive medicines has met some of the objections by targeting those most likely to benefit. Indeed, it is in nobody's interest for expensive but ineffective treatments to be sanctioned. In this respect, PHARMAC's much criticised curmudgeonly policy toward interferon beta for multiple sclerosis several years ago has been vindicated by similar restrictions following in other countries. In this case it isn't merely a matter of an expensive treatment and marginal evidence of benefit; interferons also have a myriad of toxic effects including organic brain syndromes, depression and suicide.[11] Sometimes restrictions are not just in the taxpayers' interest; they may be in our patients' interest as well.

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Can we trust scientists or are they puppets of the drugs industry?

PAY their wages but don't tell researchers what to write. That is the message to drug companies from the medical establishment this week.

Several of the world's leading medical journals, including The New England Journal of Medicine and The Lancet, announced that they are taking a tougher stance on publishing the results of clinical trials funded by the pharmaceuticals industry. Their action has been prompted by concerns that companies sponsoring the research are trying to influence the design and interpretation of trials, and that unpalatable results are being swept under the carpet.

However much the pharmaceuticals industry may protest, these concerns are well founded. Surveys show that company-funded trials are more likely to yield positive results than independent studies. The results of clinical trials that prove negative are only one-third as likely to appear in a journal as the results of successful trials.

From now on, many journals will publish papers only if the main authors, not the sponsor, make the final decision on publication. To achieve this, the journals will ask authors of papers to sign a statement declaring that they had access to all the data, and accept full responsibility for the conduct of the trial and its findings.

The measures should help put a stop to the sort of abuses that prompted this move. These include the case of Knoll Pharmaceuticals, which for seven years blocked publication of findings suggesting that generic thyroid drugs worked just as well as one of its brand-name products. We only know about such cases because a few researchers have had the courage to stand up to their sponsors.

The unpalatable truth is that some scientists still remain silent or collude in the distortion or suppression of trial results. Indeed, the pressure to obtain and maintain funding can be so great that a few even resort to fabricating data to keep their paymasters happy.

Editorial. New Scientist 2001, 15 September.

Cephalosporin Allergy

The cross-reactivity among cephalosporins and between cephalosporins and penicillins has been examined in laboratory and clinical settings; nevertheless, this complex issue remains unresolved. The specific haptens involved in hypersensitivity to cephalosporin have not been identified. The number of potential haptens is large, because both side-chain and nuclear components of the cephalosporins may participate in the hypersensitivity reaction. Laboratory tests suggest that cephalosporin derivatives have less cross-reactivity among themselves than do penicillin derivatives, but the degree of cross-reactivity between cephalosporins is greater than that between cephalosporins and penicillin. These assessments are severely limited by the fact that the cephalosporin haptenic determinants are unknown.

According to a review of the literature on allergy to penicillin, of 15,987 patients who were treated with cephaloridine, cephalexin, cephalothin, cefazolin, or cefamandole, 8.1 percent of those with a history of penicillin allergy had reactions, as compared with 1.9 percent of those without such a history. Thus, the risk of reactions was increased by a factor of approximately four among patients who were allergic to penicillin.

There have been numerous studies of patients with a history of allergy to penicillin who subsequently received cephalosporin antibiotics. Early reports from the 1960s suggested that the rate of reaction among these patients was as high as 18 percent, but a 1975 review suggested that it may be closer to 7 percent (as compared with the overall rate of reactions to cephalosporins of about 1 percent).

N Engl J Med 2001; 345: 804-9.

ORIGINAL ARTICLES

Gastro-oesophageal malignancy in New Zealand: 1995-97

Iain G Martin, ***Professor of Surgery, South Auckland Clinical School, University of Auckland, Middlemore Hospital, Auckland.***

Abstract

Aim. To assess the incidence, treatment and survival of patients with oesophago-gastric carcinoma in New Zealand.
Methods. All cases of oesophageal or gastric carcinoma diagnosed in 1995-97 were retrieved from the national cancer registry. Linked data describing all episodes of in-patient treatment for these patients were obtained from the New Zealand Health Information System. An analysis of demographics, treatment and survival was performed.
Results. A total of 1791 cases were recorded (616 oesophageal, 1175 gastric). Carcinomas of the gastro-oesophageal junction made up the majority of cases. 1138 were male. The median age was 71 years. 78.6% were of European descent, 10.4% Maori, 3.6% Pacific Islanders and 7.4% of other ethnic backgrounds. There were a total of 3403 hospital admissions (median 1.0 per patient). Overall, 29% underwent a surgical resection (15% oesophageal, 36% gastric). Exploratory surgery alone was performed in 14% operated on for oesophageal cancer and 12.3% for gastric neoplasms. Following resection 90 day mortality was 11.8% (10.5% oesophageal, 12% gastric). Overall median survival was 6.3 months (5.8 months oesophageal, 6.6 months gastric) with 16.7% of patients alive at three years. Following resection median survival was 17.8 months (16.2 months oesophageal, 18.1 months gastric) with 35.8% of patients alive at three years (34.7% oesophageal, 36% gastric).
Conclusions. These data provide a baseline for future studies of the evaluation and treatment of gastro-oesophageal malignancy in New Zealand.

NZ Med J 2002; 115: 64-7

Whilst in terms of absolute numbers, cancers of the stomach and oesophagus are not common they present significant problems in terms of diagnosis, staging, treatment and palliation.

The incidence of adenocarcinoma of the lower oesophagus, once a very rare cancer, is rising rapidly in most developed countries and at the same time gastric cancer now tends to occur in the proximal stomach and cardia.[1,2] The reasons behind these significant changes are not clear but it is likely that reflux disease and obesity are responsible in the main for the increase in oesophageal adenocarcinoma. The factors driving the proximal 'migration' of gastric cancer are not as obvious; there is little doubt that unlike distal gastric carcinoma's these tumours are not related to Helicobacter pylori.[3] The cumulative effect of these changes is that we are now being presented with a different group of cancers, centring on the lower oesophagus and proximal stomach, whose staging and treatment present particular and often new challenges.

"This patient group has very diverse, usually complex, clinical needs. Hence the primary treatment of these patients is inevitably a very selective process, requiring high levels of expertise and skill in all areas….The key to improving outcomes lies in ensuring that careful assessment of these patients allows these clinical needs to be identified and acted on by specialists in the various forms of management" – these are not the authors words but those of the introduction to a review of cancer services for patients with upper gastrointestinal cancer in the United Kingdom.[4] Given the challenges faced by clinicians in treating these cancers, the need to consider how best to deliver care to these patients and in the light of an impending review of surgical cancer services in New Zealand, it seemed opportune to review the current patterns of diagnosis and treatment for these two cancers in New Zealand.

Methods

Following ethical committee approval, the cancer registry of the New Zealand Health Information Service (NZHIS) provided two linked databases. The first contained details of all patients diagnosed with a malignant neoplasm of either the stomach or oesophagus between January 1st 1995 and December 31st 1997. At the time of the database production (December 2000), the 1997 figures were the most recent available. The second data base contained details of all admissions to a health care facility for each patient detailed in the first database following their diagnosis. Using the information from these two linked databases, a profile of the pattern of diagnosis, treatment and outcomes of malignant neoplasms of these two related organs was obtained.

Data were analysed using a combination of FileMaker Pro and SPSS version 9. Survival figures were calculated using the method of Kaplan and Meier, using overall (not cancer specific) survival.

Results

Demographics. Between January 1st 1995 and December 31st 1997 there were 1791 diagnoses of malignant neoplasms of the stomach or oesophagus. Of these 616 were coded as oesophageal and 1175 stomach malignancies. Demographic details are shown in Table 1.

Tumour Location. *Oesophagus:* Location of tumour was given as upper third of the oesophagus in 37 patients, middle third in 83 and lower third in 245 patients; the location of the remaining 251 tumours was not specified. 100 of these 251 patients had an adenocarcinoma suggesting a lower third origin.

Stomach: Of the 1175 neoplasms, 323 were at the cardia, 22 in the fundus, 73 in the body of the stomach, 137 in the antrum and 56 in the pre-pyloric area. A further 108 were said to have lesser curve tumours and 24 greater curve tumours. The remaining tumours were described as contiguous (n=106) or not otherwise specified (n=326)

Histological classification. *Oesophageal tumours:* Of the 616 cases, no histological confirmation was obtained in 60 patients (9.7%). Of the remainder, 241 (39.1%) had an adenocarcinoma, 245 (39.8%) a squamous carcinoma, 7 (1.1%) an adenosquamous carcinoma and 54 (8.8%) a carcinoma not otherwise classified. In addition 8 (1.3%) patients had a small cell carcinoma and 1 (0.2%) a spindle cell carcinoma.

Stomach tumours: Of the 1175 stomach neoplasms, 942 (80.2%) were adenocarcinomas, 95 (8.1%) carcinomas, 11 (1%) were either squamous or adenosquamous cancers and 24 (2.1%) were either sarcomas, small cell cancers or spindle

Table 1. Patient details and demographics.

	Number	Male/Female	Age (median and range)	Ethnic group	
Oesophageal carcinoma	616	411/205	71.7 (32.8-94.3)	European	538 (87.3%)
				Maori	38 (6.2%)
				Islander	4 (0.6%)
				Asian	4 (0.6%)
				Other	32 (5.2%)
Gastric carcinoma	1175	727/448	71.9 (13.5-97.1)	European	870 (74%)
				Maori	149 (12.7%)
				Islander	60 (5.1%)
				Asian	30 (2.6%)
				Other	66 (5.6%)
Total	1791	1138/653	71.8 (13.5-97.1)	Eurpean	1408 (78.6%)
				Maori	187 (10.4%)
				Islander	64 (1.9%)
				Asian	34 (3.6%)
				Other	98 (5.5%)

cell tumours. 103 patients (8.8%) had no recorded histological confirmation.

Hospital admissions. Overall there were 3403 hospital admissions for these patients following diagnosis of upper gastro-intestinal cancer. There was a median of 1.0 admission per patient (range 0-13). For those admitted to hospital there was a median total stay of 14 days (range 0-545 days).

Treatment. Interpretation of treatment data has to be treated cautiously. There is no indication as to the intent (curative or palliative) or the exact nature of the type of treatment received. However, with this caveat considered the overall patterns of treatment are clear (Table 2). The majority of patients did not receive major interventions for either potential cure or palliation. Only 15.4% of patients with oesophageal neoplasms and 35.7% with gastric neoplasms underwent surgical resection. In addition 2.4% of patients with oesophageal and 5% of patients with gastric neoplasms underwent exploratory or open – close operations; meaning that 14% of the patients with oesophageal cancer and 12.3% with gastric cancer coming to surgery did not have a resection. Overall operative mortality following resection (deaths within 90 days of surgery) was 11.8%, 10.5% oesophageal and 12.1% gastric.

Survival. Median survival was 6.26 months (95% CI 5.72 - 6.81 months). Survival for patients with oesophageal neoplasms was significantly worse than for those with stomach neoplasms (oesophagus 5.8 months, 95% CI 5.1 - 6.5 months; stomach 6.6 months, 95% CI 5.7 - 7.5 months; p = 0.005, Figure 1).

Of the 515 patients who underwent a resection, median survival was 17.8 months compared to 4.1 months in the remaining patients (p<0.0001). Somewhat surprisingly there was no significant difference in median survival following resection for patients with oesophageal or stomach neoplasms (16.1 vs. 18.1 months respectively, p=0.58). Of the 40 patients with oesophageal carcinoma who underwent chemotherapy and radiotherapy, the median survival was 15 months, no different from patients treated with surgical resection (Figure 2, p=0.8, log rank test).

Discussion

Although in absolute terms these cancers are relatively uncommon with around 200 new cases of oesophageal cancer and 400 of gastric cancer per year they still account for 8% of all male cancer deaths[5] and pose particular management difficulties. This study provides an overview of these two cancers using the most up to date national data available. The international epidemiological trends seen in the changing patterns of gastro-oesophageal cancer have been confirmed in a New Zealand population. Two decades ago, middle third squamous cancers of the oesophagus and antral gastric cancers would have predominated but lower third oesophageal adenocarcinomas and cancers of the cardia and upper part of the stomach now account for the majority of cases. Lower oesophageal adenocarcinomas now account for more than one half of all oesophageal cancers[1,2] and it is likely that reflux oesophagitis is a major factor in this change.[6] Other factors such as obesity are probably also important[7] but unlike oesophageal squamous carcinoma, smoking and

Table 2. Treatment received by the 1791 patients.

Tumour site	No specific treatment	Endoscopic Stenting / palliation	Surgery alone	Radiotherapy alone	Chemotherapy alone	Radiotherapy & Chemotherapy	Surgery & Radiotherapy	Surgery & Chemotherapy	Surgery & Chemoradiotherapy
Oesophagus n=616									
Overall	349 (57%)	79 (13%)	91 (15%)	46 (7%)	7 (1.1%)	40 (6.5%)	2 (0.3%)	1 (0.15%)	1 (0.15%)
Age <50, n=32	13 (41%)	3 (10%)	9 (28%)	2 (6.2%)	1 (3%)	3 (10%)	1 (3%)	0	0
Age 50-64, n=134	61 (46%)	14 (10%)	33 (25%)	7 (5.2%)	4 (3%)	13 (10%)	0	1 (0.8%)	0
Age 65-74, n=212	112 (53%)	30 (14%)	35 (16%)	16 (7.5%)	0	18 (8.5%)	1 (0.5%)	0	0
Age 75+ n=238	160 (67%)	32 (13%)	13 (5.5%)	21 (8.8%)	2 (0.8%)	6 (2.5%)	0	0	1 (0.4%)
Stomach n=1175									
Overall	683 (58%)	46 (4%)	411 (35%)	8 (0.7%)	12 (1%)	6 (0.5%)	3 (0.25%)	5 (0.4%)	1 (0.1%)
Age <50, n=120	60 (50%)	3 (2.5%)	43 (36%)	1 (0.8%)	7 (6%)	1 (0.8%)	1 (0.8%)	3 (2.5%)	0
Age 50-64, n=225	115 (51%)	7 (3%)	94 (42%)	4 (1.8%)	2 (1%)	2 (1%)	0	0	0
Age 65-74, n=378	184 (49%)	18 (4.8%)	164 (0.5%)	2 (0.5%)	2 (43%)	1 (0.25%)	1 (0.25%)	2 (0.5%)	1 (0.25%)
Age 75+ n=452	321 (71%)	18 (4%)	106 (23%)	1 (0.2%)	1 (0.2%)	2 (0.4%)	0	0	0

alcohol are not key players.[1] Surgeons and oncologists in the main are now treating tumours which straddle the abdominal and thoracic cavities, which require different skills and approaches than in the past when such junctional cancers were far less common.

