THE NEW ZEALAND MEDICAL JOURNAL
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This Issue in the Journal

Influence of rural background and rural medical training on postgraduate medical training and location in New Zealand
William Shelker, Tony Zaharic, Branko Sijnja, Paul Glue

Recruiting and retaining rural doctors is a pressing national problem. The Otago Medical Programme has two initiatives to increase numbers of rural doctors: to enrol students from rural backgrounds, and to offer students a year of medical training in rural communities. We looked at the influence of these programmes on where 2008-2011 graduates were working, and what training they were doing. A significantly higher proportion of graduates from rural backgrounds or who had rural training were working in rural hospital medicine or general practice, and twice as many were working outside of Major Urban Centres.

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Evan Jolliffe, Peter Flanagan

Warfarin is an effective anticoagulant used for a range of clotting disorders. Patients on warfarin therapy have a 1–3% risk of bleeding each year which may require intervention to reverse the warfarin effect. In 2013 updated guidelines for warfarin reversal were published. Prothrombinex-VF has many advantages over Fresh Frozen Plasma for the reversal of warfarin. This audit identified the suboptimal use of the reversal product Prothrombinex-VF and the overuse of Fresh Frozen Plasma for the reversal of warfarin.

The changing landscape of antimicrobial resistance in New Zealand [review article]

Deborah A Williamson, Helen Heffernan

Antimicrobial resistance is one of the greatest global health threats of the modern age. Compared with many other countries, rates of antimicrobial resistance among important bacterial pathogens are relatively low in New Zealand. However, antimicrobial resistance is increasing among bacteria isolated from patients in our hospitals and also patients in the community. There are often marked geographic differences in resistance rates within New Zealand. Factors contributing to the emergence and spread of antimicrobial-resistant pathogens in New Zealand include the use and overuse of antimicrobials, transmission of resistant organisms in healthcare facilities and the community, and importation of resistant pathogens from areas where multidrug-resistant pathogens are endemic.

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New Zealand health professional organisations' joint call for action on climate change and health

Alexandra Macmillan, Rhys Jones, Hayley Bennett

Climate change is arguably the defining health issue of our time, and 10 New Zealand health organisations have recently come together to issue a joint *Call for Action on Climate Change and Health* for New Zealand.[1]

Climate change's prominence as a mainstream public health concern is evident in the many health-focused events that took place at the Climate Summit in New York this week. The summit was convened by the UN Secretary General and attended by over 120 heads of state, as well as health leaders including the US Surgeon General, Editor-in-Chief of the Lancet and the World Health Organization. In conjunction with the Climate Summit, civil society protests calling for urgent global action have been held across the globe, involving hundreds of thousands in a People's Climate March.

Ahead of this Summit, the World Health Organization held an inaugural conference at its headquarters in Geneva to raise the profile of climate change as a crucial and urgent public health issue. The Director General of the World Health Organization, Dr Margaret Chan, stated: "[t]he evidence is overwhelming: climate change endangers human health. Solutions exist and we need to act decisively to change this trajectory."[2]

This week the World Health Organization also released a new quantitative risk assessment of the global effects of climate change. A very limited subset of causes of death in the 2030s and 2050s was included.[3] In 2030, 250,000 extra deaths per year are projected, with a sharply increasing burden of mortality attributable to heat exposure. This is an extremely conservative estimate of the adverse impacts on mortality of climate change, since major pathways of health impact could not be accounted for using current methods, such as via economic damage, major weather events and water scarcity. The likely step changes caused by crossing ecological and social thresholds were also not able to be modelled.

Also in association with the New York Climate Summit, the British National Health System has issued a collective statement of intent to deliver climate friendly health services into the future. The joint statement is the first example of one country's health sector committing to tackle climate change.[4]

It is within this context that 10 New Zealand health organisations representing doctors, nurses, midwives and medical students, have recently come together to issue a joint *Call to Action on Climate Change and Health* for New Zealand. The groups include the New Zealand College of Public Health Medicine, The Australasian College for Emergency Medicine, The New Zealand Nurses Organisation, The New Zealand College of Midwives, The Public Health Association of New Zealand, The Health Promotion Forum, OraTaiao: The NZ Climate and Health Council, Medical

Students for Global Awareness, The New Zealand Medical Students' Association and the Auckland University Medical Students' Association.[1]

In the *Call to Action* these organisations highlight human-caused climate change as an increasingly serious and urgent threat to health and health equity in New Zealand, as well as worldwide.[5–11] The *Call to Action* also emphasises that rapid and effective action to reduce greenhouse gases in New Zealand represents an opportunity to improve health and equity in this country with the right policies.[8,11,12]

Health threats from climate change in New Zealand include direct impacts (e.g. from high temperatures and other extreme weather events); biologically-mediated impacts (e.g. changing patterns of infectious disease, global rises in food prices impacting on nutrition); and socially-mediated impacts (e.g. loss of livelihoods, forced migration, and increased risk of conflict).[8–11] Māori, Pacific peoples, children, elderly and low income people are highlighted as those that are likely to be worst affected by climate health impacts.[8–11]

But opportunities to improve health and equity through climate action are also emphasised in the *Call to Action*.[5,6,8,11] Three particular policy areas hold promise for optimising health and climate co-benefits. Firstly, more walking, cycling and public transport reduces greenhouse gas (GHG) emissions, increases physical activity, and can reduce health-damaging air pollution and road traffic injuries.[5,6,11,12]

Secondly, healthy diets that include more plants and fewer animal products could reduce agricultural GHG emissions, whilst also reducing cancer and heart disease across the New Zealand population.[11,12,13] Thirdly, improving housing energy efficiency can reduce illnesses associated with cold, damp home environments (e.g. childhood asthma and chest infections which are leading causes of hospital admissions, particularly for Māori and Pacific children), whilst also cutting GHG emissions associated with home heating.[11,14]

The *Call to Action* highlights that these health co-benefits could reduce leading causes of death and illness in New Zealand, such as cardiovascular disease, respiratory disease, cancers and diabetes, with large cost savings to the health sector and society as a whole.[6,8,11]

The health professional groups are careful to point out in the *Call to Action* that measures to address climate change have the potential to widen or reduce existing health inequities, depending on design and implementation. Avoiding a disproportionate impact on low income groups and instead ensuring that co-benefits reduce social and health inequities will require careful policy design, for example by recycling carbon penalty revenue back into supporting low income households.[15]

The *Call to Action* makes a number of specific recommendations. It calls for a rapid, whole-of-society, transition to a low GHG-emitting nation in New Zealand, designed to make the most of opportunities for health and to create a fairer society. It also calls for the health sector to plan for the health impacts of climate change, and to show leadership in reducing greenhouse gas emissions – as other health systems (such as the British National Health System) are already doing. Measures that prioritise and protect groups likely to be worst affected by the health impacts of climate change are highlighted as essential; and Health Impact Assessment (HIA) is suggested as a tool to assist the planning of key climate-relevant policies in New Zealand.

The *Call to Action* highlights that no country can solve climate change singlehandedly, and that without taking rapid and sufficient action itself, New Zealand cannot effectively press for global emissions reductions in the interests of health protection. Thus the health groups specify that national emissions reduction targets in New Zealand of 80–95% by 2050 are needed, consistent with Intergovernmental Panel on Climate Change (IPCC) evidence and with our responsibilities as a developed nation with high per capita greenhouse gas emissions.

The 10 health organisations supporting the *Call to Action* also point out that New Zealand, as part of the Pacific region, will need to demonstrate leadership in protecting and promoting health in the climate-vulnerable Pacific region.

As 400,000 people hit the streets in New York for the 'People's Climate March' on the opening day of the UN Climate Summit (and thousands more in 150 countries around the world), it is clear that people everywhere are making the links between climate change, human health, and survival. The 'People's Climate March' is the largest climate protest in history and the largest social demonstration of the last decade.

The New Zealand health sector voice needs to join those voices being raised internationally – in other health systems, international medical journals and world health authorities – to make climate change a mainstream public health issue in New Zealand. The Call continues to be open to all health professional organisations in New Zealand to join. Together we must continue to press for urgent action to reduce the serious risks we face, and to seize the opportunities to improve health.

Competing interests: Nil.

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References:

1. Climate Change and Health. Health Professionals Joint Call For Action, September 2014. http://www.orataiao.org.nz/Joint+call+to+action
2. Speech by Dr. Margaret Chan, Director General of the World Health Organization. World Health Organisation Conference on Health and Climate, Geneva, August 27-29 2014. http://www.who.int/globalchange/mediacentre/events/climate-health-conference/en/
3. World Health Organization. Quantitative risk assessment of the effects of climate change on selected causes of death, 2030s and 2050s. Geneva, World Health Organization, 2014. http://www.who.int/globalchange/publications/quantitative-risk-assessment/en/
4. UN Climate Summit Cross System Statement. Sustainable Development Unit, NHS and Public Health England. http://www.sduhealth.org.uk/policy-strategy/engagement-resources/un-climate-summit.aspx

5. Smith KR, Woodward A, Campbell-Lendrum D, Chadee D, Honda Y, et al. Human Health: Impacts, Adaptation, and Co-benefits. In: Climate Change 2014: Impacts, Adaptation and Vulnerability. Contribution of Working Group II to the Fifth Assessment Report of the Intergovernmental Panel on Climate Change [Field CB, Barros VR, Mastrandrea MD, Mach KJ, et al. (eds.)]. Cambridge University Press, Cambridge, UK and New York, NY, USA, 2014. http://ipcc-wg2.gov/AR5/images/uploads/WGIIAR5-Chap11_FGDall.pdf
6. Woodward A, Smith KR, Campbell-Lendrum D, Chadee DD, Honda Y, et al. Climate change and health: on the latest IPCC report. Lancet. 2014;383:1185-9. http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(14)60576-6/fulltext
7. McCoy D, Montgomery H, Sabaratnam A, Godlee F. Climate change and human survival. BMJ. 2014;348:g2351. http://www.bmj.com/content/348/bmj.g2351
8. Jones R, Bennett H, Keating G, Blaiklock A. Climate change and the right to health for Māori in Aotearoa/New Zealand. Health and Human Rights Journal. 2014;16:54-68. http://www.hhrjournal.org/wp-content/uploads/sites/13/2014/06/Jones2.pdf
9. Howden-Chapman P, Chapman R, Hales S, Britton E, Wilson N. Climate Change and Human Health: Impact and Adaptation Issues for New Zealand. In: Nottage RAC, Wratt DS, Bornman JF, Jones K (eds). Climate Change Adaptation in New Zealand: Future Scenarios and Some Sectoral Perspectives. Wellington: New Zealand Climate Change Centre, 2010. http://www.nzclimatechangecentre.org/sites/nzclimatechangecentre.org/files/images/research/Climate%20Change%20Adaptation%20in%20New%20Zealand%20(NZCCC)%20high%208.pdf
10. Hosking J, Jones R, Percival T, Turner N, Ameratunga S. Climate change: the implications for child health in Australasia. J Paediatr Child Health. 2011;474: 93-96. http://onlinelibrary.wiley.com/doi/10.1111/j.1440-1754.2010.01699.x/full
11. New Zealand College of Public Health Medicine. Policy Statement on Climate Change. Wellington: New Zealand College of Public Health Medicine, 2013. http://www.nzcphm.org.nz/media/74098/1._nzcphm_climate_change_policy__final_comms_version2_.pdf
12. Haines A, McMichael AJ, Smith KR et al. Public health benefits of strategies to reduce greenhouse-gas emissions: overview and implications for policy makers. Lancet. 2009;374:2104-14. http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(09)61759-1/fulltext
13. Wilson N, Nghiem N, Ni Mhurchu C, Eyles H, Baker MG, Blakely T. Foods and dietary patterns that are healthy, low-cost, and environmentally sustainable: a case study of optimization modeling for New Zealand. PLoS ONE. 2013;8:e59648. doi:10.1371/journal.pone.0059648. http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0059648
14. Howden-Chapman P, Matheson A, Viggers H et al. Retrofitting houses with insulation to reduce health inequalities: results of a clustered, randomised trial in a community setting. BMJ. 2007;334:460-464. http://www.bmj.com/content/334/7591/460
15. Dhar D, Macmillan A, Lindsay G, Woodward A. Carbon pricing in New Zealand: implications for public health. NZ Med J. 2009;122:105-15. http://www.nzma.org.nz/__data/assets/pdf_file/0006/17799/Vol-122-No-1290-27-February-2009.pdf

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Medical careers – nature or nurture?

Tim J Wilkinson

There's a degree of satisfaction when one sees a gap in medical education being identified, an evidence-based intervention put in place, and then the whole thing evaluated to see if it's working as planned. Such is the case with incentives to increase the rural medical workforce.

In general, there are three pillars to influencing medical workforce, that all have to be aligned: select the right people, give them the right experiences during medical school and in postgraduate training, and provide incentives for people to work there after qualification. Rural medical workforce initiatives are no different. It has been well described internationally that choosing a medical career in a rural setting is more likely if the person comes from a rural background, has rural experiences during training and if the job at the end is sufficiently attractive.[1] There are additional, not insubstantial, social influences such as where one's spouse wants to live and work.

Some medical schools claim it is not their role to influence the medical workforce. Fortunately, neither of New Zealand's medical schools takes that stance. In this issue of the *Journal*, Shelker et al have evaluated the impact of the University of Otago Medical School's rural entry pathway and rural medical immersion programme (RMIP).[2]

The rural entry pathway is a government-led policy that ensures a certain quota of entrants into medical school comes from a rural background. The RMIP is a yearlong immersion programme in year 5 of the MBChB programme where some students spend the whole year in rural settings. Shelker et al have shown that these are associated independently and synergistically with subsequent choices to undertake rural training.[2] This is important to know. The international evidence-based best practice also works in New Zealand. These initiatives are not cheap yet seem to be delivering what was intended.

There are however important notes of caution. The effects have a significant relative effect but the absolute effect is different. While the relative effect is to approximately double the likelihood of undertaking rural training, we know that most people who have chosen a career in rural settings fit none of the criteria – many do not come from rural backgrounds and many did not have the benefit of the RMIP. Thus we are influencing choices, not determining them. This means that while 'a lot for a few' is an important aspect of medical training we must not neglect 'a little for everyone'. As well as the RMIP (for the few), all Otago students have some time in rural contexts – this (for the many) should be valued.

In addition, these findings are associations, not causations. We do not know, for example, if those students choosing to undertake the RMIP might already have decided that rural practice is for them and that the programme itself did nothing to alter that pre-existing view. Nevertheless, even if that were the case, we know that nurturing pre-existing intentions is important.

What we also know about career choices is that many people's views are very fluid until 1–4 years after graduation and that role models and intra-medical school experiences are influential.[3,4] Interestingly, our recent research has shown that extra-medical school experiences are possibly more influential, at least in choosing a career in general practice: yes, role models are important, but portrayal of various medical disciplines by the media and television shows is also influential as are the views of peers and family.[5] So medical schools can influence these things, but there are many other factors to take into account.

These findings have implications for other types of medical career as well. Given most career choices are made after leaving medical school, we need to consider medical school experience within the three pillars around career choice: selection, medical school/postgraduate experience, and postgraduate incentives.

The medical school experiences need to be positive. However, just as there is the inverse care law – those in most need of some health care services are the least likely to receive it, there could also be an inverse career law – those disciplines of greatest shortage may be the ones that provide the least positive experiences.

Consider a medical discipline that is understaffed and that needs to interest, and be considered by, more medical students. Being understaffed may also mean the few staff that are in place are over-worked and stressed. Such groups may well find it hard to provide the positive role models to medical students that we know are so important. Fortunately, these factors don't seem to be operating with these rural initiatives. But it does highlight the need to ensure there are synergies between education and service. Furthermore, increasing time in a discipline will not automatically mean more students will become interested in it.

There have been claims that some medical schools should set themselves up to train just one type of doctor. For example a medical school aimed at producing general practitioners. This is a misguided idea. Expecting an 18-year-old, at the time of selection into medical school, to be clear on career choice is naïve, especially if they have not been exposed to the full breadth of medical practice.[6]

Most choices are made after medical school, so the medical school experience is only one factor. But most importantly, the effect of these diverse experiences during medical school is just as important for people not choosing a particular career. In other words, the health service is likely to benefit from tertiary-based super-specialists also having had rural exposure. Such a person is likely to be more understanding of the context and issues affecting rural practice when being referred to from a rural-based doctor.

So are medical careers born or made? Is it nature or nurture? Clearly careers are both, but there is a third element. They are born, made, and attracted. Yes, we need to select the right people, yes we need to provide positive learning experiences, but we also need to make the job attractive enough at the end to close that loop and ensure the initiatives are sustained.

Competing interests: Nil.

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References:

1. Hsueh W, Wilkinson TJ, Bills J. What evidence-based undergraduate interventions promote rural health? New Zealand Medical Journal. 2004;117(1204):1-17.
2. Shelker W, Zaharic T, Sijnja B, Glue P. Influence of rural background and rural medical training on postgraduate medical training and location in New Zealand. New Zealand Medical Journal. 2014;127(1403).
3. Pasley T, Poole P. Characteristics of University of Auckland medical students intending to work in the regional/rural setting. New Zealand Medical Journal. 2009;122(1292):50-60.
4. Boyle V, Shulruf B, Poole P. Influence of gender and other factors on medical student specialty interest. New Zealand Medical Journal. 2014;127(1402):78-87.
5. Parker J, Hudson B, Wilkinson TJ. Influences on final year medical students' attitudes to general practice as a career. Journal of Primary Health Care. 2014;6(1):56-63.
6. Poole PJ, Moriarty HJ, Wearn AM, Wilkinson TJ, Weller JM. Medical student selection in New Zealand: looking to the future. New Zealand Medical Journal. 2009;122(1306):1-13.

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Influence of rural background and rural medical training on postgraduate medical training and location in New Zealand

William Shelker, Tony Zaharic, Branko Sijnja, Paul Glue

Abstract

Aims To evaluate the influence of the Otago Medical Programme's rural entry pathway and rural immersion programme on postgraduate medical training and location.

Methods Retrospective cohort study of 2008–2011 medical school graduates. Rural background/training included students gaining preferential entry to medical training based on rural residence or schooling, and/or those who spent a year training in a rural setting. Postgraduate medical training and location were obtained from the NZ Medical Register in December 2013.

Results 112/733 students (15.3%) had rural background/training. Significantly more students with rural background/training were training in rural hospital medicine or general practice after graduation. Multiple logistic regression identified both variables (rural background and rural training) as independently statistically significant (Odds Ratios (95%CI); rural background OR 2.1, 95%CI 1.2–3.6; rural training OR 2.5, 95%CI 1.4–4.5; p=0.002). Almost twice as many students with rural background/training were working in non-Major Urban Centres.

Conclusions These findings are similar to international reports on the influence of medical schools' rural initiatives on postgraduate training choices and practice location. University policies aimed at increasing the proportion of medical graduates practising in rural areas appear to be working as intended.

Recruitment and retention of the rural medical workforce has been highlighted as both a national[1] and global issue,[2] and that increasing numbers of rural doctors is an important step in improving the quality of healthcare delivered to rural populations. Internationally the strongest predictor to increasing graduates training in rural medical practice has been to recruit medical students from rural backgrounds,[3–9] and to provide undergraduate medical training in rural settings.[5–9]

Both the Otago and Auckland Medical Programmes have put in place initiatives to graduate doctors who are more likely to work in the rural sector.[10] The Otago Medical Programme has two approaches. The Rural Origins Sub-Category admissions pathway, started in 2003, offers preferential entry to students from rural backgrounds (determined by their residence and/or location of their primary/secondary school), who also meet academic admission standards.

The Rural Medical Immersion Programme (RMIP), started in 2007, sends 5th-year medical students to train in rural communities for one year. This research assessed the influence of the Otago Medical Programme's two rural initiatives on the proportion of

graduates training in rural hospital medicine or general practice, their location of practice, and postgraduation retention of these doctors in NZ.

Methods

This retrospective cohort study was approved by the University of Otago Ethics Committee (13/216). A database was created with the names of medical students graduating from the University of Otago from 2008–2011, along with whether they entered through the Rural Origins Sub-Category pathway and/or took part in the RMIP.

Data regarding year of birth, gender, entry pathway into medical school (Health Sciences First Year (HSFY) vs the two graduate entry pathways[11]) and year of graduation were obtained from the University of Otago student database, under the supervision of an authorised staff member.

The NZ Medical Register was accessed in December 2013 to identify which graduates were registered in NZ and their postgraduate information. This included their vocational training programme and current geographical location within NZ. Sponsored foreign students were not included in the database, nor were graduates who were one year postgraduation. Training programmes of interest to this project included the Rural Hospital Medicine Programme and the General Practice Education Programme.

Graduates' geographical location was taken from the MCNZ register as the doctor's location of practice. This was divided into one of two categories, either Major Urban Centre or non-Major Urban Centre, as described by Statistics New Zealand[12]. Anonymised data were analysed using summary statistics.

The influence of undergraduate rural exposure (graduates coming through the Rural Origins Sub-Category pathway and/or the RMIP) on training programme selection, geographical location and remaining on the NZ Medical Register were evaluated using chi square tests.

The influence of medical school entry pathway and undergraduate rural exposure on being in rural hospital medicine/general practice after graduating was evaluated using multiple logistic regression (Stata v11.2 software).

Results

The demographics of graduates, grouped by presence/absence of undergraduate rural exposure, are shown in Table 1.

Table 1. Characteristics of medical graduates from the Otago Medical Programme 2008–2011, grouped by presence/absence of undergraduate rural exposure

Rural background/experience	N	Mean (SD) age at graduation (y)	% Male	% HSFY	Number (%) remaining in NZ in Dec 2013
No	621	25.2 (3.2)	45.4%*	77.3%†	497 (80%)
Yes	112	24.8 (2.4)	33.1%*	87.5%†	94 (84%)

HSFY: Health Sciences First Year entry pathway. *p=0.02;†p=0.02.

There was a significantly higher proportion of female graduates with rural background/training (75/112; 67%) compared with those with no rural background/training (339/621; 55%; Pearson Chi^2=5.42, p=0.02), and a significantly higher proportion of graduates with rural background/training entering medical school via HSFY (98/112; 87.5%) compared with those with no rural background/training (480/621; 77.3%; Pearson Chi^2=5.33, p=0.02).

