CONTENTS

This Issue in the Journal

3 A summary of the original articles featured in this issue

Editorial

6 Making World No Smoking Day Redundant
*Chris Bullen, Marewa Glover*

Original Articles

9 Youth experiences of secondhand smoke exposure in New Zealand: evidence from 5 national surveys (2000 to 2008)
*Louise Marsh, Rob McGee, Andrew Gray, Rhiannon Newcombe, Rose Patterson*

19 Benchmarking benzodiazepines and antipsychotics in the last 24 hours of life
*Brian Ensor, Daphne Cohen*

31 Nurse titration clinics to achieve rapid control of blood pressure
*Dominic Taylor, Veronica van der Merwe, Walter van der Merwe*

41 Validation of the Edinburgh Postnatal Depression Scale (EPDS) as a screening tool for postnatal depression in Samoan and Tongan women living in New Zealand
*Alec J Ekeroma, Bettina Ikenasio-Thorpe, Sara Weeks, Jesse Kokaua, Kasalanaita Puniani, Peter Stone, Siale A Foliaki*

50 Is it NICE to monitor lithium routinely?
*Andrew McKean, Jane Vella-Brincat*

55 Trends in child and adolescent discharges at a New Zealand psychiatric inpatient unit between 1998 and 2007
*Kirsten van Kessel, Elizabeth Myers, Sarah Stanley, Peter W Reed*

Viewpoint

62 Partner notification for sexually transmitted infections. Why can’t we talk about it?
*Sunita Azariah*
Clinical Correspondence

71 Delayed puberty from partial 17-alpha hydroxylase enzyme deficiency
Michael Croxson, Megan Ogilvie, Stella Milsom, John Lewis, James Davidson, Gill Rumsby

75 Ischaemic stroke with headache as its only manifestation
Wael Radwan, Abdallah El-Sabbagh, Samir Atweh, Raja Sawaya

Letters

78 Increasing prescription part charges will increase health inequalities in New Zealand
Santosh Jatrana, Peter Crampton, Ken Richardson, Pauline Norris

81 Smokefree cars to protect children and denormalise smoking: a mini-review of New Zealand literature
Nick Wilson, George Thomson, Richard Edwards, Heather Gifford

87 Health Workforce
Bill Douglas

90 Reply by New Zealand Chiropractors' Association to Edzard Ernst's April 2012 "research"
Corrian Poelsma

100 Years Ago in the NZMJ

93 Dominion Notes: The increasing popularity of the cigarette

Proceedings

94 Proceedings of the 211th Scientific Meeting of the Otago Medical School Research Society, Wednesday 9 May 2012

Methuselah

102 Selected excerpts from Methuselah

Obituaries

104 William Leslie Francis Utley

107 Henry Stone
This Issue in the Journal

Youth experiences of secondhand smoke exposure in New Zealand: evidence from 5 national surveys (2000 to 2008)
Louise Marsh, Rob McGee, Andrew Gray, Rhiannon Newcombe, Rose Patterson

Surveys with Year 11 students (mainly 14–15 year olds) from 2000 to 2008 found declining rates of secondhand smoke exposure for young people in their homes and while travelling in vehicles. However, 35% of young people are still being exposed to secondhand smoke in their homes and 32% in vehicles. Although smokefree homes are increasing, there is still much work needed to reduce the rates of secondhand smoke exposure for our young people, and especially Māori and Pacific young people.

Benchmarking benzodiazepines and antipsychotics in the last 24 hours of life
Brian Ensor, Daphne Cohen

The use of medications at the very end of life is known to be very variable internationally, particularly regarding medications that can be sedative. Hospices in NZ considered that we needed to find out what variation exists within this country, so that we can start to reflect on our own practice, with the goal of working out why we do what we do. At this stage it is simply finding out the range of current practice, there is no attempt to make any judgements about what is ‘correct’ prescribing,. There are some expected causes of variation, such as those patients who die in a hospice may have more medication needs than those who die in the community. However there is an additional range of complex factors which may be unique for each hospice, each community and for each patient. The requirements for medications, and the goals for end-of-life care, are variable between people. The important bottom line is that there should be some dialogue and negotiation between patient, family and health professionals about what the goals are, and how medications subserve these goals. This is part of prompting further discussion in NZ about how people wish to be cared for at the end of life.

Nurse titration clinics to achieve rapid control of blood pressure
Dominic Taylor, Veronica van der Merwe, Walter van der Merwe

High blood pressure (“Hypertension”) is the most common chronic disease and the most common remediable cause of death in the western world. We set up a clinic at North Shore Hospital, Waitemata DHB, to cope with the large number of patients being referred from their GP with difficult-to-control hypertension. The patients were seen by a specialist doctor at the first appointment, and subsequently by a specialist nurse, who gave lifestyle advice and altered medications. Patients were screened for secondary (for instance, hormone-related) causes of hypertension. The nurse clinic allowed us to see and treat more patients, and the patients gave universally good
feedback about the care they received. The quality of treatment as measured by our blood pressure measurements and number of clinics required was the same as the previous clinic which was staffed solely by doctors.

Validation of the Edinburgh Postnatal Depression Scale (EPDS) as a screening tool for postnatal depression in Samoan and Tongan women living in New Zealand
Alec J Ekeroma, Bettina Ikenasio-Thorpe, Sara Weeks, Jesse Kokaua, Kasalanaita Puniani, Peter Stone, Siale A Foliaki

Depression after having a baby has been shown to be more common in Tongan than in Samoan women. A study was conducted in Middlemore Hospital to determine whether a questionnaire used routinely for screening for depression after childbirth (EPDS) should also be used in Samoan and Tongan women. The study showed that the questionnaire was acceptable and could identify about 80% of women with depression. The questionnaire should be used routinely by health workers.

Is it NICE to monitor lithium routinely?
Andrew McKean, Jane Vella-Brincat

Lithium is a mood stabiliser for the treatment of bipolar affective disorder. It has predictable toxicity at concentrations above the normal range. This study compares the monitoring of lithium blood concentrations in Canterbury, New Zealand to the current UK standard. The monitoring of lithium blood concentrations in Canterbury, New Zealand did not meet this standard which is in keeping with other published audits.

Trends in child and adolescent discharges at a New Zealand psychiatric inpatient unit between 1998 and 2007
Kirsten van Kessel, Elizabeth Myers, Sarah Stanley, Peter W Reed

Over the past decade, there has been an increase in the number of young people admitted to the regional adolescent psychiatric unit at Starship Hospital. In particular, there have been more admissions of young people with serious mental illness, such as psychosis. There has been a steady increase in the number of young Maori admitted, and psychosis was the most common diagnosis for Maori and Pacific Island patients in this child and adolescent psychiatric inpatient setting. The current unit was not designed for such large numbers of seriously unwell young people, and the resources have not increased to match the need.
Partner notification for sexually transmitted infections. Why can’t we talk about it? ((viewpoint article))
Sunita Azariah

Bacterial sexually transmitted infections such as chlamydia are very common in New Zealand. It is very important that sexual contacts of people diagnosed with bacterial sexually transmitted infections are notified of their possible exposure to an infection and are tested and treated to reduce re-infection rates and onward transmission of infection. However many health practitioners are not well trained in carrying out partner notification or feel confident in managing this process. Some practitioners commonly prescribe medication for sexual contacts of their patients without a prior consultation but this practice is not legal in New Zealand and overseas research does not support the effectiveness of such an intervention. Research does support the effectiveness of training of GP practice nurses and the use of resources such as partner notification cards in achieving better partner notification outcomes in primary care within existing legal frameworks.
Making World No Smoking Day Redundant

Chris Bullen, Marewa Glover

World No Smoking Day—May 31st—is an appropriate time for New Zealand’s medical professionals to take stock of how far we have come in the tobacco control journey—but also to consider how far we have to go to reach the goal of a Smokefree Aotearoa/New Zealand by 2025. The target has already been reached by New Zealand’s doctors—fewer than 5% are smokers—and this shows what is possible.

To see smoking prevalence among the rest of the population fall to this level within the next 13 years, business as usual—raising tobacco taxes in increments year on year, providing support for current smokers to quit, curtailing the last vestiges of tobacco promotion (through retail display bans and plain packaging), and mass media campaigns—will all be a necessary part of the tobacco control package, but will not be sufficient. Breakthroughs are needed.

Where should limited resources best be focused? Reducing smoking initiation is important but has been declining steadily for a number of years. Recent data from the ASH Year Ten Survey is encouraging, 70.4% of students were never smokers. Māori students had the biggest reduction in smoking from 2010 to 2011 of any ethnicity. But to see a step change in prevalence to achieve the national goal, the main focus must be on helping current smokers to quit.

Far more must be done to meet the high demand for cessation support among the many smokers who want to quit. All health professionals have a key role to play. Asking about smoking status, giving brief advice and providing or referring to cost-effective cessation support (such as Quitline) for smokers is not merely an optional add-on or even a target to be reached, but must be seen as a life-saving intervention and therefore an ethical obligation for doctors.

Therapeutic nihilism in the face of frequent relapse is simply not justified. Despite relapse being common and the low numbers of smokers who permanently quit as a result of making a serious quit attempt, the health benefits that accrue to those who persist and remain abstinent are such that its justifies the effort and resources applied.

But the absolute numbers of smokers who are moved towards cessation must increase dramatically if we are to halve smoking prevalence by 2020 which our new programme of research aims to inform. This will be achieved through ramping up cessation support not only in the health sector but also by expanding the reach of cessation support into workplaces and communities through lay workers, iwi, churches and other groups.

"Other innovative approaches are being considered, such as electronic cigarettes. These devices, which are marketed widely via social media rather than orthodox sources, may appeal to some smokers who have lost faith in the usual methods such as 'cold turkey', nicotine patches and gum."
There is a growing interest among tobacco control researchers in the potential of regulating down the nicotine content of tobacco in cigarettes to reduce dependence. Local research just published has shown this strategy has merit. Regulation of tobacco supply through means such as restricting the number of tobacco retail outlets is being debated in the tobacco control community – but such options are likely to be expensive to operate and may not be supported in the current political environment.

More cost-effective and acceptable than the establishment of a tobacco retailer licensing system would be a move by major retailers to voluntarily remove tobacco from sale in their stores. A handful of smaller retailers in New Zealand have already decided to stop selling tobacco products. However, this is only likely to occur on a sufficiently large scale to dent prevalence in response to a groundswell of public concern.

More fundamentally, a culture change in attitudes towards tobacco smoking, as we have witnessed with other toxic substances, such as asbestos, must be fostered and promoted, especially among population sub-groups where smoking remains the norm. As they have done on a number of other issues of public health concern, medical professionals should be among those leading the charge in advocating for such changes.

It is possible that a tipping point will be reached at some point, following which the decline in smoking prevalence will accelerate dramatically. However, no-one knows if or when that point that will be attained. In the meantime, the stakes are far too high for health professionals, researchers and others committed to achieving a smokefree Aotearoa/New Zealand within the next decade and a half to 'have a cup of tea’ and take the pressure off our policy-makers.

Competing interests: None declared.

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Acknowledgements: The New Zealand Tobacco Control Research Turanga is funded by the Health Research Council of New Zealand and Ministry of Health Reducing Tobacco-related Harm Research Partnership.

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References:


Youth experiences of secondhand smoke exposure in New Zealand: evidence from 5 national surveys (2000 to 2008)

Louise Marsh, Rob McGee, Andrew Gray, Rhiannon Newcombe, Rose Patterson

Abstract

Aims To describe trends in young people’s exposure to secondhand smoke (SHS), and to their exposure to household rules around smoking in New Zealand (NZ) over the period 2000 to 2008.

Methods We examined self-assessed perceptions of exposure to SHS in the home and while travelling in vehicles, and home smoking restrictions, both inside the home (indoor) and on the property (outside). Data were from the 2000, 2002 and 2004 Youth Lifestyle Study and 2006 and 2008 Youth In-depth Survey of 14- to 15-year-olds in NZ.

Results Downward trends in young people being exposed to SHS at home since 2000 (p<0.001) and in vehicles since 2002 (p<0.001) were found. Unrestricted indoor and outdoor smoking declined, with 31% of homes being completely smokefree in 2008. Māori and Pacific young people were significantly more likely to be exposed to SHS at home (OR 3.2 and 2.0 respectively) and in vehicles (OR 3.1 and 2.3 respectively).

Conclusions Declining rates of SHS exposure for young people in their homes and while travelling in vehicles are encouraging. However, 35% of young people are still being exposed to SHS in their homes and 32% in vehicles. Although smokefree homes are increasing, there is still much work needed to reduce the rates of SHS exposure for our young people, and especially Māori and Pacific young people.

People are regularly exposed to secondhand smoke (SHS). Worldwide in 2004 it was estimated that 40% of children aged 0-to-14-years, and 33% of non-smoking adult males and 35% of non-smoking adult females were regularly exposed to SHS indoors, resulting in an estimated 603,000 deaths and 10·9 million disability-adjusted life-years (DALYs).1

In New Zealand (NZ), SHS has been estimated to kill around 300 people per year,2-4 and cause a substantial burden of morbidity, particularly for children.5 The harmful effects of SHS in young people have been extensively researched, showing that exposure increases the risk of respiratory illnesses, ear problems, asthma, lung function,6-9 and, more recently, poorer mental health.10 In NZ, a greater risk of exposure has been found among low income individuals and for Māori.11,12

Given the association between SHS exposure and poorer health, it is important to monitor SHS exposure and examine trends over time. Decreases in SHS exposure have been seen both overseas13 and in NZ,12 but SHS is still thought of as one of the “most common indoor pollutants worldwide” (p.144).1

Despite reductions in overall exposure, there are still some areas where SHS may impact young people, in particular smoking in the home and smoking in vehicles.
These are the most significant sites of SHS exposure for most children in the USA, and in NZ, 10 to 14% of young people 15-to-19-years were exposed to SHS in their home in 2009, significantly higher than older age groups. A similar number have also been exposed to SHS in a vehicle in the past week.

Efforts to reduce the harm caused by SHS have included both legislative as well as voluntary policies. With regard to legislation, in NZ the Smoke-free Environments Act was introduced in 1990 with subsequent amendments made in 2003 banning smoking in public places including work places, restaurants and bars.

These legislative smokefree policies have been successful at reducing SHS exposure and improving indoor air quality. Furthermore, social marketing campaigns have fostered voluntary adoption of smokefree homes and cars policies by the public. Data show that these campaigns have been successful in changing behaviour in both NZ, as well as internationally. The main benefit is reduced SHS exposure for those living in the home. However, additional benefits for young people exist including reduced experimentation with smoking, and lower likelihood of smoking uptake. These findings appear to be stronger for strict smoking bans compared with partial bans, consistent with a recent review of the effect of home smoking restrictions on youth behaviour.

Research in NZ suggests that there is support for smokefree homes. There is also support for banning smoking in cars, but this has not been given a high priority by policy makers. Recently the NZ Māori Affairs Select Committee published their recommendations to the Government on achieving the goal of NZ being smokefree by 2025, and emphasising the extension of the Smoke-free Environments Act to include banning smoking in vehicles, particularly those carrying children.

The aims of this study were to describe trends in young people’s exposure to SHS, and to their exposure to household rules around smoking in NZ over the period 2000 to 2008.

Methods

Sample selection—The Youth Lifestyle Study (YLS) and Youth In-depth Survey (YIS) used methods and key measures from the international Global Youth Tobacco Survey (GYTS), developed by the World Health Organization and the Centers for Disease Control and Prevention to monitor tobacco use among youth across countries. The study data came from the 2000, 2002 and 2004 YLS surveys, and the 2006 and 2008 YIS surveys of Year 10 high school students from randomly selected secondary schools in NZ, undertaken by the Health Sponsorship Council. A two-stage cluster sample design, with random selection of participating classes was used. The sampling strategy was intended to result in a representative sample of Year 10 school students with survey weights at the individual student level used for this purpose. More details are contained elsewhere.

The survey used a self-report questionnaire for students administered during school class time. The response rate for schools was 80.5% and from students was 84.9%, giving an overall response rate of 68.3% for 2008. The response rate for schools was 78.0% and from students of 83.7, giving an overall response rate of 65.3% in 2006. The overall response rate in 2004 was 74.6% and in 2002 was 58.2%.

Table 1 describes the sample of students taking part each year. Ethical approval for this study was given by the Ministry of Health’s multi-regional ethics committee in 2008.
Measures—The YLS and YIS surveys assessed self-reported smoking attitudes, behaviours, and knowledge and information on youth culture and lifestyle. Student age, sex and ethnicity data were also collected.

Exposure to SHS around young people in their home was examined through the question: During the past 7 days, on how many days have people around you smoked in your home? From 2004 participants were also asked who the people were that had been smoking around them in their home. The response options in the 2004 survey included: mother; father; best friend; brothers and sisters; family friends; other relatives or caregivers. The two more recent surveys included grandparents and referred to older brothers and sisters.

Smoking around young people in vehicles was examined through the following two questions in 2006 and 2008: During the past 7 days, did anyone smoke in your presence while you were travelling in cars or vans? Participants were also asked: During the past 7 days, which of the following people have smoked around you while you were travelling in cars or vans? The list of options was the same for smoking exposure.

To assess what rules were in place around smoking at home, young people were asked: At your home is smoking allowed anywhere inside, only in set areas, or nowhere inside your home? A similar question was asked for smoking outside on the property.

Analysis—Descriptive statistics are provided by year of survey for all variables, including both sample characteristics and key measures. Regression models were used to investigate changes in key measures over time, adjusting for demographic variables (sex; age groups of: up to and including 13, 14, 15, and 16 and older; and ethnicity using prioritised ethnicity with the order of priority being from highest to lowest: Māori, Pacific Peoples, Asian, Other, and NZ European) as predictors of interest in themselves and to reflect changes in sample characteristics over time when looking at trends. Ordinal logistic regression was used to model days exposed to SHS at home and elsewhere and household smoking rules with outcomes dichotomised when proportionality did not hold.

Exposure to SHS in vehicles, specific people contributing to SHS, and other specified locations where SHS exposure has occurred were modelled using binary logistic regression. Interactions between survey year and other predictors (including household rules) were investigated and retained where statistically significant. All analyses included a random effect for school to model cluster effects. All analyses were performed using Stata v11.1 software. All significance tests were two-sided, with p<0.05 considered statistically significant. Adjusted odds ratios (aORs) and 95% confidence interval (CI) are presented.

Table 1. Demographic characteristics of total sample, 2000–2008 (percentages)

<table>
<thead>
<tr>
<th>Variables</th>
<th>2000 n=1610</th>
<th>2002 n=2756</th>
<th>2004 n=3400</th>
<th>2006 n=3200</th>
<th>2008 n=3066</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>47.8</td>
<td>49.2</td>
<td>50.7</td>
<td>49.3</td>
<td>50.8</td>
</tr>
<tr>
<td>Females</td>
<td>52.2</td>
<td>50.8</td>
<td>49.3</td>
<td>50.7</td>
<td>49.2</td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;14</td>
<td>0.27</td>
<td>1.4</td>
<td>1.1</td>
<td>0.6</td>
<td>0.79</td>
</tr>
<tr>
<td>14</td>
<td>56.4</td>
<td>74.6</td>
<td>61.7</td>
<td>64.5</td>
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</tr>
<tr>
<td>15</td>
<td>39.4</td>
<td>22.7</td>
<td>36.2</td>
<td>34.0</td>
<td>37.0</td>
</tr>
<tr>
<td>16+</td>
<td>3.9</td>
<td>1.3</td>
<td>1.0</td>
<td>0.81</td>
<td>1.2</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NZE*</td>
<td>58.5</td>
<td>56.2</td>
<td>48.5</td>
<td>57.1</td>
<td>52.2</td>
</tr>
<tr>
<td>Māori</td>
<td>17.2</td>
<td>20.6</td>
<td>24.9</td>
<td>20.8</td>
<td>25.0</td>
</tr>
<tr>
<td>Pacific</td>
<td>10.8</td>
<td>10.5</td>
<td>11.6</td>
<td>8.6</td>
<td>11.8</td>
</tr>
<tr>
<td>Asian</td>
<td>4.8</td>
<td>6.9</td>
<td>7.6</td>
<td>4.7</td>
<td>9.0</td>
</tr>
<tr>
<td>Other</td>
<td>8.6</td>
<td>5.8</td>
<td>7.4</td>
<td>8.8</td>
<td>2.0</td>
</tr>
</tbody>
</table>

* NZE represents New Zealand European.
Results

Sample characteristics—The total sample consisted of approximately equal number of males and females, with most participants being 14 years of age and of NZ European ethnicity (see Table 1 above).

Exposure to secondhand smoke in the home—Table 2 shows there has been a downward linear trend (adjusted linear trend p<0.001) in SHS exposure for young people in their home from 49% in 2000 to 35% in 2008. In terms of the number of days exposed, with the exception of 5-6 days, the percentage decreases seem proportional at almost all levels which appears to support the hypothesis that exposure is not shifting to a lower category as much as it is ceasing altogether (Figure 1).

Table 2. Exposure to SHS in the home, vehicles, and places other than their home in past week, and household smoking rules (%)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Year of survey</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SHS exposure</td>
<td>In home</td>
<td>48.6</td>
</tr>
<tr>
<td></td>
<td>In vehicles</td>
<td>42.1</td>
</tr>
<tr>
<td>Is smoking allowed inside your home?</td>
<td>Anywhere inside</td>
<td>17.1</td>
</tr>
<tr>
<td></td>
<td>In set inside areas</td>
<td>12.3</td>
</tr>
<tr>
<td></td>
<td>Nowhere inside</td>
<td>70.6</td>
</tr>
<tr>
<td>Is smoking allowed outside your home?</td>
<td>Anywhere outside</td>
<td>71.4</td>
</tr>
<tr>
<td></td>
<td>In set outside areas</td>
<td>10.7</td>
</tr>
<tr>
<td></td>
<td>Nowhere outside</td>
<td>17.9</td>
</tr>
<tr>
<td>Smokefree home and property</td>
<td>Total smoking ban</td>
<td>17.2</td>
</tr>
</tbody>
</table>

Note: empty cells indicate years when that question was not asked.

Females were more likely (aOR 1.1, CI: 1.1 to 1.2, p=0.001) to be exposed to SHS in their home than males. Overall, ethnicity was a significant predictor over all years (overall p<0.001) with Māori (aOR 3.2, CI: 2.9 to 3.5, p<0.001) and Pacific (aOR 2.0, CI: 1.7 to 2.3, p<0.001) young people more likely to be exposed to SHS in their home compared with NZ European (Table 3). Those identifying as Asian were less likely (aOR 0.51, CI: 0.43 to 0.61, p<0.001) to be exposed to SHS in their home than NZ European.

Participants reported who had smoked around them in their home in 2008. Mothers were reported as smoking around them most often at 46%, and one-third (35%) had fathers who smoked around them in their homes. One-quarter (25%) of older brothers and 19% of older sisters were also reported to have smoked around young people in their homes. In terms of friends, 16% of best friends and 21% of other close friends were reported as smoking in the presence of the participants in their home.
Exposure to secondhand smoke while travelling in vehicles—There was a downward linear trend in young people’s exposure to SHS in vehicles from 42% in 2004 to 31% in 2008 (adjusted linear trend p<0.001) (Table 2). Females were more likely to be exposed to SHS in vehicles than males (aOR 1.3, CI: 1.1 to 1.4, p<0.001).

Overall, ethnicity was a significant predictor over all years (overall p<0.001) with Māori (aOR 3.1 CI: 2.7 to 3.5, p<0.001) and Pacific (aOR 2.3 CI: 1.9 to 2.7, p<0.001) young people more likely to be exposed to SHS in vehicles compared with NZ European.

Those identifying as Asian were less likely (aOR 0.55, CI: 0.43 to0 .70, p<0.001) to be exposed to SHS in vehicles than NZ European (Table 3). Overall, age was a significant predictor over all years (overall p<0.001) with higher SHS exposure in vehicles for those 16 years and older compared with students under the age of 14 years (aOR 2.5, CI: 1.4 to 4.5, p=0.003).