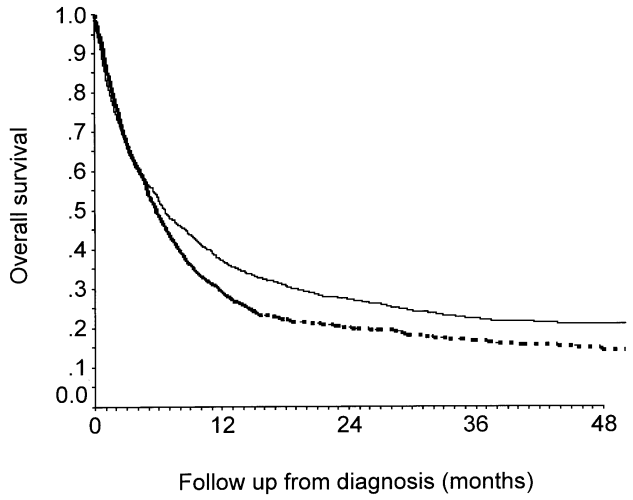

Figure 1. Overall survival. Top solid line, stomach neoplasms, lower dotted line oesophageal neoplasms. median survivals of 6.6 and 5.8 months respectively (p<0.005).

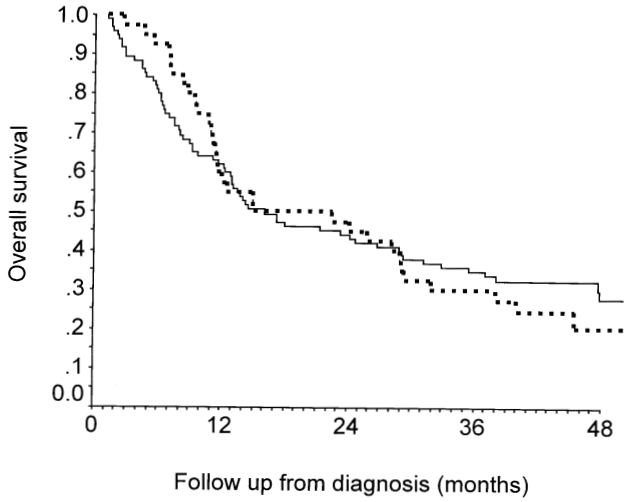

Figure 2. Survival following treatment of oesophageal cancer. Solid line indicates group treated with surgical resection (n=91) and dotted line those treated with chemotherapy and radiotherapy (n=40).

The overall gloomy prognosis associated with gastro-oesophageal cancer has been confirmed, but there are some grounds for optimism. Nearly one third of patients are less than 65 years of age and more than 50% are less than 75, at least opening the prospect of radical treatment for the majority. For both oesophagus and stomach, patients treated with surgical resection had a three year survival of more than 35%.

It is clear from the hospital admission data that these patients place a considerable burden upon the health care system, often requiring complex and demanding interventions. There is increasing evidence that both patient outcomes and costs can be optimised through the development of appropriate specialised teams treating significant numbers of such patients. In the UK, the recent cancer services review has summarised this evidence and made far reaching recommendations for the way patients with upper gastrointestinal cancer are managed.[4] Should similar proposals be considered here, New Zealand will have particular issues given its relatively small population and large geographic area.

One of the particular areas raised by the UK cancer services review was the provision of optimal staging and assessment for these patients. It is important that appropriate patients are identified early for radical and potentially curative treatment but also that patients who have incurable disease are not subjected to inappropriate or futile interventions. There is now no doubt that the optimal staging pathway should include both contrast CT scanning and endoluminal ultrasonography. Whilst CT scanning is generally available, very few patients in New Zealand have access to endoluminal ultrasound assessment. The UK review recommended that only centres able to offer the full staging investigations should be treating such cancers. Whilst this may seem excessive to some, the finding that more than 1 in 10 patients coming to surgery had an open and close procedure would suggest that staging could be improved.

Currently, surgical resection forms the mainstay of potentially curative treatment. The rates of surgical resection in this series are lower than in most comparable cancer registry based reviews from other centres. Most series report about 1/3 of oesophageal cancers were resected and nearly one half of all gastric cancers.[8-11] There are many reasons why this may not be the case in New Zealand. One issue is the use of radical chemoradiotherapy for the treatment of oesophageal cancer which seems to be the preferred option for patients in some parts of New Zealand. We know that such an approach can yield reasonable long term survival,[12] and in this series survival was similar to that with resection. There is, however, no randomised trial evidence to favour either approach and a study comparing the two approaches is badly needed although very difficult to implement.

Relatively few patients received multi-modality therapy using combinations of surgery, chemotherapy and radiotherapy. This reflects the fact that there has been, until recently, little evidence of benefit from such treatment programmes. This position is however beginning to change both for oesophageal cancer[13,14] and gastric cancer.[15] It is important that these developments are taken into consideration when planning for the future treatment of these patients. Given the uncertainties in this area, ongoing trials are vital. With the relatively low incidence of these cancers and the nature of such trials, no one centre or perhaps country will be able to answer the key questions in isolation. The establishment and co-ordination of trial networks should be an important part of service developments.

The drawing together of a team of multidisciplinary professionals treating a sufficient volume of patients with these difficult and complex cancers is, perhaps, given current knowledge, the best way to improve outcomes. This viewpoint will not receive universal approval either from other health care professionals or patients as it may be seen to be undermining locally delivered services. But if we wish to deliver optimal care without needless and expensive duplication, then such an approach is required.

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Management of acute otitis media by New Zealand general practitioners

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Abstract

Aims. To determine the current management of acute otitis media by New Zealand general practitioners (GPs).
Methods. A reply-paid questionnaire was sent to 2000 New Zealand GPs. The questions relate to management of a three year old child presenting with her first episode of acute otitis media.
Results. 95% of respondents reported they would usually or always use antibiotics. Amoxicillin was the antibiotic of choice, followed by amoxicillin/clavulanate. Cotrimoxazole was the antibiotic of choice in the case of allergy to amoxicillin. 82% of respondents recommended follow-up, with a broad range of follow-up times (24 hours to 12 weeks). Approximately half of practitioners considered 5-6 episodes of acute otitis media in a year as an appropriate threshold for referral for grommets. Most GPs had received an update on otitis media within the previous two years.
Conclusions. There is considerable variation in the management of acute otitis media by New Zealand GPs. Use of a national guideline may result in a more standardised, rational approach to the treatment of acute otitis media.

NZ Med J 2002; 115: 67-9

Acute otitis media is one of the most common childhood illnesses. Approximately 80% of children will have had the infection by three years of age.[1] It may be defined as clinical infection of the middle ear with sudden onset, short duration, and acute symptoms such as otalgia and fever. Little is known of its epidemiology in New Zealand. There is a guideline for the management of acute otitis media available on the New Zealand Guidelines Group's website, and the issue of preferred medicines has been investigated previously.[2] However, other aspects of management have not been investigated. The need for routine antibiotics in treating acute otitis media has recently been challenged by a number of papers and a Cochrane review.[3]

The purpose of this paper is to determine the current management of acute otitis media by New Zealand general practitioners (GPs). This information may assist in further developing a national guideline on the management of acute otitis media.

Methods

2000 New Zealand GPs were selected by computer randomisation from a database held by an addressing agency. Each GP was sent a reply-paid card containing a brief case history of a child with acute otitis media, followed by a series of questions regarding their management of the case. The case history read as follows: "a three-year-old child presents acutely with earache and is generally unwell. There is no past history of note. On examination the left tympanic membrane is red and bulging, consistent with an acute episode of otitis media." All replies were entered into a database in an anonymous fashion and analysed.

Results

There was a response rate of 45% (909 replies). This represents approximately 30% of the GPs in New Zealand. 907 respondents answered the first question, of which 551 (61%) stated they would always treat this case with antibiotics. 311 (34%) reported they would usually treat such a case with antibiotics, 44 (5%) would sometimes recommend antibiotics and one practitioner (0.1%) would never use antibiotics.

The GPs were asked to indicate which organisms account for at least 10% of episodes of acute otitis media, and which organism was the most common. 93% identified *Haemophilus influenzae*, and 78% *Streptococcus pneumoniae* as causative agents in at least 10% of episodes. 23% correctly identified all four organisms (*S. pneumoniae*, *H. influenzae*, *Moraxella catarrhalis*, and viruses). *S. pneumoniae* was correctly identified as the most common aetiological organism by 26% of respondents. 30% perceived viruses to be most common and 90% of those respondents would still usually or always treat with antibiotics. Some commented that although they normally prescribe an antibiotic, they would rather initially treat with analgesia then review the child at 24 hours to consider antibiotics. In their experience, however, this approach was unacceptable to many parents.

Initial choice of antibiotic is demonstrated in Figure 1. Of those that use antibiotics, 58% stated amoxicillin to be their first choice. The second most common choice was amoxicillin/clavulanate (24%) followed by cotrimoxazole (13%) and cefaclor (3%). Penicillin and erythromycin were each prescribed as a first-line agent by 1% of respondents. When amoxicillin was the first choice, the most commonly prescribed second agent in the case of allergy was cotrimoxazole (59%), followed by erythromycin (24%). Antibiotic dosage was not addressed in the questionnaire.

747 respondents (82%) would normally recommend a follow-up appointment. There was a broad range of follow-up times recommended, as illustrated in Figure 2. 25 practitioners commented that in addition to the later follow-up, they would recommend the child returned at 48-72 hours if acute symptoms persisted.

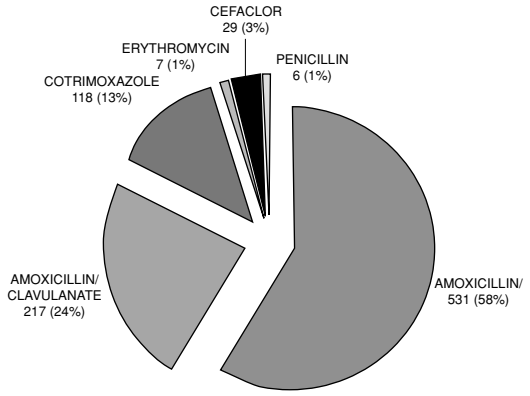

Figure 1. Antibiotic of first choice (908 responses).

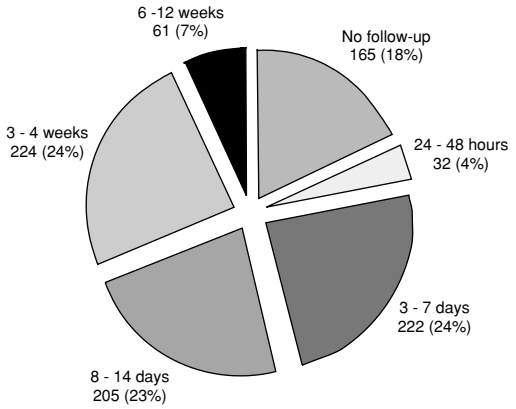

Figure 2. Follow-up times for acute otitis media (909 responses).

In order to gauge threshold for specialist referral, we asked about the number of episodes of acute otitis media in a year that would prompt referral for grommets. About half of respondents (51%) considered 5-6 episodes in a year to be appropriate for ENT referral. Some commented that parental pressure was an important factor, as was the degree of pain with acute episodes, the child's home environment, speech and language development, and hearing levels. 36 practitioners (4%) did not consider recurrent acute otitis media to be an appropriate indication for grommets. Twenty of those practitioners stated they only referred if there was a persistent effusion (or type B tympanogram), deafness, or otorrhoea.

558 respondents (61%) reported they had received an update on otitis media in the preceding two years. Only six practitioners (0.7%) had not had an update in the past ten years. The most common forms of update were reading (47%) and discussion (41%), often with an otolaryngologist or at a peer group review.

Discussion

Antibiotic treatment of acute otitis media should be based on the most current bacteriologic data. The organisms involved in acute otitis media have been identified by typanocentesis. *S. pneumonia* is the most common organism, isolated from up to 46% of middle ear fluid cultures; *H. influenzae* is the second most common (10-30%), followed by *M. catarrhalis* (0-24%).[4] *S. pneumoniae* is also the organism most likely to cause complications so antibiotic therapy should be directed against this organism. Historically, viruses have been infrequently isolated from middle ear effusions, although they are now thought to have an important aetiologic role.[5-7] Most GPs are aware of the common organisms involved in acute otitis media. Those who believe viral infections to be most common still usually prescribe antibiotics. This may reflect awareness of the likelihood of bacterial co-infection, the need to prevent suppurative complications, or parental pressure to prescribe antibiotics.

In recent years there has been an increase in the proportion of drug-resistant *S. pneumoniae*.[8-10] In New Zealand approximately 20% of isolates of *S. pneumoniae* from the ear, nose or throat show resistance or intermediate resistance to penicillin.[11] A significant proportion of these resistant organisms are also resistant to multiple other drugs. *H. influenzae* has shown a stable resistance level of 30-40% over the past decade, whereas *M. catarrhalis* has shown a steady increase in resistance level, currently approximating 100%.[12] It is postulated that increased prescribing of broad spectrum antibiotics is contributing to the rising level of resistant organisms.

Treatment should ensure that adequate middle ear levels of antibiotics are reached. Amoxicillin at 40 mg/kg/day is the only oral agent that provides adequate middle ear concentrations for the treatment of penicillin-resistant *S. pneumoniae*.[13] Cotrimoxazole is active against *H. influenzae* and *M. catarrhalis*, although *S. pneumoniae* is becoming increasingly resistant. Erythromycin ethylsuccinate provides satisfactory cover against *S. pneumoniae* but not against *H. influenzae*. Although cefaclor has stability to beta-lactamases, there is conflicting evidence regarding its efficacy in acute otitis media.[8-13] Given that there are more effective agents, cefaclor is probably not indicated as a first-line agent for acute otitis media.

Treatment of acute otitis media is controversial, and some papers have raised doubt as to whether antibiotics are necessary at all.[14-16] Antibiotics have been shown to reduce acute symptoms in a small but significant proportion of children.[14,17] More importantly however, antibiotics significanlty reduce suppurative complications such as mastoiditis and meningitis.[18,19] Antibiotic treatment has also been shown to reduce the incidence of middle ear effusion following the acute infection.[20] Only 61% of respondents in the present survey stated they would always use antibiotics for this case of otitis media, which may illustrate a tendency now to delay such prescribing. This may also explain the earlier follow-up times recommended by some practitioners.

