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Poor female representation at surgical conference

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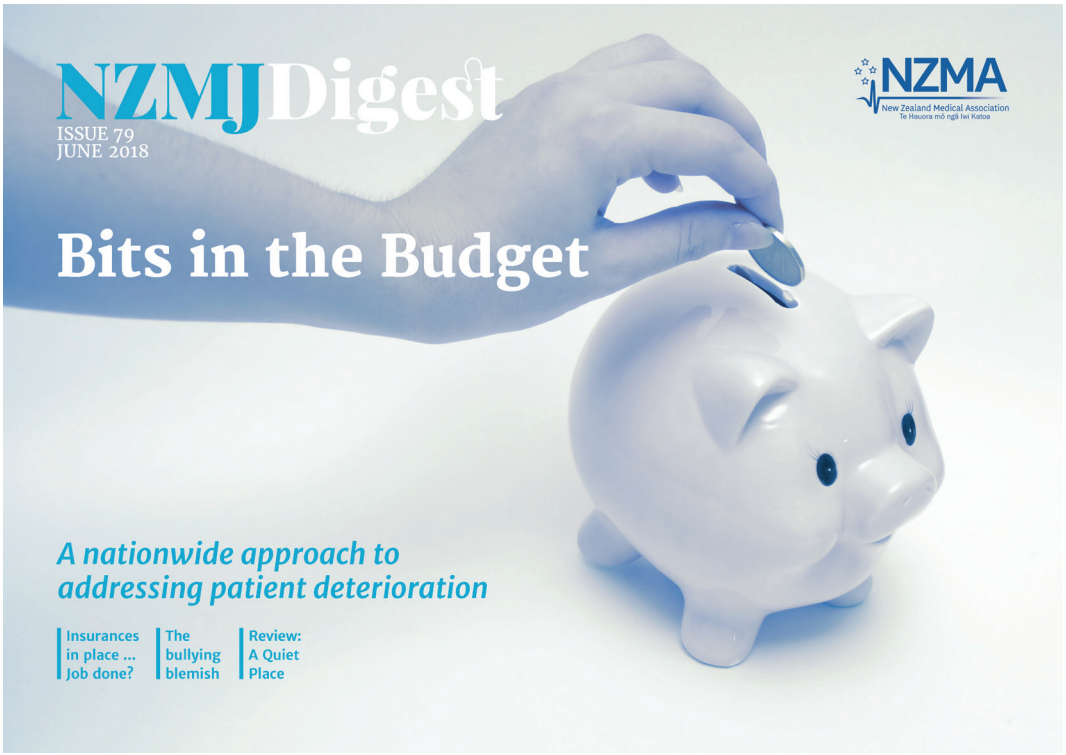

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Comparing methamphetamine, MDMA, cocaine, codeine and methadone use between the Auckland region and four Australian states using wastewater-based epidemiology (WBE)

Chris Wilkins, Foon Yin Lai, Jake O'Brien, Phong Thai, Jochen F Mueller

We aim to compare levels of drug use in Auckland with four Australian major cities using wastewater based epidemiology (WBE). A week of daily wastewater samples were selected from two Auckland and eight Australian urban wastewater treatment plants (WWTPs) during 2014 and 2015. Both Auckland and the selected Australian cities have significant methamphetamine problems compared to many European cities. MDMA and cocaine use is low in Auckland compared to sampled Australia cities.

Trends in ischaemic heart disease: patterns of hospitalisation and mortality rates differ by ethnicity (ANZACS-QI 21)

Corina Grey, Rod Jackson, Susan Wells, Billy Wu, Katrina Poppe, Matire Harwood, Gerhard Sundborn, Andrew J Kerr

Since 2006, hospitalisations and deaths from heart disease have continued to decline in New Zealand. However, rates of death are higher in Māori and Pacific, and hospitalisations higher in Indian, Māori and Pacific people, compared to Europeans. What's more, there appears to be issues with access to healthcare, with fewer hospitalisations for every death from heart disease in Māori and Pacific men and women compared to Indian, other Asian and European men and women. For Māori and Pacific men, there were approximately 3–4 people hospitalised for heart disease for every person who died from the disease. In comparison, there were approximately 7–8 Indian men hospitalised for every person who died from heart disease.

Chromoendoscopy versus standard colonoscopy for detection of nonpolypoid dysplasia in patients with inflammatory bowel disease

Anurag Sekra, Cameron Schauer, Lucy Mills, Alain C Vandal, Toby Rose, Dinesh Lal, Ravinder Ogra

Patients with inflammatory bowel disease such as Crohn's and Ulcerative colitis are on the increase in New Zealand. They have an increased risk of developing colorectal cancer. Surveillance colonoscopies should be done to detect early changes that can lead to cancer, which can then be treated. This study demonstrates that a special dye stain sprayed onto the colon wall (Chromoendoscopy) is able to improve detection of these subtle changes, compared to using standard techniques. We suggest this should be incorporated into national guidelines.

Institutional gastroenteritis outbreaks and time to notify public health services

Sarie M Sariningsih, Tui Shadbolt, Jill McKenzie, Julie Collins-Emerson, Jackie Benschop

Gastroenteritis accounts for the majority of all outbreak notifications in New Zealand. Prompt notification to the Public Health Service reduces the outbreak duration and size.

Pregabalin misuse: preventing potential problems in New Zealand

Rhys Ponton

Pregabalin has recently been made available fully funded in New Zealand. Experience from countries where pregabalin has been used widely, such as the UK, has demonstrated that pregabalin is liable to misuse and is sought after by users from prescribers such as GPs. Pregabalin is misused on its own at high dose, or in combination with other drugs. When used in combination with other drugs, particularly opioids, its synergistic effects may lead to increased risk of overdose. Prescribers, particularly GPs, need to be aware of this misuse potential and to be careful when prescribing to individuals with a history of substance or alcohol misuse, or to patients who present requesting a prescription specifically for pregabalin. All patients prescribed pregabalin should be reviewed regularly to ensure efficacy and safety.

New Zealand transplant patients and organ transplantation in China: some ethical considerations

Phillipa Malpas

In this paper, I cast an ethical lens over the situation of New Zealand patients travelling to China for an organ transplant, given evidence that China continues to take organs from executed prisoners of conscience. I consider some of the challenges facing health professionals involved in providing medical care to such patients, and propose some recommendations. I hope that this paper may start an informed conversation about this complex issue.

Transplant ethical considerations: response from the trenches

Stephen Munn

Associate Professor Malpas[1] rightly draws our attention to the historical evidence for, and possible continued practice of, commerce in deceased donor organs for transplantation in China. The moral repugnance that she expresses is not solely directed at the black market in organs but the known use of executed prisoners as an organ source and the associated targeting of prisoners of conscience, especially the Falun Gong. After describing the egregious behaviour within China's borders, we are asked what the moral imperatives might be here in New Zealand. Indeed, Associate-Professor Malpas argues that we have done little to dissuade New Zealand patients from travelling to transplant centres within China, we continue to provide medical care for such patients on their return home, and we train Chinese surgeons in the craft of transplantation, thereby indirectly aiding and abetting in a horrific abuse of our fellow human beings.

Not quite. While the arguments made about the moral implications for New Zealand clinicians might have weight, the lack of accurate data about current practices within China means that there is uncertainty about the most appropriate response and, indeed, the proportionality of that response if patient care and training of medical practitioners is to be impacted.

The Transplantation Society of Australia and New Zealand has agreed to, and affirmed, the Declaration of Istanbul (2008), a statement decrying the consequences of organ trafficking, transplant tourism and commercialism. It is unsurprising then that most transplant physicians in New Zealand try to persuade their patients that travelling to any overseas country with a view to purchasing an organ transplant is a bad idea. This is based on both ethical and medical considerations, there being clear evidence that such black market organs do not perform as well in transplant recipients. But actually banning such patients from overseas travel would be well beyond the purview of transplant physicians, would require inter-sector concurrence, and may well run afoul of the New Zealand Human Rights Commission.

Training of transplant surgeons via accredited programmes overseen by the Royal Australian College of Surgeons only occurs in one centre in New Zealand, namely Auckland, which has active liver, kidney, pancreas, heart and lung transplant programmes. There have been no surgeons from mainland China training in liver, kidney or pancreas transplantation in the last 20 years in Auckland. In terms of cardiothoracic transplantation, there has only been one locum mainland Chinese cardiothoracic surgeon employed briefly in Auckland over the same time interval—this would hardly qualify as training given that the individual was already fully certified.

Denial of medical care to patients transplanted elsewhere; be that in Australia, the UK, US or China, is not really an option for publicly funded healthcare providers in New Zealand if such patients are eligible under the current statutory requirements. While individual clinicians may object to providing ongoing medical care for those that have opted out of orthodox processes, a duty of care remains to sustain health and prevent the inevitable deterioration that would occur without transplant clinician oversight. As in poker, there are only so many times the buck may be passed before it stops on a designated dealer. Some New Zealand transplant clinician within the public health system would eventually have to provide such care. In reality, few have

qualms about this—the transplant is done and it seems foolish to sacrifice a patient's welfare because of the impropriety of a preceding, extra-mural event.

Another means of helping with what may well be an ongoing abuse of human rights in China, is to do our best to subdue the demand. To this end, New Zealand society in general and its organ donation professionals, along with its transplant physicians and surgeons in particular, is trying its best to improve access to both living and deceased donor organs. This has had a modicum of success. Organ donor rates are up, there are reimbursement provisions in law for living donors that are the best in the world, and there have been recent Ministerial reviews of both organ donation and transplantation. In crude terms, there has been, over the past three years, a 50% increase in the volume of kidney, liver and lung transplants performed in New Zealand. This does not completely remove the temptation of transplant tourism but it does help. Obviously, the more we do in this regard, the better.

Almost certainly the ethical and practical responses we have made in New Zealand to the abuses of human rights in China for transplant expediencies have been imperfect—weaker, perhaps, than what Associate-Professor Malpas would wish to see—but they are not absent.

Competing interests:
Nil.

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The Zero Carbon Bill and the health of New Zealanders—help shape this crucial health law now

Andrea Forde, Liz Springford, Scott Metcalfe

New Zealand has signed up to the Paris climate agreement, to reduce greenhouse gas emissions and limit the increase in global temperatures. The Government is consulting—with some urgency—on the institutional and legislative instruments that will give effect to our Paris agreement obligations. We urge health professionals to make submissions.

Part of the process includes the Zero Carbon Bill (ZCB), which the Ministry of the Environment (MfE) is currently consulting on[1,2] and which is far-reaching. A ZCB should commit New Zealand to limiting global average temperature rise to well below 2°C—and to pursue efforts to limit temperature increase to 1.5°C.

The Ministry of the Environment has invited submissions on this Bill closing next Thursday 19 July. Health professionals can submit easily and quickly via zerocarbonbillhealth.org.nz.