Postgraduate training choices of graduates with and without rural background/training are shown in Table 2. Graduates who had rural background/training had a higher proportion involved with Rural Hospital Medicine and General Practice than graduates with no rural background/training (Pearson Chi^2=34.2, p<0.001).

Multiple logistic regression was used to evaluate the influence of entry pathway and rural background/training on postgraduate involvement with Rural Hospital Medicine and General Practice. This showed a significant overall effect (p=0.001), with the relationship described by the formula Logit P=-2.406+(0.915 * ruralexposure)+(0.718 * entrypath).

Assessment of individual variables identified both rural background (Odds Ratio (OR) 2.5, 95%CI 1.4–4.5; p=0.002) and entry pathway (OR 2.1, 95%CI 1.2–3.6, p=0.01) as statistically significant.

Table 2. Effect of rural initiatives on postgraduate training choices of doctors

Rural background/experience	Postgraduate Training Choices [% (n)]			
	Rural Hospital Medicine	General Practice	Other	None
No	0.4% (2)	9.7% (48)	40.8% (203)	49.1% (244)
Yes	6.4% (6)*	13.8% (13)*	19.1% (18)	60.6% (57)

*=p<0.001 when combined.

The geographical location of doctors' practices in those with and without rural background/training is shown in Table 3. Although the proportion of graduates with rural background/training working outside of a Major Urban Centre was almost twice that of graduates without rural background/training (11.7% vs 6.6%), this was not statistically significantly (Pearson Chi^2=2.25, p=0.13).

Table 3. Effect of rural initiatives on geographical location of doctors

Rural background/experience	Major Urban Centre	Non-Major Urban Centre
No	93.4% (464)	6.6% (33)
Yes	88.3% (83)	11.7% (11)

There was no effect of rural exposure on graduate retention (Table 1), with 84% of students with rural background/training remaining compared with 80% of students without rural background/training (OR 1.06, 95% CI 0.61–1.87). All of the graduates (n=14) who were from rural backgrounds and who also participated in RMIP were practicing in New Zealand.

Discussion

The main finding of this study was that medical school graduates who were from rural backgrounds or who were exposed to rural medicine as undergraduates were more likely to be training in rural hospital medicine or general practice after graduation, compared with students without rural background/training.

Although not previously reported from New Zealand, these findings are consistent with an extensive international literature on this topic. An early systematic review of 12 US, Canadian and Australian case control or cohort studies identified rural background, rural schooling and rural undergraduate training as factors associated with subsequent rural medical practice[7]. Further cohort studies have confirmed this review.[8,9]

We anticipated that there would be a greater proportion of graduates with rural background/training working rurally (i.e. in non-Major Urban Centres) than graduates with no rural exposure. Although the proportion was almost two-fold higher (11.7% vs 6.6%, Table 3), this was not statistically significant. This could be due to the relatively small numbers of graduates in this study, and/or the relatively brief postgraduate period (up to 5 years), and should be re-evaluated in the future.

Our observation that there was 100% retention of graduates who were admitted to medical school via the Rural Origins Sub-Category pathway and who took part in RMIP is intriguing, but is based on a very small number of graduates (n=14), and may well be a chance finding.

Possible shortcomings of this study should be acknowledged. Because of the relatively recent adoption of the two rural initiatives, graduate data were only available for up to 5 years, and it is possible that some of the analyses could be underpowered due to relatively small numbers. " It will be important to re-evaluate this in the future. However the main finding (that rural background/training was associated with higher rates of training in rural hospital medicine or general practice) is consistent with published findings.

In conclusion, we have identified that the proportion of medical graduates training in rural medicine and general practice in the 5 years after graduation was greater in those with rural backgrounds/experience compared with graduates without rural exposure, and this finding is consistent with international literature on this topic.

Rurally-focussed medical school admission and training schemes are important ways to increase the rural medical workforce in New Zealand. University policies aimed at increasing the proportion of medical graduates practising in rural areas appear to be working as intended.

Competing interests: In the past 3 years Professor Glue has been a consultant for Kinex Pharma and involved in a clinical trial from Demerx Pharma. The other authors have no competing interests to declare.

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References:

1. Ministry of Health. Rural health and primary health care. http://www.health.govt.nz/our-work/primary-health-care/primary-health-care-services-and-projects/rural-health-and-primary-health-care Accessed 24.01.2014.
2. Dolea C, Stormont L, Braichet J-M. Evaluated strategies to increase attractions and retention of health workers in remote and rural areas. Bulletin WHO 2010;88:379-385.
3. Rabinowitz HK, Diamond JJ, Hojat M, Hazelwood CE. Demographic, educational and economic factors related to recruitment and retention of physicians in rural Pennsylvania. J Rural Health 1999;15:212-218.
4. Ward AM, Kamien M, Lopez DG. Medical career choice and practice location: early factors predicting course completion, career choice and practice location. Med Educ 2004;38:239-48
5. Rolfe IE, O'Connell DL, Pearson SA, Dickinson JA. Finding solutions to the rural doctor shortage: the roles of selection versus undergraduate medical education at Newcastle. Aust NZ J Med 1995;25:512-517.
6. Rabinowitz HK, Diamond JJ, Markham FW, Paynter NP. Critical factors for designing programs to increase the supply and retention of rural primary care physicians. J Am Med Assoc 2001;286:1041-1048.
7. Laven G, Wilkinson D. Rural doctors and rural backgrounds: how strong is the evidence? A systematic review. The Australian Journal of Rural Health 2003;11:277– 284.
8. Curran V, Rourke J. The role of medical education in the recruitment and retention of rural physicians. Medical Teacher 2004;26:265-272.
9. Jones MP, Bushnell JA, Humphreys JS. Are rural placements positively associated with rural intentions in medical graduates? Med Educ 2014;48:405-16.
10. Shelker W, Poole P, Bagg W, Wood I, Glue P. Postgraduation retention of medical students from Otago and Auckland medical programmes. N Z Med J 2014;127:47-54.
11. Shelker W, Belton A, Glue P. Academic performance and career choices of older medical students at the University of Otago. N Z Med J 2011;124:63-8.
12. Statistics New Zealand. Defining Urban and Rural New Zealand. 2004. http://www.stats.govt.nz/browse_for_stats/people_and_communities/Geographic-areas/urban-rural-profile/defining-urban-rural-nz.aspx Viewed 20.01.2014

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Poisoning following exposure to chemicals stored in mislabelled or unlabelled containers: a recipe for potential disaster

Yvette C Millard, Robin J Slaughter, Lucy M Shieffelbien, Leo J Schep

Abstract

Aim To investigate poisoning exposures to chemicals that were unlabelled, mislabelled or not in their original containers in New Zealand over the last 10 years, based on calls to the New Zealand National Poisons Centre (NZNPC).

Methods Call data from the NZNPC between 2003 and 2012 were analysed retrospectively. Parameters reviewed included patient age, route and site of exposure, product classification and recommended intervention.

Results Of the 324,411 calls received between 2003 and 2012, 100,465 calls were associated with acute human exposure to chemicals. There were 757 inquiries related to human exposure to mislabelled or unlabelled chemicals consisting of 0.75% of chemical exposures. Adults were involved in 51% of incidents, children, <5 years 32%, 5–10 years 10%, and adolescents 5%. Child exploratory behaviour was responsible for 38% of calls and adult unintentional exposures 61%. Medical attention was advised in 26% of calls.

Conclusion Inadvertent exposure to toxic products stored in unlabelled or mislabelled containers is a problem for all age groups. Although it represents a small proportion of total calls to the NZNPC it remains a potential risk for serious poisoning. It is important that chemicals are stored securely, in their original containers, and never stored in drinking vessels.

The correct storage of poisons plays a significant role in poisoning prevention. This not only includes storing poisons in locked cupboards, but also keeping products in their original containers.

Chemical containers that are mislabelled or unlabelled may increase the chance of accidental poisoning, especially when chemicals are placed into drink containers such as soft drink (soda/pop/carbonated beverage), beer or milk bottles. In these situations there are risks of poisoning not only to children, but also adults who may presume the contents are a beverage.

This risk can be exacerbated when some chemical colours are nearly identical to the colour of the original beverage (see Figure 1). Additionally, after an exposure to an unidentified chemical it is difficult for Poisons Information Centres and medical staff to perform a risk assessment of the incident and determine appropriate medical management.[1]

Figure 1. Comparison of beverage and household chemical colours

In New Zealand it is illegal to store chemicals in food and beverage containers. The Food (Safety) Regulations 2002, Part 1 Reg 6 Misuse of Food Containers[2] states that:

"No person may put, keep or sell any disinfectant, antiseptic or detergent, or a substance which could cause poisoning, in any container or package that:

a) Bears any brand, picture, word, mark or statement:
   i. indicating the presence in the container of any food; or
   ii. that is likely to mislead any person into believing that the contents of the container are intended for the purposes of human consumption; or

b) Is of a distinctive type in which articles of food have been commonly or are currently being sold, whether or not it bears any brand, picture, word, mark or statement."

Despite the Food (Safety) Regulations there have been two well publicised incidents in New Zealand in recent years in which chemicals were placed in beverage containers. In 2009 three people drank from a water jug containing an alkaline beer line cleaner. All three patients were hospitalised, two with oesophageal burns.[3]

In 2012, a benzalkonium chloride-based moss and mould cleaner was placed in a Sprite Zero® bottle at a bar. A customer was served what was believed to be lemonade from the bottle. Following ingestion of the liquid contents, the customer required medical attention.[4]

Severe poisonings including deaths have occurred overseas. A man died after ingesting paraquat that was stored in a Lucozade® bottle,[5] a 2.5-year-old boy died after ingesting diquat left in a soft drink bottle,[6] and another 2.5-year-old boy died after ingesting endosulfan also stored in a soft drink bottle.[7]

The aim of this study was to investigate the incidents of poisoning following exposure to mislabelled or unlabelled chemical products by retrospectively reviewing New Zealand National Poisons Centre (NZNPC) data over a 10-year period.

Methods

The NZNPC is the sole provider of poison information in New Zealand and receives approximately 35,000 telephone enquiries per year from throughout the country. Covering a population of approximately 4.4 million people, calls are received from both the general public and health professionals concerning acute poisoning.

An in-house computerised telephone enquiry collection database has been developed by the NZNPC. Built on Firebird™ 2.0.3 which was developed by the Firebird Project, the database is used to log information pertaining to all enquiries received by the NZNPC. This collection system utilises a poisoning incident report format and all relevant call information is entered into the database in real time as calls are received.

The current study was a single-centre retrospective review of call data from the telephone collection database regarding human acute exposures to mislabelled or unlabelled chemicals for the years 2003 to 2012 inclusively.

The retrospective review was limited to human poisoning or human exposure, excluding calls involving animal exposure, hazardous chemical inquiries (information calls without human exposure), and administrative inquiries. Calls involving mislabelled or unlabelled bottles were found using key word searches.

Data fields collected included patient age and sex, route of exposure, site of exposure, product classification, circumstances of the exposure or incident, severity of symptoms and recommended intervention.

Severity of symptoms was calculated based on The Poisoning Severity Score,[8] developed by poisons centres around the world to evaluate poisoning cases based on the most severe clinical features. Comorbidity information such as cognitive state and visual impairment was not available.

Results

The NZNPC received 324,411 calls between 2003 and 2012. Chemical exposures in humans comprised 100,465 (31%) enquiries. Of these, 757 (0.75%) were human exposures to products in unlabelled or non-original containers. These enquiries were relatively steady over the 10-year period with a mean of 75.7 (SD+21.6, range 44–110) calls per year.

The receptacles most commonly used for storing chemicals were non-alcoholic drink bottles such as soft drink, water, milk and sports drink bottles. Alcoholic containers such as beer and wine bottles also featured. Seven calls involved two products being ingested from separate containers.

Adults were involved in 51% of incidents, children <5 years 32%, 5–10 years 10%, adolescents 5% and patients of unknown age 2%. The proportion of adult exposure is different to that for overall chemical exposure enquiries—i.e. for the same time period, adults only represented 35% of total chemical exposure cases.

When the age of the adult was known, adults 18 to 29 years were involved in 32% of incidents, aged 30 to 39 years 18%, 40 to 49 years 20%, 50 to 59 years 15%, 60 to 69 years 11%, and over 70 years 4%.

Ethanol intoxication did not contribute to any of the exposures in adults nor were there any other comorbidities identified. Inadvertent exposures accounted for 99% of the total exposures (61% in adults and 38% in children) while the remaining were related to self-harm.

Male patients accounted for 58% of cases and females 41%, with 1% of unknown sex. Ingestion was the main route of exposure occurring in 93% of cases; inhalation occurred in 3%, dermal in 2% and ocular exposures in 2% of cases. The majority of cases occurred at home (84%) followed by workplace exposures (11%).

Patients were asymptomatic in 59% of cases and had minor symptoms in 35% of cases. More concerning symptoms were rare with 5% of patients developing moderate symptoms, 0.3% developing severe symptoms and no fatalities reported. Corrosive injury was the cause of all 3 cases of severe poisoning. One child developed severe symptoms (Table 1).

Table 1. Severity of poisoning based on age of patients

Age group	Severity of symptoms			
	Asymptomatic	Mild	Moderate	Severe
Child	235	78	12	1
Adolescent	22	15	1	0
Adult	190	174	25	2
Unknown	2	0	0	0
Total	**449**	**267**	**38**	**3**

Self-treatment was the most common recommended treatment to callers (56% of cases). Medical attention was advised in 26% of cases; in some cases this was because of a lack of information available to determine the toxic risk to the patient.

The substance class or type of chemical was unknown in 9% of incidents. In 81% of incidents the substance class or type of chemical was known, but due to the container being unlabelled or mislabelled the exact product name could not be established.

Table 2 represents the most common substances that were reported to the NZNPC; these were predominantly household cleaners, vehicle fuels, and glycol based products.

Potentially significant toxic or life-threatening chemicals including cyanide, paraquat and carbaryl featured in one call each.

Table 2. Top 10 most common substances involved in unlabelled or mislabelled container incidents

Substance name	Number of calls
Dishwashing liquid	51
Vehicle fuels (petrol, diesel etc.)	50
Glycols (antifreeze, brake fluids etc.)	39
Disinfectant	35
Bleach	33
Mineral turpentine	32
Glyphosate herbicides	26
Methylated spirits	23
Paint thinners	21
Multipurpose household cleaner	17

Discussion

This investigation has shown exposures to chemicals stored in unlabelled, mislabelled or non-original containers in New Zealand cross all age groups and most frequently occurs in the home setting or in the workplace. From the data, it would appear those at greater risk for poisoning are children less than 5 years and adults aged between 18 and 49 years.

Although most patients in these situations were asymptomatic or developed only mild symptoms, there is still a risk of more concerning toxicity occurring. Exposures to chemicals in unlabelled containers, particularly herbicides (e.g. paraquat), corrosive chemicals (e.g. drain cleaners), and glycols (e.g. radiator and brake fluids), can lead to more adverse clinical effects. Risks involving co-morbidities, including ethanol intoxication or cognitive and visual impairments, were not identified.

The study has also revealed that these exposures are continuing to occur despite laws prohibiting the storage of chemicals in food and beverage containers. The storage of hazardous chemicals in drink bottles can potentially cause severe poisoning or can even result in death.[6,7]

In this series, the majority of poisonings (99%) were accidental and would have been prevented if chemical storage regulations had been followed. Indeed this concern has been reflected in a recent joint advertising campaign by the Environmental Protection Agency and Ministry of Business Innovation and Employment which includes internet advertising and safety videos.[9]

Poison information centres play a vital role in the management of poisonings by determining the risk of potential adverse effects following an exposure; in the majority of cases, exposures have minimal or no clinically important toxic effects and information provided by the poison information centre can effectively reduce unnecessary presentations to medical centres or emergency departments.[10,11]

If chemicals are stored in mislabelled or unlabelled containers it may be impossible to correctly identify the actual contents; poison information centre or emergency department staff are therefore unable to do an appropriate risk assessment following accidental ingestion.[1]

In the case of an ingestion of an unknown poison, medical observation in the emergency department for the onset of adverse effects is normally recommended.[12,13] This can unnecessarily consume emergency department resources if observation and investigations are not required due to the ingestion of an innocuous substance. Conversely, delays in receiving appropriate treatment such as gastrointestinal decontamination or antidote administration may occur if a potentially poisonous chemical has been ingested.

Additionally, many commercial and household products that may be potentially hazardous are required to have child-resistant closures to prevent children from being accidentally exposed.The use of child-resistant closures has been effective in reducing accidental poisoning in children,[14,15] especially in the case of prescription medications.[15] When chemicals are transferred from their original packaging to other containers such as drink bottles, these containers will no longer provide the safety that child resistant closures may afford and could be mistaken for the original beverage content, increasing the risk of an accidental poisoning occurring.

This study has highlighted ongoing concerns pertaining to the storage of chemicals in unlabelled or mislabelled containers, despite legislation designed to prevent such incidents.

More attention needs to be given to ways of reducing accidental exposures to household and other chemicals; it is important that all hazardous chemicals are stored safely and not decanted from their original containers into vessels normally used for, or associated with, drinking.

Limitations—There are limitations that should be taken into consideration when evaluating the results of this study. The study data only relates to enquiries received by the NZNPC and therefore may not reflect all relevant exposures in New Zealand over the study period. Cases may be missed where patients present directly to medical centres or emergency departments and physicians managing these patients may not contact the poison information centre for advice. It is also possible other cases may go undetected if parents or caregivers do not witness the exposure or do not contact the NZNPC if the incident is perceived to be minor. The exposures reported may therefore suffer from bias to some degree. In addition, as incoming enquiries to the NZNPC are not routinely followed up, our study could not provide comprehensive information on morbidity or outcome. Nonetheless, despite these limitations, our data provide insight into an ongoing potential source of poisoning in New Zealand.

Competing interests: Nil.

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References:

1. Daly FF, Little M, Murray L. A risk assessment based approach to the management of acute poisoning. Emerg Med J. 2006;23:396-9.
2. Food (Safety) Regulations 2002. Part 1 r 6., (9 December, 2002).
3. Porteous D. Two remain ill after toxic tipple at RSA. Otago Daily Times. 24 Apr 2009. Accessed 25 November 2013. Available from: http://www.odt.co.nz/your-town/waikouaiti/52730/two-remain-ill-after-toxic-tipple-rsa
4. Fox M. RSA cleaner warned for toxic drink. Stuff.co.nz. 9 March 2012. Accessed 25 November 2013. Available from: http://www.stuff.co.nz/auckland/local-news/6550443/RSA-cleaner-warned-for-toxic-drink
5. MSN NZ. Man dies after mistaking weedkiller for Lucozade. MSN.co.nz. 10 December 2010. Accessed 25 November 2013. Available from: http://news.msn.co.nz/article/8180760/man-dies-after-drinking-weedkiller-kept-in-lucozade-bottle
6. Powell D, Pond SM, Allen TB, Portale AA. Hemoperfusion in a child who ingested diquat and died from pontine infarction and hemorrhage. J Toxicol Clin Toxicol. 1983;20:405-20.
7. Parbhu B, Rodgers G, Sullivan JE. Death in a toddler following endosulfan ingestion. Clin Toxicol (Phila). 2009;47:899-901.
8. Persson HE, Sjöberg, Haines JA, Pronczuk de Garbino J. Poisoning severity score. Grading of acute poisoning. J Toxicol Clin Toxicol. 1998;36:205-13.
9. Environmental Protection Authority and Ministry of Business, Innovation & Employment. Hazardous substances toolbox. Accessed 7 April 2014. Available from: http://www.hazardoussubstances.govt.nz/videos
10. Chafee-Bahamon C, Lovejoy FH, Jr. Effectiveness of a regional poison center in reducing excess emergency room visits for children's poisonings. Pediatrics. 1983;72:164-9.
11. Zaloshnja E, Miller T, Jones P, et al. The impact of poison control centers on poisoning-related visits to EDs--United States, 2008. Am J Emerg Med. 2008;26:310-5.
12. Mofenson HC, Greensher J. The unknown poison. Pediatrics. 1974;54:336-42.
13. McCoubrie D, Murray L, Daly FF, Little M. Toxicology case of the month: ingestion of two unidentified tablets by a toddler. Emerg Med J. 2006;23:718-20.
14. Krug A, Ellis JB, Hay IT, et al. The impact of child-resistant containers on the incidence of paraffin (kerosene) ingestion in children. S Afr Med J. 1994;84:730-4.
15. Rodgers GB. The safety effects of child-resistant packaging for oral prescription drugs. Two decades of experience. JAMA. 1996;275:1661-5.

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Local impact of 'Antenatal Screening for Down syndrome and other conditions' on diagnosis and outcomes in a fetal medicine centre in New Zealand

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Abstract

Aim In 2010, the National Screening Unit of the Ministry of Health launched 'Antenatal Screening for Down syndrome and other conditions'. Our aim was to assess the local impact of the new screening process on the number and outcomes of women attending a south island Fetal Medicine Centre.

Methods Retrospective audit; two time periods (T1 and T2) were reviewed. Data was prospectively collected in a viewpoint database and combined with data from other hospital databases and laboratories. Outcome measures included invasive procedures done and results and MSS1 results. Statistical analysis was done using Open Epi software.

Results 51% of women who were pregnant in T2 underwent MSS1 screening. There was a statistically significant decrease in the number of invasive procedures carried out 2.9% (175) vs. 4.1% (253), p0.0003 in T2. The proportion of procedures undertaken by Chorionic Villus Sampling and amniocentesis did not change. In both time periods no babies with Down syndrome were born following pregnancies where screening was undertaken and was low risk.

Conclusions The implementation of the new antenatal screening process in Canterbury has so far proved to be successful in maintaining detection rates of genetic anomalies whilst decreasing the numbers of invasive diagnostic procedures being done.

In February 2010 the National Screening Unit of the Ministry of Health New Zealand launched 'Antenatal Screening for Down syndrome and other conditions'. The introduction of this quality improvement process has brought antenatal screening in New Zealand in line with international best practice and offers a risk assessment for all women including those at increased risk of chromosomal anomalies.

Similar screening programmes have been trialled and found cost-effective, as judged by high detection rates for low false positive rates in other countries including the United Kingdom and the United States of America,[1–3] and provides a risk assessment of Down syndrome (trisomy 21) and other chromosomal anomalies including Patau syndrome (trisomy 13), Edwards syndrome (trisomy 18) and sex chromosome aneuploidy.