Amoxicillin remains the antibiotic of choice in uncomplicated acute otitis media,[3,9,21] and is the antibiotic most often prescribed by respondents in this study. Despite the development of resistant organisms, the favourable natural history of the disease means that only a small proportion of treatments will fail due to resistance to amoxicillin.[21] In addition, amoxicillin is safe and relatively inexpensive. Cotrimoxazole or erythromycin provide satisfactory alternatives as second line agents or when the patient is allergic to amoxicillin. Standard duration of therapy is 7-10 days, although there is some evidence that a five day course is just as effective in uncomplicated cases.[22,23]

Insertion of a ventilation tube (grommet) is appropriate in severe or recurrent acute otitis media when medical therapy has failed.[18] Other indications include chronic middle ear effusion that is unresponsive to medical management, presence of a suppurative complication, and children with cleft palate. Of our sample, about half of GPs would refer a child who was having at least five episodes of acute otitis media per year. This is consistent with current referral guidelines.

The purpose of a follow-up visit is to determine whether there has been recovery from the acute infection, and to assess the presence of a middle ear effusion. The acute symptoms should improve within 72 hours. At least 40% of children will have a middle ear effusion two weeks after the

onset of acute otitis media; about 80% of these will have resolved at two months.[1,21] For these reasons follow-up would be recommended at 48-72 hours if the acute symptoms are failing to resolve, and at 2-3 months to determine the presence of a middle ear effusion (for possible further antibiotic treatment or referral for grommets). Certain high-risk groups may require earlier follow-up.

This study demonstrates considerable variation in the management of acute otitis media by New Zealand GPs. Amoxicillin is generally the antibiotic of choice in uncomplicated cases, and there is some evidence of delayed prescribing with early follow-up. Half of respondents considered at least five episodes of acute otitis media a year appropriate for grommet insertion, consistent with current national referral guidelines. Follow-up is recommended at 48 hours if acute symptoms persist, otherwise at 2-3 months to check for resolution of effusion. Consistent use of a national guideline may result in more standardised management and a more rational approach to the treatment of this common disease.

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Postoperative epidural analgesia following elective major abdominal surgery in high risk patients: a retrospective cohort study

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Abstract

Aim. To describe the effect of post-operative epidural analgesia on morbidity and mortality rates in a group of high-risk patients undergoing elective major abdominal surgery.

Methods. Retrospective chart review of patients in American Society of Anaesthetists Physical Status (ASA) category III or IV, who underwent elective major I or II general surgical procedures between 01/01/1996 and 01/09/1998. Patients were identified from a prospective audit database. Patients who had epidural analgesia or conventional parenteral opioids were compared for outcome measures.

Results. There were 167 patients identified (72 epidural, 95 non-epidural group). There was no significant difference in demographic data, inpatient stay, intensive care unit stay, or mortality rates (11% epidural v 17% non-epidural, p>0.05). There was no significant difference in morbidity rates, however there was a non-significant trend towards a lower morbidity in the epidural group.

Conclusions. This study does not show any benefit from post-operative epidural analgesia on morbidity and mortality rates in high risk patients undergoing major abdominal surgery. It does illustrate that ASA 3 and 4 patients undergoing major abdominal surgery have a high morbidity and mortality.

NZ Med J 2002; 115: 69-72

The morbidity and mortality is high in sick patients undergoing major abdominal surgery. Epidural anaesthesia and analgesia is frequently used in an attempt to improve outcome. A number of studies have suggested advantages of epidural anaesthesia and analgesia but the superiority has yet to be demonstrated in a randomised controlled study.

Advantages of epidural anaesthesia may include improved post operative pain relief, with consequent improved respiratory function, protection against myocardial ischaemia, a decrease in the hyper-coagulable state that occurs after surgery and early recovery of bowel function. Disadvantages include the time for insertion, possible direct neurological damage, epidural abscess or haematoma formation and possible adverse effects of hypotension. Epidurals also have a failure rate of about 16% but some centres report failure rates of 30-50%.[1] Data are conflicting, but a recent meta analysis demonstrates improved outcome[2] and a large multi-centre trial is underway.[3]

The aim of the current study was to examine the effects of post-operative epidural analgesia on morbidity and mortality

rates in high risk patients undergoing major abdominal surgery, and to establish the incidence of major morbidity and mortality.

Methods

A retrospective chart review was undertaken involving patients who underwent elective major I or II general surgical procedures between 01/01/1996 and 01/09/1998 and were classified as American Society of Anaesthetists Physical Status category[4] (ASA) 111 or 1V. Operations were classified major I or II, intermediate or minor as per the guidelines of the Royal Australasian College of Surgeons. This categorisation is not a rigid one but is determined by the type of operation and its complexity. For example major I operations include aortic aneurysm, low anterior resection, oesophagastrectomy, liver resection and pancreaticoduodenectomy, while major II includes such operations as cholecystectomy, abdominal colectomy, small bowel resection and splenectomy. An open appendectomy, haemorrhoidectomy or inguinal hernia repair is considered intermediate, while excision of a skin lesion, or drainage of a simple perianal abscess is considered minor. Patients were identified from a prospective surgical audit database. Patients who had epidural analgesia and those who had conventional parenteral opioids were compared for significant differences in morbidity and mortality rates.

Inclusion criteria were:

1. Patients who had undergone abdominal surgery classified as Major I or Major II.
2. Patients that were classified as ASA III or ASA IV[4] by the anaesthetist at the time of surgery.
3. The duration of epidural analgesia had to be a minimum of 24 hours for the patient to be allocated to the epidural group.

Patients in whom epidural failed within 24 hours were excluded from analysis in either group. Patients who underwent more than one surgical procedure during the admission under review were also excluded. Aspects that were reviewed were; general demographics, inpatient stay, intensive care unit stay, and major post-operative morbidity based on the definitions used in the MASTER trial protocol (Table1).[3]

Analysis was undertaken using INSTAT. A non-parametric analysis was used with Fishers Exact and Chi squared tests as appropriate. Significance was assessed at $p<0.05$. Data are presented as mean ± standard deviation.

Results

Of 167 patients identified as defined above, 72 had post operative epidural analgesia, and 95 had parenteral opioids. There was no significant difference in age (epidural 70.1 ± 10.5 years, non epidural 69.5 ± 12.9 years) or gender (epidural m 36, f 36; non epidural m 45, f 50) between the two groups. Pre-operative morbidity and the type of surgical procedures performed are shown in Tables 2 and 3.

There was no significant difference in regard to total length of postoperative hospital stay (p=0.83) or intensive care stay (p=0.24). The inpatient stay for the epidural group was 13.8 ± 7.2 days and for the non-epidural group was 14.0 ± 8.7 days. 48 patients went to ICU (21 with epidurals, 27 with post-operatively parenteral opioids). The mean ICU stay for the epidural group was 5.2 ± 7.1 days, and for the non-epidural group was 7.1 ± 7.9 days.

54% of the epidural group had no post-operative morbidity compared with 40% of the non-epidural group (NS, $\chi^2 = 0.09$). There was no significant difference in post-operative morbidity between the two groups. In the epidural group 11% died compared to 17% of the non-epidural group. ($\chi^2 = 0.41$, Table 4).

Discussion

The study has described the morbidity and mortality in high-risk patients undergoing abdominal operations. We found no significant difference between the two groups in regard to outcome. Epidural analgesia provides superior pain relief compared to parental opioids, but there is still debate about its effect on outcome. Several effects of epidurals may, in theory, improve outcome. Thoracic epidural analgesia (TEA) is thought to protect against myocardial ischaemia.[5] The post operative stress response which increases sympathetic activity resulting in increases in myocardial oxygen demand and decreases myocardial oxygen supply,[5] is blocked. TEA also decreases myocardial oxygen demand by producing small reductions in cardiac output, heart rate and mean arterial pressure.[5] TEA increases myocardial oxygen supply by dilating coronary arterioles and optimising flow to compromised regions of the myocardium.[5] Lumbar epidural blockade may have a paradoxical effect as the hypotension and subsequent decreased oxygen supply is not off-set by a decrease in the oxygen demand.[5]

Table 1. Definitions of major post-operative morbidity*.

1. **Respiratory failure**
(a) Those patients requiring ventilatory support post-operatively.
(b) Blood gas analysis demonstrating PaC02≥50 mmHg or P02≤50 mmHg

2. **Cardiovascular morbidity**
(a) Myocardial infarction: based on elevated serum enzyme levels (troponin T, creatine phosphokinase) and ECG changes.
(b) Angina: Post-operative chest pain requiring nitrate therapy.
(c) Congestive cardiac failure: diagnosed using radiological and clinical parameters.
(d) Dysrhythmia: requiring pharmacological treatment or DC cardioversion.

3. **Cerebrovascular accident**
As diagnosed by the attending physician.

4. **Renal failure**
(a) Elevation of serum creatinine by >0.1 mmol/L
(b) The new development of a level of serum creatinine of ≥0.3 mmol/L
(c) A requirement for haemofiltration or haemodialysis

5. **Gastro-intestinal failure**
Bleeding from the gastro-intestinal tract requiring >2 units of blood in 24 hours.

6. **Hepatic failure**
A new post-operative rise of the total bilirubin to ≥100μmol/L, alkaline phosphatase rise to ≥3 times the upper limit of normal, or a rise of either the serum lactate dehydrogenase or aspartate transaminase to more than twice normal.

7. **Haematological failure**
Defined as one or more of:
(a) Haematocrit ≤20%
(b) WCC ≤2 x 10^9/L
(c) Platelets ≤40 x 10^9/L.

8. **Major inflammatory complication**
Defined as the development of infection or sepsis. Infection was diagnosed if two of the following occurred:
(a) Temperature ≥38°C
(b) While cell count >12 000
(c) Culture of a pathogen from blood or other body part.

9. **Thromboembolic events**
Deep venous thrombosis or pulmonary embolism diagnosed by ultrasound scan, angiography, or VQ scan.

10. **Mortality**
Defined as death occurring during the hospital admission under review.

*Based on the definitions used in the MASTER trial protocol.[3]

Table 2. Preoperative morbidity.

	% of patients within each study group	
	Epidural Group	Non-Epidural Group
Diabetes Mellitus	12%	8%
Chronic Renal Failure	3%	6%
Obstructive Airways Disease	25%	28%
Hepatobiliary Dysfunction	4%	6%
Congestive Cardiac Failure	13%	8%
Ischaemic Heart Disease	27%	35%
Dysrhythmias	18%	17%
Hypertension	25%	26%

These theoretical considerations have been supported in clinical studies. Beattie et al[6] compared the effects of epidural analgesia and parenteral morphine in patients with two or more risk factors for myocardial ischaemia. There was a four-

fold increased risk of ischaemic changes in the post-operative phase in the non-epidural group. Only patients who had ischaemic changes subsequently developed cardiac morbidity. Leon-Casasola et al[7] studied patients having major abdominal surgical procedures who had two or more risk factors for coronary artery disease. A significantly higher number in the non-epidural group had episodes of myocardial ischaemia although post-operative hypotension was the same in both groups. There was a trend towards a lower incidence of myocardial infarction in the epidural group. Crawford et al[8] examined whether TEA counteracted mechanisms that maintain haemodynamic stability. There was an increased incidence of hypotension at rest after epidural analgesia, but no increased risk of orthostatic hypotension. Significantly, reductions in blood pressure did not correlate with significant post-operative morbidity.

Table 3. Types of operation.

Operation	Epidural n=72 (%)	Non-epidural n=95 (%)
Upper GI	20	28
Hepatobilary	10	12
Vascular	18	7
Colorectal	44	48
Other	8	5

Table 4. Postoperative morbidity and mortality rates.

	Epidural Group (n=72)	Non-Epidural Group (n=95)	Fisher's Exact Test
Respiratory Failure	8 (11%)	16 (17%)	0.375
Myocardial Infarction	8 (11%)	6 (6%)	0.398
Angina	1 (1%)	2 (2%)	1.00
Congestive Heart Failure	13 (18%)	11 (12%)	0.270
Ventricular Tachycardia	1 (1%)	0	0.431
Supraventricular Tachycardia	8 (11%)	11 (12%)	1.00
Stroke	2 (3%)	0	0.184
Renal Failure	1 (0%)	5 (5%)	0.237
Gastro-intestinal Failure	0	4 (4%)	0.135
Hepatic Failure	0	1 (1%)	1.00
Major Inflammatory Compl	9 (13%)	18 (20%)	0.295
PE/DVT	1 (1%)	2 (2%)	1.00
Haematological Failure	1 (1%)	1 (1%)	1.00
Nil Morbidity	39 (54%)	38 (40%)	0.085
Mortality	8 (11%)	16 (17%)	0.375

The studies noted above support a protective effect of epidural analgesia on the cardiovascular system, and clinical studies have suggested that cardiac function may improve with post-operative epidural anaesthesia.[9,10] Because a patient is at greatest risk of myocardial ischaemia in the first 72 hours post-operatively, epidural analgesia should be continued over this period. In our retrospective analysis there was no difference in the incidence of cardiovascular morbidity between the epidural and non-epidural group.

Epidural analgesia is thought to reduce pulmonary morbidity by providing good analgesia, reducing diaphragmatic dysfunction and reducing the degree of post-operative hypoxaemia.[5] Jayr et al[11] studied the incidence of respiratory complications in patients undergoing major abdominal procedures. The respiratory profile in the epidural group was better in the early post-operative phase, but this did not persist after 24 hours. Overall, there was no difference in the incidence of respiratory complications between the epidural and non-epidural group. Hjortso et al[12] also showed no significant difference in rates of respiratory complications between epidural and non-epidural groups after elective abdominal procedures. In our retrospective analysis there was no difference between the rates of respiratory complications.

Surgery creates a hyper-coagulable state. It is thought that epidural analgesia may reduce this state by increasing arterial flow and venous emptying.[13] Epidural analgesia is also thought to enhance fibrinolytic activity and reduce platelet aggregation. Hjortso et al[12] found, in a retrospective study, no difference between the rates of deep vein thrombosis in the epidural and non-epidural groups. The findings of our study were consistent with this.