As with smoking in homes, parents were the most significant contributors of SHS in vehicles; 41% of mothers and 33% of fathers smoked around young people in vehicles in the past week in 2008. One-fifth (19%) of older brothers and 18% of older sisters were also reported to have smoked around young people in vehicles.

Figure 1. Percentage of young people exposed to SHS in their home 2000-2008 for numbers of days per week (excluding exposures on no days)
A significant source of SHS exposure for young people in vehicles was people other than family members; one-third (32%) reported other people, such as visitors, smoked around them in vehicles and one-quarter (26%) of respondents had a family friend smoke in their presence while travelling in vehicles.

In terms of friends, 16% of best friends and 22% of other close friends were reported as smoking in the presence of the participants in vehicles in 2008.

**Household rules around smoking**—There is evidence that both unrestricted indoor and outdoor smoking has declined between 2004 and 2008 (adjusted linear trends p<0.001 for both). Combining these, there is evidence of an increase in homes and properties being entirely smokefree from 17% in 2004 to 31% in 2008 (adjusted linear trend p<0.001). Females were less likely to live at a smokefree home or property (aOR=0.8, CI: 0.7 to 0.9, p<0.001) compared with males. There was evidence of differences between ethnicities (overall p<0.001) with Māori (aOR=0.3, CI: 0.3 to 0.3, p<0.001) and Pacific (aOR= 0.7, CI: 0.6 to 0.8, p<0.001) less likely to live at smokefree homes or properties compared to NZ European; but Asian (aOR=2.0, CI: 1.7 to 2.3, p<0.001) and those of other ethnicities (aOR=1.6, CI: 1.3 to 1.9, p<0.001) were more likely compared to NZ European (Table 3).

<table>
<thead>
<tr>
<th>Exposure</th>
<th>Ethnicity</th>
<th>aOR (CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure in the home</td>
<td>Māori</td>
<td>3.2 (2.9 to 3.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>Pacific</td>
<td>2.0 (1.7 to 2.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>Asian</td>
<td>0.51 (0.43 to 0.61)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Exposure in vehicles</td>
<td>Māori</td>
<td>3.1 (2.7 to 3.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>Pacific</td>
<td>2.3 (1.9 to 2.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>Asian</td>
<td>0.55 (0.43 to0 .70)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Household rules around smoking</td>
<td>Māori</td>
<td>0.3 (0.3 to 0.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>Pacific</td>
<td>0.7 (0.6 to 0.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>Asian</td>
<td>2.0 (1.7 to 2.3)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Reference category is NZE.

**Discussion**

This study sought to examine trends in young New Zealanders experience with SHS between 2000 and 2008. Results showed a downward trend in SHS exposure at home since 2000 and in vehicles since 2002. There may be a number of reasons for this decline in SHS exposure.

Firstly, parents are the main contributor of SHS at home, and this is in line with a drop in adult smoking in other NZ research over this time.\(^{32, 33}\)

Secondly, there is a higher awareness among New Zealanders of the dangers of SHS, and greater publicity around this issue. Social marketing campaigns targeting SHS exposure in the home and cars were implemented nationally in 2004 and 2006 respectively. There are data to show that these campaigns prompted behaviour change.\(^{19, 34, 35}\)
Thirdly, the introduction of smokefree policies (2004) in indoor areas such as workplaces, restaurants etc., may have led to an overall reduction in smoking indoors, including homes and vehicles. This current study has shown a decline in unrestricted indoor and outdoor smoking, with one-third (31%) of homes being completely smokefree in 2008; consistent with earlier NZ and international research. However, about one-third of young people are still being exposed to SHS in their home, and a similar proportion while travelling in vehicles. Additionally, Māori and Pacific young people were significantly more likely to be exposed to SHS at home and while travelling in vehicles, compared with their NZ European counterparts; consistent with previous research.

Health promotion around SHS for Māori and Pacific peoples should be a priority for the future. Further, continuing to provide appropriate cessation support for Māori and Pacific people will assist with reducing SHS exposure among young people.

Given the links between SHS and poor physical and mental health, and the risk of young people becoming smokers, it is important that NZ continue to address the issue of SHS exposure. New Zealand research has shown support for smokefree homes and vehicles, it is important now as part of the Government’s goal of making NZ smokefree by 2025.

This study is subject to some limitations. The surveys provide a series of cross-sectional snapshots, but do not allow us to disentangle causal relationships between reduced exposure to SHS and smokefree homes. Further, the same questions were not always asked each year which makes some of the comparisons from year to year more difficult.

The use of self-reported smoking data is subject to biases, including inaccurate recall of SHS exposure and social desirability bias. One of the significant strengths of this study, however, is the series analysis of five waves of national survey data to understand the patterns over time in young people’s exposure to SHS in NZ. The surveys achieved relatively high participation rates and participants were representative of NZ students.

It is encouraging that this study found declining rates of SHS exposure for young people in their homes and while travelling in vehicles. Nevertheless, significant numbers of young people are still being exposed to SHS, with Māori and Pacific young people being particularly affected.

Although smokefree homes are increasing, and more families are implementing home smoking restrictions, efforts to reduce the rates of SHS exposure for our young people are needed through more intensive tobacco control measures. These might include extending initiatives to reduce smoking in various settings such as cars, parks, beaches and shopping areas, and the provision of continuing education about the adverse health effects of SHS.
Competing interests: None declared.

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References:


Benchmarking benzodiazepines and antipsychotics in the last 24 hours of life

Brian Ensor, Daphne Cohen

Abstract

Aim To document benzodiazepines and antipsychotics (BDZ/APS) given to patients in the last 24 hours of life to establish normal prescribing patterns in hospices across New Zealand (NZ).

Methods A cross-sectional benchmarking design with retrospective chart review was carried out across 14 NZ hospices. Data (n=351) on medication use and dosages was analysed for inter-hospice variability. Analysis was shared with participating hospices for reflection.

Results There are significant differences in how these predominantly sedative medications are used within hospices in NZ, though the reasons for this cannot be commented on in this study. Diagnosis, place of death and use of the Liverpool Care Pathway influence how medications are used.

Conclusion NZ hospices are willing to submit data to enable the description of usual medication use in NZ, and have established that variations in prescribing and administration exist. This enables self reflection on the variations and the establishment of an ongoing benchmarking exercise.

The use of benzodiazepines and antipsychotic (phenothiazines and butyrophenones) medication in the final 24 hours of life is common within palliative medicine. These medications are used for a variety of indications, including nausea, delirium, anxiety, dyspnoea and seizures. However they are often grouped together as ‘sedative’ medications, regardless of the intent with which they are being used, as a side effect for most of these can be a degree of sedation.

Sedative drugs can be used as part of a targeted treatment to lower a patient’s consciousness in a titrated, proportional way for relief from intolerable and refractory symptoms. This specific use is known as palliative sedative therapy (PST), terminal sedation or palliative sedation.

Many ethical questions and controversy surround the use of PST but it has general acceptance within palliative medicine as an infrequently used end-of-life treatment option. Detailed guidelines are now available from the US and Europe, which includes the call for a regular review of practice for the purposes of improving quality of care (p921).

However BDZ/APS are frequently used at the end of life for many different and often much less clearly defined indications, including anxiolysis and terminal restlessness. For this latter indication, prescribing and administration practices may vary widely, and has both advocates and critics.
Where there is no universally agreed best practice, benchmarking is useful in enabling sometimes isolated health care providers ensure their practice is compatible with that of their colleagues\textsuperscript{8,9} and may help improve practice.\textsuperscript{10}

‘Normal’ prescribing of BDZ/APS in NZ is not well documented although there are some guidelines.\textsuperscript{11,12} Given this possible variation, hospices in NZ volunteered to submit data to establish a benchmarking cycle of these medications at the end of life in NZ. In this context, the benchmark is not against a standard or a centre of excellence, but rather it establishes a range and distribution of practice within which a hospice can orientate and understand its own practice.

This is the third cycle for benchmarking medication at the end of life, with data on opioid use previously published.\textsuperscript{13}

Method

Study design—A cross-sectional design with retrospective chart review was used. All hospices with inpatient beds (n=18) identified through the Hospice New Zealand (HNZ) website were invited to take part with a written invitation. An open invitation was also circulated to all hospices through the HNZ e-mail list. The written invitation included a document outlining the aims of the study and instructions on how to complete the electronic data collection template.

Hospices were asked to undertake a retrospective review of notes and drug charts of consecutive patients who died under their care in February and March 2008. The expectation was that this would provide at least 20 patients for each unit, recognising some small hospices would not meet this goal, and larger hospices would exceed it.

For admission to the study patients had to be under hospice care for at least the last 24 hours of their life and be 18 years or older. An accurate record of medications administered had to be available, which for many hospice teams confined the suitable patient pool to patients who had died in their Inpatient Unit (IPU).

The study variables were age, gender, diagnosis (coded using the UK palliative care minimum data set\textsuperscript{14} with the addition of Melanoma as a specific diagnosis), use of the Liverpool Care Pathway (LCP) and place of death (Inpatient Unit (IPU), Aged Residential Care (ARC), public hospital or home).

The template allowed for documentation of each medication used, the route of administration, and the total amount of medication administered in the 24 hours before death. For continuous subcutaneous medication or long-acting medication which was either started or changed during the last 24 hours, pro-rata calculation was used to ascertain the actual dosage delivered. Other medications given for symptom management and any comments thought to be relevant were also recorded.

The templates were collated, and the initial analysis shared with the contributing hospices for comment and correction. The final analysis was returned to each hospice containing their own analysed data, enabling them to compare medications and dosages used with the rest of NZ.

Analysis—Data was anonymised by allocating each hospice a number, and entered into PASW (Previously SPSS) Version 18.0 for statistical analyses. This included descriptive analysis, then analysis of variance looking for differences in practice between hospices. A log transformation of the dosage data was used to more approximate a normal distribution, and to exclude ‘nil’ dosages from the calculation of median dosages. A Haloperidol Equivalent Daily Dosage (HEDD) as described by Hui\textsuperscript{15} was used to combine haloperidol and levomepromazine (Nozinan™) as a single dosage figure.

\begin{equation}
\text{HEDD} = \text{total haloperidol dosage (mg) by any route + oral levomepromazine dosage (mg) \times 8/300 + parenteral levomepromazine dosage (mg) \times 8/100.}
\end{equation}

To facilitate an easy visual comparison between hospices, a drug ‘footprint’ was devised for both benzodiazepines and antipsychotics which records the percentage of patients in each hospice receiving a particular medication or no medication. Only the occurrence of use is displayed, regardless of the frequency or dosage of each medication administered to a patient.

Ethics—A certificate of approval was obtained from the New Zealand Health and Disability Ethics Committee (Central Regional Ethics Committee). Further ethical approval was not required for this retrospective study.
Results

Fourteen hospices across rural and urban NZ contributed data on 351 patients. There were 181 males and 170 females, with a mean age of 70 (range 21–96). 64 patients died at home, 6 in a public hospital, 251 within a hospice inpatient unit and 30 in an ARC setting. (Figure 1).

Figure 1. Percentages of patient data for each place of death over 14 hospices

302 patients (86%) died of cancer-related diseases and 49 (14%) died of non-malignant disease. The most common cancers were gastrointestinal (24%), lung (17%), prostate and breast (both 7%) and melanoma (6%), while notable non-malignant diseases included chronic respiratory disease (4%) and heart failure (3%).

Benzodiazepines included midazolam, clonazepam, and flunitrazepam, with single uses of diazepam and lorazepam. Antipsychotics were commonly haloperidol and levomepromazine. Quetiapine and risperidone were used infrequently. Phenobarbitalone was used once. Separate footprints for benzodiazepines and for antipsychotics have been generated (Figures 2 and 3).

Seventy-five percent of patients overall received a benzodiazepine. Midazolam was the most commonly used, although flunitrazepam was preferred at one hospice. The percentage of patients in each hospice receiving either midazolam or flunitrazepam in the last 24 hours of their life varied from 40%–87%. If any benzodiazepine was included, percentages ranged from 45%–93% (Figure 2).

Up to 39% of patients at each hospice received more than one benzodiazepine, with a median of 5%. The combination of benzodiazepines was always midazolam and clonazepam apart from two instances of midazolam and flunitrazepam.
Overall 62% of patients received an antipsychotic, with levomepromazine used more frequently than haloperidol (147 vs 94 patients). There was a range in the incidence of the use of any antipsychotic from 30% up to 97% between hospices (Figure 3). Up to 35% of patients at a hospice received the combination of both haloperidol and levomepromazine with a median of 2.5%.
About three-quarters of patients receiving levomepromazine were administered 12.5 mg or less in 24 hours (74%), 13% received over 25 mg.

**Dosage of medications**—Table 1 shows the range, median and mean for dosages of the five principal medications.

**Table 1. Dosage descriptors**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Range (mg)</th>
<th>Median (mg)</th>
<th>Geometric mean (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Midazolam</td>
<td>1–118</td>
<td>15</td>
<td>20.7</td>
</tr>
<tr>
<td>Flunitrazepam</td>
<td>0.5–96</td>
<td>12</td>
<td>20.5</td>
</tr>
<tr>
<td>Clonazepam</td>
<td>0.125–5</td>
<td>1</td>
<td>1.3</td>
</tr>
<tr>
<td>Haloperidol</td>
<td>0.1–10</td>
<td>2.5</td>
<td>2.73</td>
</tr>
<tr>
<td>Levomepromazine</td>
<td>0.1–275</td>
<td>12.5</td>
<td>21</td>
</tr>
</tbody>
</table>

When comparing dosages across patients who died in the different hospice IPUs, there is a significant variation between the 14 institutions in midazolam and HEDD dosages (Table 2).

**Table 2. ANOVA using hospice as dependant factor**

<table>
<thead>
<tr>
<th>Variables</th>
<th>df</th>
<th>F value</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Midazolam</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All deaths</td>
<td>208</td>
<td>1.971</td>
<td>0.025</td>
</tr>
<tr>
<td>Deaths in IPU</td>
<td>156</td>
<td>1.880</td>
<td>0.037</td>
</tr>
<tr>
<td>HEDD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All deaths</td>
<td>219</td>
<td>4.203</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Deaths in IPU</td>
<td>162</td>
<td>1.916</td>
<td>0.032</td>
</tr>
</tbody>
</table>

HEDD=haloperidol equivalent daily dosage; IPU=Inpatient Unit; df=degrees of freedom.

**Table 3. (Bivariate) comparisons of midazolam dosage**

<table>
<thead>
<tr>
<th>Midazolam</th>
<th>Geometric mean Midaz (mg)</th>
<th>N</th>
<th>df</th>
<th>F value</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>IPU death</td>
<td>14.8</td>
<td>157</td>
<td>208</td>
<td>7.950</td>
<td>0.005</td>
</tr>
<tr>
<td>Death not in IPU</td>
<td>9.8</td>
<td>52</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>13.1</td>
<td>106</td>
<td>208</td>
<td>0.050</td>
<td>0.823</td>
</tr>
<tr>
<td>Female</td>
<td>13.6</td>
<td>103</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malignant (IPU)</td>
<td>15.2</td>
<td>135</td>
<td>156</td>
<td>0.847</td>
<td>0.359</td>
</tr>
<tr>
<td>Non-malignant (IPU)</td>
<td>12.5</td>
<td>22</td>
<td>156</td>
<td>0.824</td>
<td>0.001</td>
</tr>
<tr>
<td>Died on LCP*</td>
<td>15.3</td>
<td>46</td>
<td>156</td>
<td>10.824</td>
<td>0.001</td>
</tr>
<tr>
<td>Died off LCP*</td>
<td>9.5</td>
<td>24</td>
<td>156</td>
<td>0.643</td>
<td>0.424</td>
</tr>
<tr>
<td>Died in IPU using LCP</td>
<td>15.8</td>
<td>70</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Died in IPU not using LCP</td>
<td>14.0</td>
<td>87</td>
<td>156</td>
<td>0.643</td>
<td>0.424</td>
</tr>
</tbody>
</table>

*Includes only hospices using the LCP; LPU=Liverpool Care Pathway; IPU=Inpatient Unit; df=degrees of freedom.
Some of this variation will come from the significant difference in the dose of midazolam used by patients dying in an IPU when compared with dying in places other than an IPU, (Table 3), however when considering just patients who died in IPUs, there is still a significant difference between hospices. To take this variation out of the analyses, most analyses will use data just from patients dying in IPUs.

When looking at IPU patients, there is a difference in midazolam dose between those on the LCP and those not on the LCP. However hospices that used the LCP were not using different dosages of midazolam overall. Diagnosis in IPU patients (malignant vs non-malignant) did not alter the dosage of midazolam, and gender for all patients did not alter the dosage.

Table 4. (Bivariate) comparisons of haloperidol equivalent daily dosage (HEDD)

<table>
<thead>
<tr>
<th>HEDD</th>
<th>Geometric mean HEDD</th>
<th>N</th>
<th>df</th>
<th>F value</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>IPU death</td>
<td>1.42 mg</td>
<td>163</td>
<td>219</td>
<td>6.342</td>
<td>0.013</td>
</tr>
<tr>
<td>Death not in IPU</td>
<td>0.99 mg</td>
<td>57</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male (all)</td>
<td>1.28 mg</td>
<td>108</td>
<td>219</td>
<td>0.053</td>
<td>0.819</td>
</tr>
<tr>
<td>Female (all)</td>
<td>1.32 mg</td>
<td>112</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malignant (all)</td>
<td>1.34 mg</td>
<td>193</td>
<td>219</td>
<td>7.736</td>
<td>0.189</td>
</tr>
<tr>
<td>Non-malignant (all)</td>
<td>1.03 mg</td>
<td>27</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Died on LCP*</td>
<td>1.82 mg</td>
<td>72</td>
<td>137</td>
<td>13.006</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Died off LCP*</td>
<td>1.03 mg</td>
<td>66</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IPU in LCP hospice</td>
<td>1.64 mg</td>
<td>92</td>
<td>162</td>
<td>5.298</td>
<td>0.023</td>
</tr>
<tr>
<td>IPU in non-LCP hospice</td>
<td>1.18 mg</td>
<td>71</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Includes only hospices using the LCP; IPU=Inpatient Unit; df=degrees of freedom.

Using the HEDD, patients dying outside the IPU received a lower mean dose of antipsychotics (Table 3). Comparison again showed significant differences between the 14 hospices in the use of antipsychotics (Table 1), which remained when only those who died in an IPU were analysed. In hospices that used the LCP, patients who died on the LCP received a higher mean dose of antipsychotic than those who were not on the LCP.

In contradistinction to the pattern of benzodiazepine administration, hospices using the LCP were using a higher median dosage of antipsychotics than those who had not adopted the LCP. Again neither diagnosis nor gender made a significant difference to the dosage of antipsychotic for IPU deaths.
Discussion

The purpose of this study is to provide data for hospices to reflect on their own practice in the context of NZ. The importance of having national data is demonstrated by Claessens' comprehensive review of the international literature on palliative sedation, which notes the inconsistencies in definitions of sedation, and significant variations in prevalence, indications and dosages across the literature.

Variations in practice occur between countries, between centres in the same country, and within the same centre over time. The interpretation and comparison of studies is therefore difficult as they are reporting on different patient populations, with variations in staff training, skills and resources and in the context of different cultural practices and priorities. Because of this, the usefulness or validity of applying this literature directly to NZ is questionable, other than demonstrating the potential scope of variation in the use of these medications.

This collection of data has demonstrated significant differences in medications (both benzodiazepines and antipsychotics) being used across the country. The footprints give an idea of the different frequencies of medication use, which are not amenable to statistical analyses because of the small numbers from each hospice. However, they do provide a useful start for reflection by each hospice on how their prescribing sits compared to their peers. The dosage data is robust enough for analyses, and this is discussed below.

As a country, the frequency of benzodiazepine use in NZ is as high as any international reports. The footprint for benzodiazepines shows the predominant use of midazolam as the first line benzodiazepine at the end of life, which is in line with international recommendations. The dosages are skewed as expected towards the lower amounts.

In NZ small doses of a benzodiazepine are often used for anxiolysis or to treat terminal restlessness. How significant these dosages are in lowering consciousness significantly over the 24 hours is debatable. Sykes and Thorns arbitrarily called a midazolam dosage of over 10 mg in 24 hours ‘sedative’, which would apply to 60% of NZ patients receiving midazolam. This is a similar percentage to that recorded in a UK hospice by Stephenson. Seventeen percent of patients on midazolam (10% of the total patient pool) received doses above 30 mg. When the intent is lowering of consciousness, recommendations for PST start at 0.4 mg/hr (10 mg/day) and are expected to reach as high as 20 mg/hr (480 mg/day). Midazolam dosages did not correlate to diagnosis, unlike opioid dosages which are higher in malignant disease. Patients dying in IPUs received higher mean dosages of midazolam. An assumption can be made that those dying in IPUs have higher symptom burdens and more complex needs than those dying elsewhere, but this remains an assumption.

Patients on the LCP tended to have higher dosages of midazolam, but as there was no difference in dosages between hospices that used the LCP and those that did not, it is likely that the differing dosages are a function of the disease trajectory (less rapid and more expected) of patients who are started on the LCP, rather than an effect of the LCP per se. The fact that the introduction of the LCP has no effect on the mean...
dosage of midazolam used in a hospice is supportive of the idea that the LCP is not a change in practice for hospices, but rather incorporates existing practice.

The variation between hospices of midazolam dosages is not explained, and may provoke some reflection and discussion amongst hospices. There is no clear reason for variations in midazolam dosages in the literature, although it is recognised that individual responses to these medications vary widely, particularly in the presence of renal and hepatic failure. Morita\textsuperscript{27} investigated causes for the variations in midazolam dose, but the identified factors of icterus, age, pre-exposure to midazolam and length of sedation only accounted for 36% of variation.

The use of flunitrazepam was quite confined at the time of the study, and appears less frequently in the literature. Bioequivalence may be about 5 to 10 times the potency of midazolam, with a longer half life.\textsuperscript{28,29} Although it is a hypnotic it may also have a very useful role as an anxiolytic in a palliative care setting, and perhaps as a respiratory depressant.\textsuperscript{28,30,31} European guidelines recommend starting with a bolus of 1–2 mg, then 0.2–0.5 mg/hr\textsuperscript{2}.

Similarly to midazolam dosages, antipsychotic dosages varied between hospices. They have their own specific indications, perhaps more clearly defined than benzodiazepines.

Haloperidol is a major tranquilizer and not a sedative.\textsuperscript{35} It is the drug of choice for delirium, which affects up to 85% of the hospice population in the last weeks of life,\textsuperscript{15,32} and for nausea, which afflicts up to 70% of cancer patients in the last months of life.\textsuperscript{33,34} For these common indications, there is a range of recommended dosages. When treating delirium, 0.5 mg to 2 mg every 2 to 12 hours is reasonable.\textsuperscript{32} A US panel of end-of-life experts recommend a usual maximum dose of 3 mg/day,\textsuperscript{35} though there is some debate whether this is high enough.\textsuperscript{15,36} When treating nausea, haloperidol is generally used in smaller dosages, commonly 0.5 mg to 3 mg in 24 hours.\textsuperscript{33,34,36} For any indication in this study the dosages were not large, only 3% of patients who received haloperidol had a dose over 5 mg, the largest being 10 mg.

Levomepromazine, an older typical antipsychotic, also has dual indications. It was for some years widely used as a sedative medication with analgesic properties for restlessness in the terminally ill, but more recently has been used for its antiemetic effects in a much smaller dosage.\textsuperscript{37,38}

Antipsychotic dosages for ambulant patients starting at 25–50 mg a day and increase up to 300 mg, while antiemetic dosages are as low as 2.5 mg a day and seldom above 25 mg a day. When using levomepromazine for its sedative properties, this would reasonably be within the range of 25 mg to 150 mg a day\textsuperscript{11}. This study demonstrates that when levomepromazine is prescribed, for 87% it is at the primarily antiemetic range of 25 mg or less, though for 4% of patients it is at a significantly sedative dose of >50 mg.