The impacts on human health of climate change are well recognised. Less well recognised, but just as important, is that measures to reduce emissions have substantial positive effects upon health. Tackling climate change is described as perhaps the greatest global health opportunity this century.[3] Reducing emissions from motor vehicles by changing modes of transport—walking and cycling in particular—increase activity levels with reductions in obesity and cardiovascular disease. Reducing meat consumption and changing to a plant-based diet reduces not just emissions but also non-communicable disease, including bowel cancer—a particular problem in New Zealand. Warm, dry, well-insulated homes, that do not require additional emissions to heat, reduce the incidence of respiratory infections and diseases such as asthma.[4]

In short, measures to reduce emissions in New Zealand have the potential to not just reduce the negative impacts of increased global warming, but also to positively improve health now. There are health co-benefits, and savings to health budgets, from reducing emissions. We can get important health and productivity gains from well-designed fast climate action, and the sooner we act, the easier the transition and the greater the gains. We ask that climate action be fast, fair,[5–8] firm and founded on Te Tiriti, with health at its heart. This is a potential win-win for the health of New Zealanders.

As the Zero Carbon Act will be essential for the health and wellbeing of New Zealanders, OraTaiao: The New Zealand Climate and Health Council has, with other health organisations, prepared a submission guide on the Bill for people working in the health sector. This submission guide addresses not only the importance of reducing emissions, but also the positive outcomes for health from measures that are healthy and equitable[5] (www.orataiao.org.nz/zcb). (You can choose a fast five-minute submission online or a full online submission with healthy suggestions for all the MfE's 16 discussion questions.)

This is important health legislation, and submissions close next Thursday July 19 at 5pm.

We encourage all health professionals[9] to submit on the Zero Carbon Bill. And please encourage your whānau, workmates, flatmates, friends, colleagues, professional organisations, and neighbours to have their say, for our health's sake.

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Comparing methamphetamine, MDMA, cocaine, codeine and methadone use between the Auckland region and four Australian states using wastewater-based epidemiology (WBE)

Chris Wilkins, Foon Yin Lai, Jake O'Brien, Phong Thai, Jochen F Mueller

ABSTRACT

AIMS: To compare levels of drug use in Auckland with four Australian major cities using wastewater-based epidemiology (WBE).

METHODS: A week of daily wastewater samples were selected from two Auckland and eight Australian urban wastewater treatment plants (WWTPs) during 2014 and 2015. Samples were analysed for drug residues using liquid chromatography-tandem mass spectrometry. Consumption of methamphetamine, methylenedioxymethamphetamine (MDMA), cocaine, codeine and methadone (mg/day/1,000 people) was estimated for each WWTP from mass loads using an internationally validated back-calculation formula.

RESULTS: Cocaine was not detected at either of the two Auckland WTTPs, and MDMA was detected on only one day of the sampled week in each of the Auckland WWTPs. In contrast, cocaine and MDMA was detected on every day at all eight Australian WWTPs. Methamphetamine was detected on every day at both the New Zealand and Australian WWTPs. Levels of methamphetamine consumption at the Auckland WWTPs were lower than five of the Australian WWTPs. Lower levels of codeine and methadone consumption were detected in Auckland than Australian sites.

CONCLUSIONS: MDMA and cocaine use is low in Auckland compared to sampled Australia cities. Both Auckland and the selected Australian cities have significant methamphetamine problems compared to many European cities.

Drug use can negatively affect future health and wellbeing, including mental health, family relationships, educational achievement and employment opportunities.[1] The social cost of drug-related harm in New Zealand (excluding alcohol) was recently estimated to be $1.5 billion per year, with the government spending $78.5 million on drug-related health interventions each year.[2] Monitoring levels of drug use is important to guide the delivery of health services and inform policy responses to drug-related harms. Levels of drug use in New Zealand are commonly compared to those in Australia, as the two countries are from the same global region and share similar socio-economic characteristics.[3] Traditionally the monitoring of drug use in the

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population has relied heavily on national social surveys where respondents self-report drug use. While these social surveys provide fairly good measures of drug prevalence in the population they are known to suffer from a number of limitations, including sample under-coverage depending on the means used to contact potential respondents (eg, people without landline telephones or those seldom at home), declining response rates due to high levels of commercial market surveying, and the under-reporting of drug use due to illegality and social stigma.[4–6] National social surveys of drug use are also expensive and time-consuming to conduct and analyse.[5] A common strategy to address the challenges of monitoring illegal drug use is to triangulate from a range of data sources, including health statistics (eg, drug-related hospital admissions and poisonings), police statistics (eg, drug seizures and arrests) and by conducting targeted studies of 'at risk' populations with high drug use and related harm (eg, police arrestees and injecting drug users).[7,8] Wastewater-based epidemiology (WBE) is an emerging new methodology which can provide objective measures of drug consumption based on the detection of drug residues in pooled wastewater (ie, sewage) sampled at the inlet pipe of a wastewater treatment plant (WWTP).[9–12] Sampling from a WWTP ensures all the dwellings in the WWTP's catchment are automatically covered by the estimates; thereby avoiding issues of under-coverage and under-reporting. WBE also minimises privacy issues related to drug surveying, as pooled wastewater guarantees individual anonymity.[5] Numerous WBE studies have been conducted in cities in Europe, North America, Asia and Australia in recent years.[13–17] Most recently, WBE has been applied to identify spatial variation in drug use across all Australian states, and to identify temporal changes in methamphetamine consumption from 2009 to 2016.[18–20] WBE is beginning to be utilised in New Zealand with a pilot study completed in Auckland in 2014,[21] and a larger pilot programme commissioned by New Zealand Police and conducted by the ESR in 2017.[22] However, no comparisons of WBE findings have yet to be made between New Zealand and Australian.

The aim of this paper is therefore to compare levels of methamphetamine, cocaine, MDMA, codeine and methadone measured using WBE from two urban WWTPs in the Auckland Region with eight urban WWTPs from four Australian states (ie, Queensland, New South Wales, Australian Capital Territory [ACT] and Victoria).

Methods

For the purposes of comparisons, a week of wastewater sampling from 10 urban WWTPs was selected: two in the Auckland region; one from Australian Capital Territory (ACT); two from Victoria; two from Queensland; and three from New South Wales (NSW). Urban sites were defined as WWTP with catchments of more than 150,000 people and located in major cities. The specific communities involved in the comparison were anonymised to protect confidentiality with only Region/State identified (eg, NSW-A). The selected data used for the city comparisons is taken from larger data sets, which have been previously published.[19,21]

Auckland region sampling

Wastewater sampling was completed on nearly every day from 2 May to 18 July 2014 at two urban WWTPs in the Auckland region: Auckland WWTP-A and Auckland WWTP-B. Twenty-four hour composite samples were collected at the Auckland WWTP-A using time-proportional sampling (a collection of 100mL of influent wastewater every 15 min) and at the Auckland WWTP-B using volume-proportional sampling (a collection of 200mL of wastewater in every 1,000m^3 influent wastewater) (see Lai et al[21] for sampling details).

Over the monitoring period, a total of 65 24-hour composite samples were collected at the Auckland WWTP-A. For the purposes of comparisons for this paper we selected a full week of samples from Tuesday 6 May to Monday 12 May 2014 (there was only one other instance where seven consecutive sampling days were completed over the two and half months of sampling).

A total of 40 24-hour composite samples were collected at the Auckland WWTP-B using volume-proportional sampling mode. Sampling was not routinely conducted at Auckland WWTP-B on Fridays and Saturdays. The most consecutive run of daily samples available for a week comparison

were from Monday 23 June to Tuesday 1 July (Friday and Saturday samples were not available). Note, sampling on a day represented samples from the previous night. Consequently, Sunday samples covered the previous Saturday night and so on.

Australian sampling

A week of samples was selected from the 11–17 March 2014 at urban WWTPs in the ACT and Victoria (VIC). Daily wastewater samples were collected at the inlet of the WWTPs using flow proportional sampling (sampling frequency of the autosampler proportional to the actual flow of the influent wastewater). A further week of samples was selected from urban WWTPs in Queensland (QLD), New South Wales (NSW) and Victoria using the time proportional sampling (QLD), volume proportional sampling (VIC) and flow proportional sampling (NSW) respectively. Details of the sampling have been previously reported elsewhere.[19]

Chemical analysis

Drug residues (parent drugs and metabolites) in samples were measured using an internationally validated analytical method.[14,23] The wastewater samples were filtered and spiked with deuterated chemical standards for correcting potential instrumental variability and matrix effects during analysis. Concentrations of the drug residues in the samples were identified and quantified using liquid chromatography coupled with tandem mass spectrometry.

Back-calculation

To obtain the daily mass load (mg/day) of the drug residues in the samples, the measured concentration (µg/L) of the drug residues was multiplied by the daily wastewater flow volume (ML/day). The estimated mass load of the drug residues was then corrected by the average fraction of the drug residue excreted by humans[11] to back-calculate the amount consumed (mg/day). This was further normalised to the catchment population size so as to allow comparison of data (mg/day/1,000 people) between catchments.

Statistical analysis

The Mann Whitney test was used to test for differences in estimated drug use between the Auckland region and each Australian state WWTP. For the purposes of statistical comparison with the Australian WWTP, data on the population-normalised consumption from the two Auckland sites were combined.

Results

Occurrence and consumed mass loads of drug residues

Methamphetamine was detected on every day of the selected week at both the two Auckland and eight Australian WWTPs over the selected week of sampling. MDMA was detected at the Auckland WWTP-A and Auckland WWTP-B on only one day over the sampled week, both on Sunday, representing use from the previous Saturday night. In contrast, MDMA was detected on all seven days of the selected week at all eight Australian sites. Cocaine was not detected at either the Auckland WTTP-A or Auckland WWTP-B on any of the days selected for comparison. In contrast, cocaine was detected on every day of the week at all eight Australia WWTP. Codeine and methadone were detected on every sampled day at both the Auckland and Australian sites.

Overall levels of consumption

A mean of 322mg of methamphetamine was estimated to have been consumed per day per 1,000 people at the Auckland WWTP-A, and an estimated mean of 402mg per day per 1,000 people at the Auckland WWTP-B (Table 1). The estimated levels of methamphetamine consumption at the Auckland WWTPs were higher than the ACT, but lower than QLD-A, VIC-B, VIC-A, NSW-B and QLD-B WWTP (Figure 1). There was no statistically significant difference in levels of methamphetamine consumption between Auckland and NSW-C and NSW-D WWTPs. Only low levels of MDMA consumption were found in Auckland WWTP-A and Auckland WWTP-B sites and only on a single day in the selected sampled week, preventing any comparisons to Australia sites (Table 1). A higher level of codeine and methadone consumption was found in all Australian WWTPs compared to Auckland.