Early resumption of bowel function is important, since early enteral feeding reduces the surgical stress response, reduces sepsis rates and enhances wound healing.[14] Epidural analgesia selectively blocks nociceptive afferent and efferent pathways that inhibit bowel activity.[5,14] Epidural blockade is also thought to increase blood flow to the bowel.[14] Bredtmann et al[15] showed that patients, who had post-operative epidural analgesia passed bowel motions earlier. However, this did not correlate with a shorter hospital stay. Kanazi et al[16] evaluated the effects of epidural anaesthesia on outcome after ileal pouch-anal anastomosis. They did not show a significant difference in the resumption of bowel function. Our study did not specifically test the resumption of gastro-intestinal function.

Epidural anaesthesia and analgesia have also been used in combination with a multimodal rehabilitation program including early feeding and mobilisation with reportedly reduced morbidity and hospital stay.[17-19] While initially these advantages were noted in patients following laparoscopic surgery it has now been reported in patients having open colorectal resections.[17-19]

This current retrospective analysis showing no statistical difference in morbidity and mortality rates in high risk patients undergoing either epidural or parenteral analgesia, has several weaknesses. It was open to the biases of any retrospective analysis. The size of the sample population is small and there is, therefore, a risk of missing a real difference between the groups (type 11 error). Based on our findings and review of the literature, it would appear that epidural analgesia is as safe as parenteral analgesia. There is some evidence to suggest that epidural analgesia may have a protective effect on the cardiovascular system post-operatively, the size of benefit, if present, being about 10% for major morbidity and 4% for mortality. However, there is little evidence to suggest a beneficial effect on the respiratory, coagulopathic, or gastro-intestinal systems post-operatively. To justify a procedure that is time-consuming, reasonably invasive, and one which does require stringent post-operative monitoring, further research is needed. The results of a large, prospective, randomised, multicentre study such as the MASTER trial is needed to definitively ascertain the benefits and risks of the use of epidural analgesia in the postoperative period.

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Drinking patterns among older people in the community: hidden from medical attention?

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Abstract

Aims. To determine patterns of alcohol use and misuse among community-dwelling people aged 65 years and over in Christchurch and to assess how often this comes to medical attention.

Methods. A cross-sectional survey of alcohol use and misuse was conducted followed by a self-administered postal survey among non- respondents. General practitioners (GPs) of the respondents completed a self-administered questionnaire on patients' alcohol use and misuse.

Results. The response rate was 58% (141/243). The prevalence of hazardous alcohol consumption in the past twelve months (AUDIT cut-off score 8 or more) was 9.9% (95% CI = 4.9-14.9) and the prevalence of lifetime alcohol dependence using DSM-IV diagnostic criteria was 24.8% (95% CI = 17.6-32.0). Men were more likely than women to report lifetime dependency and current hazardous patterns. The response rate among GPs was 77.7% (108/139). None of the GPs identified or diagnosed alcohol problems in the past twelve months among this group and reported a history of alcohol problems in only four (4.0%) patients. Those with current hazardous patterns of alcohol use were twice as likely to be admitted to hospital (RR=2.4; 95% CI 1.2-5.1) but significantly less likely to visit their GPs in the previous twelve months (RR=0.55; 95% CI 0.7-1.1).

Conclusion. A significant proportion of community-dwelling elderly people reported patterns of alcohol consumption that put them at risk of future damage to physical or mental health. Hazardous drinkers were less likely to visit their GPs and only in a few cases, were GPs aware of such potential problems.

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Alcohol use among older people is an issue of increasing importance. Not only is New Zealand's population – like that of other developed societies – rapidly ageing,[1] but hazardous or harmful alcohol consumption is a major independent risk factor for functional decline in elderly people.[2]

Previous work in New Zealand has established that a small proportion of residents (5.1%) report consumption of alcohol in quantities that put them at risk of future damage to physical and mental health despite advanced age.[3] A national study, the 1996/1997 New Zealand Health Survey,[4] reported that elderly people consumed alcohol more regularly than younger people but tended to drink less on single occasions. The survey also showed that a significant proportion of elderly people (4.1%) displayed a hazardous pattern of alcohol consumption.

There is a growing body of evidence that physicians often fail to identify and diagnose alcohol problems in the elderly.[5,6] There has been increasing interest in the role of general practitioners (GPs) in providing intervention[7] and several New Zealand studies support the fact that general practice is a potentially valuable point of contact for early intervention.[8,9]

The aim of this study was to determine contemporary patterns of alcohol use and misuse by New Zealand people aged 65 and over and to assess concordance with GPs estimates.

Methods

Three separate cross-sectional surveys were conducted in this study. A community survey was conducted first among people aged 65 years and older concerning their alcohol use and misuse. Later, a survey was undertaken among the GPs of community survey participants concerning their patients' alcohol use and misuse. Finally, a follow up survey was conducted among those who declined to participate in the community survey.

The study participants (n=141) were selected randomly from the electoral roll in Christchurch. All community-dwelling people aged 65 years and older, who had the ability to respond in an interview and to give informed consent to participate, were included. Subjects (n=18) were excluded if they had dementia, were terminally ill, had dysphasia or were severely deaf. Invitation letters, self-addressed postage paid envelopes and information sheets specifically designed for the participants explaining the nature, purpose and procedures of the study were posted. This was followed up by telephone calls to give further information and to attend to any queries. If a study participant did not reply or could not be contacted by telephone, a follow up letter was sent before a visit to their home was made. Finally, three home visits were attempted before declaring that they were uncontactable.

'Hazardous alcohol use' was defined as an established pattern of use carrying with it a high risk of future damage to physical or mental health but which has not yet resulted in significant medical or psychiatric ill

effects.[10] A score of 8 or more out of 40 on AUDIT[11] was used to indicate hazardous/harmful alcohol use in the past twelve months.

'Alcohol Dependence' was defined as a condition in which an individual may continue to consume alcohol, despite adverse consequences, often to avoid or to relieve symptoms of withdrawal.[12] We identified the heaviest twelve-month period of alcohol use in each participant's lifetime and then applied the DSM-IV diagnostic criteria for alcohol dependence. A cut off score of 3 or more out of 7 criteria was used to make a diagnosis of alcohol dependence in the past twelve months as well as during the lifetimes.[12]

An interview, lasting approximately 20 minutes was conducted once with each participant using the AUDIT[10] and a structured clinical interview that included DSM-IV diagnostic criteria[12] with some quantity/frequency questions and a question about treatment. To standardise for the different alcohol content of different beverages and for differences in glass size, photographs were used of standard spirit, wine, and beer glasses with markings for equivalent amounts of alcohol.[13]

Participants in the community survey were asked for consent to approach their GPs to obtain further information about their alcohol use. Only the GPs of those who gave written consent were approached (n=139) using a self-administered, semi-structured questionnaire. This was to determine if their patients' alcohol use or misuse had come to medical attention.

Statistical analysis. Assuming a true prevalence of 10%, we calculated that a sample size of 138 would allow the prevalence to be estimated to within 5 percentage points with 95% confidence. The sample size calculation was based on standard sample size formulae for estimating a binary proportion.[14] Frequency distributions were determined for categorical data. The mean and standard deviation and standard error were calculated to describe continuous data distribution. We used EpInfo software to calculate the relative risk (prevalence ratio) and 95% confidence intervals.

Results

Sample description. 272 community-dwelling elderly people aged 65 years and older were included in the initial random sample. Eighteen (6.6%) subjects were excluded and eleven (4.0%) were unable to be contacted. Of the 243 eligible subjects, 141 (58.0%) gave consent to be interviewed. 102 (42.0%) declined to be interviewed but 40 responded to the written survey. Overall, information was available from 175 of 243 eligible subjects (72.0%). Of the 141 subjects who were interviewed, 139 (98.6%) gave consent to approach their GPs. 108 (77.7%) GPs responded to our invitation and completed a self-administered questionnaire regarding their patients' alcohol use.

Most of the community survey participants were New Zealand European (75.0%), retired (92.0%), married (62.0%), had primary or high school education (57.0%), lived with their spouses (61.0%) and had national superannuation as their main source of income (51.0%). More women 79 (56.0%) than men 62 (44.0%) took part. This gender ratio was not significantly different for the non-participants with more women 66 (65.0%) than men 36 (35.3%) declining to take part in the study. Similarly, twelve (66.7%) women compared to six (33.3%) men met exclusion criteria. Of 141 participants, 71 (50.4%) were aged 65-74 years, 57 (40.4%) were aged 75-84 years and thirteen (9.2%) were aged 85-94 years. Of 141 participants, 28 (20.0%) had had a hospital admission in the past twelve months. Of these, the average length of hospital stay was four days. On average each participant had 6.2 GP visits in the past twelve months.

Prevalence of alcohol use and misuse. Alcohol was consumed in the past twelve months by 117 (83.0%) participants. Of those 141 interviewed, 38 (27.0%) had drinks containing alcohol monthly or less often, sixteen (11.3%) had alcohol 2-4 times per month, eleven (7.8%) had alcohol 2-3 times per week and 52 (36.9%) had alcohol four or more times per week. The number of standard drinks containing alcohol on a typical day when drinking was 1or 2 for 100 (70.9%), 3 or 4 drinks per day for twelve (8.5%), 5 or 6 drinks per day for three (2.1%) and 7 to 9 drinks per day for one (0.7%). Only one participant had consumed ten or more drinks per day containing alcohol during the past twelve months.

Of 141 participants, 135 (95.7%) reported to have had alcohol in their lifetime. The mean age of first alcohol use for those who used alcohol in their lifetime was 19.0 years. 62 participants had had alcohol more than ten times a month during the year of heaviest alcohol use in their lifetime, of whom 35 participants (24.8%, 95% CI = 17.6-32.0) were identified as having lifetime alcohol dependence according to DSM-IV criteria. Only two participants (1.4%, 95% CI = 0.0-3.4) were identified as having alcohol dependence in the past twelve months by DSM-IV criteria. According to AUDIT, 14 of 141 participants (9.9%, 95% CI = 4.9-14.9) were identified as having a hazardous or harmful pattern of drinking in the past twelve months. Only two of 141 participants received treatment in the past, both of whom experienced lifetime alcohol dependence; one participant continued to drink hazardously during the past twelve months.

Prevalence rates by socio-demographic variables. In Table-1 the percentage of respondents with recent hazardous drinking and any evidence of a history of alcohol dependence is outlined against key socio-demographic variables. The most notable difference recorded was for gender. The prevalence of hazardous patterns of alcohol use in the past

Table 1. Prevalence of hazardous patterns of alcohol use in the past twelve months (AUDIT) and alcohol dependence during lifetime (DSM-IV) by socio-demographic variables.

Socio-demographic Variables		n	Hazardous Patterns of Alcohol Use in the Past twelve Months (AUDIT)	Alcohol dependence During Lifetime (DSM-IV)
Gender	Male	62	20.9% (10.6-31.3)	38.7% (26.3-51.0)
	Female	79	1.3% (0.03-6.8)	13.9% (6.1-21.6)
Age Groups	65-74 Years	71	11.3% (3.7-18.7)	25.4% (15.0-35.6)
	75+ Years	70	8.6% (1.8-15.2)	24.3% (14.0-34.5)
Education	Primary School/High School	81	8.6% (2.4-14.8)	19.8% (10.9-28.5)
	Tertiary Education/ Qualification/Postgraduate	60	11.7% (3.3-19.9)	31.7% (19.6-43.6)
Marital Status	Married	87	12.6% (5.5-19.7)	26.4% (17.0-35.8)
	Never Married/Separated/ Divorced/Widow/Widower	54	5.6% (0.0-11.8)	22.2% (10.8-33.5)
Employment	Retired	130	8.5% (3.6-13.2)	24.6% (17.1-32.0)
	Self-employed/Part-time	11	27.3% (6.0-60.9)	27.3% (6.0-60.9)
Income	National Superannuation Only	71	8.5% (1.8-15.0)	19.7% (10.3-29.1)
	Private Income/National Super and Private Income/ Salary/Wages	70	11.4% (3.8-19.0)	30.0% (19.0-40.9)
Living Arrangements	Living with Spouse	86	12.8% (5.6-19.9)	26.7% (17.2-36.2)
	Living Alone//Living with Children/Relatives/ Rest Homes	55	5.5% (1.1-15.1)	21.8% (10.6-32.9)

Prevalence (%) and 95% confidence intervals.

twelve months was markedly higher in men than in women (relative risk (RR) 16.1 95% CI=2.2-119.5) as was the prevalence of DSM-IV criteria for ever being alcohol dependent (RR 2.78, 95% CI=1.4-5.6). There was little evidence for associations between the other socio-demographic variables and problem drinking. Apart from gender the most substantial socio-demographic differences were recorded for employment status (self-employed/part-time v retired RR 3.21, 95% CI=0.4-28.4), marital status (not married v married RR 0.44, 95% CI=0.1-1.6) and living arrangements (living with spouse v other RR 2.33, 95% CI=0.9-6.3).

Association between alcohol use and use of medical services. Those with current hazardous patterns of alcohol use were twice as likely to be admitted to hospital over the previous twelve months (RR=2.4; 95% CI 1.2-5.1). In contrast, they were significantly less likely to visit their GP in the previous twelve months (RR=0.55; 95% CI 0.3-1.1).

Concordance between research and clinical measures. 55 (50.9%) GPs reported their patient had had alcohol during their lifetime, 48 (44.4%) GPs did not know and five (4.6%) reported that their patient had never had alcohol in their lifetime.

Community survey participants with lifetime alcohol problems did not always come to medical attention. Of 108 patients of participating GPs, 29 (26.9%) had alcohol dependence in their lifetimes according to DSM-IV criteria. According to the GPs' assessments or medical records, only four (3.7%) of their patients were reported to have had alcohol problems during their lifetimes. When these GPs' assessments were compared with their lifetime drinking status for alcohol dependence, only two of these four patients had lifetime alcohol dependence according to DSM-IV criteria. Furthermore, of the 40 patients identified by their GPs as having no clinically apparent alcohol problems during their lifetimes, thirteen (32.5%) self-reported lifetime alcohol dependence according to the DSM-IV criteria (Table 2).

Table 2. Clinically apparent alcohol problems compared with alcohol dependence during lifetimes according to DSM-IV criteria.