When these two medications were combined as an HEDD, it was noted that there was a variation in dosage for IPU deaths amongst the hospices (p=0.032). It did not vary with diagnosis (p=0.643), but did with death on the LCP (p=0.002), and unlike benzodiazepines, dosages were generally higher in hospices that were using the LCP. (p=0.002; 1.2 vs 1.6 mg) Again, these variations are not immediately explainable. It
may be relevant that the LCP recommends haloperidol for nausea at the end of life, rather than metoclopramide which is otherwise a very commonly used antiemetic.

For these medications as a group, therefore, there is demonstrable variation of practice within NZ. Given international variations, and varying indications, this may be reasonable and expected, as long as practitioners within each community of practice are clinically astute and thoughtful in their practice. The onus is now on prescribers and those who administer and assess medication to reflect on what they do.

The dangers of uncritical use of sedative medication includes not recognising situations where more targeted intervention based on accurate diagnosis will alleviate symptoms, not recognising where non-pharmaceutical interventions may be more appropriate, or having insufficient communication between health professionals, the patient and the family regarding goals and unintended side effects of treatment.

**Conclusion**

A detailed analysis of this data was given back to the contributing hospices to enable practitioners and institutions to know and understand their current practice in the context of their peers. Participation in such a study is an indication of the need and willingness on the part of hospices to examine their practice, which in turn may increase the likelihood of changes in practice.

It shows that in NZ, as internationally, prescription and administration of BDZ/APS medications is a complex process. Whereas analgesia is titrated against pain, resulting in reasonably uniform dosages across hospices, the use of antipsychotic and sedative medication is subject to greater variability and subjective assessment.

It is important for those both prescribing and administering to be aware of factors which may influence their behaviour in any given clinical situation. This includes their own personal beliefs, skills and training, the prevailing culture of their community of practice, and the wishes and preferences of those whom they are caring.

There is no correct medication or dosage that can be applied universally, and medication may not always be the best response to a given situation. Good communication with the patient and family, and within a multidisciplinary team, is essential.

The scope of this study does not extend to identifying those factors or investigating the reasons behind this variability. However, having received this data, hospices and practitioners can (and have) embarked on discussion and reflection on their own practices for the care of the dying, informed by the knowledge of their use of various psychoactive medications. Although anonymised, there is potential for discussion between self-identified hospices who wish to compare practice directly.

These discussions may or may or not result in change in practice, which will be shown in the next cycle of benchmarking.
Competing interests: None declared.

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References:


Nurse titration clinics to achieve rapid control of blood pressure

Dominic Taylor, Veronica van der Merwe, Walter van der Merwe

Abstract

Aims To assess the effectiveness of a new hypertension clinic (in Auckland, New Zealand) using clinical nurse specialist appointments for drug titration.

Methods A new hypertension clinic was established at Waitemata District Health Board (DHB) in August 2010 using an initial registrar clinic appointment followed by fortnightly clinical nurse specialist appointments for drug titration. 50 GP-referred patients were prospectively audited and their outcomes compared to 50 patients seen in the physician hypertension clinic.

Results The comorbidities of the two groups were similar. 52–66% had the metabolic syndrome by IDF criteria. The mean number of clinic visits to discharge was not significantly different. The mean number of antihypertensive drugs at discharge was the same (2.8) for both clinics. There were significant reductions in systolic and diastolic blood pressures in both clinics, with a mean discharge blood pressure of 131/78 in the nurse clinic group.

Conclusions Nurse titration clinics are as effective as physician-only appointments in rapidly achieving target blood pressures.

Good long-term outcomes in hypertension depend on achieving target blood pressures, and, it is increasingly evident, doing so in a short period of time.1,9 In the VALUE2 and ASCOT3 trials, blood pressures attained at 3 months predicted long-term outcome. In addition, other trials, like ALLHAT4 have shown that blood pressure differences in treatment groups achieved in the first few months of a five year trial tended to persist throughout the trial, despite repeated encouragement of investigators to achieve blood pressure control.

The old adage “start low and go slow” with blood pressure medication mitigates against an aggressive approach to blood pressure management and encourages “clinician inertia” and results in patients being seen on multiple occasions with blood pressure not at target but not having their medications adjusted.5 Part of the problem is reluctance of clinicians to add medications and titrate doses upwards is a (usually misplaced) concern about inducing unacceptable hypotension,1 and also a reluctance to follow the JNC-7 guideline9 which suggests starting (previously untreated) patients with stage two hypertension (systolic ≥ 160 mmHg ± diastolic ≥ 100 mmHg) on combination therapy de novo.

Another impediment to timely blood pressure medication titration may be the need for check laboratory tests after the addition or increase in dose of RAS-blockers (angiotensin converting inhibitors/ ACE-inhibitors and angiotensin receptor blockers/ARBs) and diuretics, with the small amount of additional effort and follow-
up that that entails. There may also be patient-related factors, for example the cost and inconvenience of attending for multiple medication adjustments with their doctor.

The Waitemata Hypertension Clinic has been operating since March 2009. At one ½ day clinic per week it sees mostly GP referrals of patients with difficult or resistant hypertension, and over 300 new referrals have been seen to date. A minority of referred patients have secondary causes of hypertension requiring specialised investigation, but in the majority, the main function of the clinic is optimisation of blood pressure with the use and titration of complex multi-drug regimens. Multiple visits are often required to achieve target blood pressure, and because of pressure on clinic space these repeat visits are either far apart, or take place at the expense of valuable new patient slots.

A potential solution to this is the use of nurse or pharmacist titration clinics with which there is experience in the United States and elsewhere. The experience in some large organisations which use nurse titration clinics (e.g. Kaiser Permanente HMO in the USA) is that compliance rates are high and blood pressure control rates are excellent (80%).

In New Zealand, Clinical Nurse Specialists (CNS) are trained to provide care within a specialist area of practice, within Registered Nurse scope. This may include delegated medical responsibilities, diagnostics, and implementation of treatment protocols. Nurse-led clinics have proven beneficial in other specialties in New Zealand and have been associated with improved patient outcomes.

Nurse specialist salaries in New Zealand are approximately half of registrar salaries and one third of medical specialist salaries—if similar outcomes can be achieved in equivalent numbers of nurse-led vs doctor clinic visits, they would clearly be cost-effective. The Waitemata Renal Service appointed a Hypertension Clinical Nurse Specialist (CNS) in July 2010 and one of her roles was to establish blood pressure medication titration clinics. We audited the first 50 GP-referred patients attending these clinics, and compared their outcomes to 50 patients seen and followed up exclusively at the physician clinic.

We aimed to show that the new clinic model was at least equivalent to the previous clinic model in terms of timely achievement of blood pressure targets, and more efficient in terms of physician time. We also wished to compare number of clinic visits required to achieve target blood pressure with the two models and assess patients’ satisfaction with the new model.

**Methods**

50 consecutive patients referred from general practitioners with difficult or resistant hypertension were seen for their first clinic visit by a senior registrar. At this visit, a full history and physical examination were undertaken. The examination included careful resting blood pressure measurement with a manual oscillometric sphygmomanometer, according to the JNC-7 guideline.

Special investigations were ordered as appropriate and referrals made to smoking cessation and nutritional services if needed. In addition an initial adjustment was made to their antihypertensive medication. Other drugs, specifically aspirin and statins were added as appropriate. Cases were discussed with the consultant as required.

Patients’ next and subsequent visits were exclusively at the Hypertension CNS Clinic. They were seen at 2-4 weekly intervals until the blood pressure was at target (or as close to that as deemed achievable) on a regimen with which the patient felt comfortable.
At the initial nurse titration clinic, patients’ blood pressure was checked again according to JNC-7 guidelines, using a Microlife automated office blood pressure monitor (Microlife AG, Widnau, Switzerland). Weight, height and abdominal circumference were measured. Obstructive sleep apnoea questionnaires were performed as appropriate.

Education was provided on hypertension, cardiovascular risk, lifestyle matters, and drug-related issues particularly potential side effects. Antihypertensive medication adjustment was made according to pre-arranged algorithms. Follow up laboratory tests were performed according to protocol (for example addition of, or increase in the dose of ACE-inhibitor, ARB, or diuretic required urea, creatinine and electrolytes to be rechecked 2–3 weeks after the change). A further appointment was made for two weeks’ time if BP was not at target.

Cases were discussed at a weekly meeting between the CNS and the registrar and/or consultant, or ad hoc if needed (e.g. for deviations from the algorithms). Prescriptions were provided by the medical team. Written communication was made with the primary care physician at each visit, and once at target blood pressure a written doctor summary was provided outlining recommendations for ongoing treatment.

Data on patient demographics, comorbidities, medication changes, secondary causes of hypertension and blood pressures were recorded prospectively. Similar data from the 50 GP-referred patients seen in the physician hypertension clinic immediately prior to introduction of the new clinic were collected retrospectively, and compared to the study data.

Figure 1. Structure of new clinic model
Results

50 patients were studied from each group. Their demographic details are shown in Table 1.

Table 1. Demographic details

<table>
<thead>
<tr>
<th>Variables</th>
<th>Physician clinic</th>
<th>Nurse-led clinic</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>17 (34%)</td>
<td>23 (46%)</td>
</tr>
<tr>
<td>Female</td>
<td>33 (66%)</td>
<td>27 (54%)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>mean (range)</td>
<td></td>
</tr>
<tr>
<td>56 (26–85)</td>
<td></td>
<td>54 (19–89)</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NZ European</td>
<td>24</td>
<td>28</td>
</tr>
<tr>
<td>Other European</td>
<td>13</td>
<td>8</td>
</tr>
<tr>
<td>NZ Maori</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Chinese</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Samoan</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>East Asian</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Middle Eastern</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>South Asian</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Mixed race</td>
<td>0</td>
<td>2</td>
</tr>
</tbody>
</table>

Their comorbidities are shown in Table 2.
Table 2: Comorbidities

<table>
<thead>
<tr>
<th>Variables</th>
<th>Physician clinic</th>
<th>Nurse clinic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of hypertension &gt;10 years</td>
<td>20</td>
<td>6</td>
</tr>
<tr>
<td>Diabetes Type 2</td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td>Smoking ex-smoker</td>
<td>5</td>
<td>9</td>
</tr>
<tr>
<td>Smoking current smoker</td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>Microalbuminuria</td>
<td>13</td>
<td>13</td>
</tr>
<tr>
<td>eGFR mean</td>
<td>73ml/min</td>
<td>74ml/min</td>
</tr>
<tr>
<td>Metabolic syndrome</td>
<td>26</td>
<td>34</td>
</tr>
</tbody>
</table>

Of the current smokers, the mean number of pack-years was 22 for the physician group, 18 for the nurse group. The number of patients with the metabolic syndrome, defined by IDF criteria, was higher in the nurse clinic group.

There was no significant difference in the number of clinic visits required to reach target blood pressure (Table 3; p=0.16). The mean number of antihypertensive drugs at discharge was the same for both groups.

Table 3. Visit number and drugs prescribed

<table>
<thead>
<tr>
<th>Variables</th>
<th>Previous patients</th>
<th>Nurse-led clinic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean number of visits(range)</td>
<td>registrar/physician nurse total</td>
<td>3.6 (1–10) - 3.6 (1–10)</td>
</tr>
<tr>
<td>Mean number of drugs at first visit</td>
<td>2</td>
<td>2.2</td>
</tr>
<tr>
<td>Mean number of drugs at discharge</td>
<td>2.8</td>
<td>2.8</td>
</tr>
</tbody>
</table>

Mean blood pressure reductions are shown in Table 4.

Table 4: Blood pressure (BP) reduction by clinic

<table>
<thead>
<tr>
<th>Variables</th>
<th>Previous patients</th>
<th>Nurse-led clinic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean BP (mmHg) at first visit on discharge</td>
<td>154 87</td>
<td>161 92</td>
</tr>
<tr>
<td>Mean BP (mmHg)</td>
<td>134 74</td>
<td>131 78</td>
</tr>
<tr>
<td>Mean BP reduction (mmHg)</td>
<td>20 13</td>
<td>30 14</td>
</tr>
</tbody>
</table>

“Paired-samples” t-tests were performed to compare systolic and diastolic blood pressures at presentation and at discharge. There were significant reductions in both measurements for both clinics (table 4; p<0.01), and the reduction in systolic BP was significantly larger in the nurse clinic group (p=0.02).
Figure 3. BP measurements at presentation to, and at discharge from each clinic.

The box-and-whisker plots in Figure 5 illustrate the range of blood pressures measured at presentation to, and discharge from, each clinic. The box represents the interquartile range (IQR), the line dividing the box the median value. The whiskers indicate values 1.5 IQR lower than the first quartile and 1.5 IQR higher than the third quartile, and dots any outlying values.

The classes of drugs added in each group are shown in Figure 4. The drugs added in each clinic were similar. The number of patients discharged on the maximum dose of a thiazide diuretic or DHB calcium channel blocker was higher in the nurse clinic than the physician clinic (Figure 5).
Figure 4. Percentage of patients taking each class of drug at presentation, and at discharge or last follow-up

**Physician-only clinic**

**Nurse titration clinic**
Discussion

We trialled a new model of hypertension clinic using an initial physician visit, followed by nurse titration and education clinics, with the aim of reducing the load on the physician hypertension clinic, and achieving target blood pressures quickly and efficiently.

The groups compared were of a similar demographic, with similar comorbidities. The physician group had a longer duration of hypertension.

We found no significant difference in the total number of clinic visits needed to achieve target blood pressure between the two groups.

Blood pressures at discharge were similar between the groups, with significantly lower systolic BP reduction in the nurse clinic group. The mean number of drugs used per patient was the same.

Patients were asked to complete a questionnaire following their last visit. Feedback was uniformly positive. The majority emphasised the benefits of the extra time spent on education, which seems to have been a factor encouraging compliance both with medication and with lifestyle modifications. Patients also stated that the relaxed, unhurried atmosphere of the nurse clinic encouraged free discussion and questions, in contrast to doctor clinics where time pressure is often evident.
This model has the advantage of an initial physician assessment, and ongoing background supervision. However, because physician clinic visits are reduced by more than 2 for each patient, more new patients are able to be put through the clinic in a timely fashion (two twenty minute follow-up visits saved makes one 40-minute new patient clinic slot).

Additionally, cost-effectiveness of nurse-led clinics is evidenced by equivalent outcomes to doctor-only clinics in similar numbers of visits, given the considerably lower hourly cost of nurse specialists compared with doctors. Other advantages include accurate, unhurried electronic blood pressure measurement in the nurse clinic, and liberal time for education which is important for long-term medication compliance.14

In conclusion, hypertension nurse-specialist clinics may be a useful and cost-effective tool for management of GP-referred patients with difficult or resistant hypertension. We plan to widen the scope of the hypertension titration clinics to Nephrology patients seen in our department. We plan to encourage the development of similar projects in primary care to allow easier patient access. We continue to prospectively audit the process.

Competing interests: None declared.

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References:


Validation of the Edinburgh Postnatal Depression Scale (EPDS) as a screening tool for postnatal depression in Samoan and Tongan women living in New Zealand

Alec J Ekeroma, Bettina Ikenasio-Thorpe, Sara Weeks, Jesse Kokaua, Kasalanaita Puniani, Peter Stone, Siale A Foliaki

Abstract

Aim To validate the EPDS as a screening tool for postnatal depression in Samoan and Tongan women living in New Zealand.

Methods 85 Samoan and 85 Tongan women who delivered babies at Middlemore Hospital from February 2009 to June 2010 completed the EPDS questionnaire and from 4 weeks after delivery followed by an interview using a Composite International Diagnostic Interview (CIDI) within 4 weeks of the EPDS completion.

Results The EPDS in English, Tongan and Samoan languages is a valid and consistent tool for screening for PND in Samoan and Tongan women. A cut-off score of ≥10 for Tongan and ≥11 for Samoan women gave the best sensitivity (80%) and specificity (80%) combination whereas a higher cut-off of ≥16 for Tongan and ≥17 Samoan women gave the best positive predictive value (82%) and negative predictive value (86%) for serious depression. The lower cut-off scores correctly diagnosed 82% and the higher cut-offs more than 87% of women with serious depression.

Conclusion The EPDS was an acceptable and valid tool for PND screening in English, Samoan and Tongan languages amongst Samoan and Tongan women. The cut-offs for PND screening were dissimilar in the two groups with a ≥10 for Tongan and ≥11 for Samoan women. A higher cut-off of ≥16 for Tongan and ≥17 for Samoan women improves the predictive value of the instrument.

Postnatal depression (PND) is a serious public health issue and more so in women of Pacific ethnicity in New Zealand (NZ).¹² Pacific women have a higher fertility rate, most are untreated in the community; and depression is higher in NZ-born women than those born in the Islands.³⁻⁵

PND causes major maternal morbidity resulting in dysfunctional relationships and with effects that continue to affect the woman’s children—deficits in social, psychological, and cognitive domains and an increased risk of suffering from child abuse.⁶⁻⁷

The prevalence of PND from an aggregation of worldwide studies averages 13% (of all pregnancies)⁸ but the only study specifically on Pacific women found a prevalence of 16.4%.¹ The study cohort of 1376 Pacific women, in the Pacific Island Family Study (PIF study), found a statistically significantly difference in prevalence rates of 30.9% in Tongan women and 7.6% in Samoan women.

The PIF study used the Edinburgh Postnatal Depression Scale (EPDS), a 10-item self-report questionnaire that was developed in 1987,⁹ and has been translated into many
languages and used in many prevalence studies. Even though the EPDS had also been used in two other NZ studies,\textsuperscript{10,11} it had not been validated in Pacific or NZ populations. The PIF study administered the EPDS as an interview and “a score above 12 is widely used to indicate the presence of probable depressive disorder”.\textsuperscript{1}

The EPDS has been validated in more than 25 different ethnic groups and populations.\textsuperscript{12–14} A review of 37 validation studies of the EPDS showed a highly variable sensitivity from 34%–100% and a specificity of 44%–100%,\textsuperscript{12} therefore supporting several recommendations that validation precede clinical use in culturally diverse populations.\textsuperscript{9,15}

The purpose of this study was to validate the EPDS in Samoan and Tongan women as a pre-requisite to repeating a prevalence study. These two population groups make up 65% of all Pacific women residing in New Zealand.\textsuperscript{16}

Materials and Methods

Background—This prospective cohort study was approved by the Northern “X” Ethics Committee and was conducted at Middlemore Hospital in Auckland, New Zealand. It is the referral hospital of the Counties Manukau District Health Board (CMDHB) with a catchment population of 500,000 that includes about 36% of all 250,000 people of Pacific ethnicity in NZ.

Questionnaire—The EPDS is a commonly used screening tool and rates each of the 10 items on a four-point scale (0-3), giving a maximum score of 30. A score of \( \geq 13 \) has been used in previous prevalence studies signifying serious PND whereas women with scores of 10 to 12 were considered to have mild depression. A woman with a score of 0 to 9 was considered not depressed. The EPDS has been found to be acceptable to women\textsuperscript{17} and a useful tool in cross-cultural research on depression.\textsuperscript{18}

The EPDS was translated into the Samoan and Tongan languages and then independently back-translated, by a professional translation service. The translated versions were checked by clinical researchers AE (fluent in Samoan) and SF (fluent in Tongan) for appropriateness of language and meaning. Agreement between depression resulting from the English and translated versions were also tested using a Kappa Statistic. Each translated and English version was then piloted by five Samoan and five Tongan women who were fluent in their language.

Sample and data collection—The sample size was determined from published validation methodology for the EPDS.\textsuperscript{19,20} Names and contact details of Samoan and Tongan women scheduled to deliver the following month were communicated to the research team comprising both a Samoan and Tongan researcher. Excluded from the study were women who were critically ill, had a stillbirth, serious complications in pregnancy or delivery and who were unable to provide informed consent. Women were initially contacted by posted information followed by a phone call. Interested women were recruited in a clinic or at their home. The women could choose to complete the EPDS in English or in their own language and were not offered any assistance in completing the questionnaire. The questionnaires were completed between 4 and 7 weeks after delivery.

An interview was then arranged with one of two psychiatrists who were blind to the EPDS scores and who had received accredited training in the use of the World Health Organization Composite International Diagnostic Interview (WHO-CIDI v3). The interview was completed within 4 weeks of completing the EPDS. Psychiatrist SF who was fluent in the Tongan language interviewed Tongan women and SW who was semi-fluent in Samoan interviewed the Samoan women. Interpreters were provided where requested. Women who were diagnosed with serious depression were referred to the Maternal Mental Health Service.

Statistical analysis—The raw data was entered into an Excel Spreadsheet (Microsoft Corporation), then analysed using Stata v8.0 software (Stata Corporation, Texas, USA). SAS v9.1 software was used to analyse the CIDI data and diagnoses. Cronbach's coefficient alpha was calculated to estimate the reliability of the EPDS by determining its internal consistency or the average correlation of items within the EPDS. A value of 0.70 is considered an acceptable level for consistency.\textsuperscript{21}

Kappa statistics was used to measure the level of agreement between the EPDS and CIDI standard. A Kappa of \( >0.6 \) is an indication of substantial agreement and \( >0.8 \) is an indication of an almost perfect
agreement.\textsuperscript{22} The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) as well as the receiver operating characteristics (ROC) were used to determine the global performance of the EPDS against the CIDI and the best cut-off points in predicting PND.

**Results**

During the study period, February 2009 to June 2010, a total of 170 women (85 Tongan and 85 Samoan) completed the study and their characteristics are compared in Table 1.

There was no significant difference between the Samoan and Tongan women with regards to age, parity, country of birth and mode of delivery. However, 51% of Tongan women completed the Tongan (rather than the English) questionnaire compared to 28% of Samoan women completing the Samoan questionnaire.

**Table 1. Characteristics of the Samoan (n=85) and Tongan (n=85) women participants**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Tongan No. (%)</th>
<th>Samoan No. (%)</th>
<th>P value (df, $\chi^2$)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age groups</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤19</td>
<td>6 (7)</td>
<td>1 (1)</td>
<td>0.22 (5–7.00)</td>
</tr>
<tr>
<td>20–24</td>
<td>16 (19)</td>
<td>20 (24)</td>
<td></td>
</tr>
<tr>
<td>25–29</td>
<td>25 (29)</td>
<td>19 (22)</td>
<td></td>
</tr>
<tr>
<td>30–34</td>
<td>19 (22)</td>
<td>23 (27)</td>
<td></td>
</tr>
<tr>
<td>35–39</td>
<td>16 (19)</td>
<td>17 (20)</td>
<td></td>
</tr>
<tr>
<td>≥40</td>
<td>3 (4)</td>
<td>5 (6)</td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>28.9 (6.38)</td>
<td>29.9 (6.6)</td>
<td></td>
</tr>
<tr>
<td><strong>Parity</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>23 (27)</td>
<td>24 (28)</td>
<td>0.97 (4–0.54)</td>
</tr>
<tr>
<td>2</td>
<td>18 (21)</td>
<td>17 (20)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>15 (18)</td>
<td>19 (22)</td>
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</tr>
<tr>
<td>4</td>
<td>10 (12)</td>
<td>10 (12)</td>
<td></td>
</tr>
<tr>
<td>≥5</td>
<td>18 (18)</td>
<td>14 (16)</td>
<td></td>
</tr>
<tr>
<td>Not known</td>
<td>1 (1)</td>
<td>1 (1)</td>
<td></td>
</tr>
<tr>
<td><strong>Birthplace</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NZ</td>
<td>26 (31)</td>
<td>24 (28)</td>
<td>0.64 (1–0.22)</td>
</tr>
<tr>
<td>Pacific Islands</td>
<td>59 (69)</td>
<td>61 (72)</td>
<td></td>
</tr>
<tr>
<td><strong>Delivery</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>70 (82)</td>
<td>64 (75)</td>
<td>0.89 (2–4.8)</td>
</tr>
<tr>
<td>Caesarean</td>
<td>14 (17)</td>
<td>15 (18)</td>
<td></td>
</tr>
<tr>
<td>Instrumental</td>
<td>1 (1)</td>
<td>6 (7)</td>
<td></td>
</tr>
</tbody>
</table>

$df=\text{degrees of freedom; } \chi^2=\text{Chi squared.}$

**Are the items of the EPDS internally consistent?**—The Cronbach’s alpha for all of the EPDS language versions and English version reached acceptable levels of reliability with adjusted overall alpha values of 0.86. The English version was consistent and there was little difference observed between Tongan and Samoan women.