Prenatal diagnosis for Down syndrome and other chromosomal anomalies has been available in NZ since the early 1960s in the form of amniocentesis.[4] Historically women were offered testing based on increasing maternal age >35 years, or due to a family history of chromosomal anomalies.[3] In most developed countries, the maternal

age of pregnant women is increasing, and now about 20% of all pregnancies are to women aged >35 years.[5] Offering screening to only this sector of the maternity population is inequitable.[6]

Recently, until the introduction of the new screening process in 2010, women in NZ were offered a nuchal translucency (NT) measurement alone done by ultrasound scan at the end of the first trimester (between 11 and 13+6 weeks gestation) on an ad hoc basis. This scan measures the fluid behind the neck of the fetus and increased levels can indicate increased risk of a fetal anomaly such as Down syndrome or structural anomalies.

Accurate NT measurement has strict parameters and therefore requires significant sonographic expertise to achieve. If women presented in the second trimester they were offered the quad screen of hormones, comprising free alpha human chorionic gonadotrophin (α HCG), beta human gonadotrophin (β HCG), alpha fetoprotein (AFP) and unconjugated oestriol.[7]

The new antenatal screening test is a combined test (first trimester screening) and comprises a nuchal translucency measurement in combination with a maternal serum biochemical test measuring two hormones; pregnancy associated plasma protein A (PAPP-A) and βHCG.

This first trimester combined test has been reported to have an 83–86% detection rate compared to the old second trimester serum screening which is reported to have a 70–77% detection rate, both for a 6–9% false positive rate.[1,3,8] NT measurement alone in the first trimester only had a reported 60–70% detection rate at best for a 20–25% false positive rate.[1,3,8] Second trimester screening is a quadruple screen of hormones, comprising βHCG, AFP, unconjugated oestriol and inhibin A and has a reported detection rate of 83% for a 6% false positive rate, and is now offered only to those women who missed MSS1 but wish for a form of screening.[1,3,8]

If a woman has an increased risk of a chromosomal anomaly in either trimester she is then offered invasive testing: chorionic villus sampling (CVS) or amniocentesis. These tests are diagnostic but both carry an inherent risk of miscarriage of 0.5–1.0% in addition to the background risk of miscarriage which is higher at the gestation CVS is undertaken.[9,10]

Amniocentesis prior to 15 weeks is not recommended because of possibility of inadequate concentration of fetal cells in the sample, a higher incidence of talipes and a higher rate of miscarriage (<14 completed weeks) as found in the CEMAT study.[9,11,12] In NZ, current cut off point for annotating a pregnancy as high risk is > 1 in 300 risk of aneuploidies at term.[4]

The Royal Australian and New Zealand College of Obstetricians and Gynaecologists guidelines suggest that all pregnant women should be offered an antenatal screening assessment as soon as possible in pregnancy.[13] These guidelines are in line with the NICE guidelines produced in the UK.[14]

In New Zealand, general practitioners and family planning centres are usually the first to come in contact with newly pregnant women prior to lead maternity carers (LMCs) and so these three groups are a pivotal link to the effectiveness and success of the antenatal screening process.

In this study, we aimed to assess the local impact of the introduction of 'Antenatal Screening for Down syndrome and other conditions – quality improvement' on the numbers of women attending the regional South Island referral Fetal Medicine Centre and how this translates to the type, gestation and percentage of abnormal results of invasive diagnostic procedures.

Method

The project was a retrospective audit on the impact of numbers and timing of diagnostic invasive testing after the introduction of a formalised antenatal screening process in the Canterbury region.

Two time periods were reviewed; 1 February 2009 to 31 January 2010 (T1) and 1 May 2010 to 31 April 2011 (T2) to compare representative 1-year periods before and after introduction of the new screening. These time periods were set to enable the study to be carried out as a student research project, which is why T2 is set not long after the introduction of the new process.

Data had been prospectively collected in a viewpoint database of all women undergoing diagnostic procedures secondary to screening and this was utilised to collect data which was integrated with the information available from the Canterbury Health Laboratories on all MSS1 results. The denominator was all pregnant women in the Canterbury District Health Board catchment area during each of the time periods.

Cases were determined by putting the time periods into the viewpoint data base and extracting data and were cross checked with paper records of invasive procedures (amniocentesis and chorionic villus sampling) done at Christchurch Women's Hospital.

Ethical approval was not required and confirmation of this was sought from the Upper South B Regional Ethics Committee. Permission was sought and given by the National Screening Unit for use of MSS1 denominator data.

All those women that underwent either amniocentesis or CVS in the above two time periods had their information collected from the Fetal Medicine Viewpoint Database, including:

- Maternal age
- Risk of Down Syndrome (T21) from maternal serum screening first or second trimester (MSS1 or MSS2)
- Reason for (either increased risk MSS1/2, maternal age, abnormal USS, known familial chromosomal anomalies or previous baby with a genetic condition) and gestation of invasive procedure
- Fluorescent *in situ* hybridisation (FISH) or not
- Time to result (number of days between amnio/CVS and outcome of chromosomal testing) and what the outcome was (e.g. normal karyotype, T21, T13, T18 or another chromosomal anomaly that is tested for)
- Outcome of the baby including mode of delivery, gestation at birth and birth weight
- Miscarriages and terminations and reasons for them

Results from postnatal chromosomal testing done by Canterbury Health Laboratories was obtained to determine those babies only diagnosed as having Down syndrome after birth. We extended our catchment out to 3 months past the end date of the time periods to account for late diagnosis.

A biostatistician was consulted and assisted with the statistics. Statistics were done using the Open epi software program which was accessed at http://www.openepi.com/v37/Menu/OE_Menu.htm Mid P exact P values (2-tailed) were used and confidence intervals used were in relation to the risk difference calculation. These were calculated by the Taylor series.

Results

In Canterbury in T1 (1 February 2009- 31 January 2010), there were 6210 babies born. In T2 (1 May 2010- 31 April 2011) there were 6072 babies born. All of these women who delivered in the second time period should have been offered the new antenatal screening program at the time of their booking and 3111 of them (51%) underwent MSS1 (number obtained from the National Screening Unit, Auckland).

Table 1. Comparison of results between T1 (1 February 2009 – 31 January 2010) and T2 (1 May 2010 –- 31 April 2011)

Variables	TP1	TP2	Risk difference	95% Confidence interval^	P value
Numbers and percentage of Women Undergoing invasive Testing (% of total birthing women)	253 (4.1%)	175 (2.9%)	1.2%	0.55, 1.84	**0.0003***
Proportion of invasive testing: amniocentesis CVS	 58.7% 41.3%	 59.5% 40.5%	 -0.8% 0.85%	 -9.54, 7.83 -7.83, 9.54	 0.85 0.85
Detection rate (of abnormalities)	11.8%	15.4%	-3.08%	-9.12, 2.96	0.32
Numbers and percentage of T21 in those undergoing invasive testing	13/288 (4.5%)	14/215 (6.5%)	-1.99%	-6.07, 2.08	0.33

TP = time period.

^ Confidence Intervals calculated in relation to risk difference.

*P<0.05 level of significance.

There were no differences between the two time periods in the ages of women undertaking procedures; (mean 34.3yrs for CVS and 32.7yrs for amniocentesis) or the gestation at which the invasive procedures were undertaken at (13+0 and 17+5 days respectively) as would be expected.

The presence or absence of a nasal bone was only documented in 13.2% and then 25.6% of scans in the first and second time period (a significant increase in reporting p 0.0004). Twenty four percent of scans in both time periods reported an absent nasal bone and in 11% and then 15.4% (T1 and T2) of these babies a chromosomal anomaly was found.

Table 2. Comparison of miscarriage rates between T1 and T2

Comparison	TP1	TP2	Risk Difference	95% Confidence Interval	P value
Miscarriage rates – amniocentesis	0.6%	0.8%	-0.19%	-2.10, 1.72	0.86
Miscarriage rates – CVS	1.7%	1.1%	0.53%	-2.68, 3.75	0.81
Miscarriage rates – amniocentesis euploid	0.6%	0.8%	-0.19%	-2.10, 1.72	0.86
Miscarriage rates – CVS euploid	0%	1.1%	-1.15%	-3.39, 1.09	0.42

Overall miscarriage rates for amniocentesis were 0.3% and for CVS 1.5%. Miscarriage rate*s in euploid pregnancies* were 0.3% post amniocentesis and 0.5% post CVS.

Down syndrome (T21) diagnosis in the neonatal period

First time period—There were six babies diagnosed with Down syndrome after birth. All of these babies were born to women that did not have any NT measurements or early pregnancy scans. Two women had no scans at all throughout their pregnancy.

Second time period—In the second time period, of those six that were diagnosed with Down syndrome after birth, only two had MSS1 antenatal screening and they were both categorised high risk (>1:100). They both declined invasive diagnostic testing. Of the four that didn't have MSS1, two had increased NT results (2.5 and 2.8) and also declined invasive diagnostic testing.

Discussion

This study was aimed at analysing the impact and implementation of the new 'Antenatal screening for Down syndrome and other conditions- quality improvement' in the regional South Island referral Fetal Medicine Centre in Christchurch.

The new antenatal screening quality improvement process should be offered to all women who become pregnant and it is an individual decision as to whether they undertake the screening tests (there is a charge in most ultrasound providers for NT scanning) and, if indicated, the more invasive diagnostic procedures.

We anticipated that there would be a high uptake of screening by women in Canterbury however only 51.2% of women undertook the MSS1 testing in their first trimester in the period analysed which was early on in the new process. This study does not assess the reason for the low level of uptake; for example whether women are informed and chose not to undertake the screen or whether they are not aware of this offer.

One strength of our study was the follow up rates. Out of all the women that underwent invasive procedures, only five (1%) were lost to follow up presumed as having left the area/New Zealand.

The rates of invasive procedures (combined) have significantly ($p<0.0003$) decreased by 29% (from 4.1% of the total number of pregnant women during T1 to 2.9% in T2) after the introduction of the new antenatal screening quality improvement process.

Meanwhile the detection rates of abnormalities including Trisomy 21 have increased, although not significant. This is a statistically significant decrease in testing and is encouraging in the fact that the new antenatal screening program was designed to improve specificity without diminishing the true positive or detection rates.

The trend is suggesting that women are being given a more accurate assessment of their risk of certain chromosomal anomalies, with fewer women submitted to invasive diagnostic testing, without a diminution of detection rates. When national data are available, further analysis of this trend will be possible.

These results highlight that no babies were missed through the screening and diagnostic process as having Down syndrome. Those six babies that were diagnosed with the condition only after birth, had either not had any screening, or had, and had declined further diagnostic invasive testing (both declined after a specialist fetal medicine consultation).

The numbers in this study are too small to be able to calculate false positive and false negative rates of the new screening program.

The proportion of tests undertaken by CVS vs. Amniocentesis remained stable between T1 and T2. We expected that there may be an increase in the numbers of CVS being done as the new screening is done early so it was anticipated that invasive procedures would also be done earlier (CVS can be undertaken from 11 weeks gestation).

The static rates of CVS could reflect delays in referral (initial consult always within a week of receipt) or time taken by couples to reflect following risk assessment or patient preference to defer to amniocentesis. Unfortunately this data was not collected.

The number of tests that had FISH carried out was high in both time periods (61% and 66%). Criteria for offering FISH was risk 1:100.

The number of abnormal results which had FISH analysis ranged from 80-100% (amnio and CVS) over the two time periods. This is encouraging that those results that were abnormal were having FISH done and therefore a quicker result generated, but obviously has resource implications. Practise has more recently changed to risk 1:50. Miscarriage rates were low in these series as would be expected in a Fetal Medicine Centre where all procedures were undertaken by one of three trained specialists.

Interestingly the percentage of fetuses that had their nasal bones analysed was low, but in those scans where the nasal bone was reported as absent (24% of fetusus) there were low rates of chromosomal anomalies, however the numbers are too small to make further comment. The NSU doesn't require the nasal bone to be reported, hence likely the reason few were measured.

Our results are not in line with larger series studies which have concluded that an absent nasal bone can be seen in only 2.6% of euploid fetuses.[15] At 11-13 weeks the nasal bone is considered to be absent in 60% of those with T21, 50% of those with T18 and 40% of those with T13. [15] This perhaps raises the question of accuracy in obtaining views to visualise the nasal bone effectively.

Other studies conclude that visualisation of the nasal bone is a useful parameter and can improve the performance of first trimester screening for Down syndrome.[15]

The implementation of the new antenatal screening process in Canterbury has so far proved to be successful in maintaining detection rates of genetic anomalies whilst decreasing the numbers of invasive diagnostic procedures being done.

As the programme is still relatively new, uptake rates are modest (2011 data suggests rates are static, [16] 2013 data is pending) but we anticipate these will rise with increasing awareness of the program in years to come and its potential benefits which

also include early anatomical appraisal and early detection of multiple pregnancy with determination of chorionicity.

We hope that with increased awareness of the new program and informed LMCs and other primary health care workers, all pregnant women will be offered screening. Improved antenatal screening programs like this have increased screening uptake in parts of the UK[17] and we would hope to see this in NZ. A larger multi-centre study is needed to further evaluate the benefits of the quality improvement process.

Competing interests: Nil.

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References:

1. Wald NJ, Rodeck C, Hackshaw AK, et al. First and second trimester antenatal screening for Down's syndrome: the results of the SURUSS. Health Technol Assess. 2003;7:1-77.
2. Malone FD, Canick JA, Ball RH, et al. First-trimester or second-trimester screening, or both, for Down's syndrome. N Engl J Med. 2005;353:2001-11.
3. Tapon D. Prenatal Testing for Down Syndrome: Comparison of Screening Practices in the UK and USA. J Genet Counsel. 2010;19:112-130
4. National Screening Unit. Guidelines for maternity providers offering antenatal screening for Down Syndrome and other conditions in New Zealand. Wellington, NZ. 2009. http://www.nsu.govt.nz/health-professionals/3814.aspx Accessed April 12 2012.
5. Ministry of Health. Report on Maternity; Maternal demographic profile. 2010. p5 http://www.health.govt.nz/system/files/documents/publications/report-on-maternity-2010.pdf Accessed April 12 2013
6. Anderson CL and Brown CEL. Fetal Chromosomal abnormalities: Antenatal Screening and Diagnosis. Am Fam Physician. 2009;79:117-123.
7. National screening Unit, Ministry of Health NZ. Antenatal Down Syndrome Screening in New Zealand 2007: A Report of the Antenatal Down Syndrome Screening Advisory Group to the National Screening Unit 2007. Wellington, NZ. http://www.nsu.govt.nz/files/ANNB/antenatal-down-syndrome-screening-in-nz-2007-apr07.pdf Accessed August 5 2014
8. National Screening Unit, Ministry of Health NZ. What are the detection rates and false positive rates for the new screening options? 2012. Auckland, NZ www.nsu.govt.nz/health-professionals/3813.aspx#3909 Accessed April 21, 2013.
9. Royal College of Obstetricians and Gynecologists. Green-top guideline No.8. Amniocentesis and Chorionic villus sampling. 2010. 4Th Edition. Pg 1-13.

10. Tabor A, Vestergaard CHF, Lidegaard O. Fetal loss after chorionic villus sampling and amniocentesis: an 11-year national registry study. Ultrasound Obstet Gynecol. 2009; 34:19-24.
11. Alfirevic Z, Mujezinovic F, Sundberg K. Amniocentesis and chorionic villus sampling for prenatal diagnosis (Review). Cochrane Database Syst Rev. 2003. CD003252-1
12. The Canadian Early and Mid-Trimester Amniocentesis Trial (CEMAT) Group. Randomised trial to assess safety and fetal outcome of early and midtrimester amniocentesis. The Lancet 1998;9098:242-247
13. Royal Australian and New Zealand College of Obstetricians and Gynaecologists. College statement C- Obs4 Prenatal screening tests for trisomy 21 (Down syndrome), trisomy 18 (Edwards syndrome) and neural tube defects. 2007:1-10.
14. National Institute for Health and Clinical Evidence (NICE) guidelines. Antenatal Care: routine care for the healthy pregnant women. 2008. Updated 2010. London. http://www.nice.org.uk/CG062 Accessed April 12, 2012.
15. Kagan KO, Cicero S, Staboulidou I, et al. Fetal nasal bone in screening for trisomies 21, 18 and 13 and Turner syndrome at 11-13 weeks of gestation. Ultrasound Obstet & Gynecol. 2009;33:259-264
16. National Screening Unit, Ministry of Health, NZ. Antenatal Screening for Down Syndrome and other conditions- summary Jan to Dec 2011. https://www.nsu.govt.nz/files/ANNB/Antenatal_Screening_for_Down_syndrome_and_other_conditions_Summary_Jan_to_Dec_2011.pdf Accessed August 5 2014
17. Tringham GM, Nawaz TS, Holding S, et al. Introduction of first trimester combined test increases uptake of Down's syndrome screening. Europ J Obs & Gynae and Repro Biol. 2011;159:95-98

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Warfarin reversal: an audit of prescribing practices at Capital and Coast District Health Board

Evan Jolliffe, Peter Flanagan

Abstract

Aims In March 2013 the Australasian Society of Thrombosis and Haemostasis published an update of the Consensus Guidelines for Warfarin Reversal.[3] We reviewed the prescribing practices at Capital and Coast District Health Board (CCDHB), following publication of the updated guidelines.

Methods Patients were identified through multiple sources. CCDHB Medical Records identified admissions coded as "Haemorrhagic disorder due to circulating anticoagulants" or "Anticoagulants causing adverse effects in therapeutic use". CCDHB Haematology Laboratory identified International Normalised Ratio (INR) results ≥4.5. Wellington Hospital Pharmacy identified patients dispensed vitamin K. New Zealand Blood Service identified recipients of Prothrombinex®-VF and Fresh Frozen Plasma (FFP).

Results The management of patients with elevated INR results or bleeding on warfarin therapy was consistent with the updated guidelines in 81/149 episodes. Thirty one patients received FFP unnecessarily and 24 patients did not receive Prothrombinex®-VF when indicated. The greatest variability in management occurred in patients with bleeding complications and in patients requiring urgent warfarin reversal to allow acute surgery to proceed with only 5/31 patients and 5/21 patients having warfarin reversed as recommended. In some episodes more than one error was identified.

Conclusions The audit identified the suboptimal use of Prothrombinex®-VF and the unnecessary use of FFP in the management of warfarin reversal.

Warfarin is effectively used in a wide range of thromboembolic disorders. Patients on warfarin therapy have a 1–3% per year risk of major haemorrhage.[1] The bleeding risk increases markedly with increasing International Normalised Ratio (INR), although most bleeding events occur within the therapeutic range.[2] Patient factors, such as age, prior bleeding history, co-morbidities and concomitant medications also contribute to bleeding risk.

Despite the associated bleeding risk, warfarin remains the most commonly prescribed anticoagulant in New Zealand. Common indications for the use of warfarin include stroke prevention in atrial fibrillation, treatment of venous thromboembolism and prevention of thrombus formation in patients with mechanical heart valves.[3]

New anticoagulants such as oral direct Xa inhibitors and direct thrombin inhibitors are becoming available as alternatives to warfarin, but it is likely warfarin will continue to be prescribed to those patients already stable on warfarin, with severe renal

impairment, and for anticoagulation indications for which the new agents have not been evaluated.[3]

Warfarin lowers levels of factors II, VII, IX and X. Fresh Frozen Plasma (FFP) contains normal levels of all coagulation factors, whilst Prothrombinex®-VF is a three factor prothrombin complex concentrate (PCC) containing factors II, IX, X, and low levels of factor VII,[4] both can be used to replace these factors.

Prothrombinex®-VF is the only PCC product available in New Zealand. Due to its low levels of factor VII, previous guidelines recommended the addition of FFP to reverse the warfarin effect.[5] However, several reports have shown three factor PCCs without supplementary FFP to be effective for warfarin reversal.[6-7]

The use of FFP in the management of warfarin reversal can lead to a number of problems. The significant volume, approximately 200-250 ml per unit, can lead to transfusion associated circulatory overload. FFP is also recognised to be associated with a significant risk of allergic reactions.[8] The patient's ABO blood group must be known before the appropriate unit of FFP is selected and it must be thawed before it is issued from the blood bank.

Prothrombinex®-VF can be issued immediately from the blood bank. There is no requirement to check a patient's blood group prior to issue and it can be rapidly reconstituted into a small volume for infusion. Prothrombinex®-VF has a reduced risk of transfusion associated acute lung injury, circulatory overload and allergic reactions.[8] Prothrombinex®-VF is able to reverse an INR within 15 minutes of administration, however the infused factors have a similar half-life to endogenous factors and vitamin K should be given to sustain the reversal effect.[3]

In March 2013 an update of the consensus guidelines for warfarin reversal was published by the Australasian Society of Thrombosis and Haemostasis (ASTH) in the Medical Journal of Australia.[3] The updated guidelines provide recommendations for warfarin reversal in different clinical settings and are consistent with other international guidelines.[9-10] FFP is now only recommended in patients with life-threatening or critical organ bleeding; or in situations where PCCs are unavailable.

The New Zealand Blood Service (NZBS) as the organisation responsible for the collection of blood donations, production of blood components including FFP, and contracting the production of plasma products including Prothrombinex®-VF, has a key interest in the guideline recommendations.

The aim of this study was to review the prescribing practices for warfarin reversal at Capital & Coast District Health Board (CCDHB), in managing anticoagulated patients and warfarin-related bleeding events, following publication of the updated guidelines.

Methodology

Patients on warfarin therapy, who required intervention to reverse the warfarin effect, were identified through multiple sources. CCDHB Medical Records identified 140 admissions coded as "Haemorrhagic disorder due to circulating anticoagulants" or "Anticoagulants causing adverse effects in therapeutic use" during the 6- month audit period from the date of the publication of the updated guidelines on 4 March 2013 until 18 September 2013.

CCDHB Haematology Laboratory provided a list of all INR results ≥4.5. Wellington Hospital Pharmacy provided a list of patient's dispensed vitamin K from Pyxis MedStations®. NZBS provided a list of all recipients of Prothrombinex®-VF and FFP. Both products are routinely stored in the Blood bank in Wellington hospital and no shortages of either product occurred during the period covered by the audit.