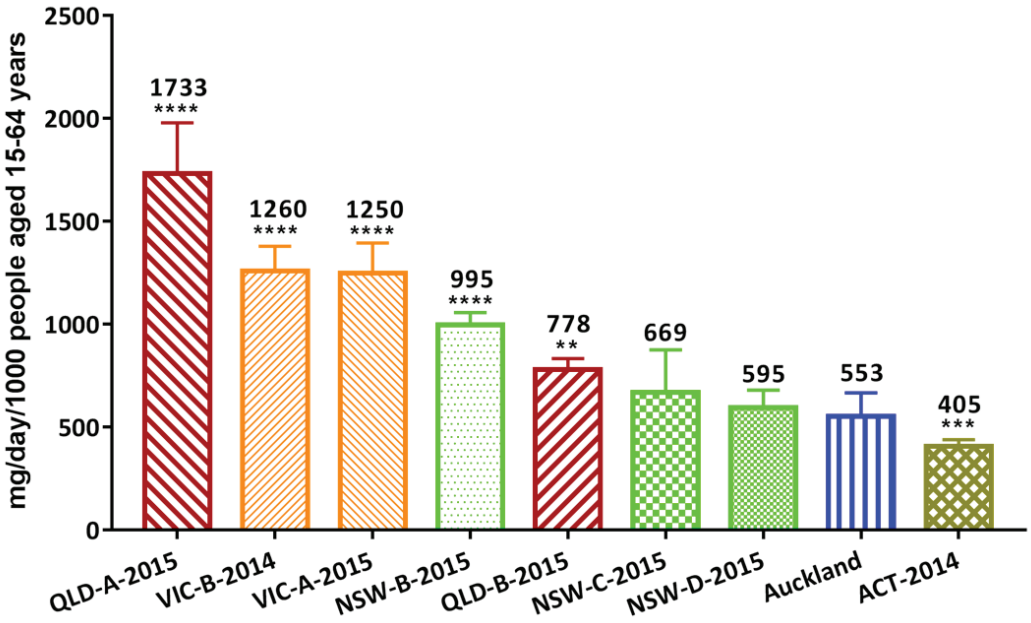
Table 1: Estimated population-normalised consumption of methamphetamine, MDMA and cocaine, codeine and methadone (mg/day/1,000 people aged 15–64 years) for Auckland, Queensland, New South Wales, ACT and Victoria urban sites, 2014 and 2015.

Location	Date	Methamphetamine	MDMA	Cocaine	Codeine	Methadone
Auckland - A	6/05/2014	433	0	0	560	32
	7/05/2014	436	0	0	572	39
	8/05/2014	481	0	0	638	41
	9/05/2014	580	0	0	594	54
	10/05/2014	506	0	0	593	36
	11/05/2014	530	70	0	628	40
	12/05/2014	475	0	0	607	45
Total (average)		**491**	-	-	**599**	**41**
Auckland - B	23/06/2014	752	0	0	961	67
	24/06/2014	493	0	0	923	44
	25/06/2014	821	0	0	1,608	94
	26/06/2014	528	0	0	665	59
	29/06/2014	637	85	0	782	90
	30/06/2014	564	0	0	917	85
	1/07/2014	501	0	0	739	55
Total (average)		**614**	-	-	**942**	**71**
Australia Capital Territory	11/03/2014	373	578	266	2,808	216
	12/03/2014	370	240	169	3,200	211
	13/03/2014	375	215	161	3,284	209
	14/03/2014	437	879	233	3,310	237
	15/03/2014	448	629	367	3,541	247
	16/03/2014	431	824	446	3,472	224
	17/03/2014	404	483	306	3,085	212
Total (average)		**405**	**550**	**278**	**3,243**	**222**
Victoria -B	11/03/2014	1,082	1,300	435	2,525	151
	12/03/2014	1,203	589	278	2,754	154
	13/03/2014	1,173	291	350	3,081	133
	14/03/2014	1,282	258	428	3,206	156
	15/03/2014	1,383	617	755	3,230	158
	16/03/2014	1,423	1,206	935	2,943	149
	17/03/2014	1,273	771	611	3,152	153
Total (average)		**1,260**	**719**	**542**	**2,984**	**151**
Queensland - A	11/03/2015	1,567	194	371	3,814	78
	12/03/2015	1,634	131	503	4,033	71
	13/03/2015	1,582	154	493	3,611	76
	14/03/2015	2,156	547	909	3,896	72
	15/03/2015	1,772	798	988	3,132	63
	16/03/2015	1,959	553	831	3,548	84
	17/03/2015	1,464	179	383	3,322	74
Total (average)		**1,733**	**365**	**640**	**3,622**	**74**

Table 1: Estimated population-normalised consumption of methamphetamine, MDMA and cocaine, codeine and methadone (mg/day/1,000 people aged 15–64 years) for Auckland, Queensland, New South Wales, ACT and Victoria urban sites, 2014 and 2015 (continued).

Queensland - B	21/04/2015	711	121	132	2,352	86
	22/04/2015	741	47	144	2,630	81
	23/04/2015	791	46	157	2,997	84
	24/04/2015	849	136	260	2,700	94
	25/04/2015	831	449	404	2,427	75
	26/04/2015	802	1,258	618	2,486	76
	27/04/2015	724	408	263	3,112	81
Total (average)		**778**	**352**	**283**	**2,672**	**82**
New South Wales - B	5/05/2015	1,012	245	638	1,752	128
	6/05/2015	1,063	369	592	1,840	188
	7/05/2015	932	263	558	1,509	223
	8/05/2015	973	253	986	2,168	198
	9/05/2015	926	11,859	1,284	1,634	130
	10/05/2015	1,064	3,117	1,301	2,404	155
Total (average)		**995**	**2,684**	**893**	**1,885**	**170**
New South Wales - D	27/04/2015	614	370	490	977	131
	28/04/2015	604	152	457	1,202	121
	29/04/2015	482	115	420	886	115
	30/04/2015	533	151	651	1,145	118
	1/05/2015	741	813	1,604	1,086	144
	2/05/2015	551	1,085	1,148	583	114
	3/05/2015	639	768	977	998	172
Total (average)		**595**	**494**	**821**	**983**	**131**
New South Wales - C	27/04/2015	994	530	587	2,071	145
	28/04/2015	616	278	399	1,713	107
	29/04/2015	831	555	329	1,472	76
	30/04/2015	758	146	311	964	83
	1/05/2015	509	231	527	650	58
	2/05/2015	386	357	489	800	48
	3/05/2015	590	1,415	871	1,166	102
Total (average)		**669**	**502**	**502**	**1,262**	**88**
Victoria - A	17/03/2015	1,174	139	118	3,418	143
	18/03/2015	1,051	61	103	3,392	138
	19/03/2015	1,235	38	112	2,806	145
	20/03/2015	1,126	62	148	3,267	140
	21/03/2015	1,464	178	268	3,771	142
	22/03/2015	1,366	458	366	3,068	132
	23/03/2015	1,329	303	230	3,350	138
Total (average)		**1,249**	**177**	**192**	**3,296**	**139**

Figure 1: Estimated methamphetamine consumption (mg/day/1,000 people aged 15–64 years) for combined Auckland urban WWTPs compared to Queensland, New South Wales, Australian Capital Territory and Victoria urban WWTP, 2014 and 2015.



**** p-value <0.0001.
*** p-value <0.0005.
** p-value <0.001.
* p-value <0.05.

Discussion

The comparison of WBE results presented in this paper confirms some important qualitative differences in the types of drugs used in New Zealand compared to Australia. Cocaine was not detected at all in the two Auckland WWTPs during the sampled weeks. In contrast, cocaine was detected on every day at all eight Australian WWTPs over the week selected. Over the whole two and a half months of sampling at Auckland WWTPs, cocaine was only detected at the Auckland WWTP-A and only on six occasions.[21] The low level of cocaine use in Auckland is consistent with previous New Zealand population drug surveying and studies of 'at risk' populations, such as frequent drug users, who report low prevalence of use and poor availability of cocaine.[7,8] Similarly, while MDMA was detected on only one day of the sampled week in each of the Auckland WWTPs, it was detected on every day at the eight Australian WWTPs over the week selected. It is important to note that as described above, sampling was not conducted at Auckland WWTP-B on Fridays and Saturdays, representing Thursday and Friday respectively, and if these days were sampled more MDMA may have been found. It should also be noted that the WBE analysis specifically detects the compound MDMA, rather than the array of MDMA analogues which are commonly sold as "ecstasy" in New Zealand. ESR (Institute of Environmental Science and Research) analysis of "ecstasy" tablets seized in New Zealand has found they contain a range of compounds other than MDMA, including methylone and MDPV.[24] Many of these substitute ecstasy compounds are associated with more serious adverse effects and hospitalisations than MDMA.[24]

Our paper also confirms that methamphetamine use is a problem in many areas of both New Zealand and Australia with methamphetamine detected on every day in all 10 WWTPs. As a point of comparison, comparable wastewater studies in 15 of 17 European countries found levels of methamphetamine consumption of less than 200mg per 1,000 people per day.[20] This reflects different drug availability between countries with high availability of methamphetamine in Oceania and Asia, while amphetamine and cocaine is more available and preferred in Western Europe. Yet even when a broader comparison is made of all

stimulants (ie, methamphetamine, amphetamine, cocaine and MDMA), Australia still ranked second compared to 17 European countries.[20] These findings are consistent with the record seizures of methamphetamine made at the border in both Australia[25] and New Zealand in recent years,[7] and with recent findings from drug monitoring studies of police arrestees and frequent drug users which found increasing methamphetamine use and availability.[7,8] The United Nations Office of Drugs and Crime (UNODC) reported the quantity of methamphetamine seized in East and South-East Asia "almost quadrupled" from 2009 to 2014.[26] Australian WBE analysis has shown rising use of methamphetamine from 2009 to 2016 in Queensland and South Australia.[18,20]

Limitations

It is important to note the WBE findings in this paper are from individual WWTP and consequently represent the drug use in a particular local catchment rather than the entire region, state or country. The more extensive WBE in Australia highlights the high level of variability in drug use between WWTP sites, detail which is often lost in the national prevalence findings from national social surveys of drug use. For example, in some Australian states the difference in mass loads of methamphetamine was more than threefold (ie, South Australia, Tasmania, Victoria).[20] WBE cannot provide data on the demographics of substance users, the distribution of consumption among users, extent of poly-drug use, routes of administration and the effects of drug use on health and social functioning.[15] As a result, WBE is generally advocated as complementary rather than a replacement for existing drug monitoring methods. The populations contributing to wastewater in each WWTP catchment are based on the most recent census, and this may have changed over time.[16] The analytical limitations of wastewater analysis have been discussed in detail elsewhere.[11,27] WBE calculations of drug consumption assume the use of a single substance and an "average" metabolism time for each drug under investigation (chronic users may have different metabolisation from occasional users).[11]

Competing interests:
Nil.

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Trends in ischaemic heart disease: patterns of hospitalisation and mortality rates differ by ethnicity (ANZACS-QI 21)

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ABSTRACT

AIM: To examine trends in ischaemic heart disease (IHD) events by ethnicity.

METHODS: All IHD deaths and hospitalisations from 2006–2015 were identified using individual-linkage of national hospitalisation and mortality data. Age-standardised IHD rates and average annual age-adjusted percent changes were estimated by ethnic group. Ratios of non-fatal to fatal events were calculated by dividing age-standardised hospitalisation by death rates.