**The EPDS scores**—About 1 in 5 (19%) of both Tongan and Samoan women had an EPDS score of 10–12. Using the cut-off points as recommended in the original EPDS
developed by Cox JL et al, the prevalence of serious depression (EPDS score ≥13) in this study would be 16.6% and for all depression (EPDS score ≥10) would be at 35.9%.

Serious depression was observed in 19% of Samoan and 13% of Tongan women with an EPDS score of 13 or more. The average EPDS score was 8.4 (SD of 5.2), Samoan average was 8.7 (SD 5.1) and Tongan was 8.1 (SD 5.1).

**The CIDI findings**—Of the 170 women interviewed, 36 (21.2%) had a positive CIDI, of which there was an equal number of Samoan and Tongan women. Of those women, 29 (17.1%) women had serious depression by interview (15 Samoan and 14 Tongan).

**How well does the EPDS compare with the CIDI diagnoses?**—The range of EPDS scores for women identified with a serious depressive disorder ranged from 5 to 24 with a median of 15 for both groups. A clear pattern of higher EPDS scores for those with diagnosed disorders was shown. The EPDS median for those with no depression and mild depression was similar in the Tongan women whereas for the Samoan group, the EPDS median was similar for serious depression. 62% of women with serious depression diagnosed by CIDI were identified by the EPDS.

If only serious depression was considered, the EPDS compared to the CIDI yielded a Kappa of 0.57, which indicates mild agreement. The prevalence of any diagnosed depression resulted in mild agreement (Kappa >0.5) for Tongan, Samoan and the combined results. A comparison between serious depression identified by the EPDS with the CIDI for serious depression resulted in mild agreement for both Tongan (Kappa = 0.58) and Samoan women (Kappa = 0.56).

The area under the ROC was equal to 0.8948 and 0.8308 for Samoan and Tongan women respectively (Figure 1). The probability that a randomly selected Samoan or Tongan woman with depression has a higher EPDS score than one selected without depression is more than 80%.

The EPDS score that gave the highest sensitivity (79%) and specificity (76%) for the Tongan women was ≥10. The best score for the Samoan women was ≥11, where both the sensitivity and specificity was 80% (Table 2).

An EPDS score of ≥10 gave a PPV of 46% and NPV of 93% for the combined EPDS in all three languages. However, an EPDS score at ≥ 16 gave a higher PPV (82%) and NPV (86%). An EPDS score of ≥16 for Tongan women gave the highest PPV and NPV whereas an EPDS score ≥17 for Samoan women resulted in an optimal PPV and NPV combination.
Figure 1: Receiver operator characteristics by ethnicity

Samoa

Tongan
Table 2. Sensitivity and specificity for depression assigned by different cut-off levels for Edinburgh Postnatal Depression Scale (EPDS) compared to diagnosed depressive disorder by ethnicity

<table>
<thead>
<tr>
<th>EPDS</th>
<th>Samoan</th>
<th>Tongan</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>C = 0.8948</td>
<td>C = 0.8308</td>
</tr>
<tr>
<td>Area under ROC curve</td>
<td>% Correct</td>
<td>% Correct</td>
</tr>
<tr>
<td>Cut-off</td>
<td>Sens</td>
<td>Spec</td>
</tr>
<tr>
<td>7</td>
<td>93%</td>
<td>44%</td>
</tr>
<tr>
<td>8</td>
<td>93%</td>
<td>49%</td>
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<tr>
<td>9</td>
<td>93%</td>
<td>64%</td>
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<td>10</td>
<td>87%</td>
<td>73%</td>
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<td>13</td>
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<td>20</td>
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Discussion

Previous validation studies had not found any issues with translating the EPDS into many languages and that was also our experience. The women found the EPDS in English and the translated versions easy to complete, confirmed by the Kappa Statistic of 0.85, which showed agreement between the English and Samoan or Tongan versions.

A significantly higher number of Tongan women preferred to complete the questionnaire in their language compared to Samoan women (p<0.003) which may mean that more Tongan women were more recent migrants.

This study found the EPDS had strong internal consistency by language and by ethnicity. It had greater consistency in those using the English version (alpha 0.85) than the Samoan version (alpha 0.75) and Tongan version (alpha 0.81). Questions 5, 8 and 9 had poor internal consistency in the Samoan EPDS and it was these three items that reduced the overall consistency of the Samoan version. The level of consistency however compares favourably with other validation studies with high Cronbach alphas, and is similar to the alphas found in the PIF study for Samoan and Tongan women.

The overall serious PND prevalence rate by CIDI was 17.1% and there was no statistically significant difference between the rates of Samoan (19%) and Tongan (13%) women. The serious PND prevalence rate of 17.1% found in our study was similar to the 16.4% prevalence found in the PIF study.

The difference in PND prevalence between Samoan and Tongan in the PIF study cannot however be explained by our findings. Methodological differences such as the administration of the EPDS by interview and by different interviewers in the PIF study may not give a full explanation. The significantly higher number of Tongan
women preferring the Tongan questionnaire suggests a higher number of them may be recent migrants and lower acculturation rates have been associated with a higher rate of depression. The difference in the EPDS cut-off points for depression between Samoan (≥11) and Tongan (≥10) women suggests that more Tongan women will have positive EPDS screening for depression given they have a lower EPDS cut-off than Samoan. Whether this difference will make a difference in PND depression prevalence between the Samoan and Tongan women will be difficult to say. The variation in cut-off scores between the different validation studies may be a reflection of the differing ethnic populations and sample characteristics of the various studied groups.

In our study, the best cut-off points for the scale were ≥10 (71%, 79%) for Tongan and ≥11 (80%, 80%) for Samoan women that gave the best sensitivity and specificity for those with postnatal depression. However, using these cut-off points gave a poor positive predictive value (PPV) and this was also found in other studies. Differences in PPV differ with the prevalence of depression which can vary between and within populations. Populations or groups with high rates of PND have better PPVs with the EPDS than those with lower prevalence of PND.

We have taken into account the prevalence rate of all PND and using the best positive and negative predictive values, alternative EPDS cut-off scores were determined. We found that the best cut-off scores were ≥16 for the English and Tongan versions (PPV 82% and 88%; NPV 86% and 88% respectively) whilst the Samoan version was ≥17 (PPV 84%, NPV 83%) for any depressive disorder.

A few validation studies have differentiated an EPDS score cut-off based solely on the sensitivity and specificity of the test or solely based on its PPV and NPV. In a systematic review of 37 validation studies, a cut-off score on the EPDS at 12/13 yielded a PPV of 17–100%. We feel that the two cut-off scores can be used simultaneously with the first being used for prevalence studies and the latter being used for clinical screening. The higher EPDS cut-off score ensures the screening test has the best performance by identifying most cases so that a diagnostic or/and therapeutic intervention could be offered.

The limitations of our study include the differing time points of administering the EPDS which was between 4 to 7 weeks postpartum and prevalence of PND by EPDS has been shown to change at different time points. The gap of up to 4 weeks between the EPDS completion and CIDI interview could have been shorter but the prevalence of diagnosed depression by CIDI should not differ as the instrument was designed to ascertain an episode of depression over a stated period.

The NZ Ministry of Health (MOH) has decided against a formal screening programme for PND following a decision of the British National Health Service citing evidence that the condition does not satisfy screening criteria. The MOH has decided instead to adopt the National Institute for Health and Clinical Excellence (NICE) guideline’s advice for the use of more focussed questioning in primary care, in the form of three questions. The routine use of the first three questions of the Patient Health Questionnaire (PHQ-3) has been promoted during the Well Child/Tamariki Ora programme, even though this tool had not been validated for PND screening in NZ and has had limited validation elsewhere.
Despite the recent recommendations by the NZ MOH, we propose that the EPDS is a valid and reliable tool for PND screening in Samoan and Tongan women and that its use should be continued in both primary and secondary care settings. Our findings suggest a cut-off score of ≥10 for Tongan and ≥11 for Samoan women was appropriate for screening whereas a cut-off of ≥16 for Tongan and ≥17 for Samoan was more appropriate where predictive value was important.

**Competing interests:** None declared.

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**Acknowledgement:** This study was supported by Mr Manu Sione (General Manager, Pacific Division of the CMDHB).

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**References:**

Is it NICE to monitor lithium routinely?
Andrew McKean, Jane Vella-Brincat

Abstract

Introduction Lithium has a narrow and well described therapeutic range.

Aim The aim of this study was to evaluate lithium blood concentration monitoring in Canterbury District Health Board (CDHB) and consider whether it meets the UK National Institute for Health and Clinical Excellence (NICE) standard (in lieu of more local standards).

Methods Lithium dispensing data for patients within the CDHB boundaries was combined with lithium blood concentrations for the period of 1 July 2009 to 30 June 2010 and the results analysed.

Results Lithium was prescribed for 1416 patients with a mean daily dose of 507 mg per day. 92% of patients in CDHB had had a lithium blood concentration performed at least once during the year. Twenty percent had had four or more lithium blood concentrations analysed. The mean (±95% CI) lithium blood concentration was 0.63 (0.62 to 0.64) mmol/L; the median (interquartile range) was 0.6 (0.43 to 0.80) mmol/L and the range was 0 to 2.8 mmol/L. The median (interquartile range) sampling interval was 35 (13–93) days. Sampling was performed approximately every 3 months (80 to 100 days) in 11 patients (<1%). Of those 56 patients that had a lithium blood concentrations >1.2 mmol/L only 7 patients had this repeated within 3 weeks.

Discussion In conclusion, lithium blood monitoring at CDHB did not achieve the NICE standard. This is in keeping with a number of other audits conducted of lithium blood monitoring.

Lithium is commonly used for the prophylaxis of bipolar affective disorder (BPAD) and in the treatment of moderate to severe mania. It has been used for more than sixty years since its role in BPAD was first described in 1949.1

Lithium has a narrow and well described therapeutic range. It is not metabolised, is excreted unchanged by the kidneys (fraction excreted unchanged 1) and has a half life of 21 hours. Lithium blood concentrations (LBC) are ideally taken just before the next dose. If this is not possible, samples should be taken at least 8 to 12 hours after a dose. Samples should ideally be performed at steady state. This is reached at 5 days on a maintenance dose. For maintenance therapy and acute mania lithium blood concentrations should be within the range of 0.4 to 0.8 mmol/L and 0.8 to 1.2 mmol/L respectively.2

Dose related adverse reactions to lithium usually occur at blood concentrations greater than 1.5 mmol/L. These include increasing anorexia, nausea, diarrhoea, muscle weakness, drowsiness, ataxia and tremor. At concentrations above 2 mmol/L increasing disorientation and seizures often occur which can progress to coma and death.3
Lithium is also subject to drug interactions. Drugs that impair the kidney’s ability to excrete sodium will also have a similar effect on lithium. Angiotensin converting enzyme (ACE) inhibitors, non-steroidal anti-inflammatory drugs (NSAIDs) and diuretics can all lead to elevated LBCs.  

Different formulations of lithium are not considered to be bioequivalent and inadvertent changing of formulations may lead to changes in LBCs.  

The UK National Institute for Health and Clinical Excellence (NICE) recently published standards for lithium monitoring. These state that patients should have a LBC performed at least once every 3 months and renal tests and thyroid function tests every 6 months.  

To encourage safe practice the NHS National Patient Safety Agency issued an alert in December 2009 requiring all health organisations in the United Kingdom to have a reliable system in place to ensure that these standards are being met.  

In this study we aim to examine lithium blood concentration monitoring in Canterbury District Health Board (CDHB) and consider whether it meets the UK National Institute for Health and Clinical Excellence (NICE) Standard (in lieu of local standards).  

**Methods**  
Lithium dispensing data for patients within the CDHB boundaries were retrieved from the national database (NZ Health Information Service) via CDHB Planning and Funding for the period of 1st July 2009 to 30 June 2010. LBCs were retrieved for the same period from all three of the laboratories in CDHB (Canterbury Health Labs; MedLab South; Southern Community). The results were combined and analysed on Microsoft Excel™ software.  

**Results**  
Lithium was prescribed for 1416 patients during the period of 1 July 2009 to 30 June 2010 with a mean daily dose of 507 mg per day.  

1342 patients had at least one sample taken. 39 of these patients were excluded from the analysis as the patient identification had not been completed correctly leaving 1303 patients. As 1416 patients were prescribed lithium and 1303 patients had at least one sample, 92% of patients in CDHB had had a LBC performed at least once during the year. Twenty percent had had four or more LBCs analysed.  

The median (interquartile range) LBC was 0.6 (0.43 to 0.80) mmol/L (mean (95% CI) = 0.63 (0.62 to 0.64) mmol/L; range = 0 to 2.8 mmol/L). A total of 136 samples (from 56 patients) were above the upper end of the therapeutic range of 1.2 mmol/L. 690 samples were between 0.8 and 1.2 mmol/L (the range for acute mania); 2687 samples were between 0.4 and 0.8 mmol/L (the range for maintenance therapy); 610 samples (from 378 patients) were below 0.4 mmol/L (subtherapeutic) and 19 results were incomplete.  

In those patients with LBCs > 1.2 mmol/L, 7 out of the 56 patients were retested within 3 weeks.  

The median (interquartile range) sampling interval was 35 (13–93) days. The median (interquartile range) number of samples per patient was 2 (1 to 3). The range was 1 to 23 samples per patient.
The median (interquartile range) LBC was from 0.57 (0.4 to 0.7) mmol/L for those patients who had one sample and 0.75 (0.58 to 0.92) mmol/L for the patient who had 23 samples taken.

Likewise the median (interquartile range) interval between samples was 149 (78 to 196) days for those sampled twice to 6 (4 to 8) days for the patient who had 23 samples taken.

Sampling was performed approximately every 3 months (80 to 100 days) in 11 patients (<1%). When the interval was widened to 60 to 130 days this increased to 42 patients (3%). 85 patients (6%) had 1 or 2 dosing intervals that were approximately 3 months (80 to 100 days) apart.

Discussion

A recent retrospective UK audit of 2976 patients taking lithium found that 30% of patients had had 4 or more LBCs analysed during a 1-year period. 9% of patients had not had a LBC analysed.\(^6\)

In comparison, 20% of Canterbury patients had had 4 or more LBCs analysed, 8% had not had a LBC analysed at all during the one year period and LBCs were taken on a regular basis (at least every 60 to 130 days) in only 3% of patients. There could be a number of reasons why the monitoring of LBCs was less than ideal. This includes lack of knowledge of lithium therapeutics, patients failing to attend laboratory appointments, differences between psychiatrist and primary care.

Other audits found that monitoring of LBCs did not meet the relevant standards.\(^7\)–\(^{13}\)

Although we could not find evidence to show a reduction in mortality with regular monitoring of LBCs, it was appear to be prudent to do so, given the predictable toxicity with elevated LBCs.

Eagles et al noted that monitoring of LBCs improved in the year after the distribution of guidelines in northeast Scotland.\(^{14}\) Fielding et al found that a dedicated lithium monitoring service in Southampton, UK led to higher compliance with the relevant guidelines.\(^{15}\) A lithium monitoring database run by a hospital pharmacy service in Norfolk, UK led to a substantial improvement in compliance with NICE standards.\(^{16}\)

Although this audit did not look at whether the monitoring of renal and thyroid function occurred every 6 months as the complete dataset was not available, other studies did. They found that these monitoring targets were achieved in between 50% and 66% of patients\(^6\)–\(^8\),\(^12\) although other audits found much lower rates had been achieved.\(^9\),\(^10\)

Eagles et al. found that this monitoring improved significantly after the introduction of guidelines.\(^{14}\) A dedicated lithium monitoring service achieved annual monitoring of thyroid and renal function test in 83.7% of patients.\(^{15}\)

The mean LBC in our cohort was 0.63 mmol/L. Other studies found similar mean LBCs of 0.69 mmol/L,\(^{13}\) 0.64 mmol/L\(^{17}\) and 0.63 mmol/L.\(^{18}\) It is reassuring that the Canterbury population has a similar mean LBC to other published mean values.

When high LBCs (>1.2 mmol/L) were examined, 12.5% (7/56) of patients were retested within 3 weeks. This is concerning as lithium has predictable toxicity when the blood concentrations are elevated. When patients present with an elevated LBC, it
should be standard practice to promptly repeat the LBC and reduce the dose if appropriate.

Other centres have improved their monitoring by either publishing and distributing guidelines or introducing a lithium patient database and monitoring service. We suggest that these improvements should be implemented in Canterbury. Patient information should be updated and a comment on pathology reports indicating how frequent LBC should occur is also desirable. We would intend to audit the monitoring of LBC after the above has been implemented.

There were a number of limitations of this audit. It was conducted retrospectively. Lithium usage was based on subsidised pharmacy dispensing data and does not reflect patient compliance with treatment. There were no patient-identifying details with the dispensing data, thus we did not have a complete record of the patients on lithium in Canterbury. Patient records were not reviewed.

In conclusion, LBC monitoring at CDHB did not achieve the targets of the NHS National Patient Safety Agency patient safety alert. This is in keeping with a number of other international audits of LBC monitoring. Given lithium’s predictable dose related adverse effects and propensity for drug interactions, it would be desirable to achieve these targets.

Competing interests: None declared.

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References:

2. The PML Committee. CDHB Preferred Medicines List 2011. Published by Canterbury District Health Board.


Trends in child and adolescent discharges at a New Zealand psychiatric inpatient unit between 1998 and 2007

Kirsten van Kessel, Elizabeth Myers, Sarah Stanley, Peter W Reed

Abstract

Aim This paper describes demographic and diagnostic data for young people discharged from a regional child and adolescent psychiatric inpatient unit in New Zealand (NZ) over a 10-year period (January 1998–December 2007).

Method Data was obtained from an electronic database, including the number of discharges, demographic characteristics (age, ethnicity, gender) and clinical data (primary diagnosis at discharge, length of stay).

Results Results showed a significant increase in number of discharges over time but no significant change in length of stay. Significant linear trends of increasing proportions of psychotic disorders and decreasing proportions of affective, bipolar affective, personality traits, suicidal/self-harm, and externalising behaviour disorders were observed. Results also found a significant decrease in the proportion of discharges of young people of European descent and a significant increase in proportion of discharges of those of Māori descent.

Conclusions This study provides evidence of changing patterns in demographic and diagnostic variables in a NZ child and adolescent inpatient population over a 10-year period. The findings have important implications for future service delivery in child and adolescent psychiatric inpatient settings.

Research on child and adolescent inpatient mental health populations can provide useful information on changes in service utilisation, psychiatric diagnoses, and demographic variables, and can have implications for service planning with regard to young people’s psychiatric inpatient care.

There has been little research in New Zealand (NZ) on trends, demographic and illness variables in child and adolescent inpatient populations. A Christchurch study gathered admission data over an 18-month period in an adolescent inpatient unit in the South Island. In a sample of 72 subjects the most common diagnosis was mood disorder (54%) followed by anxiety or adjustment disorder (25%) and major psychosis (21%). Unfortunately, no demographic information (gender, ethnicity) was reported in this study.

In terms of ethnic differences, the available evidence from the few NZ studies of inpatient populations suggests an over-representation of admissions for young Māori. A 25-year longitudinal study of adolescents looked at, among other things, ethnic identification and mental health problems. The authors described increased rates of psychiatric disorder amongst Māori youth (age 18–25 years)—depression, anxiety and substance dependence were all over-represented in the 18–21 year age group, in comparison to non-Māori.
A study on a cohort of Māori and non-Māori patients (aged between 15 and 45) admitted to inpatient services in Otago between 1990 and 1992 found Māori were over represented among first admissions. Māori were also found to be a more disadvantaged group with respect to financial support, education and other health problems. These findings are consistent with adult studies which have found that patterns of diagnosis, trends over time and use of psychiatric services in adult patients also vary between different ethnic groups in NZ, and data suggest that rates of admission to hospital are higher for Māori than non-Māori.

A retrospective file review of more than 900 adult patients from three Auckland acute inpatient psychiatric units reported that, based on the community population, Māori admissions were double the expected rate and Asian admissions were lower than expected. Compared to European admissions, Māori, Pacific, and Asian admissions were all more likely to have a diagnosis of a psychotic disorder.

Given the lack of NZ studies on child and adolescent psychiatric inpatient populations, the current retrospective analysis tried to address this gap by depicting trends in sociodemographic and diagnostic characteristics in a NZ child and adolescent inpatient unit over a period of 10 years between 1998 and 2007. It was also hoped that this information could then be used to inform future service planning.

Method

The study setting was an acute child and adolescent psychiatric inpatient unit with 23 beds, based in a public health service in the North Island. The unit includes a small eight bedded locked section, with minimal outdoor access and no capacity for family/whānau to stay. The rest of the unit is ‘open’, and more spacious, with access to a garden and activity areas. Admissions cover the age range 0–18 years, but the vast majority are for adolescents aged 13–18 years.

The geographic area served is large and encompasses both rural and urban regions. The population served is approximately 2 million, with an ethnically diverse mix including most of the Pacific Island population in NZ and a growing number of people of South East Asian descent. The model of practice used is bio-psycho-social with a strong focus on family/whānau participation and continuity of care with the referring service.

Ethical approval was obtained from the Northern Y Regional Ethics Committee and the relevant health service. All consecutive discharges between 1st January 1998 to 31st December 2007 were identified on an electronic database. Repeat discharges were examined and any temporary discharges (patients readmitted within 14 days) were re-coded as one continuous inpatient admission and one discharge. The data obtained from the electronic database included the number of discharges, demographic characteristics (age, ethnicity, gender) and clinical data (primary diagnosis at discharge, length of stay).

For the purpose of the descriptive analyses, primary diagnoses at discharge were grouped into the following diagnostic groups: Psychotic Disorders (incl. psychosis, schizophrenia), Affective Disorders (incl. depression, dysthymia), Anxiety Disorders (incl. phobia, post traumatic stress disorder, obsessive compulsive disorder, adjustment disorder), Bipolar Affective Disorder, Developmental Disorders (incl. pervasive development disorder, attention deficit hyperactivity disorder, autistic spectrum disorder), Eating Disorders (incl. anorexia nervosa, eating disorders not otherwise specified), Externalising Behaviour Disorders (incl. disruptive behaviour disorder, oppositional defiant disorder, conduct disorder), Substance Abuse Disorders, Suicide/Self-harm, Personality Traits, Other and None.

Summary statistics (proportions, means/medians, and 95% confidence intervals) were calculated for the distributions of demographic and clinical data, both overall and on a yearly basis. Trends across time for changes in annual discharge numbers were investigated by regression analyses. Trends across time for changes in annual patient proportions (and therefore controlled for any entire sample change in numbers) were investigated by the chi-square based linear trend test in the Stats Direct Version 2.7.8.software (Stats Direct Ltd, UK).
Results

There were 1109 discharges in the 10-year review period. This constituted 899 individual people, with 150 of those individuals having more than one discharge from the unit. In terms of demographic variables, 50.6% (n=561) of the discharges involved a female patient and the mean age was 15.6 years (range 2.6–19.7 years).

Over half of all discharges (53.4%, n=588) involved young people who identified as European, with the remaining sample identifying as NZ Māori (29.1%, n=321), Pacific Islander (7.4%, n=82), Asian (7.1%, n=78), or Other (3.0%, n=33). Ethnicity was not recorded for seven discharges. Māori young people were over-represented in the discharges and Pacific Island young people under-represented compared to the ethnic proportions of the relevant age group of the catchment area of the unit (Table 1, p<0.0001).