General Practitioner's Assessment (During Lifetime)	Lifetime Alcohol Dependence (DSM-IV) Alcohol Dependence	No Alcohol Dependence	Total
Lifetime Abstainer	0	5	5
Clinically Apparent Lifetime Alcohol Problems	2	2	4
No Clinically Apparent Lifetime Alcohol Problems	13	27	40
Unknown Lifetime Problem Drinking Status	2	9	11
Unknown Drinking Status (Both Current and Lifetime)	12	36	48
Total	29	79	108

Of 108 patients, eleven (10.2%) were identified as having hazardous patterns of alcohol use in the past twelve months whereas GPs of the community survey participants did not identify or diagnose any alcohol problems in the past twelve months among their elderly patients. Furthermore, of the 53 patients reported by their GPs as not having clinically apparent alcohol problems in the past twelve months, nine (17.0%) self-reported to have hazardous patterns of alcohol use (Table 3). Furthermore, according to the GPs' assessments or medical records, the current and lifetime drinking status of 48 patients were unknown. When these patients were compared with their lifetime drinking status for alcohol dependence and current drinking status for hazardous patterns of alcohol use, twelve (25.0%) had alcohol dependence and two (4.2%) had hazardous patterns of alcohol use respectively.

Table 3. Clinically apparent alcohol problems compared with hazardous patterns of alcohol use in the past twelve months as determined by AUDIT

General Practitioner's Assessment (Past 12-Months)	Hazardous Patterns of Alcohol Use (AUDIT) Hazardous Drinking	No Hazardous Drinking	Total
Lifetime Abstainer	0	5	5
Abstainer (Past 12-Months)	0	2	2
No Clinically Apparent Alcohol Problems	9	43	52
Unknown Problem Drinking Status (Past 12-Months)	0	1	1
Unknown Drinking Status (Both Current and Lifetime)	2	46	48
Total	11	97	108

Alcohol use and misuse among postal responders. Of the 40 who responded to the follow-up survey, 34 (85.0%) completed a self-administered questionnaire and six (15.0%) declined again. Among the 34 respondents, fourteen (41.2%) were male and 20 (58.8%) were female; 33 (97.0%) were New Zealand European and one (2.9%) was Maori. Alcohol was used less frequently among postal survey participants (n=34) than the main study participants. 28 participants (82.4%) reported to have had alcohol during their lifetime; 16 (47.0%) reported to have had alcohol more than 10 times a month at some point in their lifetime and 22 (64.7%) had had some form of alcohol in the past twelve months.

However, only one (2.9%) participant out of 34 was identified as having hazardous patterns of alcohol consumption that put them at risk of future physical and mental damage.

Discussion

Our study has found a high prevalence of alcohol use (83.0%) and misuse (hazardous drinking prevalence 9.9%) among community-dwelling elderly people in Christchurch. Men had more current hazardous patterns of alcohol use and alcohol dependence than women. This is consistent with a previous community-based study of people aged 70 years and older[15] showing men took alcohol more frequently and in greater quantities than women but the frequency and amount decreased with age. A recent New Zealand health survey showed that older people drink more regularly than younger people, but tend to drink less on a typical occasion.[4]

The prevalence of hazardous patterns of alcohol consumption in the past twelve months reported here for community dwelling persons aged 65 and over was higher than the prevalence of 4.1% reported for this group in a New Zealand health survey[4] and the 5.1% finding reported for rest home residents in Christchurch.[3] According to DSM-IV criteria, 35 participants out of 141 were identified as having lifetime alcohol dependence with a prevalence rate of 24.8%, which is slightly higher than the prevalence of 20.5% reported for rest home residents[3] and the prevalence of 16.3% for New Zealanders aged 45-64 years.[16] In our study, the people who responded by post had a lower prevalence than those surveyed in person. This might indicate that the people who did not responded may have an even lower prevalence.

A recent National Survey of Mental Health and Well Being (NSMHWB) in Australia reported a significantly lower prevalence (4.4%) of alcohol use disorder among people aged 55 and over in the past twelve months according to ICD-10 definitions[17] than the prevalence rates reported here. However, NSMHWB results contradict a previous national survey of alcohol use in Australian women that reported a considerably higher prevalence rate (26% prevalence of

hazardous drinking) for women aged 65 and over as identified by the Alcohol Use Disorder Identification Test (AUDIT).[18]

Our study findings are comparable to a recent study in the USA that analysed data from a NHANES I (National Health and Nutrition Examination Survey I) epidemiologic follow-up study (1982-1984). That study found that a majority (60%) of older persons who ever drank alcohol in their lifetimes were currently drinking (79%) and a substantial number (16% of men and 15% of women) were drinking currently at levels that might place them at risk of adverse health consequences.[19]

This study is unique in that it included GP estimates of alcohol use and misuse alongside other measures of alcohol use. Our findings indicate that hazardous alcohol use among elderly people in the community is either under-recognised by their GPs or that the hazardous effects of alcohol use are not yet manifest in clinical settings. Either is possible as we found that hazardous alcohol users were significantly less likely to consult their GPs. This lower rate of consultation could explain why the drinking status of a significant proportion of patients (48/108) was unknown to the GPs. This finding is consistent with the work of others who have shown that alcohol use and misuse among elderly people is often not identified or diagnosed[5,6] and is often missed in general practice.[20,21] This is important as brief medical advice can decrease alcohol use by older adults in community-based primary care practices.[22]

The low rate of clinically apparent hazardous alcohol use may also be because elderly drinkers frequently under-report their alcohol consumption and problems.[23] However, a growing body of evidence supports that information obtained from alcoholics is highly reliable and valid when obtained in a credible and respectful interviewing environment.[24]

The main limitation of this study is the low response rate (58%) in the main survey. Overall information was available for a total of 72% of participants as we were able to obtain information on a sample of non-responders. The data from the follow-up survey suggested that non-responders tended to be at low risk of problematic drinking; only one out of 34 non-responders was identified as having hazardous patterns of alcohol use according to the AUDIT. Although it is not clear if these findings for non-responders who participated in the follow-up study can be generalised to those who declined to participate in both the main study and the follow-up study, on balance it seems likely that our estimates may slightly overestimate the true prevalence of problem drinking.

This study has found a significantly high prevalence of current hazardous patterns of alcohol consumption among New Zealand elderly people in the community. Health care professionals need to be aware of the potential for alcohol-related problems in this population and to offer the support needed for successful interventions. Health care providers and administrators should plan for an expected increase in the number of older people with alcohol-related medical and social problems in the future.

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The "redisorganisation" of the NHS

The NHS is being reorganised – again. Having declared on taking office in 1997 that it recognised that the NHS had suffered too much has embarked on the largest, and least debated, reorganisation of the NHS for two decades. A consultation document, "Shifting the balance of power in NHS: securing delivery," published in July proposed abolishing the executive regional offices of the NHS and two thirds of health authorities. Only the acute NHS trusts emerge from these changes relatively unscathed. The consultation, which lasted six weeks, closed in early September and the government has yet to publish its results. But the reorganisation is steaming ahead regardless, with the aim of completing all the changes by April 2002. Few people outside the NHS management community seem to be aware of the exact nature and implications of these changes, which have their roots in growing public and political impatience with the quality of NHS services.

The NHS does not need a distracting and unproved reorganisation that, for all the rhetoric about devolution, leaves unchanged, or even strengthened, the capacity for the centre to micromanage the service into the ground. What is required is a fundamental rethinking of the relationship between central government and the NHS. The answer could lie in a move to regional government, with the NHS being transferred to the control of bodies like the Spanish regions or the Swedish country councils. Democratic renewal and devolution offer the potential to prise the NHS out from the grip of government and the hot house atmosphere of Westminster and Whitehall. The price to be paid may be greater local variation and diversity, but given that this already exists between the four countries within the United Kingdom, surely this is a price worth paying.

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MOLECULE-TO-MALADY

The role of the cytokine milieu in protecting us from allergy

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Regulating the cytokine milieu

Cytokines are messenger molecules that predominantly act on and are produced by cells of the immune system. They are produced in response to pathogenic attack that typically comes in the form of viruses or bacteria. Broadly, there are two subsets of effector cytokines that can be produced during an immune response depending on the type of microbe encountered.[1] Type 1 cytokines are produced in response to viruses and intracellular parasites and drive the immune system to lyse the cells harbouring these invaders. This type of immune response also generates a ring of macrophages around the site of infection that functions to wall off the rest of the body or tissue from the infecting pathogens. Type 2 cytokines are pivotal for inducing immune responses against large metazoan parasites and ectoparasites as they burrow through tissue. This immune response acts to both inhibit the progression of the parasite and also to warn the host of invasion (itchiness). However, in allergic individuals, 'harmless' environmental allergens such as pollen and house dust mite are inappropriately treated as dangerous and a Type 2 immune response is mounted against the allergen. An important feature of Type 1 and Type 2 cytokines is that these two arms of the immune system negatively regulate (suppress) each other. One consequence of this is that the effects of Type 2 cytokines are rarely observed during a Type 1 immune response and vice versa.

The long lasting affect of infection on the development of allergy

Infants are born with an immune system biased towards Type 2 responses that functions, in part, to protect the developing baby from cytotoxic Type 1 responses. There are two types of education thought to occur in the immune system. There is thymic and bone marrow education where only the T cell antigen receptors that do not recognise self-antigens are allowed to develop. The second type of education comes throughout life, but especially during early childhood, when our immune system is educated by the types of pathogens it is exposed to. Immune responses to these pathogens usually involve the production of Type 1 cytokines and are short-lived. After the immune response has subsided, long-lived memory cells remain that can respond much faster following re-infection. An evolving theory suggests a bystander effect of this memory may be that it biases subsequent unrelated immune responses towards the production of Type 1 cytokines. Individuals lacking this Type 1 imprint may be more likely to produce Type 2 cytokines and consequently develop allergy.

Epidemiological studies offer interesting insights into this possibility, suggesting that a lower incidence of diseases (such as tuberculosis and some upper respiratory tract viral infections) in children of the western world, has led to an increase in the incidence of allergy.[2] Such evidence culminates into what is commonly referred to as the 'hygiene hypothesis' (Figure 1). Stranchan coined this hypothesis in 1989 with a landmark study of hay fever, hygiene, and household size that proposed improved hygiene was the factor that explained the rise in allergy.[3,4] This phenomenon was subsequently reproduced in the laboratory. In 1998 it was shown that prior infection of mice with BCG, the common vaccine against tuberculosis, would protect against the induction of allergy in a murine model of asthma.[5] The mechanism of this suppression was clearly linked to the production of interferon-gamma (IFN-γ), the archetypal Type 1 cytokine. In other studies, IFN-γ has repeatedly been linked to the suppression of Type 2 immune responses both in vitro[6] and in vivo.[7]

Memory type immune cells imprint the cytokine milieu of tissues

What has been lacking in this field is elucidation of the cellular mechanism behind the hygiene hypothesis. Exciting advances in the study of immune memory may provide such a mechanism. It would appear that after most infections, memory T cells reside in both lymphoid (eg lymph nodes, bone marrow) and non-lymphoid tissues (eg lung). It is becoming increasingly clear that these memory cell types are maintained by cytokines which fall outside the Type 1 and Type 2 subsets. These cytokines play a major role in both the survival and activation of memory T cells. IL-15 is one such cytokine which is considered to have a major role in the survival of cytotoxic memory T cells (major cells involved in fighting viruses and producing IFN-γ).[8] Experiments using transgenic mice have shown that over-expressing IL-15 results in larger pools of cytotoxic memory T cells, while knocking out IL-15 gene expression ablates this memory cell population. Furthermore, IL-15 alone has been shown to induce the proliferation of cytotoxic memory cells both in-vitro and in-vivo. Recent studies have shown that another cytokine, IL-18, can activate memory T cells to produce Type 1 cytokines such as IFN-γ without requiring any other stimuli. It is now emerging that following continual exposure to viral and bacterial pathogens (or parts thereof), many tissues can produce IL-15 and IL-18. In this manner, exposure to antigentically unrelated pathogens throughout life can maintain and activate tissue resident memory T cell populations to produce IFN-γ. The resulting IFN-γ dominant cytokine milieu has the potential to bias subsequent immune responses to allergens towards Type 1 rather than allergy-causing Type 2 immune responses. Taken together, these findings describe the first cellular/ cytokine directed mechanism behind the 'hygiene hypothesis'.

Conclusions

In addition to pointing out potential therapeutic uses for the recently discovered cytokines like IL-15 and IL-18, these observations cause us to rethink our current vaccination strategies. With our current high standard of hygiene, the cytokine milieu present at many mucosal sites may lack the Type 1 imprint that populations with poorer hygiene have. Furthermore, our current vaccine strategies result largely in the production of protective antibodies rather than cell-mediated immunity that may be necessary to protect us from developing allergy. The most effective means of harnessing the power of cytokines may be to induce our immune system to focus the induction of certain cytokines in specific tissues. For example, a vaccination strategy that results in the recruitment of IFN-γ