RESULTS: IHD mortality rates declined by 3.1–5.4% per year for most groups, except Pacific women, who experienced a non-significant decline of 1.3% per year. IHD hospitalisation rates declined significantly by 3.6–8.8% per year in all groups. IHD mortality rates were highest in Māori and Pacific people, but hospitalisation rates highest in Indians. Indians also had the highest ratio of hospitalisations to deaths. For every person who died from IHD in 2014/15, 7–8 Indians, but only 3–4 Māori or Pacific people, were hospitalised with IHD.

CONCLUSION: Fatal and non-fatal IHD rates are declining in all groups, but Māori and Pacific people have disproportionately high rates of IHD mortality. The much lower ratio of IHD hospitalisations to deaths among Māori and Pacific people compared to others suggests there are still important barriers to preventive interventions and acute care for Māori and Pacific men and women.

Mortality rates from ischaemic heart disease (IHD) have been declining in New Zealand and throughout the industrialised world since the 1960s,[1] with age-adjusted mortality rates declining to less than one-third of their 1960s baseline by 2000.[2,3] These declines have been attributed to rapid progress in the prevention and treatment of cardiovascular disease, including reductions in blood cholesterol and smoking prevalence, improvements in blood pressure control and the increasing use of revascularisation in the treatment of acute coronary syndromes.[4]

However, there are concerns that rising rates of obesity and diabetes may halt, or even reverse, these favourable trends in IHD.[2] Increases in body mass index (BMI) and diabetes prevalence have been implicated in recent slowdowns in the rates of decline of IHD mortality in young adults in the US, UK and Australia.[5–7] New Zealand, however, has not yet observed this phenomenon in the total population: between 2005 and 2015 IHD event rates continued to decline in men and women of all ages.[8] However, these trends have not been examined by ethnicity, even though

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cardiovascular outcomes and the prevalence of obesity and diabetes is known to vary markedly by ethnic group. Māori, Pacific and Indian adults are known to be at increased risk of cardiovascular disease in New Zealand, with higher prevalence and hospitalisation rates compared to Europeans.[9,10] Obesity rates are highest in Pacific (67%) and Māori (47%), intermediate in European (30%) and lowest in Asian (15%) adults;[11] however, it has been shown that Indians have similar body fat levels to those of Europeans with BMI levels 4–6 units higher, so relative obesity rates in Indians may be higher than official rates suggest.[12] Estimates of diabetes prevalence range from 5.9% for Europeans to 12.3% for Māori, 17.4% for Indians and 19.5% for Pacific people.[13] It is possible that these ethnic differences in obesity and diabetes prevalence could result in differential rates of decline in IHD.

The aims of this study were therefore to: (1) investigate whether recent declines in IHD deaths and hospitalisations in New Zealand were experienced by all major ethnic groups, and (2) quantify the rate of change in fatal and non-fatal IHD events between 2006 and 2015 by ethnicity.

Methods

The study population included all New Zealand residents aged 35–84 years during the period 2006–2015. Over that time, the population in this age group increased from approximately 2.09 to 2.35 million. There is no standard age range for these types of analyses internationally; however, the upper age limit of 84 years was chosen because of concerns about the accuracy of diagnostic codes in the oldest age groups. Diagnostic uncertainty increases with age, particularly in the presence of multiple comorbidities.

IHD hospitalisation rates were estimated using discharge data for acute admissions from the National Minimum Dataset, a national collection of all ICD-10 coded public hospitalisation data.[14] IHD death rates were estimated from the Mortality Collection, a national dataset classifying the underlying cause of death for all deaths registered in New Zealand.[15] Both datasets used version ICD-10-AM (International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Australian Modification). IHD events were identified using the ICD-10 codes I20-I25.

To ensure that differing rates of re-hospitalisation by ethnic group did not skew results, a per-person-per-year, rather than a per-event, analysis was conducted. Thus, even if re-admitted, a person only contributed once to the hospitalisation numerator for each year.

For those with multiple ethnic groups recorded, a prioritisation method, modified from that outlined in the recently revised Ministry of Health *Ethnicity Data Protocols*,[16] was used to assign each individual to one ethnic group. Prioritisation occurred in the following order: Māori, Pacific, Indian, Other Asian, European/Other. There was one exception to this prioritisation process, and that was people recorded in the national datasets as belonging to both 'Fijian' and 'Indian' groups, who were categorised in these analyses as Indian rather than Pacific. The rationale for this decision came from previous analyses by our research group that have noted that people classified as both Fijian and Indian have cardiovascular risk profiles more consistent with those classified as Indians than other Pacific groups.[17] Moreover, the revised *Ethnicity Data Protocols* report that there have been data quality issues with the collection, classification and recording of 'Fijian Indian', with some respondents and some providers choosing to alter collection forms or allow respondents to select 'Fijian' and 'Indian' separately.[16]

Denominators for the calculation of rates were obtained from ethnic group population projections (2015 update), produced by Statistics New Zealand according to assumptions specified by the Ministry of Health. These projections are available by five-year age group for the following four ethnic groups: Māori, Pacific (excluding Māori), Asian (excluding Māori and Pacific) and Other (total population excluding Māori, Pacific and Asian). The Other group is mostly comprised of New Zealand Europeans, with small numbers (approximately 1%) of people identified as Middle Eastern, Latin American or African. The population projections are based on the estimated resident population of each ethnic group

at 30 June 2013 and adjusted for census undercount due to various factors, such as non-response and residents temporarily overseas on census night.

Because Indians are not identified separately in the population projections, separate denominators for Indians and Other Asians were estimated using a customised dataset from Statistics New Zealand of the numbers of Indians and Other Asians in the 2006 and 2013 censuses. The proportion of the total Asian group that was Indian was calculated for 2006 and 2013 by five-year age group and sex, interpolated for the intervening years and extrapolated for the years 2014–2015. These proportions were then applied to the population projections for Asians.

Statistical analysis

The ethnic distribution of the male and female population aged 35–84 years and of IHD deaths and IHD/MI hospitalisations were compared for the years 2006/07 and 2014/15. Average annual event rates were calculated over each two-year period because of the small number of IHD deaths in some ethnic groups. Crude rates were age standardised, using five-year age groups, to the Projected New Zealand Population 2015 by the direct method (Supplementary Table 1). Age-standardised IHD hospitalisation rates were divided by age-standardised IHD mortality rates to estimate the ratio of non-fatal to fatal IHD events for each ethnic group. Because individuals were counted only once when calculating hospitalisation rates (regardless of how many times they were hospitalised each year), this ratio represented the number of people hospitalised with IHD for every IHD death.

Temporal trends in IHD death and hospitalisation rates were examined by sex and ethnic group using negative binomial regression, with year of admission (continuous variable) and five-year age group (categorical variable) as independent variables. Interactions between year and age group were tested for, but there was no evidence of an interaction effect. The results of the final models were summarised as age-adjusted annual percent changes in IHD rates over the study period. Data analysis was performed using Stata SE statistical software version 13.0.[18]

Ethical approval

This analysis is part of the VIEW research programme, which receives annual ethical re-approvals from the Northern Region Ethics committee Y (original approval in 2003 [AKY/03/12/314]) and the Multi-Region Ethics Committee (original approvals in 2007 [MEC/01/19/EXP] and 2011 [MEC/11/EXP/078]). Individual patient consent is not required as all data are anonymised.

Results

Between 2006 and 2015, 145,929 New Zealand residents aged 35–84 years experienced at least one IHD hospitalisation and/or an IHD death. Ethnicity was not identified in 3,984 (2.7%) people. The number of men and women in the study population increased by 12.2% and 13.4% respectively between Year 1 and Year 10, but there was a steady decline in the number of people who experienced IHD events. The number of people hospitalised with IHD decreased from 21,311 in 2006 to 14,174 in 2015 (33.5% decline) and the number who died from IHD decreased from 3,624 to 2,820 (22.2% decline) over the same period.

Europeans accounted for almost 80% of the New Zealand population aged 35–84 years in 2006, but declined to approximately 75% in 2015 (Tables 1A and 1B). The four other ethnic groups all increased in size over this period, particularly the Indian and Other Asian groups. The mean age of Europeans was almost 57 years, approximately five years older than other ethnic groups. Māori and Pacific people were over-represented for IHD hospitalisations and deaths except for hospitalisations among Māori men. In contrast, Indians were over-represented for IHD hospitalisations but under-represented for mortality while Other Asians were under-represented for both hospitalisations and deaths. The European ethnic group were under-represented for deaths but their IHD hospitalisations were in proportion to their population size.

Table 1A: Proportions of the population, of IHD deaths, and of those hospitalised with IHD, in each ethnic group for men, 2006/07 and 2014/15.

Year		Māori	Pacific	Indian	Other Asian	European	Total*
2006/07	% of NZ population 35–84y	9.7%	4.2%	2.4%	4.8%	78.9%	2,030,425
	% of IHD deaths	12.5%	4.1%	1.2%	0.8%	72.3%	4,621
	% of hospitalised with IHD	9.8%	3.6%	2.7%	1.5%	80.2%	25,460
2014/15	% of NZ population 35–84y	10.5%	4.6%	3.5%	6.3%	75.1%	2,238,730
	% of IHD deaths	14.1%	5.5%	2.2%	1.2%	72.1%	3,778
	% of hospitalised with IHD	10.1%	5.3%	4.2%	2.5%	76.0%	18,513
Mean age of population 35–84y 2014/15		52.1y	51.6y	50.7y	52.3y	56.7y	

Table 1B: Proportions of the population, of IHD deaths, and of those hospitalised with IHD, in each ethnic group for women, 2006/07 and 2014/15.

Year		Māori	Pacific	Indian	Other Asian	European	Total*
2006/07	% of NZ population 35-84y	10.0%	4.2%	2.1%	5.7%	77.8%	2,179,490
	% of IHD deaths	11.3%	3.6%	1.0%	0.6%	77.1%	2,510
	% of hospitalised with IHD	12.0%	3.9%	1.8%	1.3%	79.4%	16,891
2014/15	% of NZ population 35-84y	11.2%	4.6%	3.1%	7.6%	73.5%	2,428,175
	% of IHD deaths	15.9%	6.4%	1.8%	1.2%	71.7%	1,932
	% of hospitalised with IHD	13.7%	5.2%	3.2%	2.4%	74.4%	10,192
Mean age of population 35–84y 2014/15		52.1y	52.0y	50.6y	52.1y	56.9y	

*Over two-year period.