The data sets were collated and the CCDHB electronic health record for each episode was reviewed. When multiple INRs were identified for the same patient, only those data entries used in clinical management were retained. Duplicate entries monitoring the response to an intervention were removed from the data set.

The updated guidelines provide recommendations for six patient groups, and are summarised in Table 1.

Table 1. ASTH Updated Consensus Guidelines for Warfarin Reversal[3]

Clinical setting	Recommendations
INR above therapeutic range and <4.5 without bleeding	Lower or omit the next dose of warfarin. Resume therapy at a lower warfarin dose when the INR approaches therapeutic range.
INR ≥4.5 and <10 without bleeding	Cease warfarin therapy, Vitamin K is usually unnecessary. If bleeding risk is high: consider vitamin K 1.0–2.0 mg orally or 0.5–1.0 mg IV
INR ≥10 without bleeding	Cease warfarin therapy, administer: Vitamin K 3.0–5.0 mg orally or IV; If bleeding risk is high: consider Prothrombinex®-VF, 15–30 IU/kg
INR ≥1.5 with life threatening or critical organ bleeding	Cease warfarin therapy and administer: Vitamin K 5.0–10.0 mg IV; and Prothrombinex®-VF 50.0 IU/kg IV; and fresh frozen plasma 150–300 mL; If Prothrombinex®-VF is unavailable, administer fresh frozen plasma 15 mL/kg
INR ≥2.0 with clinically significant bleeding	Cease warfarin therapy and administer: Vitamin K 5.0–10.0 mg IV; and Prothrombinex®-VF 35–50.0 IU/kg IV If Prothrombinex®-VF is unavailable, administer fresh frozen plasma 15 mL/kg
Surgery	Withhold warfarin 4–5 days before surgery Check INR day before surgery: If INR 2–3, administer vitamin K 3 mg IV Day of surgery: If INR >1.5, defer surgery or if urgent, administer Prothrombinex®-VF

Risk factors for bleeding are defined in the updated guidelines as a major bleed within the previous 4 weeks, surgery within the previous 2 weeks, known liver disease, a platelet count less than 50×10^9/L, or concurrent anti-platelet therapy.

We adopted the International Society on Thrombosis and Haemostasis definition of major bleeding as: fatal bleeding; or symptomatic bleeding in a critical area or organ; or a fall in haemoglobin of greater than 20 g/L, or leading to transfusion of 2 or more units of whole blood or red cells.[11]

Surgical procedures associated with high bleeding risk included cardiac, neurosurgical, abdominal vascular, cancer-related, orthopaedic or urological operations, and minor procedures like colonic polypectomy.[3] Liver disease was defined as: evidence of cirrhosis; or bilirubin >2 × upper limit of normal; or aspartate aminotransferase/alanine aminotransferase >3 × upper limit of normal.[12]

The updated guidelines differentiate between life threatening or critical organ bleeding, and clinically significant bleeding. Life threatening or critical organ bleeding was defined as intracranial, intraspinal, intraocular, retroperitoneal, pericardial, or intramuscular with compartment syndrome. [10] Clinically significant bleeding was defined as other major bleeding that was neither life threatening, nor critical organ bleeding, but caused a fall in haemoglobin of greater than 20 g/L, or led to transfusion of 2 or more units of whole blood or red cells.[12]

This audit was conducted in accordance with the National Ethics Advisory Committee Ethical Guidelines for Observational Studies, with specific reference to audit activities.[13]

Results

149 episodes in 136 patients required decisions on warfarin management. The management of patients with an elevated INR or bleeding on warfarin therapy was consistent with the updated guidelines in 81/149 episodes (Table 2).

In 31 episodes patients received FFP unnecessarily and in 24 episodes patients did not receive PCCs when indicated. In no instance was FFP issued by NZBS because Prothrombinex®-VF was unavailable. In 6 episodes patients received vitamin K unnecessarily and in 22 episodes patients did not receive vitamin K when indicated. In some episodes more than one error was identified.

Patients with an INR <4.5 without bleeding—Twenty-three episodes of patients with an INR <4.5 without bleeding, who had warfarin reversed, were identified. In 21/23 episodes, urgent warfarin reversal was required to allow acute surgery to proceed. Only 5/21 episodes had warfarin reversed as recommended with Prothrombinex®-VF alone. In 13/21 episodes, patients received FFP unnecessarily and in 10/21 episodes, patients did not receive Prothrombinex®-VF when indicated (Figure 1). One patient received FFP unnecessarily prior to elective surgery, and another received Prothrombinex®-VF unnecessarily after a fall.

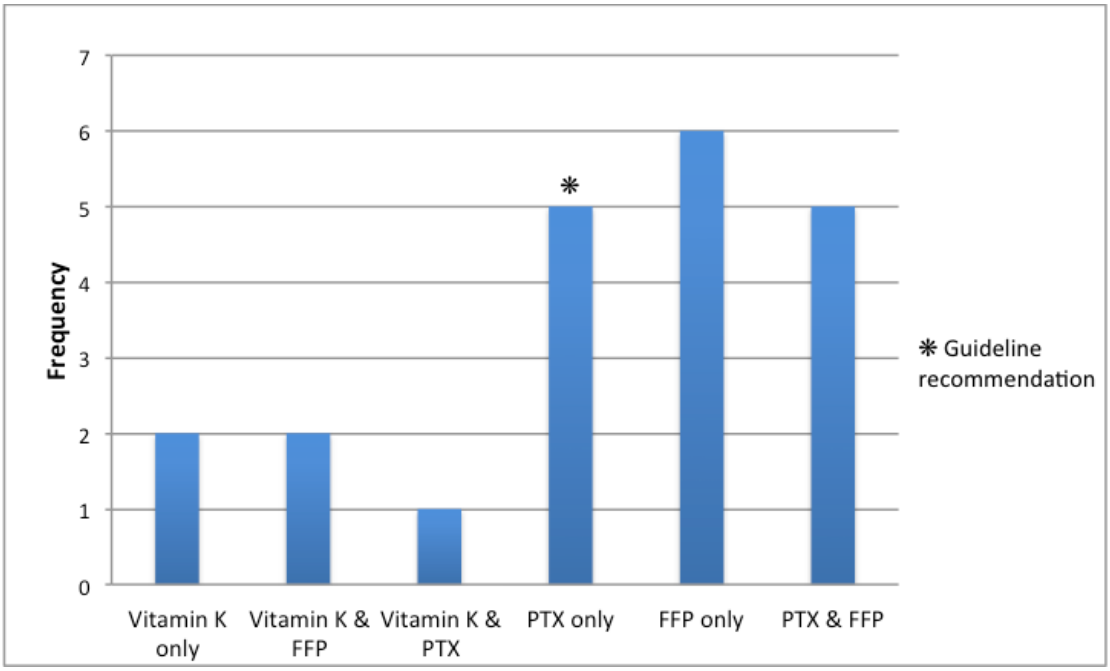
Patients with an INR ≥4.5 and <10 without bleeding—Ninety-one episodes with an INR ≥4.5 and <10 without bleeding were identified. In 25/91 episodes patients had a high risk of bleeding. Warfarin was reversed in only 10/25 episodes. 8/25 episodes had warfarin reversed as recommended with vitamin K. One patient received FFP and another received both FFP and Prothrombinex®-VF unnecessarily. In 62/91 episodes patients were not considered a high risk of bleeding. 56/62 episodes had warfarin withheld as recommended.

In the remaining 6 episodes, patients received vitamin K unnecessarily (Figure 2). The final 4/91 episodes required warfarin reversal in preparation for elective surgery and all patients received vitamin K as recommended.

Table 2. Number of episodes requiring warfarin management decisions

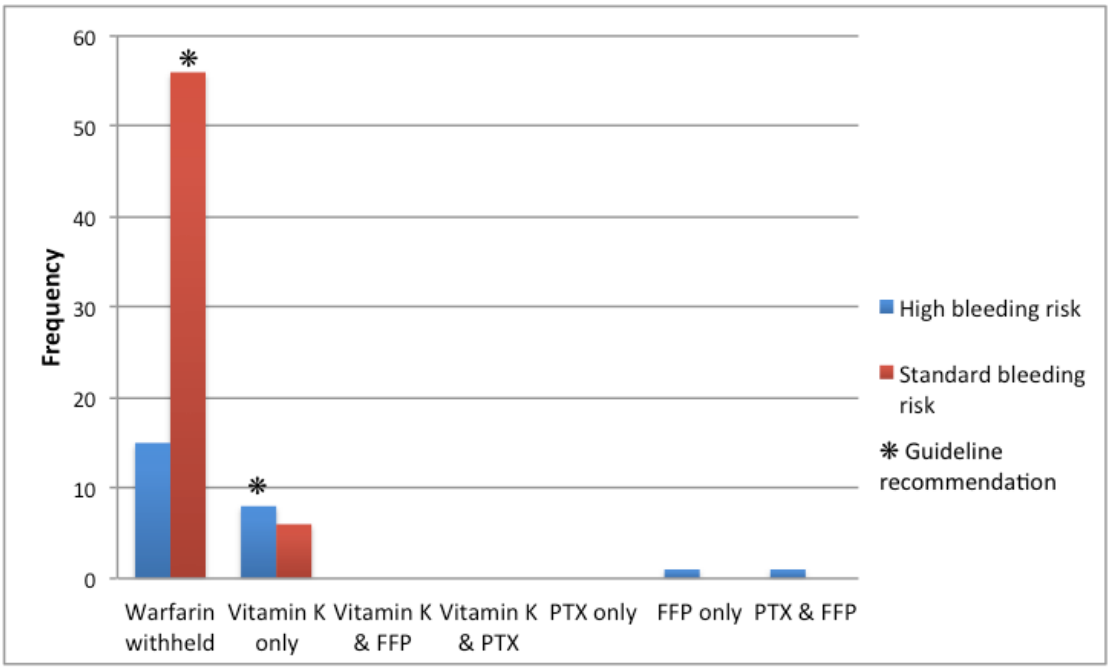
Variables	Number of episodes requiring warfarin management decisions	Number of episodes managed in concordance with the 2013 guidelines
INR <4.5 without bleeding		
Acute surgery	21	5
Elective surgery	1	0
Other	1	0
Total	**23**	**5**
INR ≥4.5 and <10 without bleeding		
High risk of bleeding	25	8
Standard risk of bleeding	62	56
Elective surgery	4	4
Total	**91**	**68**
INR >10 without bleeding		
High risk of bleeding	1	1
Standard risk of bleeding	3	2
Total	**4**	**3**
Bleeding complications of warfarin		
Life threatening or critical organ bleeding	11	4
Clinically significant bleeding	20	1
Total	**31**	**5**
Total	**149**	**81**

Figure 1. Urgent warfarin reversal for acute surgery



Note: PTX = Prothrombinex®-VF, FFP = Fresh Frozen Plasma.

Figure 2. Warfarin reversal for INR ≥4.5 and <10 without bleeding for patients at high and standard risk of bleeding



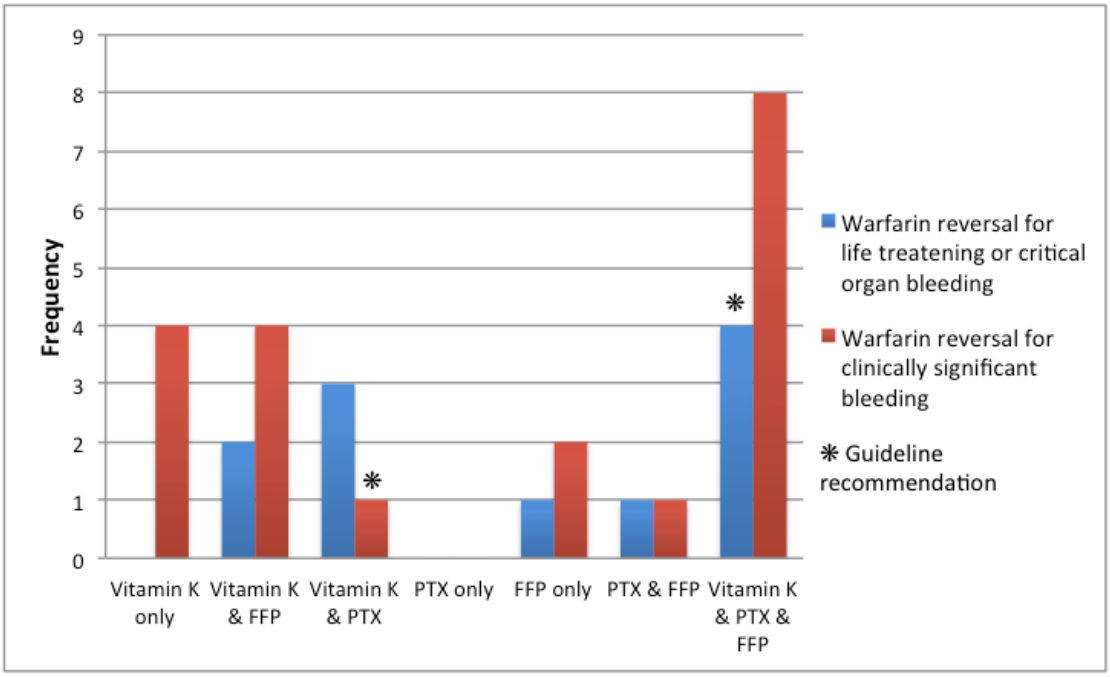
Note: PTX = Prothrombinex®-VF, FFP = Fresh Frozen Plasma.

Patients with an INR ≥10 without bleeding—Four episodes with an INR ≥10 without bleeding were identified. In one episode, a patient had a high risk of bleeding and had warfarin reversed as recommended with vitamin K and Prothrombinex®-VF. In 3/4 episodes patients were not considered a high risk of bleeding. 2/3 episodes had warfarin reversed as recommended with vitamin K. In the third episode, the patient received Prothrombinex®-VF unnecessarily.

Bleeding complications of warfarin therapy—Thirty-one episodes of patients on warfarin therapy presenting with bleeding were identified. In 11/31 episodes patients had life threatening or critical organ bleeding and in 20/31 episodes patients had clinically significant bleeding.

Only 4/11 episodes of life threatening or critical organ bleeding had warfarin reversed as recommended with Prothrombinex®-VF, FFP and vitamin K. In 3 episodes, patients did not receive Prothrombinex®-VF when indicated and in a further 3 episodes, patients did not receive FFP when indicated. Only 1/20 episodes of clinically significant bleeding had warfarin reversed as recommended with Prothrombinex®-VF and vitamin K. In 15 episodes, patients received FFP unnecessarily and in 10 episodes, patients did not receive Prothrombinex®-VF when indicated (Figure 3).

Figure 3. Warfarin reversal in patients with bleeding complications of warfarin



Note: PTX = Prothrombinex®-VF, FFP = Fresh Frozen Plasma.

Discussion

The updated ASTH guidelines provide recommendations for warfarin reversal in different clinical settings. Adherence to the guidelines for patients with bleeding complications and patients requiring urgent warfarin reversal for acute surgery was poor.

The updated guidelines differentiate between life threatening or critical organ bleeding, and other clinically significant bleeding. Had the earlier 2004 guidelines, which did not make this distinction been applied, adherence would still be poor. Only 12/31 episodes of patients with bleeding complications and 5/21 episodes of patients requiring urgent warfarin reversal for acute surgery would have had warfarin reversed as recommended compared to 5/31 and 5/21 respectively.

This audit identified the suboptimal use of Prothrombinex®-VF and the inappropriate use of FFP. FFP remains frequently used for warfarin reversal, despite its role being reduced to supplementary therapy with Prothrombinex®-VF in life threatening or critical organ bleeding, or as an alternative if Prothrombinex®-VF is unavailable. Prothrombinex®-VF is readily available and in no instance during this audit was FFP used because of unavailability of Prothrombinex®-VF.

This audit has several limitations. While the updated guidelines were circulated at the time of publication in some Wellington Hospital departments, the awareness of a change in guidelines may not have been apparent in other departments. At the time of the audit, the CCDHB “Preferred Medicines List” still contained the previous 2004 guidelines.

It is important that institutions frequently review and maintain up to date recommendations. NZBS maintains a blood resource website for all District Health Boards which provides a link to the updated guidelines. NZBS has also developed a Reversing Warfarin App based on the updated guidelines for warfarin reversal which clinicians can download free of charge.

Patients who did not receive any blood component, plasma product or vitamin K were not identified in this audit. These patients likely had their warfarin managed as recommended by the updated guidelines by lowering or omitting the next prescribed dose of warfarin.

The updated guidelines provide new dose recommendations for Prothrombinex®-VF, FFP and vitamin K. It was not possible to audit whether prescribed doses were consistent with the new recommendations. Patient weight is often not provided with requests for blood products, or recorded in the electronic health record. Pyxis MedStations® record every medication dispensed to patients but unfortunately they record dispensing of vitamin K ampoules and not the prescribed dose. Pyxis MedStations® are not used in the CCDHB Emergency Department, where vitamin K is often prescribed.

The frequency of vitamin K prescription may be underestimated in this audit. In the future, electronic prescribing may include patient factors such as weight, which will improve the accuracy of data collection and allow audit of the adequacy of prescriptions.

In summary, this audit identified that adherence to published guidelines for warfarin reversal is poor with suboptimal use of Prothrombinex®-VF and the unnecessary use of FFP. Warfarin associated bleeding is relatively common and timely and appropriate reversal of warfarin will potentially avoid major morbidity.

Competing interests: NZBS is responsible for distribution of both Fresh Frozen Plasma and Prothrombinex®-VF to hospitals across New Zealand. NZBS contracts CSL Behring Australia to fractionate plasma collected in New Zealand to produce a range of products including Prothrombinex®-VF. NZBS received an unrestricted grant from CSL Behring Australia to develop education tools to support the implementation of the updated guidelines. The grant was used to develop the Reversing Warfarin App.

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References:

1. Schulman S, Beyth R, Kearon C, Levine M. Hemorrhagic complications of anticoagulant and thrombolytic treatment: American College of Chest Physicians evidence-based clinical practice guidelines (8th edition). Chest. 2008;133(suppl 6):257S–298S
2. Palareti G, Leali N, Coccheri S, et al. Bleeding complications of oral anticoagulant treatment: an inception-cohort, prospective collaborative study (ISCOAT). Italian Study on Complications of Oral Anticoagulant Therapy. Lancet. 1996;348(9025):423–428.

3. Tran H, Chunilal S, Harper P, et al. An update of consensus guidelines for warfarin reversal. Med J Aust. 2013;198(4):198–199.
4. CSL Behring Prothrombinex®-VF data sheet. http://www.csl.com.au/s1/cs/auhq/1196562765747/Web_Product_C/11965627157 84/ProductDetail.htm
5. Baker R, Coughlin P, Gallus A, et al. Warfarin reversal: consensus guidelines, on behalf of the Australasian Society of Thrombosis and Haemostasis. Med J Aust. 2004;181(9):492–497
6. Tran H, Collecutt M, Whitehead S, Salem H. Prothrombin complex concentrates used alone in urgent reversal of warfarin anticoagulation. IMJ. 2011;41(4):337–343
7. Imberti D, Barillari G, Biasioli C, et al. Emergency reversal of anticoagulation with a three-factor prothrombin complex concentrate in patients with intracranial haemorrhage. Blood Transfus. 2011;9(2):148–155
8. New Zealand Blood Service Annual Haemovigilance Report 2012. http://www.nzblood.co.nz/assets/Haemovigilance/Haemovigilance-Annual-Report-2012.PDF Accessed 28th June 2014.
9. Keeling D, Baglin T, Tait C, et al. Guidelines on oral anticoagulation with warfarin – fourth edition. Br J Haematol. 2012;154(3):311–324.
10. Holbrook A, Schulman S, Witt D, et al. Evidence-Based Management of Anticoagulant Therapy Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012;141(2 Suppl):e152S–184S.
11. Schulman S, Kearon C. On behalf of the Subcommittee on Control of Anticoagulation of the Scientific Standardization Committee of the International Society on Thrombosis and Haemostasis. Definition of major bleeding in clinical investigations of antihemostatic medicinal products in non-surgical patients. J Thromb Haemost. 2005;3:692–694.
12. Pisters R, Lane D, Nieuwlaat R, de Vos C, Crijns H, Lip G. A Novel User-Friendly Score (HAS-BLED) To Assess 1-Year Risk of Major Bleeding in Patients With Atrial Fibrillation. Chest. 2010;138(5):1093–1100
13. National Ethics Advisory Committee. Ethical Guidelines for Observational Studies: Observational research, audits and related activities: Revised edition. July 2012. http://neac.health.govt.nz/streamlined-ethical-guidelines-health-and-disability-research Accessed 28th June 2014

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The changing landscape of antimicrobial resistance in New Zealand

Deborah A Williamson, Helen Heffernan

Abstract

Antimicrobial resistance is one of the biggest health threats of the modern age, threatening the routine treatment of many common infectious diseases. Resistance to many common antimicrobials is now endemic in New Zealand, in both community and healthcare settings. Over the past two decades, the landscape of antimicrobial resistance has changed considerably in New Zealand, with the emergence and spread of pathogens such as community-associated methicillin-resistant *Staphylococcus aureus*, extended-spectrum β-lactamase-producing Enterobacteriaceae and multi-resistant *Neisseria gonorrhoeae.*

Factors contributing to the emergence and spread of antimicrobial-resistant pathogens in New Zealand include the use and overuse of antimicrobials, transmission of resistant organisms in community and healthcare settings, and importation of resistant pathogens from areas where multi-resistant pathogens are endemic.

In this review, we provide a summary of major antimicrobial-resistant bacteria in New Zealand, with a specific focus on those pathogens that pose major threats to human health.