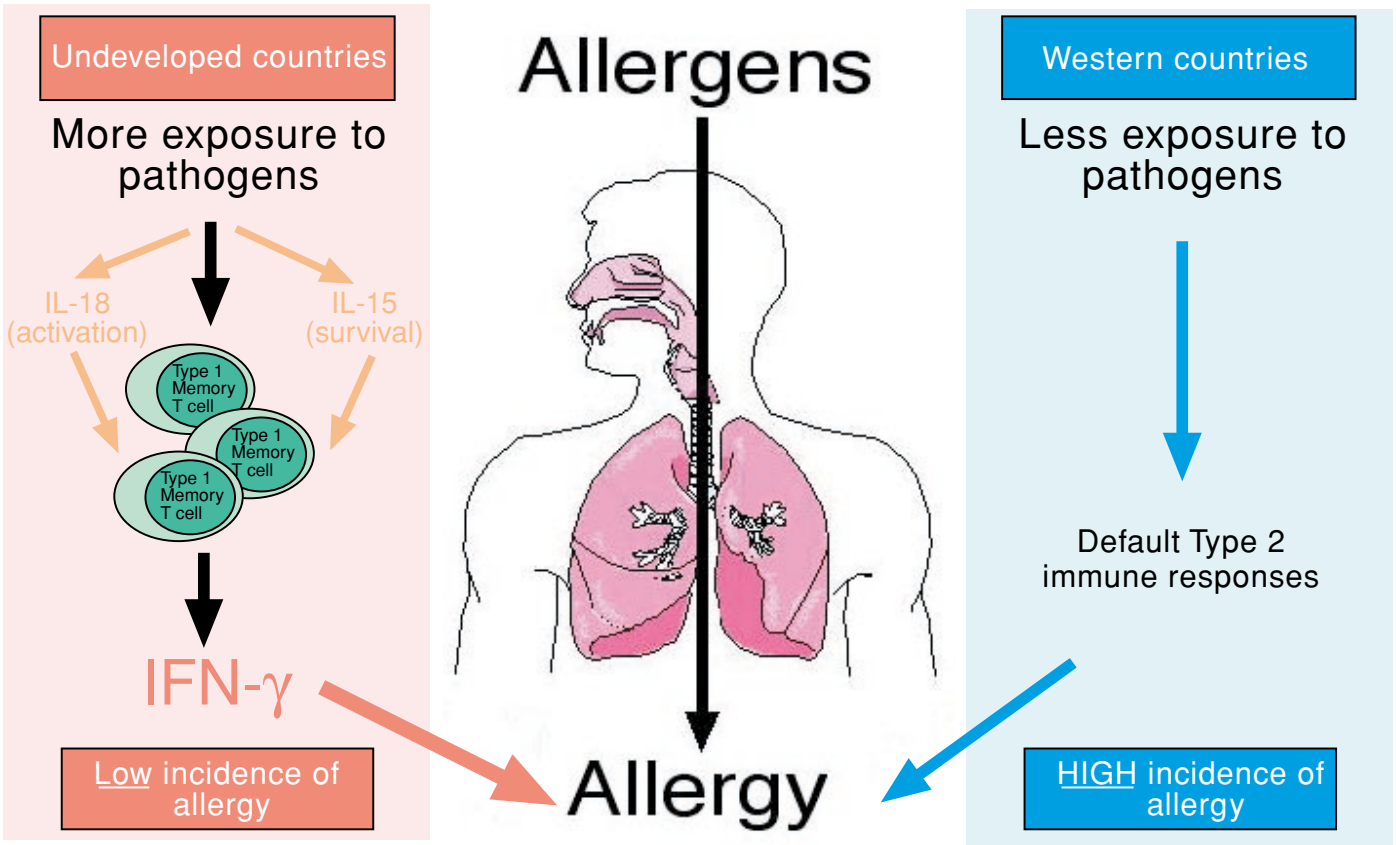

Figure 1. Reduced exposure to some pathogens has led to an increase in the prevalence of allergy in western civilisation. Memory T cells and cytokines play a pivotal role in protecting against allergy.

producing memory T cells to the lung may provide a two-tiered protection platform. On one level there is a specific response by these memory T cells against a target pathogen. On the other level is the creation of a Type 1 cytokine milieu that may bias the tissue against undesirable Type 2 responses such as asthma.

Recent discoveries in experimental immunology are providing exciting insight into memory T cells and cytokines. Cytokines are the major conductors of the immune system, whether they orchestrate an immune response against a virus or imprint tissues to protect from allergy. To balance protection from pathogens with protection from allergies, these discoveries will need to be considered in the design of future vaccines and therapies.

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VIEWPOINTS

Inadequate availability of pharmacological treatment for affective disorders in New Zealand

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The burden of affective disorders

Although many clinicians believe that affective disorders are typically self limiting and relatively benign, unipolar depression and bipolar affective disorder (BAD) are recurrent, often do not remit completely and in some cases do not respond at all to treatment. Lifelong pharmacotherapy, the side effects of which can be severe, is frequently required. We outline evidence regarding this natural history and examine the issue of availability of suitable pharmacological treatments in New Zealand. We argue that due to lack of availability of a range of drugs for affective disorder, which are available in other developed countries, New Zealand patients often receive substandard treatment, which offers less chance of effectiveness, exposes them to a higher incidence of side effects and is out of step with international guidelines.

Globally, it is recognised that BAD and severe depression are already major causes of burden of disease and will become more significant. The World Health Organisation ranked unipolar depression as the fourth highest cause of disease burden in the world in 1990 and predicts that this will rise to become the second highest cause by 2020. In terms of causing disability, major depression ranked the number one world-wide cause in 1990 with BAD ranked sixth.[1]

In both BAD and unipolar depression, research has increasingly demonstrated that treatment resistance and relapse are common problems. In unipolar depression, the long-term response rate to a first line antidepressant is approximately 50%, with a 50% response rate to subsequent trials of different antidepressants.[2] Where there is a response to antidepressants, partial remission with continuing residual symptoms occurs in approximately 30% of cases, and full relapse is also common.[3] Approximately 12% of patients do not respond to treatment and develop a chronic course.[4,5]

In BAD, Gitlin et al[6] studied 82 consecutive hospitalised patients, who all went on to take aggressive maintenance treatment with standard mood stabilisers. In the following five years, 73% had a relapse (into mania or depression) and 2/3 of these had multiple relapses. There were also considerable affective symptoms in those who did not relapse. Even in outpatients, 2/3 of whom were in employment or higher education, the response rate to either lithium or carbamazepine for one year was only 1/3. The combination of the two drugs for a further year produced a response rate of only 50%.[7] A further year on lithium plus sodium valproate and a year after this on triple therapy still left 36% of the original study group inadequately responsive.[8] This disappointing result was despite augmentation with antidepressants, antipsychotics or benzodiazepines. In another study of 155 consecutive admissions with a mania,[9] 13% developed a chronic illness. Indeed, studies of treatment of mania with currently used agents have all tended to produce a roughly equivalent response rate of only 50% within 3 weeks.[10] Amongst patients referred for treatment of resistant BAD, Cole et al found a mean length of index episode of 21.7 months.[11]

A small proportion of people with particularly severe and treatment resistant affective disorders consumes a high proportion of health care resources. Figures from the Acute Inpatient Unit in Christchurch illustrate this. In 1998, 32 patients with BAD suffered four or more relapses of sufficient severity to require inpatient admission, while 96 patients required three or more inpatient stays. During 1998 the 32 patients with four or more inpatient admissions accounted for 10% of all inpatient admissions. Patients with unipolar depression did not suffer multiple admissions but the most severe cases required particularly long admissions. The ten longest stay patients with unipolar depression accounted for 5% of total bed occupancy.

The problem of side effects

A further issue, which contributes to ongoing suffering amongst patients with affective disorders, is the high incidence of drug side effects. Side effects result in high levels of treatment discontinuation, which is an important factor in treatment failure. Tricyclic antidepressants (TCAs) and specific serotonin reuptake inhibitors (SSRIs) are the drugs most commonly prescribed for depression in New Zealand. Even in short placebo controlled trials (in which compliance tends to be better than in clinical practice) the discontinuation rate, due to side effects, is approximately 12.4% for SSRIs and 17.3% with TCAs. Total discontinuation rates were 27% for SSRIs and 31.4% for TCAs.[12] Current treatment recommendations are that antidepressant pharmacotherapy is continued for 6-12 months.[13] Of the alternatives available in New Zealand, traditional monoamine oxidase inhibitors (MAOIs) have a high incidence of side effects and there are concerns from meta-analyses about the effectiveness of moclobemide (a reversible inhibitor of monoamine oxidase A)[14,15] while nefazodone (a heterocyclic antidepressant) may cause headaches, somnolence, dry mouth, nausea and dizziness.[16]

Side effects are also a feature of mood stabilising medication. Lithium causes tremor in approximately 15% of patients, diarrhoea in 5% and an average weight gain of 4kg.[17] Drop out rate per year is approximately 25%.[18] Increasingly, sodium valproate has been used as an alternative mood stabiliser but there is a considerable burden of serious side effects including weight gain, increased risk of polycystic ovary syndrome (PCOS) in young women and adverse metabolic changes.[19] While we can discuss the pros and cons of the side effect profile of different agents, we do not believe that this is the most important point. What is important is that people are individual in their response to different drugs both in terms of response to treatment and susceptibility to side effects.[20]

While evidence suggests that the addition of cognitive therapy to pharmacotherapy may reduce rates of relapse and symptoms in patients with residual depression,[21] there is no evidence that psychological therapy alone is suitable for this group of patients or in those with severe, melancholic or hospitalised depression.[22] There is no clear evidence as yet for

effectiveness of psychological therapies in BAD although they may be useful as adjunctive strategies.

Evidence for effectiveness of newer treatments

Claims of efficacy for newer drugs in treatment resistant mood disorder are not regarded as being sufficiently evidence based by some, including the Pharmaceutical Management Agency Ltd (PHARMAC). There are several reasons for this. Firstly, in this area, the 'gold standard' of evidence based medicine, the double-blind, placebo controlled, clinical trial is difficult to conduct both practically and ethically. Groups of patients tend to be small and heterogeneous, magnitude of responses to a new agent, although important, might not be large, and placebo-controlled studies are ethically difficult. Secondly, there is a problem of funding. Pharmaceutical companies are usually reluctant to fund such studies, partly because of regulatory requirements for evidence of efficacy as first line treatment and partly because, for economic reasons, they prefer to establish their agent as first line treatment. Furthermore, in a climate of restricted research funding, such complex trials, with the methodological and ethical difficulties described above, are less likely to be funded by grant awarding bodies such as the HRC who may assume that the pharmaceutical companies will be forthcoming.

Even when such evidence is available, however, there is likely to be a prolonged delay in translating this into funding for pharmaceutical agents. First there is a lag period before publication or presentation of research findings. This is then compounded by a period of review by PHARMAC including a requirement to produce proof of cost effectiveness. Finally, as discussed below, we note a recent letter to the authors from PHARMAC which seems to suggest that even when evidence is available and published in a respected peer reviewed journal, PHARMAC are unwilling to accept this if the research was funded by a pharmaceutical company (McNee W, personal communication).

We do not suggest that attempts to produce further evidence of optimal treatment in the area of treatment resistant depression and bipolar disorder should not be made. In fact, current studies in the USA are investigating a range of treatments for nonresponders to a first line antidepressant.[23] However, this does not extend into the area of severe treatment resistance. The difficulty of conducting double-blind placebo-controlled trials for bipolar disorder has been acknowledged and much has been written about the need to review trial methodology.[24] It is acknowledged, at least in the UK and North America, that difficulties regarding methodology have led to reduced funding for research into bipolar affective disorder. Where studies have been funded, difficulties in interpreting results have sometimes occurred. A good example is a trial of lithium versus sodium valproate for prophylaxis of rapid cycling bipolar affective disorder (a variety of bipolar disorder more likely to be treatment resistant) following stabilisation on the combination of the two agents. In this study only one-quarter of patients became eligible for randomisation mainly because of poor response to the initial combination therapy.[24] The Stanley Foundation Bipolar Network in the USA has, therefore, agreed to fund a series of trials of novel clinical treatments using both case series, open and blind methodologies. In the United Kingdom a large randomised, non-blind trial of sodium valproate versus lithium versus the combination of the two agents in prophylaxis of BAD is underway.[25]

Given the paucity of large, placebo-controlled, double-blind trials in this area, clinicians and patients are faced with the problem of what to do when usual treatment modalities have failed. The current lack of availability of newer agents in New Zealand forces psychiatrists to use combinations of available drugs for which there is, in many cases, even less evidence of effectiveness and a significant potential for side effects and interactions. An example is the use of the combination of an SSRI and TCA for the treatment of depression when neither alone has been effective. While evidence for this strategy is limited, the potential for side effects mediated by both pharmacokinetic (inhibition of metabolism of TCAs by cytochrome P450 enzymes) and pharmacodynamic interactions is high.[26] A safer alternative, achieving the desired effect of combined serotonergic and noradrenergic re-uptake inhibition, would be to prescribe venlafaxine.

Venlafaxine. Here is a clear example of a drug which should be funded in New Zealand. In a rare, large (121 patients), double-blind trial in patients resistant to trials of two different antidepressants a significant advantage for venlafaxine over paroxetine was reported.[27] A further open label trial demonstrated effectiveness of venlafaxine in more severely treatment resistant depression. The criteria for treatment resistance were an adequate trial of at least three antidepressants from at least two different classes, plus a recognised augmentation strategy (lithium, carbamazepine or thyroid hormones) or an adequate trial of at least two different antidepressants plus a course of ECT. The response rate to high dose venlafaxine in this difficult situation (where the mean duration of the current episode was 4.2 years) was approximately 30% with half of these patients remaining well for at least three months. While it could be argued that the same response rate may occur in response to placebo, the placebo response tends to be small in treatment resistant/chronic depression.

There is further evidence for the usefulness of venlafaxine in affective disorder which has led to its incorporation in British and North American treatment guidelines. In inpatients, there is meta-analytic evidence that venlafaxine, at doses of 150mg per day or greater, is more effective than SSRIs and it is recommended in this situation by the British Association for Psychopharmacology[13] in their evidence-based guidelines for treating depressive disorders. A recent expert consensus report into treatment of BAD in the USA[28] suggested that for more severe depression in the context of bipolar affective disorder bupropion, venlafaxine or SSRIs are the most appropriate treatments. In New Zealand, if these guidelines are to be followed, there is little alternative should SSRIs not be tolerated. Finally, although meta-analyses of antidepressant effectiveness have generally failed to demonstrate superior efficacy of one antidepressant over others,[13] pooled data now suggest a significantly higher remission rate in patients with major depression taking venlafaxine (45%) versus SSRIs (35%) after 6 to 8 weeks.[29]

We wrote to PHARMAC drawing this study to their attention and they replied: "We note that this analysis appears to have been prepared and funded by the company marketing venlafaxine. We are aware that venlafaxine is available elsewhere, and we are also aware that it may provide benefits for some depressed patients who do not respond to currently listed SSRIs. However it yet remains to be established how the cost effectiveness of this agent compares with other potential investments PHARMAC could make, should funding for new investments become available" (McNee W, personal communication). This reply illustrates two points. Firstly, there appears to be a reluctance by PHARMAC to accept data unless it is produced independently of pharmaceutical companies, despite a lack of any constructive criticism of the data. Reputable journals are extremely careful about the review and publication of studies

with possible conflicts of interest and we have no reason to suppose that the British Journal of Psychiatry is any different in this regard. Secondly, it raises the issue of pharmaco-economic evaluation. This issue has, in fact, been addressed for the use of venlafaxine in inpatient depression.[30] A pharmaco-economic simulation model was used together with outcome data from a meta-analysis. Therapy with venlafaxine (225mg per day) demonstrated the highest level of cost effectiveness compared with TCAs, SSRIs and heterocyclic antidepressants (eg trazodone). This study was based on a theoretical model and healthcare costs in North America and was funded by the manufacturers of venlafaxine. However, an independent panel of psychiatrists, health economists, bio-statisticians, pharmacists, economists and epidemiologists guided and critiqued all aspects of the study in accord with agreed guidelines to minimise potential bias in cost effectiveness research supported by pharmaceutical companies.[31] We also note that this evaluation is of health related costs and does not take into account global socio-economic costs which, in a recurrent and sometimes chronic illness such as depression, are high.