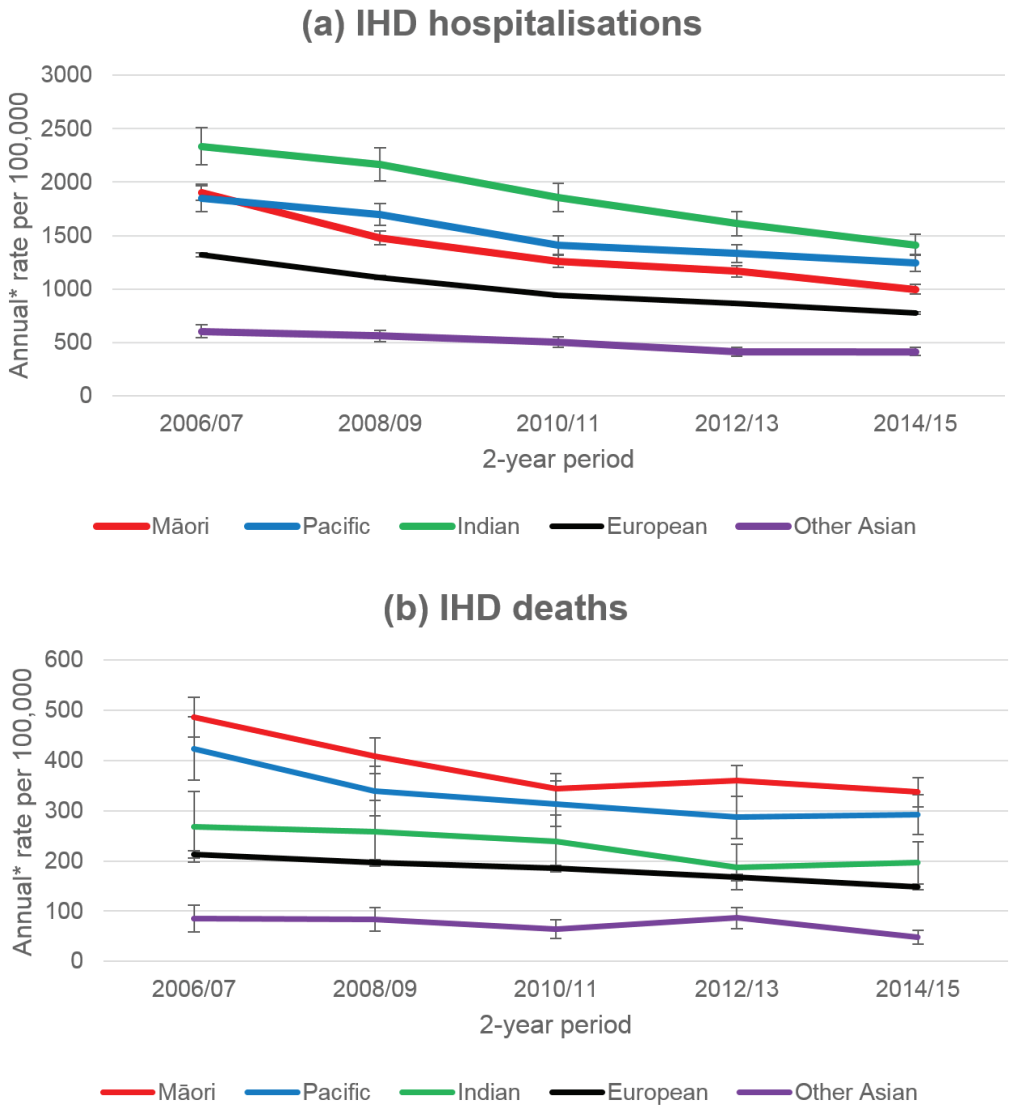
Figures 1–2 show age-standardised IHD hospitalisation and death rates in men and women. Over the 10-year study period, there was a steady decline in IHD rates in men of all ethnic groups. Indian men had the highest hospitalisation rates (1,414 per 100,000 in 2014/15), followed by Pacific (1,243) and Māori men (996), while European (779) and Asian (416) men had the lowest IHD hospitalisation rates. Mortality rates, on the other hand, were consistently highest among Māori men (337 per 100,000 in 2014/15), followed by Pacific (292), Indian (197), European (149) and Other Asian (48) men.

IHD hospitalisation rates among women were highest among Indians (706 per 100,000 in 2014/15), followed by Māori (644), Pacific (624), European (376) and Asian (211) women. Mortality rates showed a consistent decline in almost all women over this period, with the exception of Pacific women. In a pattern similar to men, Māori women had the highest IHD mortality rates (177 per 100,000 in 2014/15), followed by Pacific (171), Indian (87), European (65) and Other Asian (25) women. In 2014/15, age-standardised IHD mortality rates in Māori and Pacific women were more than twice the rate for European women.

Table 2 shows the number of people hospitalised with IHD for each IHD death that occurred in 2006/07 and 2014/15 by ethnicity. Indian and Other Asian men and women had the highest ratio of hospitalisations to deaths (7.2–8.6 IHD hospitalisations for every IHD death in 2014/15), followed by European women (5.8:1), European men (6.2:1), Pacific men (4.4:1), Māori and Pacific women (3.6–3.8:1) and Māori men (3.0:1).

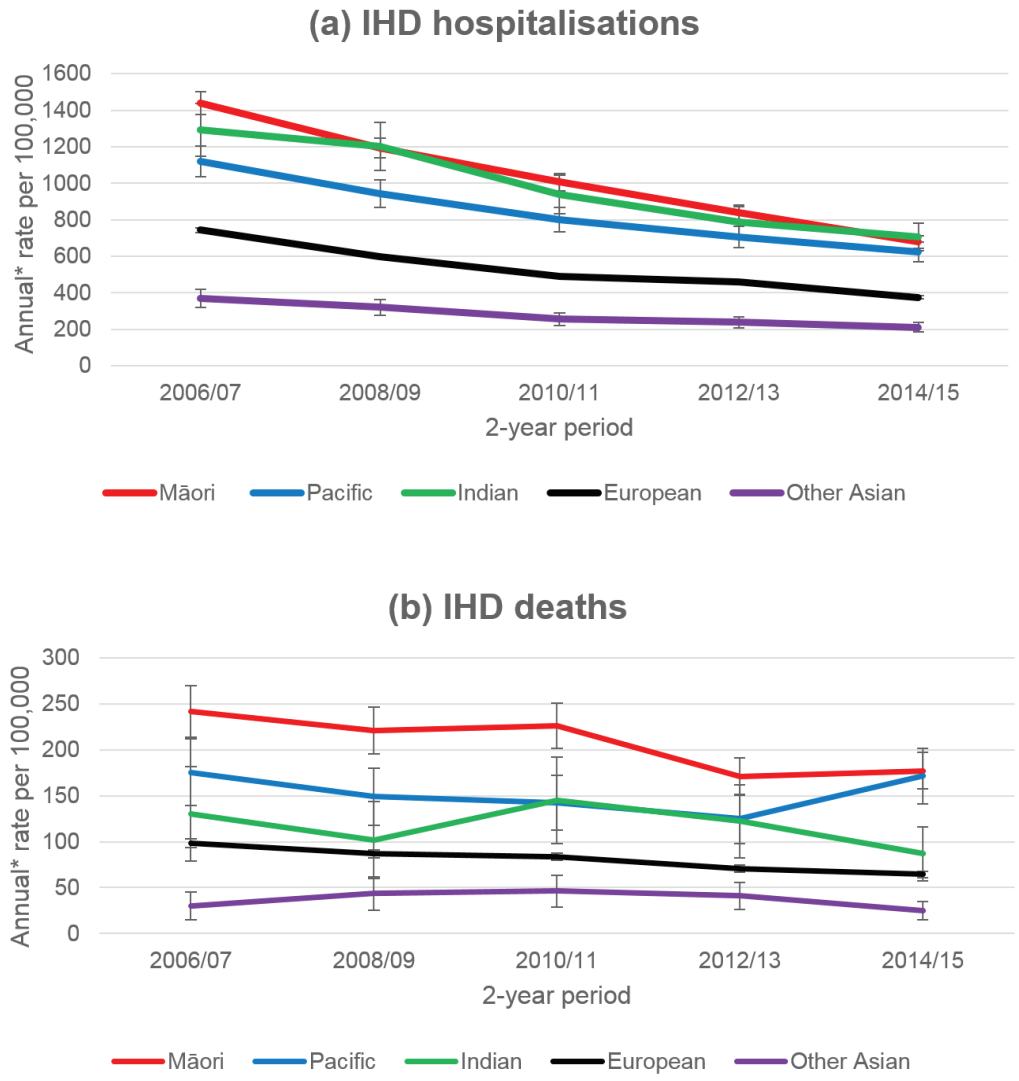
Table 3 shows age-adjusted annual percent changes in IHD deaths and hospitalisations by sex and ethnic group between 2006/07 and 2014/15. Annual declines in IHD deaths were highest among Māori and Indian men (5.0% and 4.9%, respectively) and Indian, European and Māori women (5.4%, 5.0%

Figure 1: Age-standardised* IHD (a) Hospitalisation and (b) Death Rates in Men aged 35–84y, by ethnic group, 2006–2015.



*Rates averaged over a two-year period and age-standardised to the Projected New Zealand Population 2015. Error bars denote 95% confidence intervals.

Figure 2: Age-standardised* IHD (a) Hospitalisation and (b) Death Rates in Women aged 35–84y, by ethnic group, 2006–2015.



*Rates averaged over a two-year period and age-standardised to the Projected New Zealand Population 2015.

Table 2: Number of people hospitalised with IHD for each IHD death that occurred, 2006/07 and 2014/15.*

Sex	Ethnic group	2006/07	2014/15
Men	Māori	3.9	3.0
	Pacific	4.4	4.3
	Indian	8.7	7.2
	Other Asian	7.1	8.6
	European	6.2	5.2
Women	Māori	6.0	3.8
	Pacific	6.4	3.6
	Indian	10.0	8.1
	Other Asian	12.3	8.4
	European	7.5	5.8

*Calculated by dividing age-standardised IHD hospitalisation rates by age-standardised IHD death rates.

Table 3: Age-adjusted* annual percent changes (95% confidence intervals) in IHD deaths and hospitalisations between 2006/07 and 2014/15 for men and women, by ethnic group.

Sex	Ethnic group	IHD deaths	IHD hospitalisations
Men	Māori	-5.0% (-3.8 to -6.3%)	-7.2% (-6.6 to -7.8%)
	Pacific	-3.1% (-0.9 to -5.2%)	-3.6% (-2.6 to -4.5%)
	Indian	-4.9% (-1.4 to -8.3%)	-5.7% (-4.6 to -6.8%)
	Other Asian	-4.7% (-0.4 to -8.7%)	-4.0% (-2.3 to -5.6%)
	European	-4.3% (-3.7 to -4.9%)	-6.1% (-5.7 to -6.5%)
Women	Māori	-4.5% (-2.8 to -6.2%)	-8.8% (-8.1 to -9.5%)
	Pacific	-1.3% (-4.4 to +1.8%)	-6.3% (-5.1 to -7.6%)
	Indian	-5.4% (-0.1 to –10.4%)	-7.9% (-6.3 to -9.5%)
	Other Asian	-3.1% (-9.0% to +3.2%)	-6.3% (-4.4 to -8.2%)
	European	-5.0% (-4.2% to -5.8%)	-8.1% (-7.8 to -8.4%)

*Negative binomial regression performed using five-year age bands.

and 4.5%, respectively). Pacific women had the lowest annual rate of decline in IHD mortality (1.3%). Larger declines were observed for IHD hospitalisations, with women of all ethnic groups and Māori and European men experiencing annual declines in age-adjusted mortality exceeding 6%. Pacific men had the slowest rate of decline in IHD hospitalisations, at 3.6% per year.