### Table 1. Ethnic proportions of relevant age group in catchment area (Census data) compared to unit population

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>Census 1996–2006 %</th>
<th>Unit population % (95% CI)</th>
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<tbody>
<tr>
<td>European</td>
<td>54.8</td>
<td>53.4 (50.4 to 56.3)</td>
</tr>
<tr>
<td>NZ Māori</td>
<td>21.5</td>
<td>29.1 (26.5 to 31.9)</td>
</tr>
<tr>
<td>Pacific Islander</td>
<td>12.0</td>
<td>7.4 (6.0 to 9.1)</td>
</tr>
<tr>
<td>Asian</td>
<td>8.7</td>
<td>7.1 (5.7 to 8.7)</td>
</tr>
<tr>
<td>Other</td>
<td>3</td>
<td>3.0 (2.1 to 4.2)</td>
</tr>
</tbody>
</table>

The annual changes in the numbers and proportions of discharges from 1998 to 2007 are shown in Tables 2 and 3. Table 2 shows the number of discharges over 10 years increased, with 68% more discharges in 2007 compared to 1998, and a linear trend of eight additional discharges per year (p=0.007). No significant trend of change in gender proportions was observed reflecting similar rates of male and female patients over the 10-year period.

Changes over time were observed for ethnicity, with a significant decrease in the proportion of European patients (p=0.002) and a significant increase in the numbers and proportions of NZ Māori patients (p=0.0004 and p=0.0001). However, there was little change over time in discharges from young people of Pacific Island, Asian or Other ethnicity.

In terms of clinical variables, Table 3 shows that the majority of discharges received a primary diagnosis of either Psychosis (34%, n=382), Anxiety (16%, n=181) or Affective disorders (15%, n=167). More than 50% of the total number of both Māori (321) and Pacific Island (82) patients was discharged with a diagnosis of psychosis compared to significantly smaller proportions in the other ethnic groups (p=0.0001) (data not shown). Psychosis was the most common diagnosis for Māori and Pacific Island patients in this child and adolescent psychiatric inpatient setting.
### Table 2. Number of discharges and demographic characteristics of the unit population between 1998 and 2007

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<td>(%)</td>
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<td></td>
<td>n (%)</td>
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<td>Discharges</td>
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<tr>
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<tr>
<td>Other</td>
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</table>

### Table 3. Clinical Characteristics of the unit population between 1998 and 2007

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<tbody>
<tr>
<td></td>
<td>n</td>
<td>(%)</td>
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<tr>
<td></td>
<td>n (%)</td>
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<tr>
<td>Disorder</td>
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<td>Suicide &amp; Harm</td>
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<tr>
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<td>9</td>
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A linear trend of increasing proportions of discharges of Psychotic disorders (p<0.0001) was observed. Linear trends of decreasing proportions were observed for Affective disorders (p=0.05), Bipolar Affective disorders (p=0.02), Personality Trait disorders (p=0.05), Suicidal/Self Harm (p=0.001), Externalising Behaviour disorders (p=0.06) and a diagnosis of “None” (p=0.02). There were no significant linear trends in proportions of other diagnostic groups. In terms of actual numbers, there were linear trends of increasing numbers of discharges of Psychosis (p=0.001) and Anxiety (p=0.005) at rates of five and two additional discharges per year, respectively.

There was little gender difference in the changes over time across diagnoses (data not shown), with the exception of anxiety, which in females increased on average 1.4% annually as a proportion (p=0.01), whereas in males there was a trend of essentially no change (p = 0.65). Over 90% of discharges had a Length of Stay (LOS) of less than 90 days across all years and there was no significant change over time.

**Discussion**

This study describes the demographic and clinical characteristics of young people admitted to a NZ adolescent psychiatric inpatient unit (public health facility) over a 10-year period. The findings suggest that the unit’s population has changed substantially over the last 10 years, with a marked increase in the number of discharges (which equates to number treated) over time. This increase may reflect the increase in population for the unit catchment area.

Other key findings were the significant linear trends of increasing proportions of psychotic disorders and decreasing proportions of affective, bipolar affective, personality traits, suicidal/self-harm, and externalising behaviour disorders. One explanation for these observed trends may be related to an increase in more severe presentations over time, combined with increased availability of community services in NZ for less severe presentations resulting in a decrease of some of the other diagnostic groups.

Community teams have grown in size and resourcing, and there has also been the introduction of approaches such as Cognitive Behaviour Therapy, Dialectical Behavioural Therapy and Intensive Clinical Support Services that have kept young people with mental health issues in the community for longer. Another explanation for the changes in diagnostic categories over time could be related to the reported proportional increase of young people of Māori descent in the current sample, for whom the most common diagnosis was in fact psychosis. However, due to the fact that this was a retrospective study, we can only hypothesise about the potential factors that may have contributed to these changing trends in illness variables. The results could also reflect changes in diagnostic practice, admission criteria, or actual changes in illness prevalence and further research is needed to clarify reasons for these observed findings.

Ethnic differences in the proportion of discharges included a decrease in discharges of young people of European descent compared to an increase in those of Māori descent. In tandem, there was an over-representation of young Māori being admitted to the unit compared to the catchment population. These findings are similar to results from both NZ adult and adolescent studies, yet the reasons for this over-representation are unclear.
Some authors have suggested that the elevated risk of mental disorder among young Māori may be explained by young Māori tending to come from socially disadvantaged backgrounds and having higher exposure to childhood adversity. Another explanation for increased rates of psychiatric disorder among Māori youth may be related to substance abuse; however, substance use was not robustly recorded on the database used for this study. Young Māori males have been found to have an increased use of cannabis compared to non Māori, and the development of cannabis dependence has been associated with increased rates of psychotic symptoms in young people in NZ.

Substance misuse has been associated with earlier onset of psychosis, and cannabis appears to confer an increased likelihood of developing schizophrenia in biologically vulnerable individuals. Swadi and Bobier reported that 64.5% of an inpatient youth sample had co-morbid substance use, and that 80% of those with a psychotic illness had used substances. While the scope of the current project did not allow collection of information on substance use, socioeconomic status and exposure to childhood adversity, we strongly recommend and support Kaupapa Research is carried out in this area.

The initial findings from this study suggest significant increases in the number of young people seen in the unit, significant trends in certain diagnostic categories, and significant ethnic differences in the proportion of discharges. These findings have important clinical and service implications. There is an imperative to provide culturally appropriate and acceptable services with adequate resources to engage and work with young people and their families. This could for example include providing whānau accommodation within the unit.

Given the changing nature of admissions to this inpatient unit, issues such as staffing ratios and areas of expertise may need to be reviewed to reflect the increasing complexity and severity of patients’ presentations and needs. There are also important implications for the design and resourcing of the unit, given the increase in young people presenting with acute psychosis. This could include providing an intensive care area with a higher staff presence and increasing space in the inpatient unit for low stimulus areas.

The findings from this retrospective study are limited by the extent and accuracy of the original data sources. Diagnostic data originated from a number of different service based clinicians, which may be less reliable than data from structured diagnostic interviews completed by researchers. This study included only primary diagnoses, and as such did not capture the full range of clinical co-morbid diagnoses. Similarly, definitions and/or identification of ethnicity may have varied over time, potentially influencing the size or trend in ethnic groups. Prospective study design using structured interviews with clear definitions of ethnicity could reduce these limitations.

Another limitation is that this study’s findings are based on a group of young people from a particular birth cohort residing in the northern half of the north island. The extent to which the results based on this group can be generalised to other parts of NZ needs to be determined. A final limitation is that it is as yet unclear whether the findings from this study reflect true changes in diagnostic or demographic trends or that the results reflect contextual changes such as diagnostic practice changes in
admission criteria, or access to mental health care. Further research needs to include systematic prospective studies using standardised instruments in order to more rigorously investigate trends in child and adolescent discharges in NZ inpatient units.

Despite the limitations, this study has demonstrated the unique demographic and diagnostic variables of a child and adolescent acute inpatient population, and provided the first information on changing patterns in these variables in a NZ setting. In an era of limited resources, such information is crucial for clinicians, managers and decision makers to assist with clinical and service planning in child and adolescent psychiatric inpatient settings.

Competing interests: None declared.

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References:
Partner notification for sexually transmitted infections. Why can’t we talk about it?

Sunita Azariah

Abstract

Aim Primary care practitioners need practical guidance on how to best manage partner notification for bacterial sexually transmitted infections. This paper reviews published literature on partner notification to determine whether there is good evidence to support the introduction of patient delivered partner therapy for the management of bacterial STI in New Zealand.

Method A search of CINAHL, Medline and Cochrane databases was carried out using the search terms partner notification, contact tracing, sexually transmitted infections, sexually transmitted diseases, chlamydia, gonorrhoea and trichomoniasis. After review of the abstracts the identified papers were included in the review if they addressed the research question.

Results Most people diagnosed with a bacterial STI would prefer to notify their sexual contacts themselves; therefore health practitioners need to feel competent to discuss and facilitate this process for their patients. Clinicians and patients are prepared to consider the use of patient delivered partner therapy with reservations however there is little evidence to support the effectiveness of this intervention even if it were legal under current New Zealand prescribing law.

Conclusion Training of practice nurses, the use of partner notification cards and implementation of systems to improve documentation of management of index cases are all practical ways of achieving better partner notification outcomes in primary care within existing legal frameworks.

New Zealand has a major problem with bacterial sexually transmitted infections (STI) such as chlamydia and gonorrhoea and has much higher notification rates than other similar countries, which has serious implications for use of health resources.

The estimated national chlamydia and gonorrhoea prevalence rates for New Zealand in 2010 (782 per 100,000 population) were several times higher than those most recently reported for Australia and the United Kingdom. Partner notification (contact tracing) is an important component of the management of bacterial STI however, many general practitioners (GPs) have had little training in partner notification and many feel unsure about what is best clinical practice. This needs addressing as surveillance data confirms the majority of bacterial STIs are managed in primary care settings.

A recent editorial in an Australian sexual health journal called for better guidelines on the management of partner notification. There is no doubt that practical guidance is required to enable GPs and other non-specialist sexual health practitioners to manage
partner notification in a manner that produces reasonable outcomes but also that fits within the time and cost restraints of running a busy practice.

The use of patient delivered partner therapy has been proposed as one possible solution to improving the effectiveness of partner notification. Patient delivered partner therapy is the practice of treating the sex partners of persons with bacterial STI without an intervening medical evaluation or professional prevention counselling and is used on occasion by GPs and other health professionals despite concerns about its legality.

The aim of this paper is to review published literature on partner notification to determine what is effective and whether there is good evidence to support the introduction of patient delivered partner therapy for the management of bacterial STI in New Zealand. A search of CINAHL, Medline and Cochrane databases for published literature was carried out using the search terms partner notification, contact tracing, sexually transmitted infections, sexually transmitted diseases, chlamydia, gonorrhoea and trichomoniasis and the main findings are discussed below.

**Potential risks and benefits of partner notification**

Partner notification or contact tracing is the process of identifying the relevant contacts of a person with an infectious disease (index patient) and ensuring that they are aware of their exposure. There are potential theoretical benefits to be gained from effective partner notification not only for the infected individual but also for their sexual networks.

These benefits include possible prevention of reinfection in the index case and for their contacts may include treatment of undiagnosed STI and prevention of possible morbidity and complications. There may be an added benefit of reducing the risk of further transmission of STI in the wider sexual networks of index cases and contacts.

The most commonly used method for partner notification is patient referral, whereby the index case has responsibility for informing sex partners of their exposure to a sexually transmitted infection. However the effectiveness of patient referral relies on index cases being willing or able to identify their sexual contacts. They must then be able to safely and effectively communicate to their sexual contacts of the requirement to seek testing and treatment and finally their notified contacts must be willing and able to access health services for the required testing and treatment.

Sexually transmitted infections such as chlamydia are associated with social stigma and the diagnosis may result in guilt or fear of losing a partner as well as concern about emotional or physical violence as a result of notification.

**How could the effectiveness of partner notification be improved?**

New Zealand data suggests that partner notification may not be well managed in primary care settings. A recent Waikato audit of chlamydia management in 19 different health-care sites found that most chlamydia cases had only limited documentation in the notes regarding partner notification. There appeared to be limited patient follow-up and documented outcomes of partner notification were notably lower than that reported by UK settings where partner notification is most often undertaken by specialist sexual health advisers. However, this should not be
interpreted to conclude that partner notification is best managed in a genitourinary (GU) or specialist sexual health clinic setting.

A randomised controlled trial in the UK found that with a little training GP practice nurses could manage partner notification for chlamydia as well as GU clinic health advisers.\(^8\) Overall 45% of possible contacts in the trial were considered treated; 65% in the practice nurse arm and 52% of those referred to the GU clinic. Although it is likely that that the delay in management caused by referring index cases to the GU clinic will have impacted on the results, this study illustrates that partner notification can be easily be managed in primary care and that outcomes are better than if cases are referred to another provider even if the other provider may have more expertise.

Patient delivered partner therapy is an intervention that has the potential of reducing STI reinfection rates in index cases by removing the potential barrier of a consultation before their sexual contacts can be treated. However as with patient referral, there is still a requirement for the index case to inform their contacts of their possible exposure to an STI and then they must be willing to deliver them medication. A possible disadvantage of patient delivered partner therapy is that the recipient may suffer an adverse reaction to the antibiotics.

Further because no clinical consultation has occurred, the diagnosis of other STIs may be missed\(^9\) or there may be inadequate treatment of complicated infections such as pelvic inflammatory disease. These risks could theoretically be reduced by the provision of appropriate printed information to be delivered along with the medication but this is based on the presumption the information will be read and understood and of course there is no guarantee the medication will be either delivered or taken.

Whilst the concept of patient delivered partner therapy has become increasingly acceptable internationally, it is not legal in New Zealand for a medical practitioner to prescribe medication unless it is for the treatment of a patient under his or her care (Section 39, NZ Medicines Regulation Act 1984).\(^10\) Although anecdotally it would appear that this practice is not uncommon, the evidence regarding the effectiveness and acceptability of patient delivered partner therapy needs to be critically appraised before a reasonable case could be made to revise current regulations regarding the prescription of medication.

In New Zealand this intervention could not be used for management of contacts of gonorrhoea as the prevalence of ciprofloxacin resistant *Neisseria gonorrhoeae* is widespread and there is no effective oral treatment for ciprofloxacin resistant gonorrhoea available in New Zealand.

**How effective is patient delivered partner therapy at improving outcomes of partner notification?**

Patient delivered partner therapy and similar interventions have been trialled in the US as a means of better enabling the notification and treatment of sexual contacts of bacterial STI. In 2001, SB 648 amended California law to allow patient delivered partner therapy for chlamydia, and in January 2007, AB2280 further amended the law to allow PDPT for gonorrhoea.\(^11\)

The law allows physicians to prescribe and nurse practitioners, physician assistants, and certified nurse-midwives to dispense antibiotic therapy for the male and female
sex partners of individuals infected with *Chlamydia trachomatis* or *Neisseria gonorrhoeae*, even if they have not been able to perform an examination of the patient’s partner(s). However data from 4 well conducted randomised controlled trials and 2 uncontrolled comparative trials in the US fail to make a case for the effectiveness of patient delivered partner therapy when objective outcomes such as re-infection rates in index cases are examined.\(^{12-17}\)

Although 2 of the randomised controlled trials reported better outcomes for patient delivered partner therapy, such as lower re-infection rates in index cases and index cases being more likely to report their contacts had been treated; these findings need to be placed in context.\(^{12,13}\) One of these studies(with 3 intervention arms) found that patient delivered partner therapy was more effective than standard patient referral at reducing re-infection rates for chlamydia and gonorrhoea in index cases; however the most effective intervention at preventing re-infection was giving the index case a tear-out card with information on the diagnosed STI to give to sexual contacts.\(^{12}\) In the other study, patient delivered partner therapy was more effective at reducing re-infection rates with chlamydia and gonorrhoea than standard patient referral, however the difference was only statistically significant for gonorrhoea.\(^{13}\) The participants were also a very select group comprising only 10% of total notifications for chlamydia and gonorrhoea in King County Washington during the study period and of those eligible to participate, one third declined and about half had partners who had already been treated.

Two other randomised controlled trials comparing patient delivered partner therapy with standard patient referral for women diagnosed with trichomoniasis and chlamydia respectively,\(^{14,15}\) did not find significant differences in rates of re-infection in index cases, although the former found that women were more likely to report that their partners had been treated if they were in the patient delivered partner therapy treatment arm.\(^{14}\)

Two systematic reviews of effectiveness of partner notification strategies have also not found patient delivered partner therapy to be any more effective than other methods of partner notification for bacterial STI, however simple additional measures such as provision of printed material, verbal nurse-given education or counselling by lay-workers were found to produce small increments in numbers of sexual contacts treated.\(^{18,19}\)

**What do health practitioners think about patient delivered partner therapy?**

An Australian study conducted an in-depth telephone survey of GPs from both rural and urban regions.\(^{2}\) The GPs were asked about current practice and views about partner notification, perceived barriers and useful supports, previous use of and views regarding patient delivered partner therapy.

Many cited barriers to effective partner notification including lack of time and staff, lack of contact details for sexual contacts, uncertainty about legal issues of contacting partners and whether this constitutes breach of patient confidentiality and feeling both personally uncomfortable and inadequately trained to contact someone who is not their patient. They had mixed views on the use of patient delivered partner therapy.
Many felt concerned that it was not best clinical practice but many also felt that it was better than nothing. They felt partner notification would be easier to manage if there were clear clinical guidelines, a legal framework around partner notification, a formal chlamydia screening programme and financial incentives and education and practical support for health professionals. They also felt it was important to raise awareness of chlamydia in the community, in particular amongst young people.

Another primary care study in the United Kingdom (UK) looked at practitioner attitudes towards a novel form of partner notification (“accelerated partner therapy”) whereby sex contacts of index cases had the option of either a telephone consultation with a health practitioner or attending a pharmacy for consultation before antibiotics were dispensed. Generally the participants were positive about either alternative although they preferred the former option.20

A separate UK study of non GU health practitioners examined attitudes of pharmacists, nurses and doctors towards novel methods of managing partner notification for sexual contacts of women diagnosed with chlamydia and found that the most popular novel method (chosen by 30% of doctors and 23% of nurses), was for the index case to deliver medication plus a postal testing kit to their sexual contacts.21 Standard patient referral scored very low with only 8% of doctors and 3% of nurses choosing this option. Twenty-five percent of doctors had already used patient delivered partner therapy in their clinical practice as a means of managing partner notification. Pharmacists were particularly receptive to novel methods of partner notification indicating willingness to supply free postal testing kits (98%), offer testing (75%), treatment services (100%) and give women medication for partners (80%).

In contrast, when specialist GU physicians and health advisors were surveyed; the findings were that although 50% of GU physicians had used patient delivered partner therapy in the past and were more willing to consider its use than health advisors, nearly a third of practitioners strongly objected to patient delivered partner therapy mainly because of concerns about possible adverse consequences in the recipients and concerns about the legal status of patient delivered partner therapy.22

In summary, it appears that health practitioners have mixed views on patient delivered partner therapy but most would be prepared to use it. The main concerns appear to be the legal status of such a practice and possible adverse consequences in recipients of patient delivered partner therapy such as missed infections, drug allergies and antibiotic resistance. These concerns are somewhat allayed if sexual contacts have a telephone or pharmacy consultation before antibiotics are dispensed.

Management of partner notification is an acknowledged area of difficulty for primary care practitioners, often poorly documented and complicated because of lack of clear guidelines and legal framework.

What do patients think of patient delivered partner therapy?

Shivisankar et al surveyed 500 UK GU clinic attendees about various issues including the acceptability of various methods of partner notification.23 They found that traditional patient referral was more popular for participants than patient delivered partner therapy but the difference was not statistically significant.
In another UK study, Sutcliffe et al interviewed 38 GU clinic attendees regarding 2 possible approaches for managing partner notification, which they termed “accelerated partner therapy” as patient delivered partner therapy is not legal in the UK. Participants were all either recently diagnosed with an acute STI or were contacts of people with an STI. They were given the hypothetical option for their contacts of either a telephone consultation with a GU clinic staff member followed by delivery of medication by the index case (option A) or for contacts to be referred for a consultation and treatment at a nominated pharmacy (option B). Both options were considered acceptable approaches by most participants but most also wanted the opportunity to have spoken to their partners first before they were spoken to by a health professional.

Many felt they would rather have advice from a health professional from a GU clinic than from a pharmacist. Those aged under-30 were more likely to prefer face to face advice from a GU health professional and having “proper tests”. A US study of STD clinic attendees had similar findings. When asked about preferences for partner notification, only 20% of participants (15.5% of males and 23.5% of females) preferred to “bring the medicine home for my partner(s) to take,” and of the 407 patients who tested positive for chlamydia, only 17.0% preferred the option of patient delivered partner therapy.

Other research has found patient delivered partner therapy to be generally acceptable to consumers however this depends on whether one is on the giving or the receiving end of the medication. Goldsworthy et al recruited 505 individuals to complete questionnaires regarding either willingness to deliver medication to sexual contacts or willingness for partner use, i.e. to receive medication from a sexual contact.

Whilst a majority of participants expressed willingness to engage in both patient-delivery (83%) and partner-use (69%), they found it more acceptable to deliver medication than to receive it. The facilitators most highly correlated with uptake for both patient-delivery and partner-use were: having the medicine sealed, having it in an official package, having instructions provided, having a note from the health care provider, and the presence or absence of partner trust.

In another study exploring the acceptability of patient delivered partner therapy, Macbride et al recruited 64 patients from an urban US STI clinic with the aim of developing and evaluating instructional and packaging materials for patient-delivered partner therapy. The analysis was repeated before and after participants had seen the patient delivered partner therapy materials. Prior to viewing the materials participants were largely willing (87.5%) to deliver medication to a sex partner(s), but fewer participants were willing to receive medication from a sex partner (57%).

Lack of trust in a partner and the context of the relationship (e.g. casual partner) were the primary reasons for being unwilling to receive medication from a partner. Participants also cited the need for testing and treatment by a healthcare provider before receiving treatment. After they had seen the materials participants were more likely to be willing to receive patient delivered partner therapy (89%) but were less willing to deliver patient delivered partner therapy (48%). Among those who said they would decline the medicine, all cited the need to seek services from a healthcare provider as a primary reason.
However are these study results applicable to a New Zealand context? There is some unpublished New Zealand data regarding patient preferences regarding partner notification. In a survey of 391 Auckland Sexual Health Clinic attendees, the most popular method for notifying sexual contacts was to “talk to them in person”. The majority of participants would also prefer to be told in person if they had been in contact with someone with an STI.

The least popular methods to notify sexual contacts were “send a letter” and “send an anonymous text, email or e card” Only 14% of respondents said they would like the clinic to notify their sexual contacts on their behalf. Most indicated that talking with a doctor or nurse (60%) about how to talk with their partner(s) would make it easier for them to do this. (Jenkins R, unpublished data 2011). In another Auckland study, 2 focus groups with young men and women were conducted as preparation for a pilot project for opportunistic chlamydia testing in primary care.

Both male and female participants felt that ideally partners should be notified of their exposure to an STI by the index case and that discussion of partner notification could be aided by a small card with information about the STI and contact details of health services. (They were shown contact cards similar to those used in the Kissinger trial) 12 While they considered it was possible to give antibiotics to a partner they felt that this was best done by a healthcare professional (unpublished data 2011).

In summary, these studies all highlight the complexities of issues that need to be considered in partner notification. Most people appear to be aware of their responsibilities to notify sexual contacts and would rather do it themselves than have a health professional do it for them. Although many would be willing to deliver medication to their contacts; paradoxically they would have concerns about their own health if they were to be delivered medication from a sexual contact and young people in particular would prefer to seek independent advice from a health professional.

While pharmacists are willing to provide medication, most people would prefer to speak to a clinician rather than a pharmacist about sexual health issues. The provision of printed information to be given with medication appears to reduce concerns for recipients but makes people less willing to deliver medication. This is perhaps because the provision of accurate information about STIs does nothing to reduce the stigma and concerns associated with an STI diagnosis for the index case and doesn’t make it any easier to raise an awkward subject.

**Conclusion**

New Zealand has a major problem with bacterial STI and effective partner notification is an important part of managing this significant health problem. Research has found that most people diagnosed with a bacterial STI would prefer to notify their sexual contacts themselves; therefore health practitioners need to feel competent to discuss and facilitate this process for their patients. Whilst patient delivered partner therapy appears to result in more contacts being notified and treated than standard methods of partner notification, this finding cannot be readily verified.