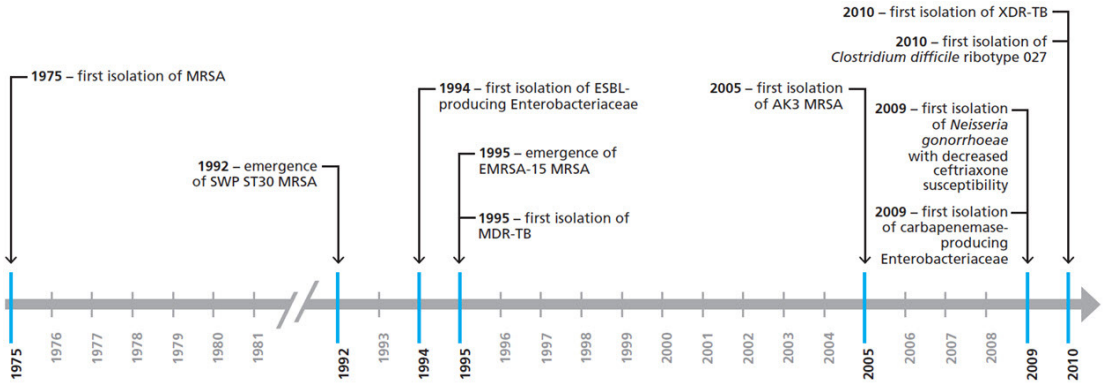
Antimicrobial resistance (AMR) is one of the greatest global health threats of the modern age.[1,2] As the prevalence of antimicrobial resistance rises, treatment of common infectious diseases, such as respiratory infections and urinary tract infections, becomes increasingly challenging, and advances made in complex medical therapy, such as organ transplantation, neonatology and intensive care, are also threatened.

Compounding this threat is the scarcity of new antimicrobial compounds in the research and development pipeline.[3] Moreover, the treatment of infections due to antimicrobial–resistant organisms places a substantial burden on healthcare systems, and has a major societal and economic impact.[1,4]

For many bacterial pathogens, resistance to major antimicrobial classes, such as penicillins, fluoroquinolones and third-generation cephalosporins, is now commonplace in New Zealand hospitals, and is increasingly found in the community setting. Examples of such resistant pathogens include *Staphylococcus aureus* (*S. aureus*), *Escherichia coli* (*E. coli*), and *Neisseria gonorrhoeae* (*N. gonorrhoeae*).

A timeline of significant events related to AMR in New Zealand is shown in Figure 1.

Figure 1. A timeline of significant events in antimicrobial resistance in New Zealand



The factors responsible for the emergence and spread of antimicrobial resistance are complex, but the key drivers in New Zealand are likely to include:

- The use and overuse of antibiotics in both human and animal populations;[5,6]
- Transmission of antimicrobial-resistant organisms in community and healthcare settings;[7,8] and
- Increasing globalisation, resulting in the importation of antimicrobial-resistant pathogens.[9–11]

One of the key components of efforts to combat the emergence and spread of antimicrobial-resistant pathogens is comprehensive and consistent surveillance.[12] Although surveillance *per se* does not reduce antimicrobial resistance, effective surveillance can provide valuable information that can be used to formulate local antibiotic guidelines, to inform policy recommendations, to identify high-priority areas for interventions, and to monitor the impact of interventions designed to prevent or reduce antimicrobial resistance.

Surveillance of antimicrobial-resistant pathogens should occur at multiple levels, including local, national and supranational, and can be structured according to factors such as the specific purpose of surveillance, available resources and testing capacity, and the likely prevalence and threat of certain resistant pathogens.

Often, a number of complementary surveillance approaches are required and may involve a combination of routine surveillance, targeted phenotypic and molecular surveys, and clear pathways for the rapid identification of resistant pathogens of major public health significance (e.g. carbapenemase-producing Enterobacteriaceae, vancomycin-resistant *S. aureus* or extensively drug-resistant *Mycobacterium tuberculosis* [*M. tuberculosis*]).

In this review, we provide a contemporary overview of the epidemiology of antimicrobial resistance in New Zealand, with a particular focus on those antimicrobial-resistant pathogens that pose a major threat to human health.

Antimicrobial resistance in specific medically important bacteria

Methicillin-resistant *S. aureus* (MRSA)—Over the past two decades, the global clinical and molecular epidemiology of *S. aureus* disease has changed dramatically, predominantly due to the emergence and spread of community-associated MRSA (CA-MRSA) clones, most notably the USA300 CA-MRSA clone in North America.[13]

Similarly, in New Zealand, there has been a considerable change in the epidemiology of *S. aureus* disease, with a significant increase in *S. aureus* skin and soft tissue infections, particularly in Māori and Pacific Peoples, and in the under-5 year age group.[14,15]

In New Zealand, the majority of *S. aureus* disease is due to methicillin-susceptible *S. aureus* (MSSA), with recent aggregate national antimicrobial susceptibility data showing a stable MRSA prevalence of approximately 8–10%, although the prevalence of MRSA differs between regions, with a generally lower prevalence in the South Island compared to the upper North Island.[14,16] However, despite this relatively stable national MRSA prevalence, there have been marked changes in the molecular epidemiology and antimicrobial resistance patterns of MRSA in New Zealand during the past decade.

Throughout the 1990s and early 2000s, the South West Pacific (SWP) clone (also known as Western Samoan Phage Pattern, 'WSPP') was the predominant CA-MRSA in New Zealand. Belonging to multilocus sequence type (ST) 30, this clone was first isolated in 1992 from patients in the Auckland community who had contact with Western Samoa.[17]

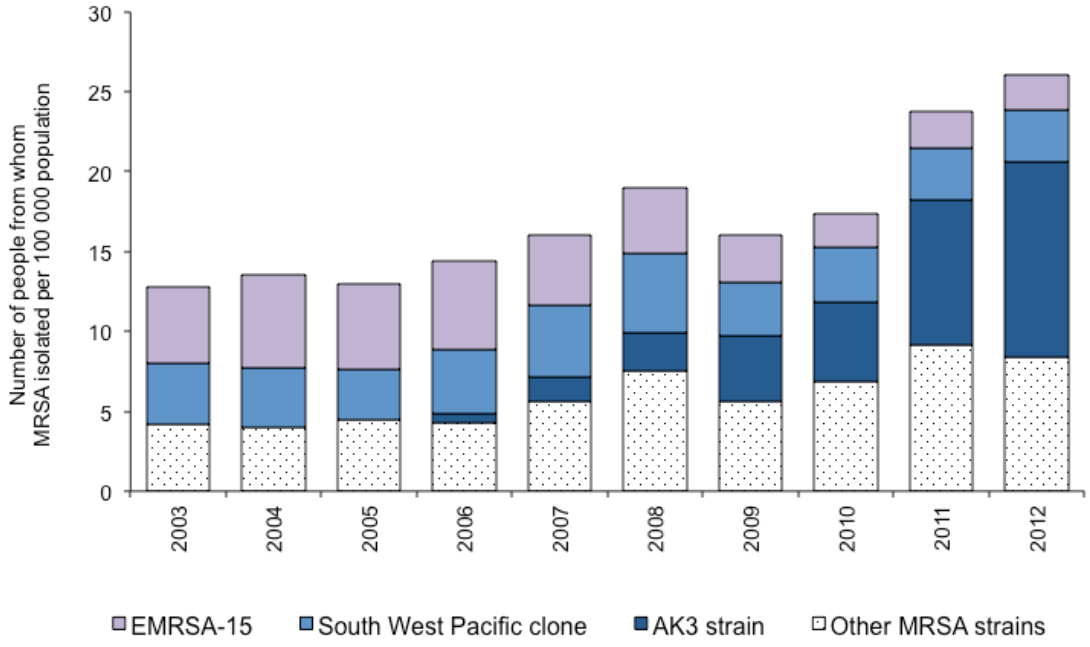
Similar to CA-MRSA clones in other parts of the world, the SWP ST30 clone is generally resistant only to β-lactam antimicrobials, and harbours the *lukF-PV* / *lukS-PV* genes encoding the Panton Valentine leucocidin (PVL) toxin.[8,18]

In 2005, a newly emerged ST5 MRSA clone (the 'AK3' clone) was identified in the Auckland region, and since then, this clone has rapidly displaced SWP ST30 as the predominant CA-MRSA clone in New Zealand (Figure 2).[8]

Although the reasons for the remarkable success of this clone in New Zealand are as yet undetermined, it is notable that, in addition to resistance to β-lactams, this clone is usually also resistant to fusidic acid, and in New Zealand, topical fusidic acid is widely used for a number of dermatological conditions.[19]

Indeed, recent data suggest that community dispensing rates of topical fusidic acid have increased significantly over the past decade (Williamson DA, Monecke S, Heffernan H, et al. A cautionary tale: high usage of topical fusidic acid and rapid clonal expansion of fusidic acid-resistant *Staphylococcus aureus.* Clin Infect Dis. 2014 Aug 18. pii: ciu658. [Epub ahead of print]), and it is likely that a key factor driving the emergence of the AK3 ST5 MRSA clone has been high and sustained usage of topical fusidic acid in the New Zealand community.

Figure 2. Annual point-prevalence rates of methicillin-resistant *Staphylococcus aureus*, 2003–2012, showing the relative prevalence of the AK3 MRSA strain, South West Pacific clone and EMRSA-15 strain



Note: Data based on annual 1-month national surveys and rates calculated using the mid-year population estimates.[22]

In addition to these two major CA-MRSA clones, a number of prominent global clones have been detected in New Zealand, such as the ST8 ('USA300'), ST93 ('Queensland') and ST772 ('Bengal Bay') clones.[8] Furthermore, a recent study described the isolation of clonal complex (CC) 398 MRSA from nine patients in the South Island.[20] In other settings, particularly in Europe, the CC398 clone has been strongly associated with exposure to livestock, most commonly swine.[21]

In contrast to the diverse range of CA-MRSA clones, MRSA clones in the hospital setting are more genetically restricted and more commonly resistant to a wide range of antimicrobial agents, with the predominant healthcare-associated MRSA (HA-MRSA) clone being ST22 'EMRSA-15', which is typically resistant to several non-β-lactam antimicrobials, particularly ciprofloxacin and erythromycin.[8,22]

In keeping with other countries, recent data suggest an infiltration of CA-MRSA clones into the healthcare setting in New Zealand,[8] and it has been suggested that due to an increasing community reservoir, CA-MRSA clones will ultimately replace HA-MRSA clones in the hospital setting.[23] This is of concern given the apparent high transmissibility of CA-MRSA clones,[24] and highlights the need for ongoing systematic molecular surveillance to track MRSA clones in the New Zealand setting.

Resistance in Enterobacteriaceae—Enterobacteriaceae, particularly *E. coli* and *Klebsiella pneumoniae* (*K. pneumoniae)*, are major human pathogens in both community and healthcare settings, and over the past decade, the prevalence of

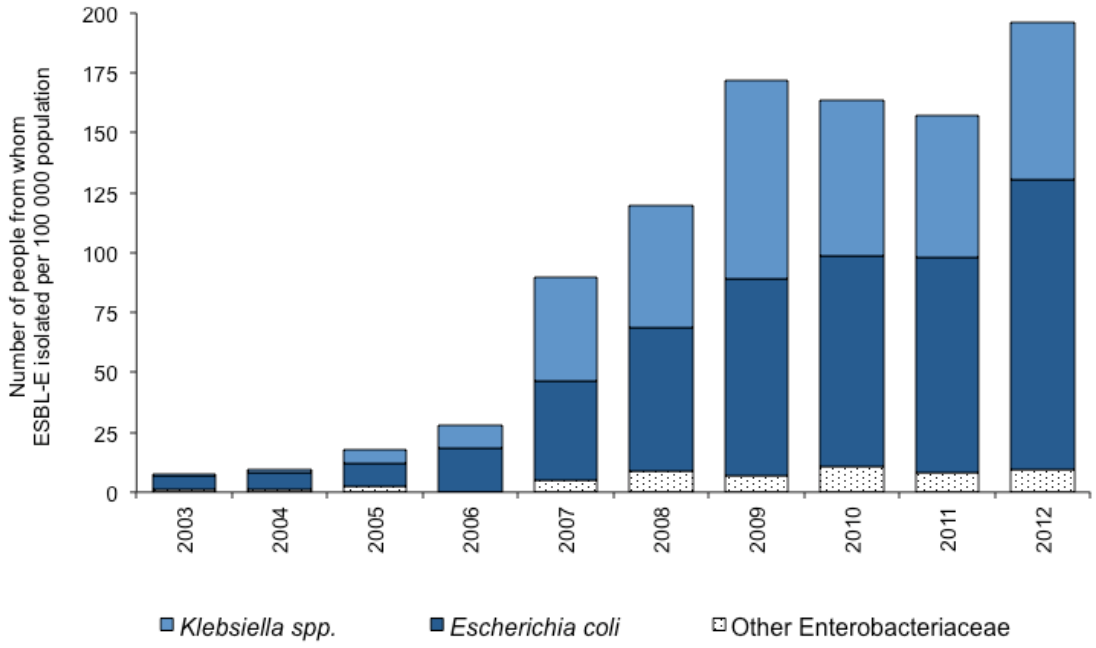
antimicrobial-resistant Enterobacteriaceae has increased dramatically in many parts of the world.[2]

In particular, resistance in Enterobacteriaceae to third-generation cephalosporins (e.g. ceftriaxone, ceftazidime) due to extended spectrum β-lactamase (ESBL) production, or to carbapenems (e.g. ertapenem, meropenem) due to carbapenemase enzymes, has reached disturbing levels in several regions. [2] For example, data from the Asia-Pacific region collected as part of the Study for Monitoring Antimicrobial Resistance Trends (SMART study) reported an ESBL prevalence of ≥60% in *E. coli* urinary tract isolates from China and Vietnam.[25]

Of even greater concern are reports of the widespread dissemination of carbapenemase-producing Enterobacteriaceae (CPE) in certain geographic regions, most notably the Indian subcontinent.[26]

Data from national surveillance demonstrates an increase in the incidence of ESBL-producing Enterobacteriaceae (ESBL-E) isolation over the past decade in New Zealand (Figure 3), with marked geographic variation in incidence rates, such that ESBL-E isolation rates are consistently higher in the greater Auckland region.[27] However, these geographic differences are likely to be due, in part, to regional variation in infection control screening policies, differences in patient case mix and any concurrent local outbreaks.

Figure 3. Annualised point-prevalence rates of extended-spectrum β-lactamase-producing Enterobacteriaceae (ESBL-E), 2003-2012



Note: Data based on annual 1-month national surveys with rates calculated using mid-year population estimates.[27]

Based on aggregate susceptibility data,[28] the overall prevalence of ESBL production in *E. coli* bloodstream isolates has remained stable in New Zealand over the past

decade at <5%, whereas the reported prevalence of ESBL production in *K. pneumoniae* bloodstream isolates is higher at 10–15%.

In keeping with these aggregate national data are recent data from Auckland demonstrating an ESBL prevalence of 5.6% in *E. coli* bloodstream isolates, [29] and an ESBL prevalence of 5.1% in Enterobacteriaceae from faecal samples submitted to a community pathology laboratory.[30]

Several studies have attempted to identify specific epidemiological associations for ESBL-E colonisation and/or infection in New Zealand. Such information may be useful in informing decisions around infection control practices and empiric therapy.

A case-control study conducted in Auckland in 2003-2004 identified residence in a long-term care facility (LTCF) [odds ratio (OR) 6.1, 95% confidence interval (CI) 1.6–23.2] and concurrent chronic obstructive pulmonary disease (COPD) (OR 10.6, 95%CI 1.04–107.7) as strong independent risk factors for ESBL-E infection in the community setting.[31] These authors postulated that the association of ESBL-E isolation and COPD might reflect frequent exposure to healthcare and/or multiple prior courses of antimicrobials.

Another study conducted in the Auckland community in 2009 also identified LTCF residence as an independent risk factor for ESBL-E colonisation (OR 19.8, 95%CI 7.0–56.2).[30] In addition, a retrospective case-control study conducted between 2003 and 2007 in South Auckland identified known colonisation with an ESBL-E as a particularly strong risk factor (OR 46.2, 95%CI 3.5–619) for subsequent bloodstream infection with ESBL-E.[32] The authors of this study suggested the importance of considering ESBL-E colonisation status when choosing empiric therapy in such patients.

Throughout the 1980s and 1990s, the most common reported types of ESBL were either TEM- or SHV-type ESBLs. However, during the 2000s, the CTX-M-type ESBLs rapidly emerged and spread to become the most commonly identified ESBL type worldwide.[33] In particular, CTX-M-15 has emerged to become the most globally prevalent CTX-M enzyme, and in keeping with these findings, a molecular epidemiological study conducted in 2006 identified CTX-M-15 as the most common ESBL type in New Zealand.[34] In this study, 81/83 (98%) of ESBL-E isolates produced CTX-M enzymes, with the most common CTX-M types being CTX-M-15 (63/81; 78%) and CTX-M-14 (11/81; 14%).

A strong association has been described between CTX-M-15 producing *E. coli,* and a global 'pandemic' clone of *E. coli* known as ST131.[35] This clone is notable for its ability to harbour numerous genes associated with both antimicrobial resistance and virulence,[35] and in addition to resistance to β-lactam resistance, it is also commonly resistant to fluoroquinolones. The ST131 clone has been identified as a cause of bloodstream infections in the Auckland region, most notably following prostate biopsy in patients who had recently been treated with a fluoroquinolone antimicrobial.[36,37]

The endemicity of ESBL-E in New Zealand is posing an ongoing therapeutic challenge to the treatment of infections caused by such organisms, particularly community-onset urinary tract infections. In particular, suitable oral antimicrobial options may be limited to agents such as fosfomycin and mecillinam, although the latter is not routinely available in New Zealand.

In contrast to ESBL-E, it is fortunate that the isolation of CPE continues to be relatively infrequent in our setting. In addition to hydrolysing penicillins and cephalosporins, CPE hydrolyze carbapenems such as ertapenem and meropenem, and similar to ESBL-E, CPE usually harbour genes conferring resistance to other classes of antimicrobials such as aminoglycosides and fluoroquinolones.

As a result, there are little or no available treatment options for infections caused by such organisms. To date however, all CPE in New Zealand have been isolated from patients who have recently returned from areas in which CPE are endemic.[9,10,38,39] For example, one study between 2009 and 2010 described the identification of New Delhi metallo-β-lactamase (NDM)-producing Enterobacteriaceae from four patients in New Zealand hospitals, all of whom had received recent medical care in India.[10]

Similarly, an OXA-181-producing *K. pneumoniae* was isolated in 2010 in Auckland from a patient who had recently been hospitalised in Asia.[9] These reports highlight the requirement for vigilance, both in surveillance and infection prevention and control policies, in monitoring the importation of such extensively resistant organisms.

***Mycobacterium tuberculosis*—**Tuberculosis (TB) remains a significant global public health issue, with an estimated 8.6 million people developing TB in 2012 and a global incidence rate of 122 per 100,000 population.[40]

One of the most challenging problems in TB control is drug-resistant *M. tuberculosis*, specifically multidrug-resistant TB (MDR-TB, defined as *M. tuberculosis* that is resistant to at least isoniazid and rifampicin), and extensively drug-resistant TB (XDR-TB, defined as MDR-TB plus resistance to a fluoroquinolone and a second-line injectable agent).

TB is a notifiable disease in New Zealand, and the 2012 notification rate was 6.6 per 100,000 population, with the highest notification rate in the Asian ethnic group (41.4 per 100,000 population).[41] Methods for the laboratory diagnosis of drug-resistant TB have changed considerably over the past decade, with a shift towards rapid genotypic detection of resistance-conferring mutations. In particular, the Cepheid Xpert® MTB/RIF assay, which simultaneously identifies *M. tuberculosis* and common mutations in the *rpoB* gene that are used as a surrogate marker for MDR-TB, has been widely adopted globally. This assay is also used in New Zealand, and was useful in detecting four cases of MDR-TB that were not identified by conventional phenotypic testing.[42]

Fortunately, MDR-TB remains relatively rare in New Zealand. Between 1995, when national antituberculosis-drug resistance surveillance began, and 2013, a total of 48 MDR-TB cases were identified, with the vast majority of cases occurring in patients born overseas.[41] In keeping with the predominantly overseas origin of MDR-TB in New Zealand are recent molecular epidemiological data demonstrating an association between distinct phylogenetic lineages of MDR-TB and patient country of origin,[43] although the clinical relevance of this finding has not yet been determined.

Importantly, the first reported case of XDR-TB in Australasia was identified in 2010 in Otago, New Zealand.[44] This patient, an emigrant from Myanmar, had no reported history of TB or prior receipt of anti-tuberculous therapy, suggesting that XDR-TB strains are circulating within Myanmar.

Of particular concern in the New Zealand setting was the approximate 2-month delay between specimen collection and final reporting of XDR-TB. [44] Fortunately this

patient did not have active pulmonary TB, although this case highlights the value of risk-based laboratory testing algorithms and emphasises the importance of cohesive laboratory networks.

Neisseria gonorrhoeae—Antimicrobial-resistant *N. gonorrhoeae* has been identified as an 'urgent threat' to public health.[4] Over the past four decades, *N. gonorrhoeae* has developed resistance first to the penicillins, and subsequently to macrolides, tetracyclines and fluoroquinolones.[45]

Currently, the recommended empiric treatment of *N. gonorrhoeae* infection in many countries, including New Zealand, is ceftriaxone (intramuscularly, 250–500 mg) plus azithromycin (orally, 1 g).[45] Beyond third-generation cephalosporins such as cefixime and ceftriaxone, treatment options are extremely limited. Of concern therefore, are worldwide reports of *N. gonorrhoeae* strains displaying decreased susceptibility to third-generation cephalosporins, typically with minimum inhibitory concentrations (MICs) of ≥0.06 mg/L, with sporadic reports of treatment failures in patients infected with such strains.[46,47] In these strains, decreased susceptibility is due to the presence of mosaic penicillin-binding proteins, which have reduced affinity for extended-spectrum cephalosporins such as ceftriaxone.

More alarming is the description of two multi-drug resistant *N. gonorrhoeae* strains (H041 and F89) from Japan in 2009 and France in 2010 respectively.[48–50] In addition to displaying resistance to almost all classes of antimicrobials, both strains exhibited high-level resistance to ceftriaxone, with a ceftriaxone MIC of 2 mg/L.

In New Zealand, sexually transmitted infections, including gonorrhoea, are not notifiable diseases, and monitoring of gonorrhoea cases is performed predominantly by laboratory-based surveillance. Aggregate susceptibility data indicates that, during the 10 years 2003-2012, rates of penicillin resistance in *N. gonorrhoeae* increased only modestly from 5.1% to 11.3% compared to fluoroquinolone resistance which increased from 8.1% to 40.6%.

Fortunately, no ceftriaxone-resistant *N. gonorrhoeae* strains (MIC >0.25 mg/L) have been detected in New Zealand to date; however, isolates with decreased susceptibility to ceftriaxone (MIC 0.06–0.25 mg/L) have been detected in the Auckland region.[51]

Currently, one of the major challenges in monitoring the emergence and spread of antimicrobial resistance in *N. gonorrhoeae* is the shift from culture-based to molecular diagnostics, using nucleic acid amplification tests (NAAT). Although NAAT assays are rapid, sensitive and specific, bacterial culture is still required to provide information on antimicrobial susceptibility.