Discussion

To our knowledge, this is the first study to examine recent IHD trends at a country-wide level by ethnicity. Between 2006 and 2015, IHD deaths and hospitalisations declined in all main ethnic groups and in both sexes. There were no clear differences in pattern of decline by ethnicity with the possible exception of smaller declines among Pacific people, particularly IHD deaths in Pacific women. Among both men and women, IHD mortality rates were highest in Māori and Pacific people, intermediate in Indians, and lowest in Europeans and Other Asians. However, IHD hospitalisation rates were highest in Indians, who also had high age-standardised IHD hospitalisation to IHD death rate ratios. For every Indian man or woman that died from IHD in 2014/15, approximately seven Indian men and eight Indian women were hospitalised with IHD. In contrast, for every Māori or Pacific man or woman who died from IHD in 2014/15, approximately three or four people were hospitalised.

The sustained decline in IHD deaths and hospitalisations in all ethnic groups is encouraging and likely due to continued improvements in the acute and long-term management of coronary disease as well as favourable risk factor trends, such as for smoking and blood cholesterol.[19,20] The slower declines in IHD among Pacific people, however, needs to be monitored carefully, especially in light of the high and increasing rates of overweight and obesity in this population group.[11,21] Our finding of a small and statistically non-significant decline in IHD mortality in Pacific women is consistent with other New Zealand studies that have noted slower declines in stroke and all-cause mortality among Pacific people over a similar time period.[22,23]

Marked ethnic disparities in IHD mortality continue to be a cause for concern. Age-standardised IHD mortality rates for Māori and Pacific people are more than twice as high as those for Europeans, and the even lower rates among the Other Asian population indicate what could be possible for all groups if socioeconomic determinants of health and preventive and treatment strategies were optimised. As well as obesity, smoking is known to be a key contributor to health loss in New Zealand,[24] and smoking prevalence is substantially lower among Asian and European New Zealanders. Smoking rates have been less than 10% for Asian New Zealanders since 2006 and 15% for Europeans since 2011.[20] By contrast, an

estimated 38% of Māori and 25% of Pacific people are current smokers.[11]

Our study also highlights a potential problem with differential access to care in different ethnic groups, as reflected in the markedly lower ratios of hospitalisations to deaths in Māori and Pacific men and women. Previous studies have noted a discrepancy between IHD mortality and hospitalisation rates for Māori, concluding that despite high need, Māori receive relatively poor access to appropriate care for IHD.[25,26] Our study confirms these previous observations, and assuming that the ratio of non-fatal to fatal IHD events should be relatively constant across different incidence rates, suggests that access to care is an important issue for both Māori and Pacific people. These findings are consistent with studies that have shown lower rates of revascularisation and higher rates of out-of-hospital IHD deaths in Māori and Pacific people.[27–29]

Māori and Pacific people are significantly more likely to report unmet need for primary care than people from other ethnic groups, with one in five citing the cost of a general practitioner as a major barrier.[11] Māori and Pacific patients suffering from an acute coronary syndrome were less likely to call an ambulance in a South Auckland study, a factor which contributed to greater delays to acute care.[30] Transport by ambulance is associated with a significant cost (~$100) to the patient. Māori are also less likely to report having a positive experience of care in hospital.[31] Other barriers to healthcare for Māori and Pacific people include: transport, availability of appointments, previous poor experiences, costs, perceptions of negative or racist health provider attitudes, and language and cultural fit barriers, such as a preference for Māori or Pacific clinicians or a lack of cultural competency.[32,33] Strategies to overcome these barriers should therefore focus on increasing the availability of public and/or private transport, extending opening hours, operating flexible and accommodating approaches to appointment times, increasing the Māori and Pacific health workforce and supporting cultural competence across the entire health services workforce.[33]

Limitations

While data-linkage is a powerful way to examine event rates on a large scale, there are also associated limitations. First, analyses were reliant on the accuracy and validity of routinely collected data through which IHD events were identified using ICD-10 codes. Studies from several European countries have reported high sensitivity and positive predictive values for ICD-coded IHD events in national datasets,[34] but there are no published validation studies over a contemporary period in New Zealand. Our group have compared ACS diagnoses in hospitalisation data with a clinical registry and found 95% agreement (unpublished data). Second, our analyses are unlikely to have captured all non-fatal IHD events, as some people will have been undiagnosed or treated in the community. Third, because of the way ethnicity is currently coded in the national datasets, Indians are able to be identified as a separate group, but not the small number of other people identifying with other South Asian groups (eg, Pakistani, Bangladeshi), who are also at increased cardiovascular risk. In these analyses, therefore, other South Asian groups are included as 'Other Asians', rather than Indian.

Fourth, denominators for the Indian and Other Asian populations were not readily available using Ministry of Health population projections (only 'total Asian' numbers are published). We therefore derived Indian and Other Asian denominators by calculating the proportions of the total Asian group that were Indian in the 2006 and 2013 census and linearly interpolating and extrapolating these proportions for each sex and five-year age group. We believe this method is valid because there is no reason to believe that there were any differences in the proportions of Indians and Other Asians represented on the Census nights. Indeed, because Indians represented approximately one-third of all Asians, it was very important to calculate their rates of IHD separately, as the extremely low rates of IHD in the total Asian group would have masked the high risk experienced by Indians.

Conclusions

IHD death and hospitalisation rates continue to decline in all ethnic groups in New Zealand, but the decline in mortality was slowest in Pacific people, particularly Pacific women. Māori and Pacific people also have disproportionately high rates of IHD mortality compared to hospitalisations, suggesting poor access to care. More effective strategies are required to improve both access to CVD prevention and to acute care for these population groups.

Appendix

Supplementary Table 1: Standard Population used for age standardisation.

Projected New Zealand Population 2015 (35-84 years)		
Age group	**Number**	**% of population**
35–39	274,950	11.68
40–44	310,120	13.17
45–49	314,425	13.35
50–54	319,175	13.55
55–59	287,985	12.23
60–64	251,080	10.66
65–69	226,430	9.62
70–74	165,555	7.03
75–79	120,835	5.13
80-84	84,150	3.57
Total	2,354,705	99.99

Note: Because of the very low number of IHD deaths in the younger age groups, age standardisation was performed based on the following three age groups: 35–64y, 65–74y, 75–84y.

Competing interests:
CG has been the recipient of a Health Research Council Clinical Research Training Fellowship and a National Heart Foundation Research Fellowship. SW has received a grant from the Stevenson Foundation during the conduct of the study and grants from Roche Diagnostics Ltd and the National Heart Foundation outside of the submitted work. KP holds the National Heart Foundation Hynds Senior Fellowship. This research is part of the VIEW research programme, which is funded by the Health Research Council.

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Chromoendoscopy versus standard colonoscopy for detection of nonpolypoid dysplasia in patients with inflammatory bowel disease

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ABSTRACT

AIM: Inflammatory bowel disease (IBD) is associated with an increased risk of colorectal cancer. Studies show that chromoendoscopy (CE) can increase the detection of dysplasia at surveillance colonoscopy, compared to standard white light endoscopy (WLE). We performed a retrospective cohort study to compare standard WLE to CE with targeted biopsies in detecting nonpolypoid dysplasia in IBD patients undergoing surveillance colonoscopy at a single tertiary centre.

METHOD: Data was collected on 110 consecutive patients with IBD who underwent surveillance colonoscopy from 1 August 2015 to 31 July 2017 at Counties Manukau District Health Board, Auckland. Patients had either WLE or CE. Patient characteristics, endoscopic and histologic descriptions were reviewed. Rates of dysplasia detection by the different endoscopic techniques were compared using an exact Poisson test.

RESULTS: 76/110 (69%) had WLE (mean age 56y; median disease duration 18y) and 34/110 (31%) had CE (median age 59y; median disease duration 19y). Nonpolypoid dysplasia was detected in 0/76 (0%) patients who had WLE. Seven nonpolypoid dysplastic lesions were detected in 4/34 (11.8%) patients who had CE. Dysplasia pick up rate was significantly higher in the CE group with a risk difference of 11.8%, 95% confidence interval (0.93, 22.59), p=0.008. Dysplasia detection rate per patient was also significantly higher in the CE group with a rate difference of 20.6 lesions per 100 patients, 95% confidence interval (5.3, 35.8), p=0.0003. As expected, there was no difference between the number of polypoid dysplastic lesions found between the two groups (p=0.12).

CONCLUSION: In our cohort of IBD patients undergoing surveillance colonoscopy, CE with targeted biopsy is associated with a significantly increased nonpolypoid dysplasia detection rate when compared to WLE. These results are comparable to studies performed in the rest of the world.

Patients with chronic inflammatory bowel disease (IBD) are at increased risk of colorectal cancer (CRC). IBD is the third-highest risk factor for CRC.[1] The cumulative probability of development of CRC in ulcerative colitis (UC) is estimated at 2% by 10 years, 8% by 20 years and 18% by 30 years.[2] Compared to sporadic CRC, these patients may have a higher histologic grade[3] with greater mortality,[4] accounting for one-sixth of deaths in IBD patients.[5] In New Zealand, this risk is reflected in our national guideline for Surveillance for People at Increased Risk of Colorectal Cancer,[6] which recommends one-, three- or five-yearly intervals for colonoscopic surveillance depending on additional risk factors.

Chromoendoscopy (CE) describes the segmental, topical application of 0.4% indigo carmine or 0.1% methylene blue dye onto colonic mucosa. This provides contrast enhancement to improve detection and visualisation of subtle colonic lesions which may be flat, not easily visible with regular white light endoscopy (WLE) used during

standard colonoscopy. Reference to CE was removed from the national guidance statement[6] as it was not available at the time in New Zealand. The alternative option recommends quadrantic random biopsies every 10 centimetres. Critics of this method note that it may only sample 0.03% of the mucosal surface from the recommended minimum 33 biopsies and has a dysplasia detection rate of <2 per 1,000 biopsies.[7] In addition, many clinicians did not follow this protocol.[8,9] This has led to a transition to CE which is associated with a 7% greater yield in detecting nonpolypoid dysplasia, a 40% lower miss rate compared to WLE[10] and greater proportions of detected neoplasia.[11,12] CE also has similar withdrawal times and requires fewer biopsies taken overall, improving efficiency and cost effectiveness.[13–15] Current society guidelines have updated their approach in light of this evidence to include a preference for CE.[16–19] Despite this, there has been some reluctance within the gastroenterology community to take up CE,[20] with some studies suggesting little benefit, [21–26] adding to clinical equipoise and debate about its utility. Variance in study results may be attributed to local expertise and experience with differences in practice, newer high-definition scopes and use of virtual chromoendoscopy with narrow band imaging (NBI). Newer imaging technologies such as NBI, i-Scan[24] (electronic staining) or Fuji Intelligent Color Enhancement[27] (FICE) technology may increase lesion detection rates further. No local data exists from New Zealand on nonpolypoid dysplasia detection rates for CE as compared to standard colonoscopy.