Patient delivered partner therapy is not the most effective intervention at reducing re-infection rates in index cases, therefore a case cannot be made to change current New
Zealand prescribing laws and the use of patient delivered partner therapy should be reserved for only a minority of situations.

Guidance from the Medical Council of New Zealand would be helpful to advise practitioners in what circumstances it would be acceptable to use patient delivered partner therapy and what precautions need to be taken to reduce the risk. The development and use of partner notification cards of a similar design to those used in the Kissinger trial should be encouraged as they have been shown to reduce re-infection rates in index cases. Training of nurses is an effective method of managing partner notification therefore nursing staff should be utilised in health care settings for the follow-up of all patients diagnosed with bacterial STIs.

Partner notification activities need to be accompanied by full documentation in medical records in order to properly audit partner notification outcomes. Finally, improving knowledge and awareness about STIs in the community is important to reduce the stigma associated with an STI diagnosis and will help normalise conversations about STIs for health practitioners and their patients.

**Competing interests:** None declared.

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**References:**


Delayed puberty from partial 17-alpha hydroxylase enzyme deficiency

Michael Croxson, C Megan Ogilvie, Stella Milsom, John Lewis, James Davidson, Gill Rumsby

Abstract
An 18-year-old woman with primary amenorrhoea and pubertal delay was investigated for mild labile hypertension and secondary hypogonadism. Low renin and normal aldosterone levels combined with evidence of primary adrenal insufficiency suggested partial 17-alpha hydroxylase enzyme deficiency. The diagnosis was confirmed by measurement of 24-hour urine steroid metabolites and whole gene sequencing of CYP17A1 that demonstrated c.160_162delTTC (p.Phe54del) homozygous mutation. Ultrasound showed bilateral small ovaries with multiple cysts. The serum anti-Mullerian hormone concentration was unremarkable at 6.6 (normal <12.6 ng/ml) but the outlook for her future ovulatory potential is uncertain. Dexamethasone 0.25 mg pre-bed and hydrocortisone 5 mg on waking normalised her hormonal profile and her blood pressure without side-effects.

Failure of puberty to progress to onset of menarche by age 15 in young women usually requires further investigation. The distinctive triad of hypogonadism, low-renin hypertension and primary hypocortisolism in a young woman suggested the presence of congenital adrenal hyperplasia caused by partial deficiency of 17α (alpha) hydroxylase enzyme.

Case report
An 18-year-old daughter of unrelated Indian parents was referred for further endocrine assessment of primary amenorrhoea and pubertal delay. Early growth had been unremarkable with height on the 50th percentile, BMI 18 kg/m². Breast development as well as axillary and pubic hair had begun 3 years earlier but progressed only to Tanner Stage II. She was found to have normal external genitalia and vaginal appearances.

Ultrasound showed bilateral small ovaries with multiple cysts and a normal uterus. Serum gonadotrophins were not raised, her karyotype was 46XX normal as was a pituitary CT scan. Her blood pressure ranged from 120/80 to 150/100 mmHg and she had occasional migraine-type headaches. A raised plasma ACTH and low basal serum cortisol indicated primary hypocortisolism but plasma active renin level was undetectable, suggesting mineralocorticoid excess rather than deficiency. Basal hormone values and the response to 250 mcg Synachthen (tetracosactide) are shown in Table 1.
Table 1. Pre and post-glucocorticoid treatment steroid, peptide and blood pressure measurements indicate primary adrenal insufficiency. Serum progesterone and corticosterone levels are raised, active renin is suppressed and there is pre-treatment hypertension.

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<td>FSH</td>
<td>5.6</td>
<td></td>
<td>3–10 IU/l</td>
</tr>
<tr>
<td>LH</td>
<td>4.3</td>
<td></td>
<td>2–8 IU/l</td>
</tr>
<tr>
<td>Anti-Mullerian hormone</td>
<td>6.6</td>
<td></td>
<td>&lt;12.6 ng/ml</td>
</tr>
<tr>
<td>Blood pressure*</td>
<td>130–150/80–100</td>
<td>98/70</td>
<td>&lt;120/80 mmHg</td>
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*Normal reference ranges for age, weight and Tanner Stage II.

Hydrocortisone replacement led to increased wellbeing and a slight fall of blood pressure to 130/90. Measurement of urinary steroids and further investigation of a possible CYP17A1 mutation were carried out by Dr Gill Rumsby at UCL Hospitals, London. 24-hour urine adrenal steroids and metabolites were measured by gas chromatography mass spectrometry.

Cortisol and metabolites were reduced while intermediate mineralocorticoid precursors proximal to 17α hydroxylase action were increased, consistent with 17α hydroxylase enzyme deficiency. Whole gene sequencing of CYP17A1 demonstrated c.160_162delTTC (p.Phe54del) homozygous mutation.

Figure 1 illustrates the hormonal consequences of the partial enzyme deficiency.

On confirmation of the diagnosis, her glucocorticoid supplements were modified to maintain diurnal ACTH suppression using dexamethasone 0.25 mg pre-bed and hydrocortisone 5 mg on waking. Her blood pressure fell further to 90/60 and both serum progesterone and ACTH also fell appropriately. Weekly percutaneous oestradiol was added to advance puberty. Additional radiology showed epiphyseal closure but osteopenia with a t score of -2.6 prior to beginning estradiol replacement.
Congenital adrenal hyperplasia due to 17α hydroxylase deficiency is a rare form of congenital adrenal hyperplasia with less than 200 cases reported and approximately 50 different mutations of the CYP17A gene identified. Partial CYP17A1 deficiency associated with the homozygous phenylalanine 53 or 54 deletion was first described by Yanese et al who showed <37% wild type 17α hydroxylase activity and < 8% 17,20 lyase activity in a cell expression system.

The first case was initially reported as an example of dexamethasone suppressible aldosteronism. Three 46XX women with the Phe53 deletion had no sexual abnormalities on physical examination and regular or irregular menstruation. Gonadotrophin levels were normal. One 46XY phenotypic male had hypospadias and cryptorchidism. Hypospadias or microphallus has been reported in a further two phenotypic 46XY males due to partial loss of function mutation at the same site (p.Phe54del) in CYP17. Overt cortisol deficiency and adrenal crises are rare because the increased corticosterone production has glucocorticoid activity.

The finding of low renin hypertension with normal aldosterone levels reflects the mineralocorticoid activity of corticosterone and deoxycorticosterone. Delay in recognition of hypertension may occur unless normative childhood values are used for comparison. With hindsight, unexpected elevation of serum progesterone was a clue to the presence of increased steroid precursors and the true diagnosis. Both parents are normotensive and her 24 year old brother has a normal male phenotype and normal steroid values, but mildly elevated plasma corticosterone and corticosterone/cortisol.
ratios both basally and after ACTH stimulation, as has recently been shown in genotype-proven heterozygous individuals. The outlook for her future fertility remains uncertain.

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**References:**
Ischaemic stroke with headache as its only manifestation

Wael Radwan, Abdallah El-Sabbagh, Samir Atweh, Raja A Sawaya

Abstract

We present two cases of middle-aged men with chronic hypertension presenting with acute severe hemicranial headache with otherwise a normal neurological examination. Investigation revealed occlusion of the ipsilateral middle cerebral artery. We reviewed the literature of ischaemic strokes with headache as the only manifestation and elaborated on the pathophysiology of headaches in ischaemic strokes.

Headache is frequently associated with cerebrovascular disease.\(^1\) Cerebral haemorrhage can cause headache by increasing intracranial pressure, while ischaemic cerebrovascular disease causes headache by disruption of intracranial vessel walls leading to seepage of neurotransmitters and stimulation of receptors on sensory nerve terminals. Infratentorial infarcts are reported to produce more headaches than supratentorial lesions because of the dense sensory innervations of the posterior cerebral vessels.\(^2\)

We present two cases of middle-aged patients presenting with severe periorbital and hemicranial headaches with otherwise normal neurologic examination. Investigation revealed middle cerebral artery thrombosis with large territorial infarcts.

We attempt to explain the pathophysiology of isolated headaches in ischaemic cerebral disease.

Case reports

Case 1—A 53-year-old man with controlled hypertension presented with acute severe persistent right hemicranial headache associated with nausea. No previous history of headaches or other complaints in the days prior to presentation. Blood pressure was 140/85. Completely normal neurological examination. Headache did not resolve on simple analgesics. MRI of the brain revealed large acute infarct in the right temporal lobe. MRA revealed occlusion of the distal branches of the right middle cerebral artery (MCA) with patency of the other cerebral and carotid arteries. The patient was treated with heparin, fearing thromboembolism or paroxysmal atrial fibrillation, followed by anti-platelet therapy with eventual resolution of the headache.

Case 2—A 60-year-old man with controlled hypertension presented with acute severe persistent right periorbital pain associated with nausea and vomiting. No previous history of headaches or other complaints in the days prior to presentation. Normal vital signs and full neurological examination. MRI revealed acute infarction in the vascular territory of the right MCA (Figure 1). Cerebral angiography revealed filling defect in the distal branches of the right MCA and a thrombus in the common carotid artery which was the source of the embolus. The patient was treated with heparin fearing thromboembolism or paroxysmal atrial fibrillation, followed by anti-platelet therapy with eventual resolution of the headache.
Discussion

Headache can be a manifestation of an ischaemic cerebral lesion, together with the corresponding neurological deficits, in about 34% of cases. On the other hand, isolated and severe headaches, with no neurologic deficits, associated with MCA infarctions have rarely been reported in the literature.

Headaches may be associated with infarcts of the posterior circulation because of the dense sensory innervations of the posterior cerebral vessels by the trigeminovascular system. Supratentorial vessels are sparsely innervated by sensory and autonomic fibres of the trigeminal nerve and thus lesions in these vascular territories usually present with focal neurological deficits rather than headaches. The occasional patient who presents with acute severe headache associated with an MCA infarction confirms the innervation of supratentorial arteries with sensory nerve terminals.

Cerebral arteries are innervated by the trigeminovascular system. The trigeminal nerve terminals are responsible for vascular nociception. The sympathetic fibres induce vasoconstriction and the parasympathetic fibres vasodilatation. Pathological studies have confirmed that arteries and arterioles of the brain are enclosed by a plexus of adrenergic nerves which are superimposed on the media and covered by the adventitia.

The pathology behind headaches secondary to ischaemic strokes is either secondary to mechanical stretching of the thrombotic artery, as described in the mechanism of post endarterectomy headache, or secondary to the release of vasoactive neuropeptides, and the potent vasodilator calcitonin gene related peptide, from the sensory fibres of
the trigeminovascular system. The release of these neuropeptides causes the resulting increased nociceptive input into the nervous system. \(^3,7\)

The vascular theory that claims that headache is secondary to cerebral tissue infarction with corresponding thrombosis of the vasa nervosum seems less probable considering that a minor proportion of patients with infarcts present with severe headaches and that the severity of the headache is not proportionate to the size of the infarct and paranchymal damage. \(^2\)

The headache associated with ischaemic cerebral disease is usually frontal and periorbital because the intracranial vessels are innervated by the ophthalmic ramus of the first branch of the trigeminal nerve that arises from unipolar neurons located in the trigeminal ganglion. \(^7\)

We conclude that headache as the only manifestation of cerebral infarction is not rare and can be seen in patients with supratentorial vessel thrombosis. The reason for the headache is most probably the release of vasoactive neuropeptides such as calcitonin gene related peptide. We recommend MRI rather than CT scan imaging of the brain in patients who present with unexplained, isolated, severe hemicranial or periorbital headaches, especially in patients with increased risk for vascular disease and no explanation for their headache.

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**References:**

4. Ruskell GL, Simons T. The internal carotid artery has a sleeve of increased innervations density within the cavernous sinus in monkeys. Brain Res 1992:116–120.
Increasing prescription part charges will increase health inequalities in New Zealand

Prescription charges will increase from $3 to $5 under the latest Budget announcement. The new charges will apply up to a maximum of 20 items and the Government argues that money saved would be reinvested in other health initiatives.

The changes to prescription charges will impact negatively on health and healthcare costs, and increase health inequalities. Our research based on 2004 data clearly showed that while 7% of respondents deferred picking up a prescription in the previous 12 months because they could not afford the cost of the prescription, a much higher proportion of Māori (14%) and Pacific people (15%) reported putting off paying for prescription medication.

The most recent release of the Statistics New Zealand Survey of Family Income and Employment longitudinal dataset showed that the number of people who could not pick up a prescription because of cost dropped to 4% in 2006 and 2009. A similar trend is seen for European (non-Māori-non-Pacific-non-Asian) people: 5% deferred picking up a prescription in 2004, decreasing to 3% in both 2006 and 2009. However, the numbers still remained much higher for Māori and Pacific people: 8% and 10%. Thus while deferring collection of prescription medication because of cost has decreased over time for everyone, the proportion has remained much higher among Māori and Pacific people.

There are two reasons for concern. Firstly, Māori and Pacific people are more likely to have fewer resources and high unmet health needs. Deferral of necessary drugs is only going to make their conditions worse, resulting in needless suffering and increased costs for themselves and the health system. Secondly, the encouraging trend toward lower deferral rates amongst all ethnic groups is threatened by the proposed increase in charges.

The importance of prescription medications for treating chronic conditions and preventing a deterioration of health status is well-known. There is strong research evidence that when people have to pay more for their prescriptions they sometimes stop not only ‘non-essential’ medicines, but also medicines for serious and potentially life-threatening illnesses such as hypertension, hyperlipidaemia, depression, osteoporosis, prevention of stroke, asthma and diabetes.

In the US, people who can’t afford their medicines either go without and often end up needing hospital care, or they ration their tablets and take lower doses so the prescription lasts longer. Cost barriers to drugs are associated with increased rates of non-elective hospitalisations, visits to the emergency departments, and death costs. This in turn has substantial economic consequences for society, especially as health care cost containment becomes an increasingly important policy issue.

To many people in New Zealand, the difference between $3 and $5 seems inconsequential. It’s the sort of money you might pay for coffee or a parking meter. But to people on low incomes this can make the difference between getting the
medicines they need or going without. Because poorer people are more likely to have multiple health problems, they are likely to be prescribed many items in one doctor’s visit. Increased prescription charges mean that 6 items, they have to find $30, rather than $18, on top of the cost of getting to, and seeing, the doctor. If other family members also need to see the doctor, this can lead to some tough decisions about which drugs to get, and which to go without.

New Zealand pharmacists frequently report that patients with limited budgets are forced to choose which of their medicines they will take and which they will leave. This can have disastrous and expensive consequences. For example, if someone with gout cannot afford to pick up their allopurinol, which is an effective and safe way to prevent gout attacks, they can end up later purchasing over the counter anti-inflammatory to deal with gout attacks. This is both more expensive for them in the long term, but can also cause serious stomach and kidney damage.

The increase in prescription co-payment from $3 to $5 per item is for up to 20 items per year. After that medicines become free again, until the start of the next year. But this initial $100 outlay can be prohibitive for people on low incomes with multiple health problems.

Before the introduction of the $3 prescription fee, New Zealand had a lower charge for low-income people. The increase to $5 is the first time prescription fees have been raised across the board, so everyone pays the same rate. This move to increase these charges without any concession for low income people will undermine other attempts to increase equity of access to healthcare or to improve health outcomes. Those who already have the most health problems will be the ones most affected by this policy.

Given the importance of prescription medication in maintaining health and treatment of both acute and chronic illness, the decision to increase the co-payment for a prescription should be reconsidered. While the policy issues regarding prescription drug coverage are complex, the public health message is simple: it is important to reduce the cost barriers to drug access to improve population health and reduce ethnic health inequalities and subsequent increased costs for hospital care.

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Statistics New Zealand Security Statement: Access to the data used in this study was provided by Statistics New Zealand in a secure environment designed to give effect to the confidentiality provisions of the Statistics Act, 1975. The results in this study and any errors contained therein are those of the author, not Statistics New Zealand.

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References:

Smokefree cars to protect children and denormalise smoking: a mini-review of New Zealand literature

The Associate Minister of Health (Hon Tariana Turia) has signalled interest in the New Zealand Government developing legislation to protect child health by limiting smoking in cars with children.¹ Such a move would be part of an international trend that has seen such laws covering most Australian states, Canadian Provinces and some US States (including California).² ³ It would also be consistent with other actions to limit hazards and improve safety within cars: compulsory seat belts, compulsory car seats for infants, and bans on mobile phone use while driving (as recently enacted by the last National Party-led Government in New Zealand).

Smokefree cars would help reduce the burden of child illness, given the evidence for the role of secondhand smoke (SHS) in “sudden infant death syndrome (SIDS), asthma, altered respiratory function, infection, cardiovascular effects, behaviour problems, sleep difficulties, increased cancer risk, and a higher likelihood of smoking initiation”.⁴ Reducing these impacts could in turn reduce both private and tax-payer funded health system costs (given international evidence on SHS impacts on health costs⁵–⁷). It is expected that the move would help reduce smoking uptake in children by providing positive smokefree modelling (given New Zealand evidence⁸ and international evidence⁴).

To provide background and context to further policy-maker discussions on this topic, we tabulate the New Zealand literature relevant to smokefree car policies that we could identify on Medline and on health organisation websites in New Zealand (Table 1).

Table 1. Research relating to smoking in cars in the New Zealand setting (peer-reviewed journal publications and research on health organisation websites)

<table>
<thead>
<tr>
<th>Topic area</th>
<th>Main findings of studies identified</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Exposure data</strong></td>
<td></td>
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<tr>
<td>Observational studies of smoking in cars</td>
<td>The first observational study in New Zealand (NZ) collected data in 2005 and reported a 4.1% point prevalence of smoking in cars (95%CI: 3.8% to 4.4%).⁹ It found a higher prevalence of smoking in cars from a more deprived suburb compared to a less deprived one.</td>
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<td>The second observational study collected data in 2011 and involved the observation of 149,886 vehicles at two sites with different levels of socio-economic deprivation.³ The mean point prevalence of smoking in vehicles at the two sites combined was 3.2% (95%CI: 3.1% to 3.3%). Of those vehicles with smoking, 4.1% had children present. There were marked gradients in all the smoking patterns seen by deprivation area of observation. For example, for smoking with children in the car it was 10.9 times (95%CI: 6.8 to 21.3) higher in the more deprived suburb relative to the least deprived suburb.</td>
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<td>A University of Otago “smartphone app” for counting smoking in cars has recent data from a number of NZ settings (data collated online at:</td>
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<tr>
<td>Topic area</td>
<td>Main findings of studies identified</td>
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<tr>
<td>Air quality hazard inside the car</td>
<td>A small experimental study found extremely high levels of fine particulates were associated with in-car smoking in a NZ setting. As of early May 2012, over 4100 vehicles were counted, with 2.5% having in-car smoking occurring. Such smoking is in the presence of others 32% of the time, and children 6% of the time.</td>
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<td>Self-reported behaviours (2004)</td>
<td>A national telephone survey in 2004 reported that 71% of smokers smoked in their cars. In response to the question “It’s OK to smoke around non-smokers inside cars if windows are open”, 64% of respondents “strongly disagreed” and another 12% slightly disagreed (all 2731 respondents, including non-smokers).</td>
</tr>
<tr>
<td>Exposure data in 2009 (national)</td>
<td>In the 2009 NZ Tobacco Use Survey, 6.1% (95%CI: 5.3–7.0) of non-smoking adults self-reported being exposed to SHS in the car they usually travel in during the past week. Rates were highest in Māori (14.7%, equivalent to 25,900 people exposed weekly), then Pacific (12.4%, equivalent to 13,300 people), then European/Other (5.5%, equivalent to 89,200 people) and then Asian (4.9%, equivalent to 14,800 people). After adjusting for age, the prevalence of this form of SHS exposure in the most deprived areas was nearly four times higher than in the least deprived areas (13.9% vs 3.5%). Similar ethnic and deprivation gradients for SHS exposure in cars were apparent in an earlier Tobacco Use Survey (2006) and in the NZ Health Survey (2006/07).</td>
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<td>Youth exposure (HSC 2008)</td>
<td>The Health Sponsorship Council’s (HSC) 2008 Year 10 In-depth Survey found that around a quarter of students (26.8%) reported that someone had smoked in their presence while travelling in cars or vans in the seven days prior to the survey. A higher proportion of Māori and Pacific students reported that someone smoked around them in cars or vans in the seven days prior to the survey (45.9% and 35.1%, respectively), compared with New Zealand European/Pakeha students (20.1%). “Students from low decile schools had the highest prevalence of reporting that someone had smoked around them in cars or vans, compared with students from mid and high decile schools (39.5%, 29.2% and 14.3%, respectively).”</td>
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<td>Impact of exposure on subsequent smoking uptake</td>
<td>Analyses of survey data from the “Keeping Kids Smokefree” study, found that “after controlling for all variables reported exposure to smoking in cars and homes were significantly associated with increased risk of initiated smoking (RR 1.87, 95% CI 1.43-2.44, and RR 1.5, 95% CI 1.13-1.97, respectively). Exposure to smoking in cars was substantially and significantly associated with risk of current smoking (RR 3.21, 95% CI 1.45-7.08).” The authors noted that “smoking in cars is under parental control and therefore modifiable”.</td>
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<tr>
<td>Attitudinal data – public and smokers</td>
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<td>Public attitudes (1997)</td>
<td>A study in 1997 involved surveying the public in Wellington. It reported that around a half (53.5%) thought that “smoking should be banned in cars when there are passengers”. But 94% agreed that cars with children in them should be smokefree (86% of smokers).</td>
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<td>Review of attitudes to smoking in cars (published 2005)</td>
<td>A review article focused on NZ and published in 2005, included data from a tobacco-industry commissioned survey that reported: “For private cars, 58% of non-smokers and 18% of smokers wanted no smoking at all”. An analysis of three national surveys commissioned by the HSC was also included in this review. The “not at all” response to the question “People should be able to smoke in private cars” was reported as: 29% (in 1999); 23% (2001); 41% (2003), (trend: p&lt;0.00001).</td>
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| Smoker attitudes (ITC Project)                | The nation-wide “ITC Project” study reported that the overall support by NZ smokers for smokefree cars containing preschool children was very high at
<table>
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<th>Topic area</th>
<th>Main findings of studies identified</th>
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<td>2007/2008)</td>
<td>96%. This high support was across all socio-demographic groups (with no statistically significant differences between European smokers and smokers who were: Māori, Pacific or Asian). The data also indicate that NZ smokers have nuanced views around new smokefree areas which sometimes contrasts with the overwhelming support for smokefree cars e.g., most are supportive of smokefree outdoor eating areas, council-owned playgrounds, but voice only minority support for smokefree lifeguard-patrolled beaches and for some of the outdoor seating areas of restaurants/cafés and pubs. In general however, Māori, Pacific and Asian smokers (relative to European smokers) are more in favour of new types of smokefree areas.</td>
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<td>Public attitudes (HSC 2008)</td>
<td>A national HSC survey of the public in 2008 asked for responses to the statement “smoking should not be allowed in cars with children under the age of 14 in them”. Overall 91% of respondents agreed and 49% “strongly agreed”. Similarly, 82% of current smokers agreed and 33% “strongly agreed”.</td>
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**Attitudinal data – policy-makers**

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<td>Another publication from the same dataset reported some potentially conflicting beliefs and attitudes. For example, there were “very strong themes of policy-maker concern for the vulnerability of children and the need for their protection from secondhand smoke; however, there were mixed reactions to the idea of a smokefree law for cars with children in them. These themes and mixed reactions spanned both the ‘left’ and ‘right’ political parties.” A lack of policy-maker awareness in some areas was also identified (e.g., of relatively high “public support for banning smoking in cars with children and of the progress elsewhere on such laws…”). Additional aspects of these themes were explored in another publication. It concluded that: “The results indicate the need for good communication of the acceptability and benefits of legislative smokefree changes to both the political and public arena.”</td>
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<td>Another case study interviewed politicians, officials and non-governmental organisation staff in 2008. It also found a lack of support by interviewees for giving smokefree car legislation a high priority. The authors argued that there was a need for “more information on the extent of current child exposure to tobacco smoke in New Zealand cars” and for “wider dissemination to policy-makers of New Zealand public and smoker support for banning smoking in cars, and of the progress overseas on smokefree car laws…”</td>
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<td>Māori policy-maker attitudes</td>
<td>A qualitative study of Māori policy-makers (MPs and officials in 2008/09) indicated that “there was a strong theme that the rights of children clearly outweigh the individual rights of adults to smoke in privately owned spaces, for instance homes and cars, and that adults have a duty of care to protect children from harm.” However, despite this there were mixed views on legislating to ban smoking in cars with children.</td>
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<tr>
<td>Pacific policy-maker attitudes</td>
<td>A qualitative study of Pacific policy-makers in 2008 identified a general reluctance to consider smokefree regulation extensions e.g., to smokefree cars. The authors noted that this finding was “at odds with surveyed attitudes of Pacific peoples in New Zealand”.</td>
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<td>Previous political considerations</td>
<td>The landmark Māori Affairs Select Committee Inquiry into the tobacco industry included a recommendation in their Report to investigate extending the Smoke-free Environments Act to legislate against smoking in additional settings including vehicles (especially those carrying children).</td>
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</table>
As detailed in the above table, a large amount of research has been done in the New Zealand setting around smokefree cars. The overall thrust of this work is that smoking in cars is an important public health issue and one that is likely to contribute to health inequalities in New Zealand (both ethnic inequalities and by area deprivation).