In New Zealand, as in other settings, it is vital that regular, systematic monitoring of antimicrobial resistance in *N. gonorrhoeae* is undertaken to inform empiric therapy guidelines and to track the inevitable emergence of resistant strains.

Clostridium difficile—*Clostridium difficile* (*C. difficile*) is the commonest cause of healthcare-associated diarrhoea, and *C. difficile* infection (CDI) has been associated with increased morbidity and mortality in overseas settings.[52,53] Although acquired antimicrobial resistance in *C. difficile* is not a problem *per se*, its intrinsic resistance to many common antimicrobials, typical occurrence after exposure to antimicrobial agents, and propensity for transmission in healthcare settings poses a major challenge.

Over the past decade the clinical and molecular epidemiology of CDI has changed considerably with several important observations from other developed countries. These include:

- An increase in infection rates in younger populations;[54]
- The emergence of "epidemic" ribotypes of *C. difficile*, most notably ribotype 027, which has been associated with increased morbidity and mortality;[55] and
- Infections in patients who would not previously have been considered to be "at risk" for CDI, most notably patients with no prior healthcare exposure.[54]

At present, there are no formal systems in place for coordinated surveillance of CDI in New Zealand. To date, two national "snapshot" surveys have been conducted, one in 2009 and the second in 2011.[56] These surveys indicated a diverse range of circulating ribotypes, with no single dominant strain.

Although these ad-hoc surveys provided useful information on the molecular epidemiology of circulating *C. difficile* ribotypes in New Zealand, minimal accompanying clinical metadata were obtained. As such, relatively little is known about the clinical epidemiology or prevalence of CDI in New Zealand. Such information is crucial in determining the most appropriate strategies for prevention and control of this important infection.

Other antimicrobial resistance threats—In addition to the pathogens above, there are numerous other bacteria in which antimicrobial resistance poses a major threat. For example, vancomycin-resistant enterococci (VRE) continue to be regularly isolated from patients in New Zealand,[57] often as the result of importation from overseas settings. Reassuringly however, the prevalence of VRE in New Zealand has not reached the concerning levels seen in some Australian healthcare settings.[58]

Penicillin non-susceptibility is prevalent among *Streptococcus pneumoniae* in New Zealand, with 17.2% of invasive isolates recorded as penicillin resistant (MIC ≥0.12 mg/L) and 25.1% of non-invasive isolates recorded as penicillin non-susceptible (MIC ≥0.12 mg/L) during 2012.[59]

It is disappointing that there has been little change in penicillin or cefotaxime susceptibility among pneumococci since the addition of pneumococcal conjugate vaccine to the childhood immunisation schedule in 2008, given that the pneumococcal serotypes covered by the conjugate vaccines are those types that were most commonly associated with resistance to penicillin and third-generation cephalosporins in the pre-vaccine era. However, as has been observed globally, non-vaccine serotypes have in part replaced vaccine types, and in New Zealand one of the two most common replacement serotypes, 19A, is often penicillin resistant.[59]

Finally, despite the large agricultural sector in New Zealand, relatively little is known about the contemporary prevalence and epidemiology of antimicrobial resistance in zoonotic bacteria in animals.

A study conducted in New Zealand over a 12-month period in 2009 and 2010 found that the prevalence of antimicrobial resistance among potential human pathogens isolated from food-producing animals (including very young calves, pigs and broiler poultry) was comparatively less than that reported for human isolates of the same bacterial species, especially for antibiotics of particular importance in human medicine, such as third-generation cephalosporins and fluoroquinolones.[60]

However, a study assessing antibiotic sales in the veterinary sector in New Zealand between 2009 and 2011 identified increasing use of third-generation cephalosporins as a potential antimicrobial resistance threat at the human-animal interface.[61] Of particular concern was the finding of a 26% increase in sales of cefovecin, a long-acting third-generation cephalosporin used in the companion animal population. The authors of this study suggested that overuse of such compounds could result in significant antimicrobial resistance in bacteria infecting companion animals**.**

Identifying knowledge gaps

Although recent data from the 2014 World Health Organization (WHO) Global Antimicrobial Resistance report indicate that New Zealand has comparatively low rates of antimicrobial resistance (particularly when compared to countries in neighbouring regions such as South-East Asia), New Zealand is not immune to the threat of antimicrobial resistance, and we should not become complacent.[2] Although there are existing programmes of antimicrobial resistance surveillance, there remain a number of important 'knowledge gaps' and 'action gaps' around antimicrobial resistance in New Zealand.

Importantly, there are few New Zealand data on the extent and impact of antimicrobial usage, both in hospital and community settings. Such information may permit benchmarking comparisons at national or international levels; guide the development of treatment guidelines and formularies; assess the public health consequences of antimicrobial use (and misuse) and evaluate the impact of any educational or regulatory interventions that encourage prudent antimicrobial prescribing.

In addition, there are no data available on the clinical and economic impact of antimicrobial resistance in New Zealand; this information is particularly important in informing policy decisions around health and research funding for antimicrobial resistance-related activities.

Notably, a recent UK study analysing infection-related research funding between 1997 and 2010 found that only 5.5% of such funding was allocated to the area of antimicrobial resistance.[62] These authors highlighted the importance of prioritising such funding, given the potentially devastating public health consequences of increasing antimicrobial resistance.

Conclusions

Antimicrobial resistance is one of the biggest man-made public health threats of modern times, and similar to other settings, New Zealand must confront this challenge. Noteworthy contemporary issues in New Zealand include fusidic acid-resistant *S. aureus*, the endemicity of ESBL-E in the community setting, and the alarming global reservoir and importation of drug-resistant TB.

It is imperative that, in the face of the threats and realities of antimicrobial resistance, New Zealand builds on existing linkages and infrastructure, and adopts a cohesive, proactive and multi-regional approach that combines expertise from across the medical, academic, and veterinary sectors.

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References:

1. Laxminarayan R, Duse A, Wattal C, et al. Antibiotic resistance-the need for global solutions. Lancet Infect Dis. 2013;13:1057-98.
2. World Health Organization. Antimicrobial resistance: Global report on surveillance. 2014. Available at http://www.who.int/drugresistance/documents/surveillancereport/en/
3. Boucher HW, Talbot GH, Bradley JS, et al. Bad bugs, no drugs: No ESKAPE! An update from the Infectious Diseases Society of America. Clin Infect Dis. 2009;48:1-12.
4. Centers for Disease Control and Prevention (CDC). Antibiotic resistance threats in the United States. 2013. Available at http://www.cdc.gov/drugresistance/threat-report-2013
5. Norris P, Horsburgh S, Keown S, et al. Too much and too little? Prevalence and extent of antibiotic use in a New Zealand region. J Antimicrob Chemother. 2011;66:1921-6.
6. Pleydell EJ, Souphavanh K, Hill KE, et al. Descriptive epidemiological study of the use of antimicrobial drugs by companion animal veterinarians in New Zealand. N Z Vet J. 2012;60:115-22.
7. Freeman JT, Williamson DA, Heffernan H, et al. Comparative epidemiology of CTX-M-14 and CTX-M-15 producing *Escherichia coli*: Association with distinct demographic groups in the community in New Zealand. Eur J Clin Microbiol Infect Dis. 2012;31:2057-60.
8. Williamson DA, Roberts SA, Ritchie SR, et al. Clinical and molecular epidemiology of methicillin-resistant *Staphylococcus aureus* in New Zealand: Rapid emergence of sequence type 5 (ST5)-SCCmec-IV as the dominant community-associated MRSA clone. PLoS One. 2013;8:e62020.
9. Williamson DA, Heffernan H, Sidjabat H, et al. Intercontinental transfer of OXA-181-producing *Klebsiella pneumoniae* into New Zealand. J Antimicrob Chemother. 2011;66:2888-90.
10. Williamson DA, Sidjabat HE, Freeman JT, et al. Identification and molecular characterisation of New Delhi metallo-beta-lactamase-1 (NDM-1)- and NDM-6-producing Enterobacteriaceae from New Zealand hospitals. Int J Antimicrob Agents. 2012;39:529-33.
11. Williamson DA, Masters J, Freeman J, et al. Travel-associated extended-spectrum beta-lactamase-producing *Escherichia coli* bloodstream infection following transrectal ultrasound-guided prostate biopsy. BJU Int. 2012;109:E21-2.
12. O'Brien TF, Stelling J. Integrated multilevel surveillance of the world's infecting microbes and their resistance to antimicrobial agents. Clin Microbiol Rev. 2011;24:281-95.
13. Klein EY, Sun L, Smith DL, et al. The changing epidemiology of methicillin-resistant *Staphylococcus aureus* in the United States: A national observational study. Am J Epidemiol. 2013;177(7):666-74.

14. Williamson DA, Lim A, Thomas MG, et al. Incidence, trends and demographics of *Staphylococcus aureus* infections in Auckland, New Zealand, 2001-2011. BMC Infect Dis. 2013;13:569.
15. Williamson DA, Zhang J, Ritchie S, Roberts S, Fraser J, Baker MG. *Staphylococcus aureus* disease in New Zealand, 200-2011. Emerg Infect Dis, in press.
16. Huggan PJ, Wells JE, Browne M, et al. Population-based epidemiology of *Staphylococcus aureus* bloodstream infection in Canterbury, New Zealand. Intern Med J. 2010;40(2):117-25.
17. Smith JM, Cook GM. A decade of community MRSA in New Zealand. Epidemiol Infect. 2005;133:899-904.
18. Vandenesch F, Naimi T, Enright MC, et al. Community-acquired methicillin-resistant *Staphylococcus aureus* carrying Panton-Valentine leukocidin genes: Worldwide emergence. Emerg Infect Dis. 2003;9:978-84.
19. Best Practice Advisory Committee. Management of impetigo. 2009. Available at http://www.bpac.org.nz/BPJ/2009/february/docs/bpj19_impetigo_pages_8-11.pdf
20. Williamson DA, Bakker S, Coombs GW, et al. Emergence and molecular characterization of clonal complex 398 (CC398) methicillin-resistant *Staphylococcus aureus* (MRSA) in New Zealand. J Antimicrob Chemother. 2013;69(5):1428-30.
21. Fluit AC. Livestock-associated *Staphylococcus aureus*. Clin Microbiol Infect. 2012;18:735-44.
22. Heffernan H, Bakker S. Annual survey of methicillin-resistant *Staphylococcus aureus*, 2012. Institute of Environmental Science and Research, Wellington, New Zealand. Available at https://surv.esr.cri.nz/antimicrobial/antimicrobial_resistance.php
23. D'Agata EM, Webb GF, Horn MA, et al. Modelling the invasion of community-acquired methicillin-resistant *Staphylococcus aureus* into hospitals. Clin Infect Dis. 2009;48:274-84.
24. David MZ, Daum RS. Community-associated methicillin-resistant *Staphylococcus aureus*: Epidemiology and clinical consequences of an emerging epidemic. Clin Microbiol Rev. 2010;23:616-87.
25. Lu PL, Liu YC, Toh HS, et al. Epidemiology and antimicrobial susceptibility profiles of gram-negative bacteria causing urinary tract infections in the Asia-Pacific region: 2009-2010 results from the study for monitoring antimicrobial resistance trends (SMART). Int J Antimicrob Agents. 2012;40 Suppl:S37-43.
26. Sheng WH, Badal RE, Hsueh PR, et al. Distribution of extended-spectrum beta-lactamases, AmpC beta-lactamases, and carbapenemases among Enterobacteriaceae isolates causing intra-abdominal infections in the Asia-Pacific region: Results of the study for monitoring antimicrobial resistance trends (SMART). Antimicrob Agents Chemother. 2013;57:2981-8.
27. Heffernan H, Woodhouse R. Institute of Environmental Science and Research. Annual survey of extended-spectrum β-lactamase (ESBL)-producing Enterobacteriaceae, 2012. Available at https://surv.esr.cri.nz/antimicrobial/antimicrobial_resistance.php
28. Institute of Environmental Science and Research. Antimicrobial resistance data from hospital and community laboratories, 2012. Available at https://surv.esr.cri.nz/antimicrobial/antimicrobial_resistance.php
29. Williamson DA, Lim A, Wiles S, et al. Population-based incidence and comparative demographics of community-associated and healthcare-associated *Escherichia coli* bloodstream infection in Auckland, New Zealand, 2005 -- 2011. BMC Infect Dis. 2013;13:385.
30. Upton A, Eyres S, Heffernan H, et al. Background prevalence of extended-spectrum beta-lactamase-producing Enterobacteriaceae in the Auckland community. N Z Med J. 2011;124:102-4.
31. Moor CT, Roberts SA, Simmons G, et al. Extended-spectrum beta-lactamase (ESBL)-producing Enterobacteria: Factors associated with infection in the community setting, Auckland, New Zealand. J Hosp Infect. 2008;68:355-62.

32. Freeman JT, McBride SJ, Nisbet MS, et al. Bloodstream infection with extended-spectrum beta-lactamase-producing Enterobacteriaceae at a tertiary care hospital in New Zealand: Risk factors and outcomes. Int J Infect Dis. 2012;16:e371-4.
33. Pitout JD. Extraintestinal pathogenic *Escherichia coli*: An update on antimicrobial resistance, laboratory diagnosis and treatment. Expert Rev Anti Infect Ther. 2012;10:1165-76.
34. Heffernan HM, Woodhouse RE, Pope CE, et al. Prevalence and types of extended-spectrum beta-lactamases among urinary *Escherichia coli* and *Klebsiella* spp. in New Zealand. Int J Antimicrob Agents. 2009;34:544-9.
35. Rogers BA, Sidjabat HE, Paterson DL. *Escherichia coli* O25b-ST131: A pandemic, multiresistant, community-associated strain. J Antimicrob Chemother. 2011;66:1-14.
36. Williamson DA, Freeman JT, Porter S, et al. Clinical and molecular correlates of virulence in *Escherichia coli* causing bloodstream infection following transrectal ultrasound-guided (TRUS) prostate biopsy. J Antimicrob Chemother. 2013;68(12):2898-906.
37. Williamson DA, Roberts SA, Paterson DL, et al. *Escherichia coli* bloodstream infection after transrectal ultrasound-guided prostate biopsy: Implications of fluoroquinolone-resistant sequence type 131 as a major causative pathogen. Clin Infect Dis. 2012;54:1406-12.
38. Williamson DA, Freeman JT, Roberts SA, et al. Rectal colonization with new Delhi metallo-beta-lactamase-1-producing *Escherichia coli* prior to transrectal ultrasound (TRUS)-guided prostate biopsy. J Antimicrob Chemother. 2013;68(12):2957-9.
39. Heffernan H, Dyet K, Munroe S, et al. First cases of KPC-type carbapenemase-producing bacteria in patients in New Zealand hospitals. J Global Antimicrob Resist. In press 2014. Available at http://dx.doi.org/10.1016/j.jgar.2014.07.002
40. World Health Organization. Global tuberculosis report. 2013. Available at http://www.who.int/tb/publications/global_report/en
41. Institute of Environmental Science and Research. Tuberculosis in New Zealand: Annual report. 2012. Available at https://surv.esr.cri.nz/surveillance/AnnualTBReports.php
42. Williamson DA, Roberts SA, Bower JE, et al. Clinical failures associated with rpoB mutations in phenotypically occult multidrug-resistant *Mycobacterium tuberculosis*. Int J Tuberc Lung Dis. 2012;16:216-20.
43. Yen S, Bower JE, Freeman JT, et al. Phylogenetic lineages of tuberculosis isolates in New Zealand and their association with patient demographics. Int J Tuberc Lung Dis. 2013;17:892-7.
44. Goh TL, Towns CR, Jones KL, et al. Extensively drug-resistant tuberculosis: New Zealand's first case and the challenges of management in a low-prevalence country. Med J Aust. 2011;194:602-4.
45. Whiley DM, Goire N, Lahra MM, et al. The ticking time bomb: Escalating antibiotic resistance in *Neisseria gonorrhoeae* is a public health disaster in waiting. J Antimicrob Chemother. 2012;67:2059-61.
46. Ison CA, Hussey J, Sankar KN, et al. Gonorrhoea treatment failures to cefixime and azithromycin in England, 2010. Euro Surveill. 2011;16:19833.
47. Tapsall J, Read P, Carmody C, et al. Two cases of failed ceftriaxone treatment in pharyngeal gonorrhoea verified by molecular microbiological methods. J Med Microbiol. 2009;58:683-7.
48. Unemo M, Golparian D, Nicholas R, et al. High-level cefixime- and ceftriaxone-resistant *Neisseria gonorrhoeae* in France: Novel penA mosaic allele in a successful international clone causes treatment failure. Antimicrob Agents Chemother. 2012;56:1273-80.
49. Ohnishi M, Saika T, Hoshina S, et al. Ceftriaxone-resistant *Neisseria gonorrhoeae*, Japan. Emerg Infect Dis. 2011;17:148-9.
50. Ohnishi M, Golparian D, Shimuta K, et al. Is *Neisseria gonorrhoeae* initiating a future era of untreatable gonorrhea?: Detailed characterization of the first strain with high-level resistance to ceftriaxone. Antimicrob Agents Chemother. 2011;55:3538-45.

51. Institute of Environmental Science and Research. Sexually transmitted infections in New Zealand: Annual surveillance report, 2012. Available at https://surv.esr.cri.nz/surveillance/annual_sti.php
52. Hensgens MP, Goorhuis A, Dekkers OM, et al. All-cause and disease-specific mortality in hospitalized patients with *Clostridium difficile* infection: A multicenter cohort study. Clin Infect Dis. 2013;56(8):1108-16.
53. Bouza E. Consequences of *Clostridium difficile* infection: Understanding the healthcare burden. Clin Microbiol Infect. 2012;18 Suppl 6:5-12.
54. Rupnik M, Wilcox MH, Gerding DN. *Clostridium difficile* infection: New developments in epidemiology and pathogenesis. Nat Rev Microbiol. 2009;7:526-36.
55. Aldeyab MA, Devine MJ, Flanagan P, et al. Multihospital outbreak of *Clostridium difficile* ribotype 027 infection: Epidemiology and analysis of control measures. Infect Control Hosp Epidemiol. 2011;32:210-9.
56. Roberts S, Heffernan H, Al Anbuky N, et al. Molecular epidemiology and susceptibility profiles of *Clostridium difficile* in New Zealand, 2009. N Z Med J. 2011;124:45-51.
57. Institute of Environmental Science and Research. Vancomycin-resistant enterococci: Annual report. 2012. Available at https://surv.esr.cri.nz/antimicrobial/vre.php
58. Coombs GW, Pearson JC, Daley DA, et al. Molecular epidemiology of enterococcal bacteraemia in Australia. J Clin Microbiol. 2014;52:897-905.
59. Institute of Environmental Science and Research. Invasive pneumococcal disease in New Zealand, 2012. Available at https://surv.esr.cri.nz/surveillance/IPD.php
60. MAF Technical Paper No: 2011/53. A baseline survey of antimicrobial resistance in bacteria from selected New Zealand foods, 2009-2010. 2011. Available at http://www.foodsafety.govt.nz/elibrary/industry/antimicrobial-resistance-in-bacteria.pdf
61. Ministry for Primary Industries. Antibiotics sales analysis: 2009-2011. MPI technical paper no: 2013/62, 2013. Available at http://www.mpi.govt.nz/news-resources/news/monitoring-the-potential-for-antibiotic-resistance
62. Head MG, Fitchett JR, Cooke MK, et al. Systematic analysis of funding awarded for antimicrobial resistance research to institutions in the UK, 1997-2010. J Antimicrob Chemother. 2014;69:548-54.

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New Zealand's mental health legislation needs reform to avoid discrimination

Sarah E Gordon; Anthony O'Brien

Abstract

New Zealand's Mental Health (Compulsory Assessment and Treatment) Act (the Act) is now over 20 years old. As has occurred historically our conceptualisation of humane treatment of people with mental illness has altered significantly over the period in which the Act has been in force. The emergence of the philosophy of recovery, and its subsequent policy endorsement, has seen a significant shift in mental health service delivery towards a greater emphasis on autonomy.

Human rights developments such as New Zealand's ratification of the 2006 United Nations Convention on the Rights of Persons with Disabilities have resulted in compulsory treatment, where it is justified in whole or part by a person's mental illness, now being considered antithetical to best practice, and discriminatory. However the number of people subject to the Act is increasing, especially in community settings, and it is questionable how effective the mechanisms for challenging compulsion are in practice. Moreover, monitoring of the situation at the systemic level lacks critical analysis.

Complacency, including no indication that review and reform of this now antiquated legislation is nigh, continues a pattern of old where the situation of people with experience of mental illness is largely ignored and neglected.

It is with interest that we read "Treatment of the Insane", the reproduced article from 100 years ago in the *New Zealand Medical Journal*.[1,2] In that article the authors attest to the deplorable state of the insane as a result of the carelessness and negligence of government in addressing facilities that were 25 years behind the times.

Many of the sentiments expressed relate to present-day analysis of New Zealand's current mental health legislation, the Mental Health (Compulsory and Treatment) Act 1992 (The Act). New Zealand takes pride in its reputation for socially progressive legislation. However, some areas of the Act belie this self-belief.

In this paper we argue that although by some measures the Act can be said to be working well[3] in certain important respects the Act is out of step with contemporary thinking about mental health and human rights. There are three strands to our argument. These are: increasing use of compulsion under the Act; the movement towards recovery philosophy in mental health; and recent developments in human rights under the 2006 United Nations Convention for the Rights of Persons with Disabilities (UNCRPD).

The UNCRPD has led to questioning of mental health legislation which is based, as in the New Zealand case, on mental illness (or disability) as one of its criteria for treatment without consent.

One consequence of the UNCRPD is a developing body of literature critiquing separate mental health legislation in favour of generic legislation based on capacity.

We argue that it is time for New Zealand to respond to this international trend and consider adopting a single capacity based standard across the entire health sector for treatment without consent. In addition to legislative reform we recommend that rates of use of mental health legislation are closely and critically monitored and reported, with a view to reducing the overall use of compulsion in mental health care.