Methods

We retrospectively collected data on 110 consecutive patients with IBD who underwent surveillance colonoscopy from 1 August 2015 to 31 July 2017 at Counties Manukau District Health Board. Colonoscopies were classified as a surveillance procedure when the endoscopy report explicitly stated this as the indication for the procedure.

We targeted a total number of 35 and 70 participants under CE and WLE respectively as a compromise between feasibility and power. First, these recruitment figures appeared achievable in two years of data collection. Secondly, the 1:2 proportion reflected the relative availability of endoscopists trained vs not trained to perform CE. Finally, simulations using a Poisson model and a grid of relative rates showed that these numbers were sufficient to detect a relative rate of detection of 9 between CE and WLE with 80% power at a 5% significance level against a two-sided alternative, under the assumption that two lesions per 100 participants be detected under WLE as per Rutter et al.[13] Although this was a high detectable relative rate, local experience indicated that it was plausible.

Patients had surveillance with either WLE or CE at the endoscopists' discretion. All endoscopists were gastroenterology consultants experienced in colitis surveillance. A single operator (AS) completed the majority (27/34) of the CE cases. Targeted biopsies were taken in the CE group and random quadrantic biopsies every 10cm with additional targeted biopsies in the WLE group. Colonoscopy was carried out primarily using standard Olympus colonoscopes (CF-H190I series). CE was completed with either 0.1% methylene blue or 0.4% indigo carmine, and distributed using the waterjet channel using the auxiliary foot pump. The dye was sprayed in a segmental fashion and excess dye was suctioned before visual examination. Biopsy specimens were processed according to standard procedures and read by gastrointestinal pathologists. Patient demographics, relevant background, endoscopic and histologic descriptions were reviewed from the computerised clinical and endoscopic database.

The primary endpoint was the number of patients with nonpolypoid dysplastic lesions detected. The secondary endpoint was the number of polypoid dysplastic lesions detected.

Baseline age at colonoscopy was compared between the two modalities using Wilcoxon's two-sample test. Baseline categorical variables between the two modalities were compared using Fisher's exact test, producing an observed significance level. Duration of disease was compared between the two modalities using the log-rank test. Rates of dysplasia detection by the different endoscopic techniques were compared using an exact Poisson test.

Results

One hundred and ten IBD surveillance colonoscopies were reviewed, including 76 (69%) who had WLE and 34 (31%) who had CE. The mean age was 56 years old (Standard Deviation 14), with the median duration of disease 18 years (IQR 16.5). 43/76 (57%) in the WLE cohort had UC, compared with 22/34 (65%) in the CE cohort. Fifty-eight percent of patients had pancolitis, with the majority having no (51%) or mild (34%) inflammation. The groups were well-matched for all demographic and colonoscopic variables that were collected (Table 1).

Seven nonpolypoid dysplastic lesions were detected in 4/34 (11.8%) patients, all in the CE group (Table 2). Five lesions had low-grade dysplasia and two had high-grade dysplasia. There were no invasive cancers. Five were dysplasia with tubular architecture and two had serrated dysplasia (Table 3). None were detected using WLE. This pick-up rate was significantly higher in the CE group with a risk difference of 11.8%, 95% Confidence Interval (CI) [0.9–22.6], p=0.008. Nonpolypoid dysplasia detection rate per patient was also significantly higher in the CE group with a rate difference of 20.6 lesions per 100 patients, 95% CI [5.3-35.8], p=0.0003.

Table 1: Patient and colonoscopy information for WLE and CE.

Characteristic	**All cohort (n=110)**	**WLE (n=76)**	**CE (n=34)**	**p-value**
Age, mean years	56	55	58	0.26
Male gender, n (%)	59 (46)	42 (45)	17 (50)	0.68
Ulcerative colitis or Crohn's disease				
Ulcerative colitis, n (%)	64 (59)	43 (57)	22 (65)	0.53
Crohn's disease, n (%)	45 (41)	33 (43)	12 (35)	
Duration of disease				
Median (years)	18	18	19	0.88
<8 years, n (%)	15 (13)	11 (14)	4 (12)	0.96
8–15 years, n (%)	25 (23)	18 (24)	7 (21)	
15–25 years, n (%)	35 (32)	24 (32)	11 (32)	
25+ years, n (%)	35 (32)	23 (30)	12 (35)	
Disease extent				
Pancolitis, n (%)	64 (58)	41 (54)	23 (68)	0.16
Left-sided colitis, n (%)	18 (16)	13 (17)	5 (15)	
Right-sided colitis, n (%)	1 (1)	0 (0)	1 (3)	
Ileocolonic Crohn's disease, n (%)	27 (25)	22 (29)	5 (15)	
Family history of bowel cancer, n (%)	1 (1)	0 (0)	1 (3)	0.31
Primary sclerosing cholangitis, n (%)	5 (5)	5 (7)	0 (0)	0.32
Mucosal inflammation				
None, n (%)	56 (51)	36 (47)	20 (59)	0.64
Mild, n (%)	38 (34)	27 (36)	11 (32)	
Moderate, n (%)	15 (14)	12 (16)	3 (9)	
Severe, n (%)	1 (1)	1 (1)	0 (0)	

Table 2: Nonpolypoid and polypoid dysplastic lesions found for WLE and CE, patient frequency and lesion counts.

	All cohort (n=110)	WLE (n=76)	CE (n=34)	p-value
Nonpolypoid dysplastic lesions				
Patients with nonpolypoid dysplastic lesions detected, n (%)	4 (4)	0 (0)	4 (12)	0.008
Number of nonpolypoid dysplastic lesions	7	0	7	0.0003
Polypoid dysplastic lesions				
Patients with polypoid dysplastic lesions detected, n (%)	14 (13)	7 (9)	7 (21)	0.12
Number of tubular adenoma detected	14	7	7	0.41*
Number of tubulovillous adenoma detected	6	6	0	
Number of sessile serrated adenoma detected	8	4	4	

*p-value comparing total number of lesions detected (17 for WLE vs. 11 for CE).

As expected, there was no difference between the number of polypoid dysplastic lesions found between the two groups (p=0.12). One patient with pancolitis was discovered to have a neuroendocrine tumour using WLE. No other malignancy was identified.

Discussion

This study demonstrates that in our setting, use of CE with targeted biopsies for colonoscopic surveillance in IBD is associated with a higher nonpolypoid dysplasia detection rate as compared with WLE. These findings are similar to those found in international studies with a meta-analysis[10] of six prospective studies involving 1,277 patients demonstrating a difference in yield of nonpolypoid dysplasia between CE and WLE of 7% (95% CI 3.2–11.3).

With the rising incidence of IBD both internationally[28] and in New Zealand,[29,30] it is vital for both general physicians as well as colonoscopists to be aware of CRC risk and appropriate and timely referral to enter into surveillance programs. Previously, New Zealand colonoscopists demonstrated poor understanding of the importance of

Table 3: Histology and location of nonpolypoid lesions identified on CE.

Patients with nonpolypoid lesions (n=4)	No. of lesions (n=7)	Location	Paris classification	Histology
Patient 1	1	Ascending colon	0-IIa	Low-grade serrated dysplasia
Patient 2	1	Ascending colon	0-IIb	High-grade serrated dysplasia
Patient 3	1	Sigmoid colon	0-IIa	Low-grade dysplasia with tubular architecture
Patient 4	4	Ascending colon	0-IIa	Low-grade dysplasia with tubular architecture
		Hepatic flexure	0-IIa	Low-grade dysplasia with tubular architecture
		Sigmoid colon	0-IIb	High-grade dysplasia with tubular architecture
		Rectum	0-IIa	Low-grade dysplasia with tubular architecture

dysplasia associated with colitis.[9] There was also variance in surveillance practice, both timing of procedure and biopsy protocols, which will only compound the technical and practical limitations of dysplasia detection outlined in this paper.

The clinical implications of this study, although not able to be formally addressed by this study design, include the potential for increased targeted endoscopic resection of the identified dysplastic lesions. In addition to close follow-up, this treatment method has been shown to be a safe alternative to colectomy in selected patients.[31,32]

The retrospective nature of the study, with its inherent limitations restricts interpretation with potential for confounders and bias. However, this study demonstrates real-life practice of surveillance methods at our centre, with endoscopists left to decide based on their clinical judgment which method to use. The lack of randomisation may lead to differences in patient characteristics, yet pseudo-randomisation by enrolment of consecutive patients apparently matched all measured variables between the two groups, allaying the likelihood of confounding. Further limitations include potentially important non-measured variables such as the patients IBD treatment modalities, bowel preparation scores and previous surveillance outcomes.[6] We also did not record data on number of biopsies, time taken for procedure and the potential cost implications of these, although CE is thought to be overall less costly than WLE.[15]

One endoscopist (AS) performed 27/34 (79%) of the CE procedures. This may have introduced selection bias, with more difficult or higher-risk patients being referred to this procedure list. All endoscopists who completed CE in this study were already experienced with this modality. No learning curve was taken into account. However, studies have presented data demonstrating no difference between expert (performed >20 CE-based dysplasia surveillance procedures) and non-expert endoscopists for dysplasia detection.[23] The multiple operators in this study introduce risk of inter-observer variability, but allows for real-world results.

In conclusion, CE with targeted biopsy is associated with a significantly increased nonpolypoid dysplasia detection rate when compared to WLE for dysplasia surveillance in patients with IBD. With the accumulated high-quality international evidence, subsequent international societal guidelines and similar findings from this retrospective study in our local setting, CE certainly warrants consideration of incorporation into the next New Zealand CRC surveillance recommendations for patients with IBD.

Competing interests:
Nil.

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Institutional gastroenteritis outbreaks and time to notify public health services

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ABSTRACT

AIM: We report a quantification and visualisation of the association between the time to notify public health service (PHS) and the duration and size of institutional gastroenteritis outbreaks, and explore the seasonality and trend of the outbreaks.

METHOD: Descriptive analysis was performed on institutional gastroenteritis outbreak data from a North Island PHS (1 January 2009–31 December 2014). Time-series analysis was used to explore the seasonality and trend of outbreaks. Multivariate analyses were performed to quantify the association between the time to notify PHS and the duration and size of outbreaks.

RESULTS: One hundred and seventy-five gastroenteritis outbreaks (from 58 facilities) were included in descriptive analyses. A significant increasing trend (p=0.01) without seasonal pattern was confirmed by time-series analysis. Shorter notification time was associated with shorter duration and smaller size of outbreaks, eg, duration of outbreaks when time to notify was ≥7 days, was 3.4 days (p=0.001, 95% CI=3.1–3.7) longer than baseline time to notify (0–1 day).

CONCLUSION: Prompt notification to the PHS appears to be a factor associated with reduced outbreak duration and size.