Smokefree car laws have been successfully introduced in other countries. Furthermore, the evidence indicates that there is high public support and indeed high smoker support for requiring smokefree cars carrying children especially in groups most impacted on by smoking e.g., Māori and Pacific populations. However, although the statements of policy-makers appear to give the protection of children’s health from proven hazards a high priority, they have (at least until recently), been less in favour of smokefree car laws than the public.

The most critical research need now is intervention and evaluation research, where before and after data collection occurs around a national smokefree cars law. Such research could assess the impact of the new law on:

(i) the occurrence of smoking in cars (especially with children present);
(ii) denormalisation relating to acceptability of smoking indoors and exposure of children to SHS; and
(iii) trends in youth smoking uptake. Monitoring trends in denormalisation are particularly relevant to informing on-going strategies around the tobacco endgame in this country and achieving the national goal of “Smokefree New Zealand 2025”.

Further information is also needed from overseas jurisdictions where there are smokefree car laws. Nevertheless, the 2007 smokefree vehicle law in South Australia (which only applies to vehicles carrying children), was reported to result in an increase in smokefree vehicles with children from 69% in 2005 to 82% in 2008. 30

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Competing interests: Although we do not consider it a competing interest, for the sake of full transparency we note that all of the authors have previously undertaken work for health sector agencies working in tobacco control.

References:


Health Workforce

The idea that the public appeal to the Whanganui District Health Board (DHB) over the shortage of obstetricians and gynaecologists has made the slightest jot of difference is ludicrous. In an under-supply and over-demand situation as currently exists and following on from the major overtime payment changes of the late 1980s a major factor influencing medical practitioners choice of work places is the lifestyle and on-call requirements.

In 1984, Wanganui had 3 obstetrician/gynaecologists, no obstetrics and gynaecology (O&G) registrars, and 1 O&G house surgeon. Palmerston North had 4 O&G specialists, 1 full-time registrar, 1 GP who also performed minor gynaecological operations and Caesarean sections, and 3 O&G house surgeons who were doing the then 6-month rotation to complete the requirements for the Diploma of O&G before entering general practice.

At that time all hospital doctors from trainee interns to specialists were on a unified pay scale regulated by the higher salaries commission which also set the pay for judges and MPs. In 1984, house doctors working a 1 in 3 roster were on-call and worked every third weekend from 8 am Friday till 5 pm Monday when the award required them to have a regulated 8 hrs rostered off duty. For rosters of greater than 72 hours per week, house surgeons received their basic pay plus overtime payments of a maximum of 42% for hours on-call and worked during the call period. The consultants worked a 1 in 4, sometimes a 1 in 5, and sometimes a 1 in 3 if covering leave.

With the Nurses Amendment Act 1989, taxpayer funding for private obstetrics dried up and in a low socioeconomic area like Wanganui few young couples could afford the $4000 plus that a private obstetrician needed to charge. For the last 20 odd years there has been no private obstetrics in most of New Zealand. The same act also has virtually killed off GP obstetrics in New Zealand which has further reduced a potential workforce for performing Caesarean sections.

Most Wanganui GPs now only see women (who are pregnant) requesting terminations. Because of vocal resistance to these being performed locally around 150 Wanganui women a year travel 400 km to a tertiary centre for these to be carried out. The Whanganui DHB funds the operations and 60,000 km travel out of its O&G budget.

The changes to the Employment Acts of the late 1980s and early 1990s saw the hospital doctors’ terms and conditions of employment turned upside down with the formation of the Resident Doctors’ Association (RDA) and the Association of Salaried Medical Specialists (ASMS). The RDA reasoned that working an extra 32 to 80 hrs for 42% of base salary was nuts and negotiated the overtime pay rate up to 200% of base salary for a 1 in 3 roster.

The net outcome of that was that hospitals needed to employ twice as many junior doctors as before the changes to do the same workload. To meet roster requirements
and avoid paying 300% to 1 junior doctor for an 80-hour week it was cheaper to employ 2 doctors and pay 200% of the base rate. The problem with that was that the supply of junior doctors had not doubled overnight to match the fiscal and physical demand. Consequently many junior doctors moonlighted for other Crown Health Enterprises on their days off commanding high locum rates, but they couldn’t be required to work the same hours for their main hospital employer.

Jump forward 20 years to 2012 and those junior doctors of the 1980s are now older specialists and for a rapidly decreasing proportion of the group, business owning General Practitioners. The specialists have had 20 years of not doing call without junior medical staff screening the brunt of the workload overnight and on weekends. Rosters of less than 1 in 4 or preferably 5 are no longer considered normal or acceptable working conditions for the majority of doctors. There is a requirement for registrar cover, specialist doctors in training to work between the undifferentiated house officers and the consultants, which lessens the burden of call.

According to the Medical Council, Palmerston North has 8 resident O&G specialists, there are 4 or 5 registrars and a number of house surgeons. Following on from the RDA roster negotiations of the 1990s the Diploma of Obstetrics went from a 6-month residency to a 9-month residency in order to provide enough clinical experience.

The 1986 Census had the combined population of Manawatu/Wanganui at 220,000. In 2012 the estimated population of the region has increased to 232,000, not enough to provide sufficient work for a large Wanganui-based workforce in order to provide reasonable after hours rosters and workloads. The private surgical pool is miniscule in comparison to larger centres like Auckland, and unlike orthopaedics, ACC is not a big payer in the private O&G market. Statistics New Zealand expects the regional population to decrease in the future. The Primary Health Organisation 3-monthly registers on the Ministry of Health website are showing the local population is decreasing by several hundred a year.

Over the years, Wanganui has employed solo vascular surgeons, psychogeriatricians, pathologists, ENT surgeons, eye surgeons and radiologists but the small population base and changing work expectations and conditions means some of these positions will have gone forever and others are provided at the beneficence and goodwill of the incumbent individuals albeit at a premium in some cases. Supervision means employing 2 people to do the work of 1 until the Medical Council, the supervisor and the employers are happy that the standard of work and level of expertise are commensurate with the position filled.

Health Workforce New Zealand doesn’t seem to have managed to rationalise the training and workforce with the places and positions of need and it is largely the clinicians who hold all the trump cards in dictating their terms and conditions of employment. It is not possible to bond medical students to progress to certain specialties or general practice to fill a perceived need and the time lag from student to fully qualified GP or specialist is at least 10 to 12 years.

Shorter periods of student allowances and higher student costs will inevitably push up the required levels of remuneration and that will further strain the relationship between cash-strapped medical employers and the increasingly casualised and short-term locum workforce seeking to pay off student loans at the same time as having the
ideal work/life balance. This balance is pushed by many of the increased number of locum agencies, each of which takes their fee for making the locum’s life easier.

Distorted financial returns and risks have (in the past) led to shortages of hospital midwives, house surgeons, ultra-sonographers, physiotherapists, paediatricians, other specialists, and GPs to name but a few.

What is bizarre is that often it is the taxpayer representatives, in the guise of ACC or the Ministers of Health with unrealistic goals, that are creating the pay discrepancies. It is as if the left hand and right hand are not connected and communicating with their one integrated brain.

Bill Douglas
Wanganui
Reply by New Zealand Chiropractors’ Association to Edzard Ernst’s April 2012 “research”

Dear Editor

It is disappointing to see that you have once again through your journal allowed Professor Edzard Ernst the opportunity with the 20 April 2012 publication to stimulate fear and suspicion about manipulation, and more specifically about the chiropractic profession. He has on numerous times in the past been identified as publishing misleading articles on chiropractic\(^\text{1-3}\) and has been described by Dr Gordon Waddell, a leading UK orthopaedic surgeon and back pain authority, as offering “inter-professional confrontation under the guise of scientific objectivity.”\(^\text{4}\)

Among the numerous journals that he cites as failing to report adverse events [AEs] are prestigious journals such as *Spine*. The editors of such high ranking journals would surely be experts regarding the requirements around this topic. Ernst implies that chiropractic is unsafe because adverse events are often not reported. Even if this is the case, this is not a uniquely chiropractic issue, as he implies. As recently as 2007, the task force set up by the International Society of Pharmacoepidemiology found that “many major journals have minimal requirements for publishing adverse event reports, and some have none at all”.\(^\text{5}\)

The “numerous prospective studies specifically designed to investigate AEs of chiropractic manipulation”, quoted by Ernst, refer to only three studies and they do not “agree” on the figure of 50% experiencing mild to moderate AEs after such treatments. However; this is not, as implied, an unreasonably high reaction rate unique to chiropractic. A recent review found around half manual therapy patients may experience minor to moderate adverse events after treatment\(^\text{6}\) (a moderate adverse event can be defined as transient disability with medical care sought or needed but not hospitalization and minor adverse event as self limited which did not require additional medical care\(^\text{7}\)). This brings into question whether Professor Ernst is purposely exaggerating the information available and placing undue emphasis on certain issues for effect.

This incidence of AEs is not to suggest that manual therapies are somehow more dangerous than pharmaceutical treatments. Soon to be published research conducted in Sweden by an expert panel of pharmacists estimate 61% of all patients attending healthcare suffer from drug related morbidity (DRM)\(^\text{8}\) and of those 29% will suffer from a new medical condition. A similar study by an expert panel of Swedish physicians estimated that every other outpatient and inpatient experiences DRM. They will either suffer an ‘adverse drug reaction’ – which could be any reaction from insomnia to death – get ‘intoxicated’ from an overdose or become dependent on the drug.\(^\text{9}\)

Ernst’s persistence in peddling his particular brand of scaremongering is made all the more disturbing by the way he neglects to refer to any research that contradicts his
point of view. In this particular case, it occurs when he refers to the “expressed doubts about the safety of spinal manipulation. A particular concern [which] relates to vascular accidents caused by arterial dissection after upper spinal manipulation”. An objective and impartial reviewer would make some reference to the most comprehensive research carried out on this subject, (Cassidy) which found no evidence of greater risk of stroke from chiropractic care when compared with seeing a primary care physician. This was carried out under the direction of The Bone and Joint Decade and looked at over 100 million person years worth of data, finding only 818 cases or examples.\(^{10}\) The association with chiropractic or spinal manual therapy for 7% of these cases was considered likely to be due to patients with headache and neck pain from a pre-existing tearing of the vertebral artery seeking care before their stroke. This is termed “Stroke in Evolution” and can be difficult to diagnose.

His statement that “the opinion of most chiropractors that such complications are extreme rarities is partly based on the fact that clinical trials of chiropractic manipulation fail to demonstrate the existence of such events”, is artfully worded to sow suspicion without having to make any reference to the vast amount of data available that contradicts his position.

The best evidence indicates that the incidence of vertebro-basilar artery injuries associated with high-velocity upper neck manipulation is extremely rare – about 1 case in 5.85 million manipulations\(^ {11}\) and as previously discussed form only 7% of all causes of such events. These are indeed tragedies; however, the overwhelming evidence for the much higher risk of serious side effects and death from properly prescribed and properly administered pharmaceutical medication is also tragic, far more common, and therefore represents a much higher risk to the public. We acknowledge that spinal manipulation does carry some risk. As a profession we take this seriously. However, when put in perspective with the risks associated with other common medical treatments, the side effects from manual therapies are minimal. Add to this recent evidence that has shown that spinal manipulation is more effective than medication both in the short and long term for acute and subacute neck pain\(^ {12}\) and Ernst’s arguments just do not add up.

It would appear that Prof. Ernst is “manipulating” his presence in the sceptic blogosphere by publishing in the \textit{NZMJ}. This appears to do little more than promulgate misinformation. A careful review of the article in \textit{The Guardian}, published shortly after the \textit{NZMJ} article, would appear to confirm this.

In summary, the chiropractic profession is happy to debate issues surrounding shortcomings, patient management, safety and effectiveness. However we hope that we do not have to witness repeated publications of articles that mismanage the evidence in what can only be interpreted as an attempt to discredit.

Corrian Poelsma  
President  
New Zealand Chiropractors’ Association (NZCA)
References:


Dominion Notes: The increasing popularity of the cigarette

Excerpt from ‘Dominion Notes’ published in NZMJ 1911 May;11(42):35–37.

The steadily increasing popularity of the cigarette among all classes of smokers has been a matter of frequent comment of late years. That it is well grounded is demonstrated by the figures, which show that while the importations of tobacco – under which heading, presumably, both pipe and cigarette tobaccos are included – have grown at a rate roughly corresponding to the growth of population, the importation of cigarettes, has increased out of all proportion by leaps and bounds.

It has been calculated that during the past ten years the quantity of tobacco, imported into New Zealand has risen by about 30 per cent, while the increase in the case of cigarettes has been about 250 per cent. And these figures, it must be noted, take no account of the fairly large amount of tobacco made up into cigarettes in the Dominion.

The following table shows the importations under each heading at the four chief ports for the years 1900, 1905, and 1910:

<table>
<thead>
<tr>
<th>Year</th>
<th>Tobacco</th>
<th>Cigarettes</th>
</tr>
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<tr>
<td>1900</td>
<td>1,417,209</td>
<td>143,177</td>
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<tr>
<td>1905</td>
<td>1,742,412</td>
<td>220,522</td>
</tr>
<tr>
<td>1910</td>
<td>1,954,057</td>
<td>465,566</td>
</tr>
</tbody>
</table>
Proceedings of the 211th Scientific Meeting of the Otago Medical School Research Society, Wednesday 9 May 2012

Establishment of a photothrombotic stroke model in rats for investigations into therapies for improving recovery after stroke. L Boddington, J Gray, J Reynolds. Brain Health Research Centre, Department of Anatomy, Otago School of Medical Sciences, University of Otago, Dunedin.

Stroke is a leading cause of disability with many survivors showing some degree of motor impairment. After a stroke the brain undergoes remapping, allowing limited recovery of lost motor function. However, recovery is potentially hindered by changes in neuronal excitability. This study set out to establish a photothrombotic stroke model in rats to be used for future investigations into therapies to improve recovery after stroke.

Photothrombotic lesions were induced in the motor cortex of three rats. The photosensitive dye ‘Rose Bengal’ was injected intravenously and the motor cortex illuminated with intense light for 30 minutes to induce local platelet aggregation and thrombus formation. Another three rats underwent stroke induction surgery and light exposure, however no lesion was induced (unlesioned shams). Deficits in forelimb coordination were assessed using a grid-walking task and any asymmetry in exploratory forelimb use was detected using a cylinder task.

Before stroke induction, no significant asymmetry in forelimb use was observed, however after surgery, lesioned rats showed a persistent significant bias in using their unaffected forelimb (61.0% ± 5.9, mean ± SD, P < 0.05, One-way ANOVA). Unlesioned sham rats showed no significant bias in paw use after surgery. Prior to surgery, rats showed good co-ordination when walking across a wire grid, with less than 3% of the total steps taken being considered as stepping errors. During the first week after stroke induction, stepping errors in lesioned rats rose significantly (9.9% ± 3.6, mean ± SD, P < 0.05) compared to baseline assessments, but recovered to baseline levels after four weeks. Unlesioned rats showed no significant change in stepping errors over the course of the study.

Establishment of this reproducible model of stroke and functional deficit in rats will allow for future studies of the application of stimulation protocols thought to improve functional recovery after a stroke.

Nanomicelle-encapsulated RL71 (SMA-RL71) retains cytotoxicity against estrogen receptor negative breast cancer cell lines. J Diong1, R Rosengren1, L Larsen2, K Greish1. 1Department of Pharmacology and Toxicology, Otago School of Medical Sciences, 2Department of Chemistry, Division of Sciences, University of Otago, Dunedin.

Triple negative breast cancer (TNBC) is an aggressive subset of breast cancer lacking targeted drug treatments. The novel drug RL71 is cytotoxic toward TNBC cell lines.
with submicromolar EC50 values. To effectively deliver RL71 utilising the enhanced permeability and retention (EPR) effect, this study aimed to optimally encapsulate RL71 into styrene-maleic acid micelles (SMA-RL71) and examine the in vitro cytotoxicity of SMA-RL71 towards estrogen receptor negative breast cancer cell lines.

To synthesise micelles, RL71 and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide were added to hydrolysed styrene-maleic acid. Micelles were precipitated at pH 5, centrifuged, solubilised in water at pH 11 and then neutralised. The release rate of RL71 from micelles was determined by dialysis in a water bath at pH 7.4 and pH 5.5. The size of micelles was established using dynamic light scattering. MDA-MB-231, MDA-MB-468, Hs578T and SKBr3 cells were treated with RL71 or SMA-RL71 (5% or 15% loading).

Synthesised micelles had diameters of 130 nm (5% loading) and 182 nm (15% loading) which were large enough to utilise the EPR effect. In tumour-like conditions at pH 5.5, 24.5% ± 0.14% and 8.28% ± 0.7% (5% and 15% loading, respectively; mean ± SEM, n = 3) of RL71 was released from micelles after 6 hours. SMA-RL71 (15% loading) was the most cytotoxic towards MDA-MB-231 cells (EC50 of 0.54 µM compared with 0.78 µM for free RL71). SMA-RL71 (15% loading) was also more cytotoxic than RL71 towards MDA-MB468 and Hs578T cells, with EC50 values of 0.98 µM and 0.61 µM, respectively (compared with 1.05 µM and 0.88 µM for RL71). SMA-RL71 (5% loading) was less cytotoxic than RL71 and SMA-RL71 (15% loading) in all cell lines.

These results indicate that cytotoxicity was maintained for both constructs of SMA-RL71, largely in the submicromolar range. Furthermore, the micelles possessed desirable characteristics for further in vivo examination.

Changes in rat supraoptic nucleus gene expression in pregnancy and lactation. A Seymour, R Augustine, V Scott, C Brown. Centre for Neuroendocrinology and Department of Physiology, Otago School of Medical Sciences, University of Otago, Dunedin.

Birth and lactation are partly controlled by the hormone oxytocin, which is synthesised in the hypothalamic supraoptic nucleus (SON) of the brain. This study used quantitative PCR to investigate changes in gene expression of oxytocin, c-Fos, JunB and prodynorphin at different stages of reproduction to determine whether these might be involved in the driving activity of the oxytocin system in pregnancy and lactation.

Conscious rats that were either non-pregnant diestrous (NP, n = 8), pregnant at day 7 (P7, n = 6), 14 (P14, n = 6), or 21 (P21, n = 7), lactating at day 7 (L7, n = 5) or post-weaning (PW, n = 4) were euthanised by decapitation. Micropunches were taken from the SON and RNA was extracted and reverse-transcribed to cDNA that was then amplified using primers specific for the gene of interest. Gene expression was calculated relative to the housekeeping gene β-actin and expressed as a percentage of NP levels.

SON oxytocin gene expression was not different between groups (P = 0.18, one-way ANOVA). Similarly, SON c-Fos expression was not different between groups (P =
0.29) By contrast, SON JunB expression was different between groups (P = 0.02), as was SON prodynorphin expression (P < 0.01). SON JunB expression was lower than NP at P7 (61.8 ± 8.6% of NP, mean ± SEM, P < 0.05, Dunnett’s post-hoc test), P14 (55.6 ± 5.1%, P < 0.05) and L7 (58.5 ± 5.4%, P < 0.05). SON prodynorphin expression was higher at L7 than NP (235.1 ± 67.9% of NP, P < 0.05).

The results from this study provide evidence that decreased JunB expression and increased prodynorphin expression might be associated with altered functioning of the oxytocin system in pregnancy and lactation.

Microbiological quality of imported sexual performance medications. W Shen\(^1\), S Mros\(^2\), M McConnell\(^2\), S Hook\(^1\), C Strachan\(^1\). \(^1\)School of Pharmacy, \(^2\)Department of Microbiology and Immunology, Otago School of Medical Sciences, University of Otago, Dunedin.

Counterfeit medicines, adulterated natural products and invalidly imported prescription medicines are examples of importations that are seized by the border control pharmacist. While the pharmaceutical quality of such products have been found to be sub-standard, there is a lack of appreciable data on the microbiological quality of these imported products, usually purchased via the internet. This study therefore examined the microbiological quality of confiscated medicines and natural products produced for aiding sexual performance, which make up a large proportion of the items seen and detained by border control.

The products provided by border control included: counterfeit Viagra® (sildenafil), counterfeit Cialis® (tadalafil), three generic sildenafil medications and seven natural products. Additionally, four natural products were purchased locally, as well as genuine Viagra® and Cialis®. Testing methods were based on those given by the European Pharmacopoeia. Product contamination was quantified by the enumeration of total aerobic micro-organisms, yeast and moulds, and bile-tolerant, Gram-negative bacteria. Absence/presence testing for faecal coliforms, \textit{Salmonella} spp., and \textit{Clostridium} spp. were carried out by enriching then sub-culturing onto differential agars. Results were then compared to pharmacopoeial acceptance criteria.

Seventeen of the 18 products tested conformed to pharmacopoeial standards. One of the imported natural products recorded an aerobic microbial count of \(5.74 \times 10^5\) colony-forming units per gram of product (CFU/g), exceeding the pharmacopoeial limit of \(1.0 \times 10^5\) CFU/g for herbal products. The presence of \textit{Enterobacter} and \textit{Clostridium} were detected following enrichment, suggesting possible faecal contamination. No faecal coliforms should be present in oral dosage forms for human use.

This is the first study to examine the microbiological quality of confiscated imported medicinal products in New Zealand. While it is pleasing to note that all but one of the products were of an acceptable microbiological quality, the pharmaceutical quality of these products, particularly those claiming to be natural, should be examined.
“Mummy, Are There Bugs in My Mouth?”: Investigating the Oral Bacterial Diversity of Dunedin Children. D Sundaresan¹, M Cullinan¹, B Drummond¹, J Stanton², G Seymour¹, N Heng¹. ¹Sir John Walsh Research Institute, Faculty of Dentistry, ²Department of Anatomy, Otago School of Medical Sciences, University of Otago, Dunedin.

The adult oral cavity is thought to harbour > 700 microbial species, some of which cause oral diseases such as periodontitis. However, little is known about the number and types of oral species present during a child’s dental development. This project aimed to characterise the oral bacterial diversity of children at key stages of dental development using next-generation DNA sequencing technology and bioinformatics. Samples were taken from the teeth of 12 dentally-healthy children across four age groups ranging from 10 months to 7 years. A fifth group (3 children, aged 4 - 5) with confirmed active caries lesions was also included. The highly-conserved bacterial 16S rRNA genes were PCR-amplified from each sample and sequenced using the GS-FLX Titanium pyrosequencer. All sequence data was processed using the CLOTU (CLuster Operational Taxonomic Unit) bioinformatics suite.