Current legislation

New Zealand mental legislation is based to a significant extent on the UK Mental Health Act of 1983 and was last revised 22 years ago. The 1992 Act strengthened procedural safeguards in committal processes, introduced a narrower, phenomenological, definition of mental disorder, and moved away from the previous "need for treatment" standard towards a standard based on the dual criteria of mental disorder and dangerousness.[4]

The Act also introduced community treatment orders, justifying this intrusion into individuals' autonomy on the grounds that it would facilitate the process of deinstitutonalisation and reduce the rate of involuntary hospitalisation.

A leading commentator on mental health legislation, has argued that all such legislation should be reviewed every 20 years or so.[5] Although there appears currently to be little appetite for such a review, it is timely to reflect on how the Act has performed against its original aspirations, and how it stands in relation to contemporary treatment philosophy and international human rights developments that New Zealand has committed to since the legislation was enacted.

How is the Act currently working?

Since 2006 the Office of the Director of Mental Health has produced an annual report on key aspects of the functioning of the Act.[6-12]

Data from the annual reports (Table 1) show that since 2005 coercive uses of the Act have increased both absolutely and as a proportion of population numbers.

The data suggest that the total number of people subject to both community and inpatient compulsory treatment is growing. An increase of 2 per 100,000 equates to 80 more individuals subject to the Act, and an increase of 25 equates to an additional 1000 individuals.

These numbers mean that New Zealand's use of community treatment orders is amongst the highest in the world.[13]

Table 1. Legislative activities under the Mental Health (Compulsory Assessment and Treatment) Act (1992) 2005–2011[1]

Legislative activities	2005	2011
Initial assessments that progress beyond the second assessment to an application for a compulsory treatment order	45%[2]	67%
Applications for compulsory treatment orders or extension	4291	4755[3]
Compulsory treatments orders granted	3671 (85.6% of applications)	4181[3] (87.9% of applications)
Average number subject to a compulsory treatment order: Community treatment (section 29) Inpatient treatment (section 30)	 60[2] (per 100,000 population) 17[2] (per 100,000 population)	 85 (per 100,000 population) 19 (per 100,000 population)
Number of applications for review received by Family/District Court	950[2]	1070
Number of applications for review heard by Family/District Court	640[2]	592
Decisions of Family/District Court to release following section 16 inquiries	44[2] (4.6% of applications received/6.9% of applications heard)	37 (3.5% of applications received/6.3% of applications heard)
Number of applications for review received by Mental Health Review Tribunal	133[2]	144
Number of applications for review heard by Mental Health Review Tribunal	78[2]	72
Decisions of Mental Health Review Tribunal to release following section 79 inquiries	5[2] (3.8% of applications received/6.4% of applications heard)	2 (1.4 of applications received/2.9% of applications heard)
	2007	2011
The number of seclusion events	3148[3]	3410
The average number of seclusion events per patient secluded	2.75	3.5

1. Data source (except where indicated): Ministry of Health. Office of the Director of Mental Health: Annual Report 2011, Ministry of Health; 2012. The most recent (2013) report could not be used because some of the data is reported differently in that document.
2. Ministry of Health. Office of the Director of Mental Health: Annual Report 2005, Ministry of Health; 2006
3. Numbers for applications and orders granted represent increases of 9.8% and 10.1% respectively against a population increase of 6.3% from 2005 to 2011 (http://www.stats.govt.nz/).
4. Ministry of Health. Office of the Director of Mental Health: Annual Report 2007, Ministry of Health; 2008 (This data was reported for the first time in 2007).

During the two initial assessment periods (the first for up to 5 days and the second for up to 14 days) consumers can apply to have their compulsory assessment status reviewed by a Family Court or District Court judge.

At the conclusion of the assessment period a Family or District Court judge decides whether or not to issue a compulsory treatment order. If a compulsory treatment order is issued, consumers can apply to have their legal status reviewed by the Mental Health Review Tribunal.

Despite the number of applications received having increased, the number of applications heard by the Family/District Court and the Mental Health Review Tribunal and the numbers of successful applications for release from compulsory status have all decreased. The small number of patients seeking review under section 79, and the rarity of discharge decisions has previously been noted.[3]

The United Nations Working Group on Arbitrary Detention conducted a country visit to New Zealand from 24 March to 7 April 2014.

At the completion of that visit the Working Group held a press conference[14] where they drew the Government's attention to a number of issues of concern. In relation to the detention of persons with mental disability under the Mental Health Act they expressed concern that, in practice, compulsory treatment orders are largely clinical decisions, and difficult to effectively challenge. More specifically they identified that the Family Court is not a specialist court in mental health and seems to have the tendency to heavily rely on medical reports by merely one clinician and one other medical professional, who, in most cases, is a registered nurse.

Although the Mental Health Act guarantees the right to legal advice for all patients, the Working Group observed that persons undergoing compulsory assessments are often unrepresented in practice, as they do not have access to legal aid. They also expressed concern about the widespread practice of seclusion in psychiatric units. Whilst recognising the Government's achievement in reducing the incidents of seclusion since 2009, the Working Group urged authorities to eliminate this practice.

There is a notable variation between DHBs in rates of use of the Act. In 2011 the rates of use of community treatment orders (CTOs, section 29) ranged from 33–151 per 100,000 per month; from 3–55 per month per 100,000 for compulsory inpatient treatment orders (section 30); and from 5 to 16 per 100,000 acute assessment and treatment (section 11).[12]

Rates of seclusion varied from 20–500 for seclusion events per 100,000 population; and ECT administrations without consent from 0-61%. The variability in use of the Act between regions suggests that the decision to invoke the Act might be governed not by a widely agreed 'clinical necessity' but more by locally determined administrative practice.

It is quite possible that the basis on which the figures have been collected have changed over time, affecting their reliability. However, whilst there might be different opinions as to the reliability of official data and the reasons for the apparent increases, these concerns about coercion demand attention. It is perhaps the lack of critical analysis that is the biggest issue.

In contrast to New Zealand, Australia, England, Scotland, Ireland, and Canada all have Commissions that have some form of independent monitoring function and/or initiative to reduce the use of involuntary treatment. Notably most of them refer to human rights imperatives as the justification for doing so.

Whilst the increase in coercion is common to many countries, there is an apparent difference in response:

> "It should be a source of considerable concern to the health and social care system in this country that use of the MHA continues to rise – despite the objectives of the national mental health policy and the investments in community services of recent years. We will be working across the system to consider possible changes to practice and policy that could result in a reduction or reverse to this trend".[15]

Changes in service philosophy

Increases in use of coercion sit uneasily with other developments in mental health care over the last two decades. The treatment philosophy of recovery, in which service users are supported to live well in the presence or absence of continuing symptoms, is one of the most prominent of these developments.

Recovery philosophy explicitly supports individual autonomy.[16] It is seen not only as good practice, but as the explicit Governmental goal of mental health services in New Zealand,[17] as it is in the United Kingdom, the United States, Australia and many other developed nations.[18]

If governmental commitment to recovery based services is to have effect, this needs to be reflected in the legislative framework supporting mental health services. Recovery philosophy explicitly recognises service users' experiences of adversity, including compulsory detention and treatment, but also draws attention to how the mental health service system can give greater recognition to the service user voice, even in situations of crisis where compulsory treatment might be considered.

The current definition of mental disorder in the Act is antithetical to recovery because it implicitly suggests that people with mental illness pose such a degree of risk that this risk needs specific legislative recognition.

The Convention on the Rights of Persons with Disabilities

Recent developments in international human rights have important implications for mental health legislation internationally and within New Zealand. The 2006 United Nations Convention on the Rights of Persons with Disabilities (UNCRPD) clarifies the application of human rights to persons with disabilities, including people with mental illness.

New Zealand has signed and ratified the UNCRPD, thereby assuming an obligation under international law to ensure and promote the full realisation of all the rights it contains. Within the UNCRPD the term 'disability' is given an inclusive meaning which incorporates all forms of physical, psychosocial and learning disabilities.

From the perspective of mental health legislation, the UNCRPD calls into question the legitimacy of legislation, such as New Zealand's, which includes disability as one of its criteria.[19]

Legislation which includes disability as a criterion is held to be discriminatory, an interpretation reflected in the following advice on mental health legislation from the Office of the United Nations High Commissioner for Human Rights (OHCHR):

> Prior to the entrance into force of the Convention, the existence of a mental disability represented a lawful ground for deprivation of liberty and detention under international human rights law. The Convention radically departs from this approach by forbidding deprivation of liberty based on the existence of any disability, including mental or intellectual, as discriminatory
>
> ….[Un]lawful detention encompasses situations where the deprivation of liberty is grounded in the combination between a mental or intellectual disability and other elements such as dangerousness, or care and treatment. Since such measures are partly justified by the person's disability, they are to be considered discriminatory and in violation of the prohibition of deprivation of liberty on the grounds of disability, and the right to liberty on an equal basis with others prescribed by article 14.[20]

New Zealand submitted its first report on implementing the Convention in March 2011[21]. That report correctly noted that the threshold for compulsory care under New Zealand's legislation is that the person concerned must be clinically assessed as having an abnormal state of mind, of such a degree that it poses a serious danger to the health or safety of the person or of others, or seriously diminishes the capacity of the person for self-care. On this basis, it was stated that the trigger for detention is not disability *per se*, but the risk of harm to self or others, so there is no breach of the Convention.

Based on the OHCHR explication of this matter, that interpretation is incorrect: the Act's criteria for compulsion remains discriminatory because mental disability is still a central part of the legal test.

More recently the UN Committee on the Rights of Persons with Disabilities has taken a very definitive stand in response to the reports of a number of countries, including Australia, that have similar mental health legislation to New Zealand.[22]

In particular the Committee concluded that legislation allowing detention in a psychiatric facility "when [a person has] a psychosocial disability and it is forecast that they might endanger themselves or other persons" is in conflict with Article 14's prohibition of deprivation of liberty based on an actual or perceived disability.[23]

The Committee advocated that countries should also take all measures to ensure that no one is detained against their will, on grounds of disability, in any kind of mental health facility.[23] The Committee also urged that countries whose legislation includes the dual criteria of disability and risk should repeal these provisions,[24] and should "abolish norms that authorise deprivation of liberty based on disability".[25]

The Committee's recommendations were not limited to detention in inpatient facilities, but included the more prevalent form of compulsion in New Zealand, community treatment orders.[24]

Given that New Zealand's rate of use of CTOs is amongst the highest in the world,[13] this opinion of the Committee is one of great significance in the New Zealand context.

Altogether, the CRPD and subsequent interpretations by UN committees signal a pressing need to review New Zealand legislation to reflect current human rights concerns.

Suggestions for reform

Commentators responding to challenges posed by the CRPD have proposed reforming legislation, most notably through the adoption of so called "fusion" legislation in which a single standard for capacity (or incapacity) is adopted across the health sector for all situations in which treatment is given without consent.[26]

Calls to abolish separate mental health legislation date as far back as 1994[27] and are based on an argument that treatment without consent should not be based on "status" (i.e. membership of a particular group) but on the patient's capacity to give informed consent. Fusion law is based solely on impaired decision making capacity rather than what is believed to cause that incapacity. The same standard applies to the person with a diagnosis of schizophrenia, dementia or delirium, or the person with no diagnosis at all but who lacks capacity.

This approach to lack of decision making capacity addresses the issue raised by the CRPD that separate legislation with a criterion of disability is discriminatory.

Capacity standards for are not without their critics.[28] Skipworth[29] argues that a system based on capacity for treatment decisions (but not for detention) could prove problematic for forensic patients (people that have committed crimes and have experience of mental illness), particularly in terms of the impact on long-term prison to hospital transfers and the criminal courts potentially being unwilling to consider therapeutic dispositions if they are unable to secure treatment.

67.6% of a sample of forensic patients currently compulsorily treated under The Act were found to have treatment-relating decision-making capacity, and hence would not meet criteria for continued compulsory treatment under capacity based legislation.[30]

One of the arguments against introducing capacity-based legislation is that it could result in an epidemic of detained yet untreated patients in both prisons and mental health facilities and additional pressures for already overburdened systems. However, Skipworth et al[30] found that very few of these people would refuse treatment, particularly if their liberty is at stake. They therefore conclude that there is no evidence to support the proposition that increased risks to third parties would commonly arise if there was a change to legislation based on capacity to consent to treatment. However the issue of whether even a small number of competent patients who will refuse treatment can be safely accommodated within tight budgetary constraints needs to be considered.

> …because of the limited numbers, the risks of permitting treatment refusal by patients with capacity might be seen as manageable, and it may be considered that the disadvantages of that outcome are outweighed by the advantages of promoting patient autonomy if capacity principles are fully respected (p. 449).

In recent legislative reforms some jurisdictions have moved to introduce a capacity based standard[31] however to our knowledge, none have so far adopted the "fusion" model of a single standard across the health sector. (A draft Mental Capacity Bill based on the fusion principle has recently been developed for Northern Ireland[32].)

The fusion model proposes a single legislative vehicle, based on a capacity standard, for treatment without consent for both physical and mental illness.[33]Such a model

would combine adult guardianship and civil commitment provisions within a unified legislative regime.

Kelly explains that such a change represents a radical departure from the present position, and there is little evidence that any jurisdiction, including the UK, is ready for such profound change.[34] Arguably these are similar sentiments to those expressed when de-institutionalisation was first mooted. However, at least these jurisdictions have begun the discussions. If New Zealand values its reputation for socially progressive legislation this issue must be faced.

We have raised two main issues in this paper. First, use of compulsion, especially use of community treatment orders, appears to be increasing in New Zealand. Second, New Zealand's mental health legislation, like that of other western countries could be considered to be in breach of our obligations under the UNCRPD. Legislative reform could address the second of these issues but is unlikely to address the first.

Experience has shown that the criteria of legislation is at best a blunt instrument for reducing rates of compulsion, with clinicians continuing to apply their own clinical and moral intuition in the face of legal criteria that are perceived as restrictive [35,36]. But resistance to change is not a good reason to maintain the status quo.

While it might be expected that politics would not be an issue given successive Governments' commitments to recognition of human rights, in a risk averse social and health climate such commitments will not necessarily trump domestic political whim. The literature on mental health commissions indicates that mental health reform is much more likely succeed with an independent monitor with influence at the highest levels of government.

Monitoring is essential to champion the transition to more evidence-based, community-centred, recovery-oriented, consumer, family and human rights-focused mental health services[37].

Conclusion

In the last 20 years the emergence and promulgation of the philosophy of recovery, subsequent policy endorsement of that philosophy, and international human rights developments, have significantly altered conceptualisations of humane treatment of people with mental illness.

New Zealand's mental health legislation is now in conflict with the philosophical approach required by Government; and in breach of our international treaty obligations. At the same time, compulsion under mental health legislation in New Zealand appears to be increasing, and it is questionable how effective the mechanisms for challenging detention are in practice.

Moreover, monitoring of the situation at the systemic level lacks critical analysis. There is no indication that a review of the Act is nigh. So, just like 100 years ago, many people with experience of mental illness find themselves taken charge of, and managed, by a State that is not fulfilling its concomitant moral, ethical and political duties to ensuring the most humane treatment of people with mental illness.

Consequently New Zealand's mental health legislation is in urgent need of review and reform. In the meantime, current reporting of rates should continue, with critical analysis of trends over time and of variation between regions.

Competing interests: Nil.

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References:

1. Treatment of the insane (part 1). New Zealand Medical Journal. 2013;126(1378). (Original work published 1913). Retrieved from http://www.nzma.org.nz/journal/read-the-journal/all-issues/2010-2019/2013/vol-126-no-1378/5746
2. Treatment of the insane (part 2). New Zealand Medical Journal. 2013. 126(1379). (Original work published 1913). Retrieved from http://www.nzma.org.nz/journal/read-the-journal/all-issues/2010-2019/2013/vol-126-no-1379/100yrs
3. Dawson J, Gledhill K. Introduction. In J Dawson, K Gledhill (Eds.). New Zealand's Mental Health Act in Practice. (2013). Wellington: Victoria University Press, pp. 17-25.
4. Brookbanks W. Introduction. In W Brookbanks, S Bell. Mental health law in New Zealand (2nd ed.). (2005).Wellington: Brookers Ltd, pp. 3-12.
5. Dawson J. The 'No Force' Report. NZLJ. 2006; June:167-169.
6. Ministry of Health. Office of the Director of Mental Health: Annual Report 2005, Ministry of Health; 2006.
7. Ministry of Health. Office of the Director of Mental Health: Annual Report 2006, Ministry of Health; 2007.
8. Ministry of Health. Office of the Director of Mental Health: Annual Report 2007, Ministry of Health; 2008.
9. Ministry of Health. Office of the Director of Mental Health: Annual Report 2008, Ministry of Health; 2009.
10. Ministry of Health. Office of the Director of Mental Health: Annual Report 2009, Ministry of Health; 2010.
11. Ministry of Health. Office of the Director of Mental Health: Annual Report 2010, Ministry of Health; 2011.
12. Ministry of Health. Office of the Director of Mental Health: Annual Report 2011, Ministry of Health; 2012.
13. O'Brien AJ. Community treatment orders in New Zealand: regional variability and international comparisons. Australas Psychiatry. 2014; doi: 10.1177/1039856214531080 [Epub ahead of print].
14. United Nations Working Group on Arbitrary Detention. Statement at the conclusion of its visit to New Zealand. [Press release]. 7th April, 2014. Retrieved from http://www.scoop.co.nz/stories/PO1404/S00106/un-working-group-on-arbitrary-detention-statement.htm
15. Care Quality Commission. Monitoring the Mental Health Act in 2012/2013. Care Quality Commission, 2013, p. 80. Retrieved from http://www.cqc.org.uk/public/reports-surveys-and-reviews/reports/mental-health-act-annual-report-2012/13, p. 80.
16. Leamy M, Bird V, Le Boutillier C, et al. Conceptual framework for personal recovery in mental health: systematic review and narrative synthesis. Br J Psychiatry. 2011;199:445-452.
17. Ministry of Health. Rising to the Challenge: The Mental Health and Addiction Service Development Plan 2012–2017. Wellington, Ministry of Health; 2012.

18. Compagni A, Adams N, Daniels A. International pathways to mental health system transformation: strategies and challenges. California Institute for Mental Health, 2006.
19. Szmukler G, Daw R, Callard F. Mental health law and the UN Convention on the rights of persons with disabilities. Int J Law Psychiatry, pii: S0160-2527(13)00126-X. doi: 10.1016/j.ijlp.2013.11.024. [Epub ahead of print] [Cited 27 February 2014]. Available from: http://dx.doi.org/10.1016/j.ijlp.2013.11.024
20. Office of the United Nations High Commissioner for Human Rights. Thematic Study by the Office of the United Nations High Commissioner for Human Rights on enhancing awareness and understanding of the Convention on the Rights of Persons with Disabilities, UN Human Rights Council; 2009, p. 15.
21. Human Rights Commission. First New Zealand Report on Implementing the United Nations Convention on the Rights of Persons with Disabilities. Wellington, Human Rights Commission; 2011.
22. Minkowitz T. UN Prohibition of Psychiatric Commitment: Review and Analysis, Mad in America; 2013. Retrieved from http://www.madinamerica.com/2013/10/un-leaves-doubt-end-mental-health-detention/
23. Committee on the Rights of Persons with Disabilities, Consideration of Reports Submitted by States Parties under Article 35 of the Convention: Concluding Observations of the Committee on the Rights of Persons with Disabilities (Austria), CRPD/C/AUT/CO/1, 10th sess, (30 September 2013).
24. Committee on the Rights of Persons with Disabilities, Consideration of Reports Submitted by States Parties under Article 35 of the Convention: Concluding Observations of the Committee on the Rights of Persons with Disabilities (Australia), CRPD/C/AUS/CO/1, 10th sess, (30 September 2013).
25. Committee on the Rights of Persons with Disabilities, Consideration of Reports Submitted by States Parties under Article 35 of the Convention: Concluding Observations of the Committee on the Rights of Persons with Disabilities (El Salvador), CRPD/C/SLV/CO/1, 10th sess, (30 September 2013).
26. Dawson J, Szmukler G. Fusion of mental health and incapacity legislation. Brit J Psychiatry. 2006;188(6):504-509.
27. Rosenman S. Mental health law: an idea whose time has passed.[see comment]. Australia. Aust NZ J Psychiatry. 1994;28(4):560-565.
28. Anand S, Pennington-Smith P A. Compulsory treatment: Rights, reforms and the role of realism. Aust NZ J Psychiatry. 2013;47(10):895-898.
29. Skipworth J. Should involuntary patients with capacity have the right to refuse treatment? In J Dawson, K Gledhill (Eds.). New Zealand's Mental Health Act in Practice. (2013). Wellington: Victoria University Press, pp. 213-228.
30. Skipworth J, Dawson J, Ellis P. Capacity of forensic patients to consent to treatment. Aust NZ J Psychiatry. 2013;47(5):443-450.
31. Callaghan S, Ryan C. Rising to the human rights challenge in compulsory treatment – new approaches to mental health law in Australia. Aust NZ J Psychiatry. 2012;46(7):611-620.
32. Ministers launch consultation on Mental Capacity Bill. Retrieved from http://www.dhsspsni.gov.uk/pr-mentalcap270514
33. Szmukler G, Dawson J. Reducing discrimination in mental health law – the 'fusion' of incapacity and mental health legislation. In T. W. Kallert, J. E. Mezzich and J. Monahon (Eds.) Coercive Treatment in Psychiatry. Clinical, Legal and Ethical Aspects. Chichester, Wiley-Blackwell, 2012, pp. 97-120.
34. Kelly B. An end to psychiatric detention? Implications of the United Nations Convention on the Rights of Persons with Disabilities. Brit J Psychiatry. 2014; 204(3):174-175.
35. Appelbaum PS. Standards for civil commitment: a critical review of empirical research. Int J Law Psychiatry. 1984;7:133-144.
36. Durham ML, La Fond JQ. The empirical consequences and policy implications of broadening the statutory criteria for civil commitment. Yale Law Policy Review. 1984;3:395-446.

37. Rosen A, Goldbloom D, McGeorge P. Mental health commissions: making the critical difference to the development and reform of mental health services. Curr Opin Psychiatry. 2010;23(6):593-603.