Lamotrigine. Of the newer treatments for bipolar disorder, perhaps the most researched is lamotrigine.[32] This is a new anti-convulsant medication funded in New Zealand as an antiepileptic with the Special Authority of a neurologist. Open label studies have consistently found a beneficial effect as an add-on treatment in refractory BAD in various phases of the illness and several double-blind studies have also now been reported.[33] The role of lamotrigine in the treatment of bipolar depression is of interest, given the evidence that antidepressants may precipitate mania and rapid cycling (four or more mood episodes per year),[34] which is associated with poor treatment response.[35] A large, double-blind placebo controlled study suggests that lamotrigine, at a dose of 200mg per day, is effective in the treatment of bipolar depression.[36] In addition, studies suggest good efficacy of lamotrigine in treatment of rapid cycling BAD.[37,38] In the latter study, 182 patients with rapid cycling bipolar affective disorder were randomly assigned to maintenance with lamotrigine or placebo. The proportion of patients who were clinically stable for the six months of the study was significantly higher in the lamotrigine group. While this was a trial of monotherapy, it may be that lamotrigine in combination with other mood stabilisers is even more useful in rapid cycling and a trial of this is currently underway.[36]

Finally, there is evidence in patients with epilepsy that where obesity and PCOS do occur as a result of treatment with sodium valproate, substitution of lamotrigine may be a useful alternative which also allows reversal of these changes in some cases.[39] Although lamotrigine is not yet licensed for use in bipolar disorder, it has been funded and used for this purpose in other countries for several years.

The processes of funding

In New Zealand, funding for drug treatments is controlled by PHARMAC who currently use a policy of reference pricing based on a number of criteria. The lack of consistency or logic with which these policies have been employed has recently been well documented.[40] We believe that in the area of treatment-resistant affective disorder, the criteria employed by PHARMAC are even more problematic. We have argued that the criterion of demonstrable superiority to currently available drugs is difficult to meet in an area where clinical trials are extremely difficult and unlikely to be funded. Secondly, even where a drug does not show evidence of superior efficacy, we argue that in treatment-resistant affective disorder, too few drugs are available as options for patients who either do not respond to, or do not tolerate the side effects of, the currently available drugs. When evidence of efficacy is available PHARMAC appear to doubt this if it is funded by a pharmaceutical company, even though they may be unable to find grounds to criticise the data itself. Furthermore, even when the criterion of efficacy is met, a further criterion of economic viability comes into play. In this complex area, the validity of pharmaco-economic models can easily be disputed, studies are often funded by pharmaceutical companies and wider health care costs are not taken into account. In our opinion, the result of this process is that when evidence becomes available, and PHARMAC eventually accepts this evidence, there is likely to have been an unacceptable delay.

Summary

Both BAD and unipolar depression are common, serious and, in some cases, chronic conditions which often require long term pharmacotherapy. Drug side effects can be severe, contribute to poor compliance and are therefore a factor in maintaining illness and precipitating relapse. Treatment resistance is common. Current evidence suggests that a number of pharmacological agents which are available in other countries (and in some cases have been for many years) may be useful when side effects or treatment resistance occur. In some cases these alternatives are part of recommended algorithms for treatment. In New Zealand, when side effects occur, the options are limited and the problem of treatment resistance is usually approached by using poorly researched combinations of the currently available drugs, thus increasing the likelihood of side effects and adverse drug interactions. The current system is failing to provide appropriate or adequate treatment for people suffering from affective disorders and should be urgently reviewed.

Conflicts of interest. Dr Porter has received support for attendance at conferences and honoraria from a number of pharmaceutical companies including the manufacturers of venlafaxine. Associate Professor Mulder has received support to attend conferences and honoraria from a number of pharmaceutical companies.

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Reducing the uncertainties of withdrawing or withholding treatment

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Death is inevitable but death with dignity is not, particularly in the 'unnatural' situations created for many patients by modern medicine. Withdrawing or withholding treatment embraces the art as well as the science of medicine and confronts clinicians with the true meaning of beneficence. This includes the reduction of unnecessary suffering by measures which may hasten death.

Much has been written about withdrawing or withholding treatment from patients in intensive care units.[1-4] In areas such as general medical wards the question develops insidiously against a background of the mental, physical and social incapacities of old age compounded by co-morbidities. Although the impact of uncertainty on such decisions may be considerable, relatively little has been written about the responses to it[5] despite their potential for being contrary to patient's best interests: for example, the implicit or explicit imposition of preconceived ideas with consequent suppression of questioning or expression of different views. In highlighting the relative certainty of processes to determine what is best for patients rather than wrestling with treat/not treat dilemma, this paper emphasises the importance of anticipation with particular attention to the advance directive.

Uncertainties may be considerable and extend far beyond clinical outcomes to include patient perspectives and ethical and legal concerns. Clinicians' responses often reflect their rationalist training and preoccupation with the physiological aspects of illness.[6,7] As a result patients may become pawns in their battles with illness in which futile imperatives to carry out more investigations or step up treatment under the banner of beneficence reflect unwarranted optimism at best[8] or at worst, deceit. Whilst patients and their relatives generally respond to uncertainty by accepting clinicians' decisions some make unrealistic demands and, fired up by the language of rights,[9] may confront what they regard as paternalism or even arrogance.[10]

The influence of clinicians' use of words on their decisions made in the face of uncertainty may be considerable.[7] For example, use of the term 'medical futility' which appeared to offer a trump card to assert medical authority[11] and obscure the doctor's uncertainty, was widely promoted until critical examination revealed the term's own inherent futility[12,13] and its potential for creating unnecessary conflict.[9] Clinical guidelines, which by their very nature obscure uncertainty, are of only limited help in value-laden and emotionally charged situations.[5,14]

It is important that patients or their advocates understand their condition and the implications of treatment or non treatment. The achievement of the mutual trust fundamental to reaching the best decision may be hampered by difficulties in communication with the patient, compounded by lack of continuity of carers and, in the case of some minority groups and the socially deprived, negative social experiences.[15]

The process

Informed consent requires that the patient is competent, that sufficient information is disclosed and that the choice is voluntary. The approach to the obviously incompetent patient is quite different and will be discussed. Unfortunately in clinical practice the competence of the patient is often either unclear or variable. In such cases considerable sensitivity and thought must be given to ensure the individual's rights are respected.

A good process facilitates decision making by enhancing confidence and trust in difficult life-ending discussions. Being explicit also increases legal security for clinicians who must balance their medical perspectives with respect for the rights and autonomy of the individual. It must be emphasised that the decision to withhold or withdraw treatment does not mean that the patient will be abandoned or their symptomatic care neglected.

The following steps are suggested:

- Anticipation
- Data collection and identification of issues
- Consultation and decision making
- Closure

Medical leadership must be evident, though its style may vary.

Anticipation

Uncertainty may be reduced and unnecessary intervention and suffering avoided by clinicians anticipating the likely need for a decision to withhold or withdraw treatment in

either informal discussion with the individual or formally through an advanced directive or living will.

The right of self determination is enshrined in the Bill of Rights Act 1990. This includes the right of a competent person to refuse treatment. An advanced directive gives an individual the ability to extend their autonomy and right to self determination. Legal standing has been given to advance directives through the Health and Disability Commissioner Act 1994 and in particular, the code of Health and Disability Services Consumers' Rights 1996 ('the Code').

An advance directive is defined in the Code as a written or oral directive:

a. By which a consumer makes a choice about a possible future health care procedure.
b. That is intended to be effective only when he or she is incompetent.

A valid advance directive must provide clear evidence that the patient is competent, free from pain or fatigue, has been advised about treatment options and understands the implications of the choice not to receive treatment. Further, that choice must be voluntary and the person is under no pressure from relatives or others.

The patient must be sufficiently informed of the relevant risks and alternatives to the procedure. In an English decision, the Court found that the patient misunderstood the alternatives available to blood transfusions and had not contemplated her refusal as being life threatening. As the patient had not anticipated this particular event the consent was not valid.[16]

Unlike Canada, USA and parts of Australia, New Zealand does not have specific legislation that sets out what the requirements are for a valid advance directive.[17] Experience of other countries shows legislation can be too limiting and does not take into account all personal health areas over which a person may want to exercise control. This results in the patient not having control over certain treatments after becoming incapacitated.[18]

The difficulties arising in assessing the validity of advance directives include the vagueness of wording used, how informed the person was when the decision was made, and the length of time since the directive was made.

Informed discussions with patients whose condition is deteriorating or who are considered at high risk of sudden, irreversible deterioration, can be extremely helpful in clarifying and even correcting expectations and wishes. Many doctors are still reluctant to discuss the extent of future emergency treatment with patients at risk of sudden deterioration[19,20] despite the high probability of exposing them to interventions which may be inappropriate and unwanted.[20]

Many elderly people wish to limit their health care if they become terminally ill[21] and have expressed interest in living wills or advance directives. The drawing up of an advance directive has been shown to facilitate discussion between doctors and patients.[20] The ability of patients to understand prognostic information is often under-estimated.[22]

Documentation of the content and process of such discussions is essential and may form part of an advance directive. The clinical situation(s) to which the advance directive applies must be specified. A clearly expressed refusal by a competent patient must be accepted in line with S11 Bill of Rights Act 1990.

The New Zealand Medical Association (NZMA) has developed a policy to assist practitioners dealing with advance directives.[23] The policy outlines the doctor's obligation to comply with the terms of the advance directive. A model has been developed and practitioners have been advised to keep stock of NZMA directives in their general practice. However, the practitioner must ensure the needs of individual patients are met when using a standard form. It is also important to document when the advance directive was made and to revisit the patient's wishes on a regular basis (1-2 yearly), as appropriate.

Data collection and identification of issues

Decision making, whether anticipatory or immediate, is based on personal as well as clinical information. The uncertainties inherent in this process must be recognised. There are inevitable limitations to predicting the outcome for an individual based on clinical assessment, medical knowledge and individual clinical experience, however detailed or extensive.[24] It is important to have some understanding of the patient's beliefs and values and to take time to elicit misconceptions where expectations appear inappropriate.

When patients are incapacitated and/or unable to communicate, attempts must be made under Right 7(4) of the Code to ascertain whether they have previously expressed any views or wishes about lifesaving interventions or the quality of life measurements. Right 4 of the Code requires relatives' views to be taken into account in the decision making process. This is to assist the doctor in making a decision and does no imply that the relatives take this role.

Many relatives incorrectly assume that a next of kin is the legal representative. A patient may assign another person to be their Enduring Power of Attorney (EPOA). That person's responsibility commences when the patient begins to lose the capacity to make competent decisions and understand the consequences of those decisions. The EPOA then has the legal responsibility for making treatment decisions for the patient according to the scope of the deed and will advise the doctor of those decisions. Practitioners who are assessing whether they should rely on the attorney's opinion must consider the deed which sets out the attorney's power. The EPOA does not have the power to refuse consent to medical treatment to save the person's life or prevent serious danger to their health, eg amputation. However, when the EPOA and the doctor are discussing the withdrawal or treatment then they can together make the decision as to what is in the best interests of the patient in accordance with the Code.

Review of the clinical, personal and other data may prompt the need for further consultation with experts, both medical and non medical: for example, with regard to particular cultural attitudes to death and dying. Further discussion with other members of the clinical team may not only resolve areas of concern but also raise others requiring further exploration with the patient or family. The doctor conducting the interview should also anticipate any additional potential queries. These may challenge traditional medical beliefs and dogma as has happened with the imperative to hydrate dying patients.[25] The added uncertainty which paradoxically such preparation may at times create is probably best expressed and shared with the patient since its denial may impair communication and even give the impression of deceit.

Consultation and decision making

Careful thought should be given to the manner and place of discussion with the patient and/or family. Patients have a right to choose whether or not they have a support person or family member present. Practical issues such as privacy, the number of participants, the setting and seating and avoidance of interruption especially by bleepers and telephones are important. Whether dealing with competent patients or in the case of the incompetent their advocates, it is imperative to encourage them to express feelings, ask questions and raise

other matters of concern rather than dominate the discussion by talking at them.

For incompetent patients Right 7(4) of the Code requires the clinician to ascertain what the patient's views would have been and to ensure that the treatment decision is in accordance with the choice the patient would have made if he were competent. If the patient's views are not known the clinician must take into account the views of other suitable persons interested in the welfare of the patient and available to give advice.

Different cultural and religious beliefs and values relating to life and death must be recognised and acknowledged. It should be clearly understood the final decision for incompetent patients according to the Code rests with the doctor, not the patient's relatives or advocates. As part of establishing trust with either the competent patient or advocates, the clinician should be prepared to share any uncertainties. Where there is any possibility of conflict, either within the family or with the doctor, the involvement of someone they know and trust such as a priest, general practitioner or even a facilitator, may be considered.

Closure

Recognition that the views of patients and health professionals may change[26] permits review and reassessment of decisions including advance directives: none is irrevocable, merely the best that could be made at the time. Closure should allow for differences in the speed of handling and accepting information and only occur when all involved, including clinical staff, feel comfortable with both the process and final decision.

In the event of failure to agree there are a number of options.[27,28] Review of the process rather than just the content of discussions may identify corrective steps such as allowing more time for clarification and review. It may be appropriate to obtain expert medical, legal or ethical advice or to offer referral to another clinician for either a second opinion or further management. Occasionally formal mediation may be necessary. Whilst doctors are not obliged to provide useless treatment in response to inappropriate demands they must nevertheless respond in ways which show recognition of concerns expressed.

The doctor in charge must review the moral and legal validity of the process which has been followed and ensure that all steps have been appropriately documented from both legal and clinical perspectives.

Conclusion

A formal process which emphasises the importance of anticipation in reaching a decision to withdraw or withhold treatment has been described. Whilst not a guarantee of the best outcome, it should, by providing relative certainty and security, help doctors better manage this challenging and important aspect of care. Most importantly, it allows for greater involvement of patients, either directly or through their advocates, in determining how they end their lives. Doctor's denial of their own uncertainties or failure to address the patient's personal and legal issues adequately may lead to abdication of their responsibilities to lawyers - with consequences over which they may have little control.

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What's happening in New Zealand emergency departments?