Analysis of the bacterial diversity in all of the children’s dental samples revealed only 40 to 128 distinct species. At 10 - 12 months of age, bacteria on the teeth are predominantly Gram-positive with 35% - 46% of sequences classified as Streptococcus spp. and Abiotrophia. In contrast, at 6 - 7 years, dental surfaces comprise mainly Gram-negative taxa including Leptotrichia (~25%) and Fusobacterium (~10%). Genera such as Rothia were found in comparatively constant proportions (~10%) across all age groups. Interestingly, higher levels of Streptococcus sanguinis (~19%), and not the expected Streptococcus mutans, were detected in children with active caries relative to their age-matched dentally-healthy counterparts.

In summary, despite an overall limited range of species, age-dependent shifts in oral bacterial diversity were evident at different stages of a child’s life. The consistent presence of under-studied genera such as Leptotrichia and Rothia, and the prominence of S. sanguinis in carious samples, demonstrate the need for further research into their respective roles as potential microbial markers of oral health status.

Delayed post-treatment with bone marrow-derived mesenchymal stem cells affects the proliferation of progenitor cells in the subventricular zone after neonatal rat hypoxic-ischemic brain injury. S Cameron, L Goddard, R Sizemore, D Oorschot. Department of Anatomy, Otago School of Medical Sciences, University of Otago, Dunedin.

Hypoxic/ischemic (H/I) brain injury is a major contributor to neurodevelopmental deficits such as cerebral palsy. Striatal medium-spiny neurons die after this injury. The absolute number of striatal medium-spiny neurons is restored at one week after delayed treatment with bone marrow-derived mesenchymal stem cells (MSCs). The adjacent subventricular zone (SVZ) is a source of progenitor cells that may restore these neuronal numbers. Whether treatment with exogenous MSCs facilitates
neurorestoration via progenitor cell proliferation, migration, survival and differentiation is unknown. Hence, we investigated whether MSCs affect progenitor cell proliferation in the SVZ after neonatal hypoxia-ischemia.

Postnatal day (PN) 7 male Sprague Dawley rat pups underwent ligation of the right common carotid artery followed by exposure to 8% oxygen/92% nitrogen for 1.5 h. On PN14 a subcutaneous injection of cultured bone marrow-derived MSCs (126,000 cells), sourced from rat femurs, or diluent (saline) was administered to four H/I rats, respectively. Animals were perfused on PN21, each cerebrum was serially sectioned, and the sections processed for immunohistochemistry. The primary antibody MIB-5 raised against Ki-67, a specific marker of cellular proliferation, was utilized. The primary antibody was detected using biotinylated secondary and streptavidin-peroxidase antibodies, with aminoethylcarbazole as the end label. Stereological methods were used to measure the absolute number of Ki-67-positive cells in the SVZ.

There was a statistically significant reduction in the absolute number of Ki-67-positive cells in the SVZ of H/I animals treated with MSCs (1380 ± 120, mean ± SEM, n = 3) compared to H/I diluent-treated animals at one week after treatment (3390 ± 537, n = 4, unpaired two-tailed Student’s t-test; \( p = 0.03 \)). This decrease in the number of proliferating progenitors in the SVZ suggests that MSCs may be effective in stimulating the migration, survival and differentiation of SVZ progenitor cells into nearby striatal neurons. This is currently being investigated.

Upregulation of chemokine expression is associated with oestrogen deprivation in ER+ breast cancer. B Hunter, A Dunbier. Department of Biochemistry, Otago School of Medical Sciences, University of Otago, Dunedin.

Breast cancer is the most common cancer amongst women and the leading cause of cancer-mortality in females, with particularly high incidence amongst those living in developed countries. Approximately 80% of breast cancers express oestrogen receptor-\( \alpha \) (ER) and use oestrogen as a key growth stimulus. Aromatase inhibitors (AIs) reduce tumour cell proliferation by blocking the production of oestrogen. Despite this, up to 50% of patients receive little to no benefit from this therapy and many ultimately relapse. Treatment failure has recently been found to be associated with increased immune cell infiltration and inflammatory gene expression. Chemokine production by tumour cells represents one mechanism through which immune cells could be recruited. This study aimed to investigate the effect of oestrogen deprivation on expression of chemokines in the human cancer-cell line MCF-7 and in patients treated with AIs.

To mimic AI therapy, MCF-7 cells were cultured for 5 days in steroid-stripped fetal bovine serum and chemokine expression was measured at days 0, 1, 3 and 5 using quantitative real-time PCR. Chemokine expression was measured relative to the housekeeper genes FKBP, PUM1 and TPB that are known not to change during oestrogen deprivation.

Oestrogen deprivation induced cells to up-regulate expression of CCL5, CCL22 (8-fold and 9-fold of control cultures respectively \( P < 0.05, \) unpaired two-tailed t-test) and CXCL16 (2-fold, \( P = \text{ns} \)) after 3 days. Bioinformatic analysis of gene expression
data from AI-treated patients revealed up-regulation of CCL5 and CXCL16 ($P < 0.05$). Genetic data was derived from patients involved in two clinical trials by Dunbier et al. and Miller et al. High pre-treatment expression of CXCL16 and CXCL14 were also associated with increased survival.

These data suggest that oestrogen deprivation induces chemokine expression in ER+ve tumour cells in vitro and in vivo. Chemokines have the potential to recruit immune cells that could facilitate tumour growth in the absence of oestrogen. Targeting these cells could provide a novel therapeutic approach to improve response to treatment.

Does the schizophrenia-inducing cytokine IL-6 alter neurite outgrowth in the developing brain? S Murray, C Jasoni. Department of Anatomy, Otago School of Medical Sciences, University of Otago, Dunedin.

Maternal infection during pregnancy is a risk factor for schizophrenia. Maternal immune activation (MIA) in rodent models causes up-regulation of cytokines that can access the fetus, leading to schizophrenia-like behaviours in adult offspring. Pro-inflammatory cytokines, especially Interleukin-6 (IL-6), are strongly implicated in the development of this schizophrenic phenotype, however little is known about what effect cytokines may be having in the brain during development. The growth of neurites and formation of neuronal connections are essential for development of functional neural circuits in the brain. Therefore, the present study aimed to investigate the effect of IL-6 on neurite outgrowth in the developing hippocampus.

Hippocampi obtained from gestational day 17.5 (GD17.5) and postnatal day 0 (P0) mice, were cut into 300µm explants and plated in a 3D collagen gel containing either 10 ng/ml IL-6 or vehicle (phosphate buffered saline). The plated explants were incubated for 24 or 48 hours, then fixed and stained with the neuron-specific antibody TuJ1. Images were obtained using confocal microscopy and analyzed using computer software ImageJ. A ratio of outgrowth was calculated using the number of pixels outside the explant divided by the number of pixels inside the explant.

Neurite outgrowth in the treated group was expressed as a percentage of outgrowth in the control group. At P0, outgrowth of IL-6 treated explants (n = 6 explants) was 95.9% of control outgrowth (n = 5) at 24 hours, however at 48 hours outgrowth in the treated group (n = 21) was significantly reduced to 35.3% of control outgrowth (n = 15, $P < 0.05$, Student’s $t$-test). At GD17.5, outgrowth of IL-6 treated explants was not significantly different from controls at either 24 or 48 hours.

These results suggest that exposure to elevated IL-6 found in MIA can disrupt hippocampal wiring, forming a mechanism for schizophrenia risk in offspring.
Reduced cardiac response to β-adrenergic stimulation in the diabetic rat heart. H-Y Wang¹, J Baldi², R Lamberts¹. ¹Department of Physiology, Otago School of Medical Sciences, ²Department of Medicine, Dunedin School of Medicine, University of Otago, Dunedin.

Diabetes mellitus has a profound detrimental effect on the heart, with diabetic patients having a greater risk in the development of cardiovascular complications during and after surgery. It is established that the diabetic myocardium has a reduced cardiac response to β-adrenoceptor (β-AR) stimulation by catecholamines, but whether this is due to decreased inotropy (contractile force), chronotropy (heart rate) or both is unknown. Therefore, this study aimed to determine whether myocardial inotropic and chronotropic responses to β-AR stimulation are reduced in diabetes, using the isolated hearts of Zucker-diabetic-fatty (ZDF) rats.

Langendorff-perfused hearts of non-diabetic and diabetic ZDF rats (male, 16 weeks, n = 8) were randomly assigned to paced (5 Hz) or unpaced (intrinsic) heart rate. After basal functional parameters were measured, the hearts were exposed to incremental concentrations of dobutamine (10⁻⁹ to 10⁻⁶ M), a β-AR agonist. Left ventricular pressure (PᵥLV) and intrinsic heart rate (HR) were measured to assess inotropic and chronotropic response, respectively.

In the paced hearts, no change in basal PᵥLV was observed. In unpaced hearts, a depression in basal HR was detected in diabetic compared to non-diabetic (250 ± 15 versus 178 ± 9 bpm, P < 0.05), whereas the proportional HR increase in dobutamine concentrations was similar in both groups. There was a reduced response in PᵥLV to incrementing dobutamine concentrations in the diabetic group, which was more pronounced in the unpaced heart (∆EC₅₀ between non-diabetic and diabetic group: 0.47x10⁻⁷ M paced versus 1.76 x 10⁻⁷ M unpaced, P < 0.05).

The reduction in basal heart rate and compromised inotropic response to catecholamine in the diabetic heart is likely to be caused by the sympathetic overdrive present in diabetic rats in vivo. Although chronotropic modulation by dobutamine is unaltered, the HR-dependent inotropic response shows a reduced association between HR and contractility (Treppe effect) in the diabetic heart.

Apoptotic cell death in the rat hippocampus following a single binge alcohol exposure. C Smith¹,², L Fisher², R Napper¹,². ¹Brain Health Research Centre, ²Department of Anatomy, Otago School of Medical Sciences, University of Otago, Dunedin.

Drinking alcohol during pregnancy can result in profound developmental defects in the child, especially in learning and memory. Animal studies show that apoptotic cell death occurs in the developing brain soon after alcohol exposure. During apoptotic degradation, the contents of the cell are destroyed, presenting a challenge in determining which cell type is dying. Many of the neuronal populations vulnerable to ethanol toxicity are postmitotic and neuronal deficits will result in changes in brain circuitry. A deficit of hippocampal CA1 neurons in mature animals, exposed to alcohol on postnatal day 6 (PN6) suggests acute CA1 neuronal death. This study
investigated the time interval during which apoptotic cells can be phenotyped after the initiation of apoptosis.

Alcohol was delivered to rat pups on PN6, as two gavages of alcohol, administered two hours apart. A high dose (6 g/kg body weight) was used to achieve a high blood alcohol concentration (greater than 400 mg/dl). Animals were sacrificed 4, 8, and 12 hours after the initial alcohol exposure. Tissue sections were labelled using immunohistochemistry methods to detect astrocytes (GFAP/Vimentin), neurons (NeuN), and apoptotic cells (activated caspase-3 and Hoescht 55542).

The results showed an increase in apoptotic cell death in hippocampal sections between 4 to 12 hours (from 56 ± 13 to 246 ± 32 respectively). Maximal co-localisation of NeuN/activated caspase-3 occurred at 4 hours, with a significant decrease in NeuN/activated caspase-3 from 4 to 12 hours (57.29% ± 1.94% to 11.91% ± 1.73% respectively, $P < 0.001$). Activated caspase-3/Hoescht co-localisation was high at all time points (100% at 4 hours, 93.45% ± 2.61% at 8 hours, and 87.78% ± 1.03% at 12 hours). Data was analysed using one-way ANOVA and Newman-Keuls post-hoc test (Graphpad Prism).

The results confirm that CA1 neurons undergo apoptotic cell death following ethanol exposure in the CA1 region. Phenotypic identification is optimal at 4 hours after activation of the apoptotic cascade.
Lithium toxicity

Clinical practice guidelines have long recommended lithium as a first-line long-term treatment for bipolar disorder but its use has decreased, partly because of safety concerns. These are related to the drug’s low therapeutic index and the need to monitor its serum concentration and also monitor endocrine and renal function. This systematic review and meta-analysis aims to quantify the potential risks of lithium. They have included 385 studies in their analysis and their conclusions were:

“Lithium is associated with increased risk of reduced urinary concentrating ability, hypothyroidism, hyperparathyroidism, and weight gain. There is little evidence for a clinically significantly reduction in renal function in most patients, and the risk of end-stage renal failure is low. The risk of congenital malformations is uncertain; the balance of risks should be considered before lithium is withdrawn during pregnancy. Because of the consistent finding of a high prevalence of hyperparathyroidism, calcium concentrations should be checked before and after treatment”.

An accompanying editorial notes that this study provides timely clarification of the toxicity associated with lithium therapy and, on balance, reaffirms its role as a treatment of choice for bipolar disorder.


Reproductive technologies and the risk of birth defects

There is evidence from many studies that demonstrate there is an increased risk of birth defects among births conceived with assisted reproductive technology as compared with births from spontaneous conception.

This paper seeks to elucidate whether this is a true association or if is explained by other underlying parental factors. Data obtained from over 300,000 births, including 6163 resulting from assisted conception, was analysed. The unadjusted odds ratio for birth defects involving assisted conception versus natural conception was 1.47. However, the increased risk associated with in vitro fertilisation was no longer significant after adjustment for parental factors.


Abdominal computed tomography (CT) in the diagnosis of appendicitis

CT is now recognised as being superior to other tests, including abdominal ultrasound, in the diagnosis of acute appendicitis. However, many patients in whom appendicitis is suspected are children or young adults, and radiation exposure from CT is of particular concern in the population.
Hence this randomised trial which has evaluated the rate of negative (unnecessary) appendectomy after low-dose versus standard-dose abdominal CT in young adults with suspected appendicitis.

The researchers randomly assigned 891 patients with suspected appendicitis to either low-dose CT (444 patients) or standard-dose CT (447 patients). The median radiation dose in terms of dose-length product was 116 mGy⋅cm in the low-dose group and 521 mGy⋅cm in the standard-dose group. The negative appendectomy rates were 3.5% in the low-dose CT group and 3.2% in the standard-dose CT group.

The researchers conclude that low-dose CT was noninferior to standard-dose CT with respect to negative appendectomy rates in young adults with suspected appendicitis.


Self monitoring of blood glucose in people with non-insulin treated type 2 diabetes

Such monitoring is useful in those diabetes who are treated with insulin as they are at significant risk of hypoglycaemia or hyperglycaemia. This paper gets to grips with the usefulness of self monitoring in non-insulin treated type 2 diabetics. They reviewed 6 randomised trials an they report a small but statistically significant reduction in HbA1C levels at 6 months in those who have used self monitoring. The mean pooled reduction in HbA1C at 6 months was 9.6 mmol/L in the monitored group compared with 7.5 in the controls. They felt that the evidence was not convincing enough to support the routine use of self monitoring in such patients.

BMJ 2012;344:e486.

Incidence of diabetic retinopathy in people with type 2 diabetes and how should they be screened?

The author of this study note that screening for diabetic retinopathy is cost effective, although the current policy of screening every person with diabetes each year might not be necessary.

They have done a retrospective analysis of data from 49,763 with type 2 diabetes mellitus and no evidence of diabetic retinopathy attending systematic screening provided by the Diabetic Retinopathy Screening Service for Wales between January 2005 and November 2009. They report the annual incidence of referable retinopathy remained low at 2.02 and 3.54 per 1000 people in the first and fourth follow-up year, respectively.

They conclude that these findings lend support to the use of risk stratification to define the most appropriate screening interval, with less frequent screening needed in people at low risk of developing retinopathy, therefore allowing more frequent screening in those at high risk. Those at higher risk seem to be those who have had diabetes for 10 years or more and those requiring insulin treatment.

BMJ 2012;344:e874.
William Leslie Francis (Bill) Utley

OBE, MB.ChB(NZ), FRCS (Eng) FRACS (born 6 August 1922, died 14 April 2012)

Bill graduated from the University of New Zealand in Dunedin in 1945. He married Patricia Gardiner in 1946.

After hospital residencies in Christchurch and a short spell in general practice, in 1948 he went to England as a ship’s surgeon and began as a house surgeon at the Royal Post-graduate Hospital at Hammersmith.

He passed the Fellowship of the Royal College of Surgeons of England and then had a registrar position at All Saints Hospital, London under Terence Millin who popularised the retropubic approach to open prostatectomy, which was safer than the trans-vesical method introduced earlier by Freyer.

Bill then was appointed as Urology Registrar at St Peter’s Hospital, Covent Garden in 1951–1952.

There followed short appointments at St Mark’s Hospital for rectal diseases and then 8 months at the Whittington Hospital in London.

He returned to Christchurch in 1952 first as a resident surgical officer and senior registrar and then consultant in Urology working in the Urology Department with E R (Steve) Reay and Norman Greenslade. He was involved in some seminal research on the prevalence of vesico-ureteric reflux in neonates and in early childhood and the relationship to its grading severity to the risk for renal scarring. He collaborated with George Rolleston, and Fred Shannon. George Abbott, and Ross Bailey, and later Tom Maling (radiologist) were also involved.

Bill’s father had spinal vertebral injuries in WWI, and subsequent osteomyelitis, a spinal abscess resulting in tetraplegia. He died soon after when Bill was 2. Perhaps this was one of the triggers that stimulated his interest in spinal urology.

Knowledge of the neurological problems in spinal injuries was thin in the 1950s and on a sabbatical leave Bill went to the UK to Stoke Mandeville Hospital to learn more and to upskill under the tutelage of Sir Ludwig Guttman. On the return trip he visited Ernst Bors at the Long Beach Spinal Center in Los Angeles California.

On return to Christchurch he was convinced that New Zealand needed a dedicated Spinal Unit. He wished to adopt Guttman’s philosophy first that patients should be admitted as early as possible after injury to a specialised spinal unit, and secondly that the Unit should make the patient as independent as possible and rehabilitate him/her so that life was worth living. These principles remain the firm basis of the
independent living paradigm espoused strongly by Allan Clarke and the Burwood Spinal Unit and its Academy of Independent Living. In 1974 Ludwig Guttmann visited Christchurch and the Ministry of Health, adding weight to Bill’s efforts to establish a standalone Unit.

He was also involved in establishing the Paraplegic Federation, Parafed, to encourage rehabilitation through sport, and was active in supporting patients to compete in the first Paralympic Games in New Zealand held in Dunedin in 1974. Later he was made an honorary member of Parafed, which continued with Guttmann’s philosophy by emphasising the importance of sport to the gaining of independence and quality of life. He supported the formation of Kaleidoscope, an organisation to help people spinal patients back into the workforce as another means of restoring patients to independent useful living.

He also visited the Spinal Unit in Perth and held fruitful discussions with Sir George Bedbrook, on developing the shape of the new Unit. Allan Bean and later Angelo Anthony did further training in managing those with spinal injuries at the Perth Unit.

With advice, persistence and enthusiasm he was the prime mover in establishing a Spinal Unit in Christchurch Hospital initially in 1968 assisted by Bill Liddell Orthopaedic surgeon and J Cunningham, neurologist. Later he succeeded after much lobbying and political persuasion in establishing a purpose-built Spinal Unit at Burwood Hospital, Christchurch in 1979. This unit accepted patients from as early as possible after the injury so rehabilitation could begin straight away. He was the director of the Spinal Unit from 1964 to 1999.

At the beginning the Urology Ward had its own operating theatre, purportedly for doing cystoscopies and minor procedures. Major procedures were allowed on a trial basis. The trial lasted 30 years. The theatre staff introduced themselves on the day of the patient’s admission and would explain any details. On arrival in the theatre next day for the operation, the patient would be greeted by familiar faces. The same theatre nurses would visit the patient in the ward post-operatively, and many patients appreciated that. It did not last, as there was no staffed Intensive Care Unit close by.

Similarly a cystoscopy and minor procedures theatre was incorporated in the new Spinal Unit in 1979. It was not long before even major procedures were undertaken there for a time, before the requirement these be done in the main operating theatre suite was enforced for safe post-op recovery care.

He trained many urology registrars over the years, including two from USA: Dale Vermillion (Billings, Montana) and Bob Donohue (Denver, Colorado). Together with Bob he undertook the first kidney transplant in the South Island of New Zealand in 1972.

Bill was awarded the OBE in 1972 for services to medicine.

He developed a liaison with the Pacific Islands and was instrumental in aiding some Fijians to advance in training as specialist surgeons and one did complete the Urology training for the RACS.

Together with the other urologists in Christchurch, in 1981 he assisted in the establishment of a renal transplant program in Riyadh, Saudi Arabia where earlier a
Christchurch renal physician Peter Little had established the Kingdom’s first unit for managing end-stage renal disease.

Bill was far-sighted in introducing a partnership model in specialist private practice in 1978, which has continued successfully in Christchurch ever since. At the time this type of specialist group practice was practically unknown in New Zealand.

Bill was a urology examiner for the Royal Australasian College of Surgeons from 1978 to 1982. He was President of the Urological Society of Australasia in 1980.

Aside from medicine, Bill was active politically both as an elected member of the Christchurch City Council, and an elected member of the then North Canterbury Hospital Board. While in that capacity he served as the Chair of its Works Committee for 9 years. He also served on the Executive of the St George’s Hospital and in 2010 was made a Life Member of the St George’s Hospital Society.

He farmed a small property on the outskirts of Christchurch and often after a busy operating list he would drive home and get on the tractor do the ploughing and other work as needed. He chaired the New Zealand Murray Grey Beef Cattle Society for 3 years. He had enormous enthusiasm and energy in all he took on.

Bill died on 14 April 2012 after a period of illness precipitated by a fall at home.

Bill is survived by his wife Pat, daughters Frances and Juliet, sons-in-law Ross and Steve, and daughter-in-law Marie, and their families. Their son John was a general surgeon in Christchurch and had died a few months earlier in 2011.

To Pat and the family, we extend our sincere sympathy, and trust that this acknowledgment of his many contributions to Urology and Spinal injury in Christchurch and the rest of New Zealand will help in some way to bear their loss in his passing.

Written by Ted Arnold, with assistance from Pat and other colleagues in New Zealand.
Henry Stone

Henry was born in Warsaw, Poland on 9 September 1922. His parents were Gershon and Racal Leah Norodworski. He was called Asher Anshell until his name was changed when he left Europe in the late 1920s. With his two sisters and two brothers he enjoyed a traditional Jewish upbringing rich in education. Gershon was keen to improve the family's situation.

He and his siblings emigrated to all corners of the world—including Argentina, USA, UK, France, and New Zealand.

Gershon himself initially explored Central America spending 6 months in Panama and Cuba before heading to Australia.

The rest of the family then travelled by sea from Marseille to Sydney to join Gershon. A year or so later they all moved to Auckland.

When the family arrived in Auckland, Henry's first languages were Yiddish and Polish but he quickly learnt English and spoke without the trace of an accent for the rest of his life. Growing up in Ponsonby he attended the local school, and then Mount Albert Grammar.

He was an academic and despite his small stature was also a keen sportsman. In Otago he gained University Blues in fencing and hockey. Henry spent 5 years in Dunedin at Medical School, followed by hospital work around the country.

He went to England in the early 1950s to further his studies, focusing on respiratory medicine. Research into tuberculosis took him to Kitwe, and the Copper Belt of Northern Rhodesia (now Zambia). While there in 1955 he met Joan Kaye who was travelling from England. In December 1955 Joan and Henry married in Salisbury; a marriage which was to last 56 years.

By early 1958 they returned to New Zealand; Henry completed his MD and also a Diploma in Public Health. After posts around the country he established himself as Medical Superintendent at Green Lane Hospital where he stayed for over 20 years. During his tenure he assisted the team at Green Lane to create a world class centre of excellence.
Henry was admired for his extensive general knowledge; the family frequently sought his opinion on all manner of subjects. Until the year before he died he still played a competitive game of tennis, and walked daily. His bridge was almost as sharp as his general knowledge. He read avidly and loved to pass on his thoughts and knowledge to the family. Typical of Henry he always encouraged others to participate.

All who knew him understood he was a modest, kind, caring man always keen to put others first. Henry passed on a great legacy to his family and those who knew him of intellectual pursuit and education, kindness, medical endeavour, strong work ethic and family values. He is survived by his wife Joan, sons Marcus and Tony and six grandchildren.

Marcus Stone wrote this obituary.