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DTCA in New Zealand, finding a healthy balance

To compare United States (US) pharmaceutical companies' spend and associated operating standards regarding Direct to Consumer Advertising (DTCA) with those of New Zealand—as Sarah Every-Palmer, Rishi Duggal and David B Menkes do in their article published by the *NZMJ* (Vol 127 No 1401: 29 August 2014)—is to compare apples with oranges.

The dynamics of medicines supply New Zealand are very different from those operating in the US and the provision of information to consumers through advertising of prescription medicines is a healthy balancing of the heavy restrictions on supply that PHARMAC generate.

The New Zealand direct-to-consumer advertising (DTCA) environment is very different to that found in the USA. For a start, all local advertising must comply with Advertising Standards Authority's (ASA's) Codes of Practice and in particular the Code for Therapeutic Products. In addition, industry agreed as a condition for allowing DTCA in New Zealand that all advertising be independently checked for compliance with the ASA Codes by the Therapeutics Advertising Pre-vetting Service (TAPS). Since inception, when DTCA was first approved, the TAPS Adjudicators work closely with Medsafe, the ASA and media companies to ensure DTCA meets the high standards of social responsibility required by the Codes.

At any time a complaint may be made to the ASA regarding advertising, in any media that may be considered in breach of the Codes. Complaints regarding DTCA are extremely rare, reflecting the value of independent pre-approval.

At Medicines New Zealand we go beyond the call of legal duty in publishing an additional set of requirements in our Code of Practice that the pharmaceutical companies we represent are obliged to follow in all realms of their operational activity including DTCA.

It is ironic in a sense that the Every-Palmer, Duggal and Menkes article raises the issue of being misleading when they proceed to lump all advertising together. We are concerned at the view expressed that advertisements promote products for which there is limited evidence of effectiveness. Prescription medicine regulation means that there is robust evidence for a medicine's efficacy before it is allowed to be sold or advertised in New Zealand under the Medicines Act.

It is also worth remembering whilst reading the views put across in the said article regarding television advertising that, as the world becomes increasingly digitally orientated, the access individuals have to information about different pharmaceutical products is only going to grow and even now if a person is looking for an alternative product to that which they are currently being prescribed, they will easily find it online irrespective of whether they'd seen it advertised on TV.

By allowing DTCA in New Zealand consumers are empowered to discuss alternative pharmaceutical products with their trusted GP and that is exactly the point: a medical practitioner will always have the opportunity to present their own professional view

on what they think is the best option for their individual patients—and write the prescription accordingly.

In summary, New Zealand is not the United States and the fact that both countries happen to have DTCA is where the comparison ends.

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Potential for electronic household food purchase data to enhance population nutrition monitoring

Population diets are commonly monitored using national nutrition surveys that employ traditional dietary assessment methods such as 24-hour dietary recalls. However, national nutrition surveys typically occur only every 10 years or so in New Zealand, largely because of high costs. Moreover, traditional dietary assessment methods such as the 24-hour recalls are prone to bias and measurement errors due to reliance on self-report.[1,2] An alternative is to use electronic food purchase data linked with information on the nutrient composition of foods, as has been done in the United Kingdom,[3,4] and for a small number of nutrition intervention studies, including in New Zealand.[5,6]

Although food purchase data are usually collected at household rather than individual level, they are a good proxy for food and nutrient intakes.[7] Furthermore, their objective nature means they are less affected by individual biases.

In New Zealand, Nielsen (a market research company) collects electronic food purchase data using their Homescan® panel, a national, geographically and demographically representative panel of ~2,500 New Zealand households who scan all foods and beverages purchased for consumption in the home. [8] The Nielsen Homescan® panel has been in existence for 16 years, and the weighted data represent ~75% of the ~$11 billion annual total retail grocery sales in New Zealand.

Since 2011, The National Institute for Health Innovation (NIHI) at the University of Auckland has been undertaking annual systematic surveys of the nutrient composition of packaged foods available in New Zealand supermarkets and fast food restaurants (the Nutritrack database).[9] We (NIHI) recently combined Nielsen Homescan® and Nutritrack data to (1) assess population exposure to sodium, saturated fat, and sugar in New Zealand, and (2) identify key opportunities for reformulation of processed foods with the largest potential population health benefits.

Analyses were undertaken using data on more than 16,800 packaged, processed New Zealand food and non-alcoholic beverage products ($3.7 billion total annual sales). Crude and sales-weighted means (weighted by number of units sold) were calculated overall and by food category, and major contributors to household purchases of sodium, saturated fat, and sugar were identified.

Figure 1 shows the proportional contribution major processed food groups make to sodium, saturated fat, and sugar purchases in New Zealand. Specific food categories within those food groups contributing most to nutrient purchases are where the largest population health gains could be made via reformulation and/or reduced consumption (Table 1).

The full report is available on request from the lead author (HE).

Figure 1. Percentage contribution of specific food groups to annual purchases of sodium, saturated fat, and sugar

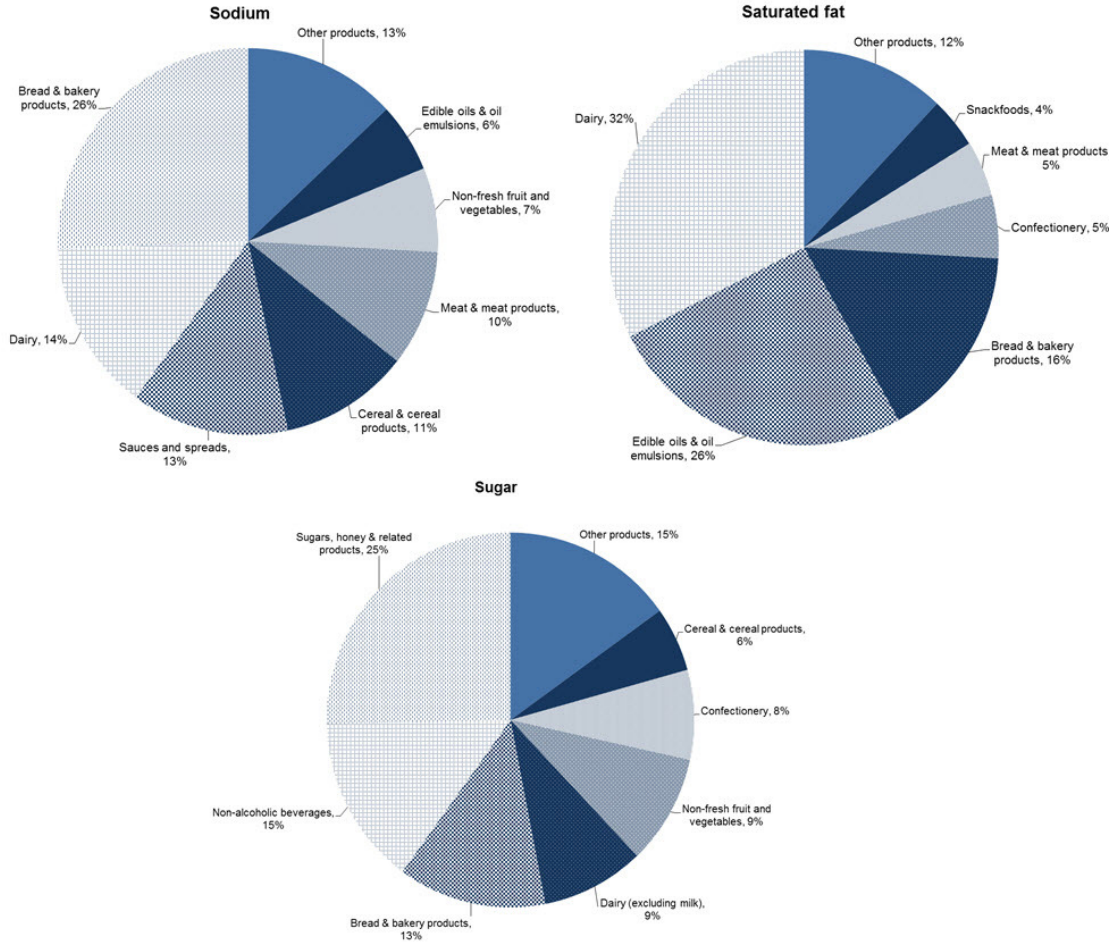

Table 1. Percentage contribution of specific food categories to annual purchases of sodium, saturated fat, and sugar

Sodium		Saturated fat		Sugar*	
Key opportunities for reformulation / intervention/policy	**% contribution to total sodium purchases**	**Key opportunities for reformulation / intervention policy**	**% contribution to total saturated fat purchases**	**Key opportunities for reformulation / intervention/policy**	**% contribution to total sugar purchases**
Bread	17%	Edible oils (butter, margarine, and spreads)	23%	Plain sugar	22%
Processed meat	10%	Cheese	13%	Biscuits	9%
Savoury sauces	9%	Biscuits	12%	Chocolate & sweets	8%
Cheese	8%	Chocolate & sweets	5%	Soft drinks	7%
Edible oils (margarine, butter, and edible oil spreads)	6%	Processed meat	4%	Ice cream & edible ices and non-fresh fruit	5% each

* Excluding milk.

Our findings align with analyses of Australian and United Kingdom processed foods.[3,4] Although New Zealand food manufacturers have already removed some sodium from bread,[10] bread remains the single biggest source of dietary sodium and hence a primary target for continued reformulation, intervention, and policy. Secondary yet still important targets for sodium reduction are processed meat, savoury sauces, cheese, and edible oils (margarine, butter, and spreads).

Corresponding targets for saturated fat reduction are edible oils, cheese, and biscuits, which combined account for 48% of saturated fat purchased by New Zealand households. In order for New Zealanders to meet the new suggested World Health Organization (WHO) guideline for sugar intake,[11] food manufacturers should work on reduction of sugar in biscuits, chocolate and sweets, and soft drinks, particularly as these are foods consumed in high quantities by New Zealand children.[12]

Increased consumer awareness via targeted nutrition education campaigns and policies is also important, especially as plain sugar, which is unlikely to be reformulated, is the top contributor to sugar purchases in New Zealand.

These analyses illustrate the potential of electronic household food purchase data to guide important improvements in population diets. Moreover, they show important potential as a way of objectively monitoring food and nutrient availability and purchases between infrequent national nutrition surveys.

Linked sales and food composition data also offer unique opportunities to identify where healthier reformulation of specific processed food products is likely to have the largest population health benefits. Finally, such data could be used to provide independent evaluation of the impact of industry initiatives, national nutrition interventions, and policies to improve the processed food supply.

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References:

1. Block G. Human dietary assessment: Methods and issues. Prev Med. 1989;18(5):653-60.
2. Winkler JT. Nutritional survey data are inaccurate. Brit Med J. 2014;348:g3204.
3. Eyles H, Webster JL, Jebb SA, Capelin C, Neal B, Ni Mhurchu C. Impact of the UK voluntary sodium reduction targets on the sodium content of processed foods from 2006 to 2011: Analysis of household consumer panel data. Prev Med. 2013;57:555-60.
4. Ni Mhurchu C, Capelin C, Dunford EK, Webster JL, Neal BC, Jebb SA. Sodium content of processed foods in the United Kingdom: analysis of 44,000 foods purchased by 21,000 households. Am J Clin Nutr. 2011;93(3):594-600.

5. Ni Mhurchu C, Blakely T, Jiang Y, Eyles H, Rodgers A. Effects of price discounts and tailored nutrition education on supermarket purchases: a randomized, controlled trial. Am J Clin Nutr. 2010;91:736-47.
6. Smith C, Parnell WR, Brown RC, Gray AR. Providing additional money to food-insecure households and its effect on food expenditure: a randomized controlled trial. Pub Health Nutr. 2013;16(8):1507-15.
7. Hamilton S, Mhurchu CN, Priest P. Food and nutrient availability in New Zealand: an analysis of supermarket sales data. Pub Health Nutr. 2007;10(12):1448-55.
8. Nielsen. Consumer panels. What we measure. http://www.nielsen.com/nz/en/solutions/measurement/consumer-panels.html 2014
9. National Institute for Health Innovation. Nutritrack: Reformulation of processed foods to promote health. Accessed 12th February 2013. http://nihi.auckland.ac.nz/page/current-research/our-nutrition-and-physical-activity-research/nutritrack-reformulation-processe 2013
10. Dunford EK, Eyles H, Mhurchu CN, Webster JL, Neal BC. Changes in the sodium content of bread in Australia and New Zealand between 2007 and 2010: implications for policy. Med J Aust. 2011;195(6):346-9.
11. World Health Organization. WHO opens public consultation on draft sugars guideline. Accessed 3rd June 2014. Available: http://www.who.int/mediacentre/news/notes/2014/consultation-sugar-guideline/en/ 2014
12. Ministry of Health. NZ Food NZ Children: Key results of the 2002 National Children's Nutrition Survey. Wellington: Ministry of Health; 2003.

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British Medical Association (NZ Branch): Annual Report

Excerpt published in NZMJ 1914 March;13(49):39–59.

The annual report and statement of accounts was taken as read and adopted as follows:–

Your Council have pleasure in reporting a continued steady increase in the membership, 48 new members having been added to our roll during the past year. The membership of the Branch now numbers 530.

The death of five of our members Drs G. A. Harrison, S. B. Axford, B. Locking, P. V. N. Hammersley, and K. McAdam, is recorded with deep regret.

At the quarterly meetings held during the year the majority of the Divisions were well represented, and a considerable amount of business was dealt with.

New Divisions

In response to applications received from members resident in Wanganui and District and Palmerston North and District, the Manawatu and West Coast Division was divided into two separate Divisions of the N. Z. Branch. The Manawatu and West Coast Division thus ceases to exist. The newly constituted Divisions are known as the Wanganui and Palmerston North Divisions respectively.

Lodge Practice—Proposed Standard Agreement

With a view of bringing about a greater degree of uniformity in Lodge practice, a form of Standard Agreement between Medical Officers and Friendly Societies has been drawn up by the Council, and, with certain amendments, has been generally approved by the Divisions of the N. Z. Branch. This proposed Standard Agreement has now been printed and circulated to every member of the Branch. Already replies have been received from a large number of members, in almost every case expressing approval. The Draft Agreement will be submitted to the Annual General Meeting in February for confirmation.

Medical Defence Scheme

Your Council have been engaged during the past year in inquiring into the best means of creating a Medical Defence Scheme to apply to all members of the Branch. A favourable offer of Defence Insurance received from a company doing business in New Zealand will be placed before a Special General Meeting in February next. The offer, if accepted, will necessitate a small increase in the Annual Subscription of Members of the Branch.

Accident Insurance Certificates

As it has been found that in many cases where a medical certificate is given to an injured worker it is impossible to recover payment either from the worker, the employer, or the Insurance Company, the Underwriters' Association has been asked to co-operate with your Council in endeavouring to bring about a uniform practice with

regard to payment for such certificates. Unfortunately, the Underwriters' Association is not disposed to meet us in this matter, and it becomes necessary, therefore, to instruct members to give no accident insurance certificates unless payment for same is made or guaranteed.

Scale of Fees

During the year a revised scale of fees was drawn up and submitted to the Divisions of the N.Z. Branch for approval or for suggestion. The scale of fees has now been finally revised, adopted, and printed for circulation to members.

New Zealand Medical Journal

There has been a good supply of original matter for insertion in *The Journal*, but the Secretaries of the various Divisions, almost without exception, neglect to send reports of meetings for publication. It is impossible for the Editor to supply Association news without the aid of the local Divisions. *The Journal* has been increased in size, new features introduced, and the printing much improved.

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Tobacco in the USA

A *Lancet* editorial notes that the adult smoking rate in the USA has dropped from 42.4% in 1965 to 18.1% in 2012. In spite of this, tobacco use is still the biggest cause of preventable death in the USA where 42 million adults and 3 million children smoke. The 2014 US Surgeon General's report has concluded that changes in the design and composition of cigarettes have increased smokers' risk for lung cancer and obstructive pulmonary disease.

A new report by the Campaign for Tobacco-Free Kids describes how the tobacco industry has made cigarettes more addictive (e.g. increasing nicotine levels), more attractive to children (e.g. by adding flavourings such as chocolate), and even more deadly (e.g. increased levels of carcinogenic nitrosamines). The report calls for the US Food and Drug Administration to use its regulatory power to enforce reductions in the addictiveness and harmfulness of cigarettes.

Lancet 2014;384:2.

Risk of complications after total hip arthroplasty

This study investigates whether there is a cut point in annual surgeon volume associated with increased risk of complications after primary elective total hip arthroplasty.

The researchers included 6716 patients who were operated on by a surgeon who had carried out ≤35 such procedures in the 365 days before the index surgery. These patients were matched each (1:1) to a patient who received arthroplasty from a surgeon who had carried out more than 35 procedures in the 365 days before the surgery using a propensity score that included several variables, including age, sex, comorbidity and various socioeconomic indicators.

Patients with hip replacement carried out by a surgeon with an annual volume of ≤35 procedures had a higher rate of dislocation (1.9% *v* 1.3%; P=0.006) and revision (1.5% v 1.0%; P=0.03) within 2 years of their surgery.

BMJ 2014;348:g3284.

Revascularisation versus medical treatment in patients with stable coronary artery disease

Does revascularisation using coronary artery bypass grafting or techniques for percutaneous revascularisation (balloon angioplasty, bare metal stents, early and new generation drug eluting stents) improve survival compared with medical treatment among patients with stable coronary artery disease?

That is the question evaluated in this meta-analysis. 100 trials involving 93,553 patients were included. The primary outcome was all-cause mortality and researchers'

conclusions were that “coronary artery bypass grafting and new generation drug eluting stents (everolimus eluting and zotarolimus eluting (Resolute) stents) but no other percutaneous revascularisation technology were associated with improved survival compared with medical treatment among patients with stable coronary artery disease.”

BMJ 2014;348:g3859.

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Diana Edwards (nee Montgomery)

Home was in Christchurch. School was in Hawke's Bay. Diana Edwards commuted between home and boarding school each term by inter-island ferry and train.

It was the family spirit, Edwards' daughter Shan says. It was a spirit of get on in life, face your challenges, do your thing. Edwards demonstrated the spirit in the whirl of family and social life, in her profession as an obstetrician and gynaecologist and as a champion for women's rights.

She had to be, and was, determinedly strong to work in the controversial areas of contraception and abortion in Christchurch for 20 years from the 1980s.

Born Diana Montgomery, she excelled in sports at Woodford House School, Havelock North, enjoyed holidays at the Grigg family's Longbeach farm, Mid- Canterbury, and revelled in equestrian pursuits, including "riding to hounds" in North Canterbury.

Her parents instilled in her the belief that education was important for girls. When she told her father she wanted to study medicine, he applauded the decision.

She completed a year's study at Canterbury University, while taking night classes in Latin for entry to medical school. She received university blues for hockey and netball (then called basketball) and represented Canterbury at netball.

While at Otago Medical School she captained the university and provincial hockey teams and was a member of the university ski team. She qualified in 1948 and served as a house surgeon and registrar at Dunedin and Melbourne before travelling by ship to Britain. She worked in various hospitals in England while achieving specialist qualifications in obstetrics and gynaecology (O and G).

A "difficult" house surgeon under her supervision brought himself very much to her notice. He was Welshman Bill Edwards. They married and worked together in Nigeria in 1962.

A six-month break in New Zealand followed before the couple formed a specialist O and G team for the Isle of Wight hospitals. A decade later they moved to Canada. She worked as a research assistant, clinical associate and staff physician at St John's, Newfoundland, over a 10-year period. She and Bill returned to New Zealand in 1985.

Shan remembers her mother through these years as highly sociable. She made many friends and extended generous hospitality to them, making a name for herself as a gracious host and a great cook.

“What a fantastic mother she was, always positive, keen for us to give everything a go,” Shan says. Do what you want and be what you want, and if it fails, it is character building, was her advice.

The family settled on an orchard near Blenheim in 1985. Edwards took up the role of medical director of the Family Planning Association in Christchurch and, being accustomed to commuting, drove between the two towns weekly for several years. She still found the energy to work in the orchard at weekends. A few speeding tickets later, she re-located to Christchurch.

Her Family Planning role included delivering and monitoring clinical services and teaching doctors, nurses and medical students across Canterbury, West Coast and Marlborough. She continued her long involvement in research, teaching, and writing for medical journals.

Her work involved her in the acrimonious public debate over abortion. Shan says her primary focus was on advocating for all aspects of women’s rights. Her fight for the right to abortion grew out of this.

“She promoted women’s choice. She was always championing women and standing up for them,” Shan says. She was particularly concerned about the growth of Muslim fundamentalism and its impact on women.

Friend and colleague Dr Robyn Hewland says Edwards was “a pioneer for women's health”. The two served jointly on the NZ Medical Women's Association and attended conferences of the international body. Edwards represented the association on the National Council of Women.

Edwards became clinical director of Lyndhurst Hospital, on Bealey Ave. She was registered as a certifying consultant for women seeking abortions, a role required under the new law. In later years she was a co-director of Istar, a company with charitable trust status that imported the so-called “abortion pill”, the drug RU486. Revenue from the venture was paid into a fund to assist women in need.

Friend and colleague Helen Eskett says Edwards was a woman of “enormous talent, intellect, tenacity and love of life”.

“I never met anyone with so much energy, enthusiasm and commitment for the work she undertook,” Eskett says.

Edwards retired at 75, though she sustained her determination to work for women well into her 80s. After her husband died, she remained a keen bridge player and enthusiast for horses. She was dedicated to family, visiting her daughter in England often. She died at 90.

Diana Edwards, born Christchurch, April 21, 1923; died Christchurch, March 10, 2014. Pre-deceased by husband William; survived by daughters Anne and Shan, son John and six grandchildren.

Mike Crean wrote this obituary. It originally appeared under the heading *Medical Specialist Advocate for Women’s Rights* in *The Press* newspaper (Christchurch) on 15 April 2014 . We thank them for reprint permission.

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Erratum

The authors advise the following in regards to the first author's name:

Stefanie Honegger Bloch, David Semple, Karishma Sidhu, Ralph Stewart, Helen Pilmore. *Prognostic value and long-term variation of high sensitivity troponin T in clinically stable haemodialysis patients*. N Z Med J 12 September 2014;127(1402):97–109.

http://www.nzma.org.nz/journal/read-the-journal/all-issues/2010-2019/2014/vol-127-no-1402-12-september-2014/6296

Previously listed as: Stefanie Honneger

Correct: Stefanie Honegger Bloch

Please refer to the link above for the corrected copy.

NZMJ