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Where we have been

The first fulltime casualty director in Australasia was appointed at Christchurch Hospital in 1963. In the 1970s and '80s specialist training programmes were established in the UK, USA and Canada. Australasia followed, culminating in recognition of emergency medicine as a specialty in New Zealand in 1990.

The International Federation for Emergency Medicine (IFEM) was formed in 1991, the founding members comprising the Australasian College, the American College, the Canadian Association and the British Association. It now has a further eleven full members and one associate member. There have been, as a consequence, enormous advances in emergency medicine internationally. However, the evolution of emergency departments (EDs) in New Zealand has been disappointing. When the first casualty director was appointed in New Zealand, EDs were somewhat ad hoc and opportunistic, utilising whatever space was available somewhere near the front of the hospital. Equipment tended to consist of a variable feast of 'hand me downs' and medical staff were rotated, with unsupervised junior staff often there to cut their teeth at the medical frontline. There was little or no

medical leadership, and standards were variable. Standards tended to be externally derived, from inpatient units, not taking into account the ED context, nor the undifferentiated nature of ED patients.

Where we are going

The ideal ED is purpose-built to international standards and with equipment to practice Emergency Medicine to that standard. There should be dedicated staff working under guidance and supervision and with expert medical and nursing leadership. Staff should have an Emergency Medicine focus, and the standards and guidelines used to deliver care should be appropriate for an ED and for the patients they receive. Although models of this sort do exist in New Zealand it is fair to say that a variable passion for progress and differing degrees of inertia have seen the EDs of our country scattered randomly along the line from where we have been to where we are going.

The ideal model is not just idealistic. International precedents suggest that EDs of high standard are the expectation, and in New Zealand, The Health and Disability Consumer's Code of Rights demands that of us.[1] However, the Commissioner has identified numerous instances where appropriate standards have not been met in New Zealand EDs (Office of the Health and Disability Commissioner). Before describing how our EDs might consistently achieve an appropriate standard of service, it is worth reviewing the specialty of Emergency Medicine and what happens in an ED.

The specialty of emergency medicine

The IFEM defines Emergency Medicine as a medical specialty based on "the knowledge and skills required for the prevention, diagnosis and management of acute and urgent aspects of illness and injury, affecting patients of all age groups with a full spectrum of episodic and undifferentiated physical and behavioural disorders; it further encompasses an understanding of the development of pre-hospital and in-hospital emergency medical systems and the skills necessary for this development." The Health Funding Authority emergency department specifications 2000, state that emergency medicine is suited to episodes of acute care for which the services are not available in the community.

In practical terms, and in keeping with the vocational description of emergency medical practice in New Zealand, Emergency Medicine is predominantly (although not exclusively) the practice of medicine in hospital-based EDs. Clearly the care of a patient with an emergency involves a continuum from the community to definitive care in the hospital. The ED phase is only one link in the chain and is no more or less important, nor should it be more or less strong, than any other link. The 'roadside to bedside' project of the Ministry of Health[2] emphasises the importance of the links between each phase of care, and it behoves Emergency Medicine, as defined above, to have a close, convivial and collaborative relationship with pre-hospital and inpatient providers of emergency care.

In addition it is a responsibility of the specialty that those who claim it, encourage an appropriate fit with emergency nurses, general practitioners (GPs), ambulance staff, other pre-hospital carers, hospital medical officers of special scale, accident and medical practitioners, inpatient specialist teams, and others with whom they interact. The appropriate fit is that which brings about the best care for the patient.

The Australasian College for Emergency Medicine has approximately 40 specialists working in our EDs distributed from Whangarei to Invercargill. In addition, there are more than 110 advanced trainees of the College. It has been estimated by the College, and by the Clinical Training Agency[3] that the country needs a minimum of 150 Emergency Medicine specialists to provide an adequate level of direct patient care, supervision of junior doctors, and leadership in all of our EDs.

What happens in an emergency department?

The EDs in our country vary in size and role delineation. Consequently there is variation in who presents for care and what subsequently happens to them. Most EDs admit approximately one third of presenting patients (range about one fifth to one half). The remaining two thirds are discharged from the ED having had definitive care, or with care to be continued by their GP. Although with a greater range of variation, approximately one third of patients have been referred by a GP for secondary care, approximately a third have been brought by ambulance and approximately one third are self referred and arrive by car. There is a common perception that many patients presenting to EDs should be presenting to primary care providers instead, and that their ED presentation is inappropriate. This perception is not based on evidence. What evidence does exist suggests that the inappropriate attendance rate is relatively small.[4]

Patients on arrival in the ED are triaged according to the Australasian Triage Scale,[5] which defines their urgency for care. This scale has been well validated as a tool to define urgency as well as to describe the complexity of case mix presenting to EDs. It was not designed, nor validated for, the identification of patients who might be sent to an alternative provider of care. Further research is required to define the population attending our EDs and why they attend. The temptation to restrict access to ED care, in response to growing numbers of attendances and a misperception that many are inappropriate, should be resisted. Appropriateness or otherwise is not accurately identified by the process of triage, and turning patients away or triaging them to another service carries considerable risk in addition to limiting a patient's rights to access care. Furthermore, appropriateness of attendance is dependent on what other services are accessible, and will therefore vary from place to place, from time to time, and from patient to patient. The decision to attend the ED is made by the patient (or their proxy or community health care provider) and a subsequent assessment in the ED does not alter the fact that there was a perceived need for emergent hospital care. In this respect, the appropriateness of attendance is determined by the patient's perception of the problem and not by the subsequent medical determination of what the problem is. The solution to minimising any inappropriate use of services is to lower barriers to appropriate care (education, cost, accessibility in place and time) rather than raising barriers to perceived inappropriate care (restricting access or triaging away).

Patients in an ED have access to a variety of hospital-based assessments and treatments. In some departments in this country patients are assessed and managed by probationary house surgeons in their first year after graduation from medical school. These house surgeons take responsibility for the safety of patients and for the judicious use of costly hospital-based resources. In other departments in New Zealand, patients are assessed by doctors in postgraduate year two or above, registrars, medical officers of special scale, or by doctors who are specialists in emergency medicine. International precedent, the Health and Disability Commissioner,[6] the Medical Council of New Zealand[7] and common sense tell us that patients should not be managed by junior doctors, unless they are working with continuous onsite supervision from a senior ED doctor.

Education in the emergency department

Our EDs are major contributors to undergraduate education and postgraduate training for general registration as well as vocational training for Emergency Medicine and for some

other vocations. Undergraduate education in Emergency Medicine is well developed in some centres, with academic positions in all four clinical schools and the country's first Chair in Emergency Medicine at the Christchurch School of Medicine. EDs provide an excellent learning environment, giving an intense and practical experience and straddling community and hospital aspects of care.

Doctors in their first year postgraduation are expected to gain appropriate experience for general registration and some work in EDs under the constraints of Medical Council guidelines, which restrict them from unsupervised ED practice in their first six months.[7] Such unsupervised practice by a junior doctor can be destructive for the patient and the doctor, thus the Medical Council guidelines are appropriate. Indeed, a variety of precedents and opinions suggest the restriction should be extended to include the entire probationary year.[8] However, the absence of ED experience in the probationary year serves to prolong a range of incompetencies with many general registrants, who are then disseminated to small hospitals with inadequate experience of acute care skills. The solution is to have all probationary registrants in EDs working in a supervised environment which is stimulating, formative and safe for them and for their patients. It is worth stressing that junior doctors are infrequently at risk due to an inability to resuscitate patients, since resuscitation skills tend to be readily mobilised when the need is apparent. Instead, junior doctors are most at risk in our EDs because of insufficient experience to recognise the subtle presentations of serious illness and to know when they need help. Supervision, therefore, must be on site and continuous so that both junior doctors and their patients are protected from errors of judgement due to inexperience. The compulsory rotation of postgraduate year one doctors to EDs as supernumerary members of staff under the supervision of senior doctors is a feature of the Australian pre-registration year and should be a feature of New Zealand's also. However, resourcing is needed to achieve this. Increasing restrictions on the rostering of junior doctors in EDs will force many hospitals to exclude junior doctors from EDs altogether, replacing them with more senior doctors. The consequences will be an inevitable protraction of the doctors' inexperience, transferring the risk of this inexperience into subsequent years of practice.

How do we get there?

EDs in this country need to be taken seriously. High expectations should be matched by adequate resourcing along with support from the medical community, to ensure EDs fit smoothly and competently into the chain of care. There are a number of specific initiatives which will help achieve this.

1. National leadership. The good EDs in this country have staff with their heads down battling to improve their lot locally. Other EDs without adequate resources or expertise may be somewhat isolated and untroubled by the expectations of progress. The Ministry of Health as both policy maker and funder, has established a national committee to define three key areas of ED care. The first is to provide a database of EDs in this country. This database would define a common language, describing where our EDs are (in terms of regional relationships) and what they do (in terms of role delineation). The second function would be to define the standards required of those EDs, including ED specifications for the purposes of funding and audit. The third task would be to define the national data set. This describes the data that should be collected, and how it should be collected, so that each Department in New Zealand can speak in a language which is intelligible and comparable.

2. Local leadership. EDs need leadership from those who have demonstrated a specialist standard and who have dynamic links to progress in the specialty and to international benchmarks. The Australasian College for Emergency Medicine and the newly formed Emergency Nurses College are able to contribute to this leadership.

3. Support in the interim. Specialist medical and nursing leadership in all EDs of this country may not be achievable immediately, but will be achievable within a matter of years. In the interim, regional networks should define the interaction required to support service delivery in a region, as well as to provide education and oversight for general registrants in EDs. Specialists in Emergency Medicine who work in larger centres have a responsibility for providing support, by a variety of means, to smaller EDs in their region. This support may include rotation of senior staff, the provision and implementation of standards and guidelines, assistance with audit and education and oversight of general registrants. The Australasian College for Emergency Medicine's Maintenance of Professional Standards programme is available to all ED doctors, and training programmes such as that defined by the Accident and Medical Practitioners' Association, are interim alternatives available to those who cannot, or choose not to, undertake specialist training.

4. Roadside to bedside. It behoves EDs to be a strong link in the chain of care from roadside to definitive bedside. National and local ED leadership, and the establishment of regional Emergency Care Co-ordinating Teams is essential to strengthen these links.

5. Education in emergency medicine. Strengthening undergraduate education in Emergency Medicine and rotating first year postgraduate doctors to EDs under appropriate supervision, is a sensible use of an excellent educational resource and enthusiastic educators, as well as a means of assuring greater competence in the general registrants we disseminate to all corners of our country.

Five initiatives over five years

Emergency Medicine is at an exciting stage of development in New Zealand. There are pockets of expertise, but there are concerns that progress has been variable and without clear direction. We have the opportunity to achieve five relatively simple outcomes by 2006:

i) Specialist medical and nursing leadership established in every ED.
ii) Standards of care, including staff expertise, staff numbers, space, equipment and systems comparable to the best in the world.
iii) A strong Emergency Medicine contribution to undergraduate and postgraduate medical education.
iv) Nationally standardised specifications for EDs, with variations according to the local context and role delineation.
v) Regional networks of care which provide service and educational links between EDs in the region, as well as a robust chain of care from roadside to bedside.

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Erratum

In the article by Tony Blakely and colleagues, the following Table was printed without the key boxes at the foot. (NZ Med J 2002; 115: 43-8).

Figure 2a. Males

Figure 2b. Females

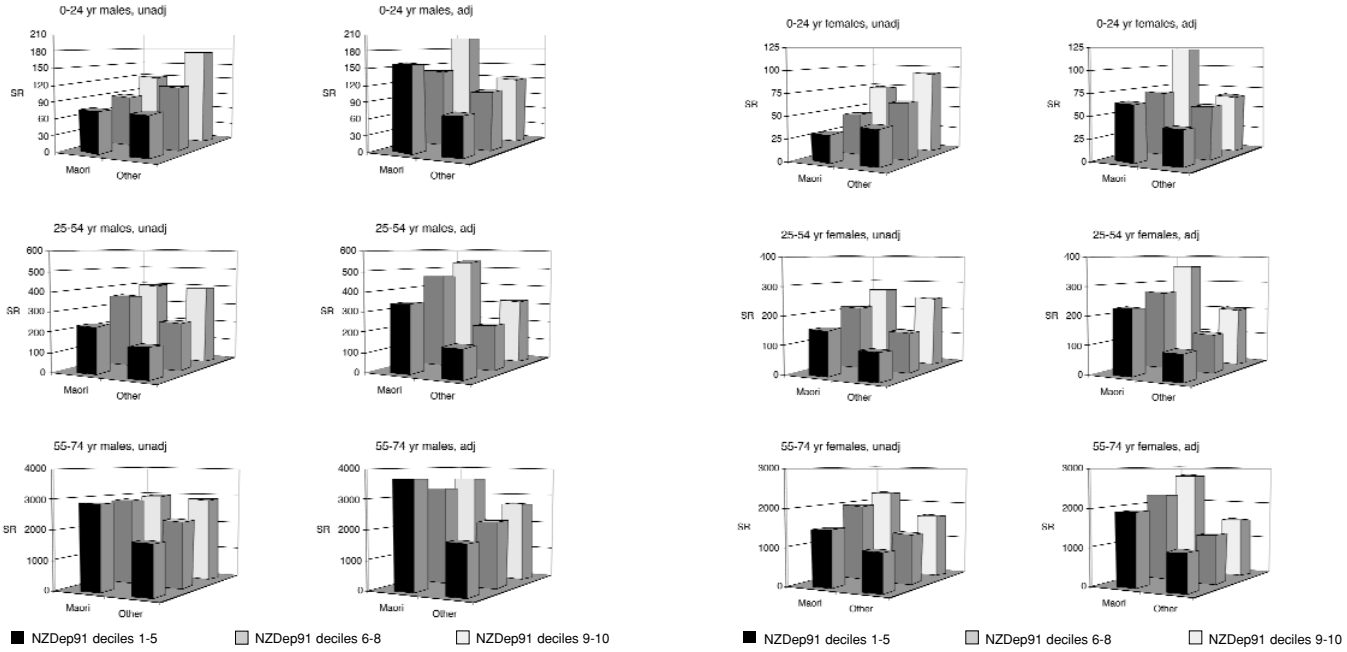

Figure 2. Standardised rates of mortality (per 100 000; deaths during 1991-94) for Mäori and Non-Mäori non-Pacific by small area deprivation (NZDep91), unadjusted and adjusted for numerator-denominator bias.