Gastroenteritis is a non-specific term indicating pathological states of the gastrointestinal tract which manifest in diarrhoea, nausea, anorexia, fever, abdominal pain and/or vomiting.[1] Children under five, adults over 65, pregnant women and immunocompromised people are at increased risk of developing gastroenteritis.[2,3]

Gastroenteritis in infants and children is a common cause of infant mortality in developing countries.[1] Gastroenteritis incidence is lower in adults compared to children. However, it is well known that old age is a risk factor for gastroenteritis associated with a risk for death.[4,5] The elderly are vulnerable to gastroenteritis because of pre-existing conditions such as chronic disease, weakened immune function, malnutrition, malabsorption and communal living in a long-term care facility.[6,7] In developed countries including the US, residents of the long-term care facility are four times more likely to die from gastroenteritis than those in the community.[8]

A gastroenteritis outbreak is defined as an increase in cases of gastroenteritis which is beyond that normally expected.[9] In 2014, gastroenteritis accounted for the majority of all outbreak notifications in New Zealand (95.0%, 820/863) and 37.3% (322/820) of these outbreaks were confirmed as due to the pathogen norovirus.[10] Institutional outbreaks are those confined to the population of a specific residential or other institutional setting including aged care, early childhood education (ECE) centres, hospitals and defence facilities.[10] Outbreaks in facilities have constituted about half the gastroenteritis outbreaks in New Zealand every year since 2006. Since then, the outbreak numbers have continued to increase.[10] In 2014, 34.9% (301/863) of

gastroenteritis outbreaks in New Zealand were notified from aged care institutions.[10] Individuals living in aged care institutions are more vulnerable than the general population and communal living facilitates the spread of infection.

Norovirus is the most common cause of epidemic non-bacterial gastroenteritis worldwide.[11] In New Zealand, norovirus has been the most common pathogen implicated in institutional gastroenteritis since 2007.[10] Either foodborne or person-to-person contamination is the most common transmission route of norovirus outbreaks. The overall attack rate in New Zealand outbreaks is approximately 40–60% of the total population exposed, but can be higher in institutional outbreaks.[12]

Gastroenteritis outbreaks also cause a considerable burden to the economy. This is related to staff absenteeism due to illness and additional resourcing to implement appropriate controls in outbreaks, including staffing, cleaning, investigation, treatment and laboratory costs.

Thus, it is important to manage institutional gastroenteritis outbreaks. This includes the timely identification of outbreaks, implementation of controls and accessing expert advice through notification to public health services (PHSs). Early recognition of an outbreak and rapid implementation of appropriate control measures can reduce the impact of disease. This is supported by early notification to PHSs and identification of the likely causal organism. Confirmation of the casual organism provides reassurance that the best control measures are in place and improves knowledge around best practice to prevent and manage future outbreaks. The timely identification, notification and institution of control measures have been identified as important to limiting the size and duration of gastroenteritis outbreaks. To date, the present study collaborating with a North Island PHS is the first New Zealand study that aims to explore the seasonality and trend of institutional gastroenteritis outbreaks and to quantify the association between the length of time it takes for the facility to notify the PHS and the duration and size (incidence risk) of the outbreaks.

Methods

Ethical considerations for this project were evaluated by peer review and judged to be low risk. This has been recorded on the Massey University Low Risk Database.

Anonymised data provided by the PHS from the case logs of gastroenteritis outbreaks at institutions (1 January 2009–31 December 2014) were validated and standardised. The facility types included aged care, ECE, hospitals and defence facilities which fell under PHS' remit.[13] Time to notify PHS was the length of time it takes for the facility to notify PHS, ie, days between the date of the onset of symptoms of the second case and the date when an outbreak was first notified. Duration of outbreak was approximated by the number of days between the date of the onset of symptoms of the second case and the date of the onset of symptoms of the last case of an outbreak. Population at risk was the number of residents/attendees and staff members of the facility in which each outbreak happened. Calculation of the population at risk for each outbreak occurred during investigation of the outbreak. Incidence risk (IR) was calculated by dividing the number of gastroenteritis cases with the population at risk. All data analyses were performed using R version 3.1.0.[14]

Investigation of seasonality and trend

The date of onset of an outbreak was taken as being the date of onset of the second case in a given outbreak. Dates of onset were aggregated to the week, month and year and plotted as a time-series. Loess smoothing was applied to emphasise the trend and seasonality and to reduce distraction from random variation.[15,16] A non-parametric Spearman-test was used to test if an increasing or decreasing trend existed in the time-series plot.[17] Monthly box plots and periodograms of the raw data were produced to investigate seasonality and cyclicity.[18]

Modelling the duration of outbreaks

The 'nlme' package version 3.1-117[19] in R version 3.1.0[14] was used to build a linear mixed-effects model of the association between time to notify PHS (main

Table 1: Descriptive statistics of main variables.

Variable	Minimum	25th percentile	Median	75th percentile	Maximum
Population at risk	20	44	70	100	1,993
Total number of cases	3	11	17	32	320
Duration of outbreak (days)	1	5	9	15	55
Time to notify (days)	0	1	3	6	35

covariate) and log duration of outbreak (outcome). Other covariates available for inclusion in the model were pathogen, type of facility, number of gastroenteritis cases, size of the population at risk, year and sequence of outbreaks, ie, some facilities experienced multiple outbreaks over the course of the study. To adjust for repeated outbreaks within the same facility, a random effect term for facility was fitted. Bivariate analysis, analysis of collinearity and backward selection (multivariable models) were performed to select covariates. Those associated ($p \leq 0.20$) with the outcome in bivariate analysis were included in a preliminary multivariable model. The main covariate was maintained and other covariates were removed, one by one, while those with a $p \leq 0.05$ were retained and/or if removal altered the regression coefficient (β) estimate (>20%) or SE (>20%) of the main covariate. To determine if there was any interaction with the main covariate, interaction terms were tested for significance. The Akaike Information Criterion (AIC), Bayesian Information Criterion (BIC) and log likelihood were used for model selection. The Goodness-of-fit tests in the 'nlme' package,[19] focusing on the distribution of the random effects, were used to test the model fit.

Modelling the size of outbreaks

The 'glmmADMB' package version 0.8.0[20] in R version 3.1.0[14] was used to build a zero-truncated, negative-binomial, mixed-effect (ZTNBME) model of the association between time to notify PHS (main covariate) and size of the outbreak (IR). The 'epi-bohning' test of the 'epiR' package version 0.9-58[21] was run to investigate over-dispersion of Poisson data. The procedure of inclusion of covariates in the ZTNBME model was the same as the procedure in the LME model. The diagnostic tests in the 'lme4' package,[22] which was integrated to 'glmmADMB', were used to test the model fit.

Results

In 58 facilities, 175 outbreaks (with 141 of 175 having population at risk data available) were notified: 64 outbreaks (notified within 1 day), 46 outbreaks (2–3 days), 29 outbreaks (4–6 days) and 36 outbreaks (≥7 days). In total, 4,562 cases comprising 3,077 residents, 1,316 staff and 154 visitors were involved. In the multivariable analysis, 154 visitors were excluded. The facilities included 31 aged care, 23 ECE, three hospitals and a defence facility. Summary statistics for variables are displayed in Table 1.

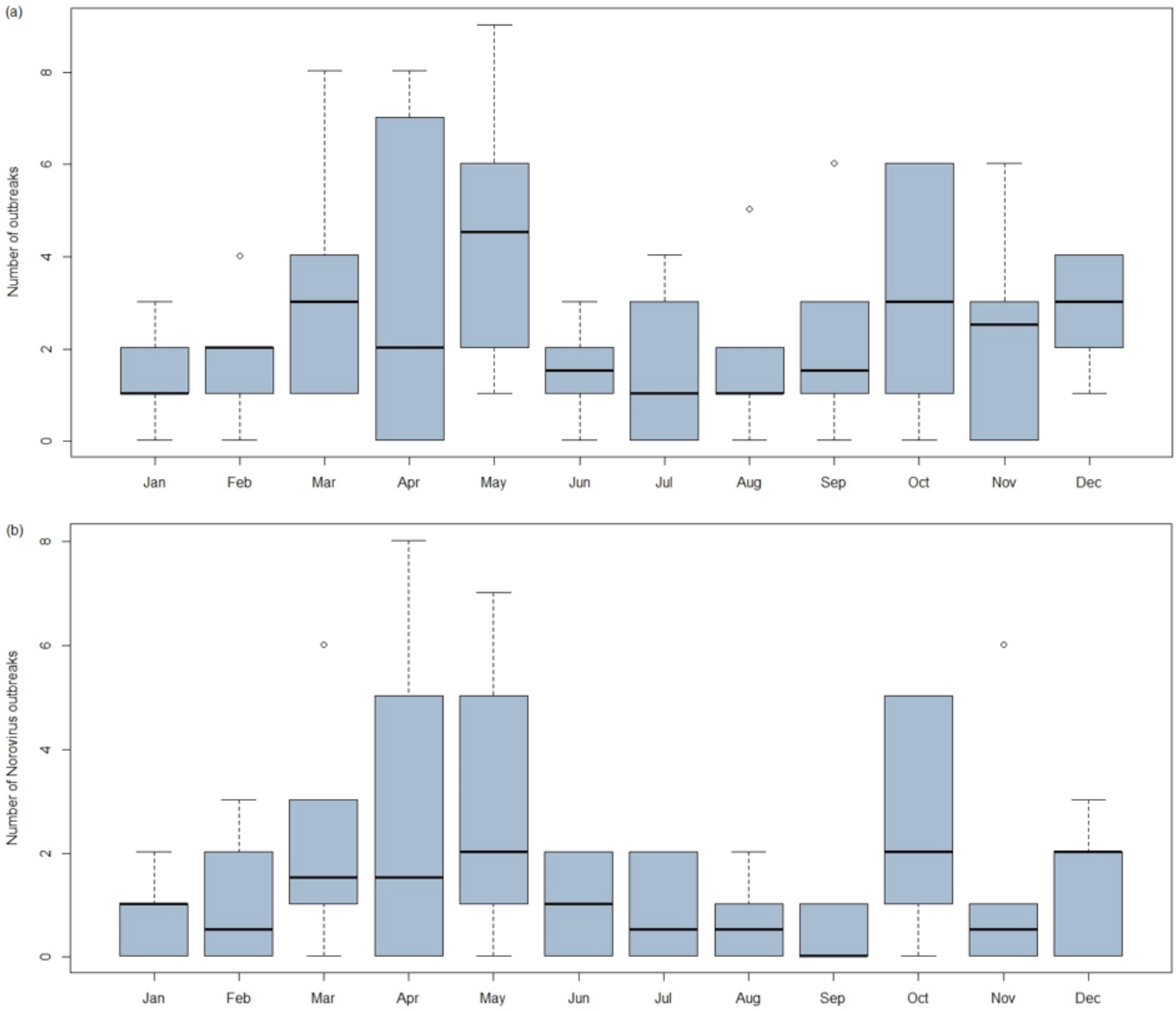
Norovirus was the most commonly identified pathogen (108 outbreaks), followed by rotavirus (14 outbreaks) and sapovirus (9 outbreaks). Other pathogens, ie, *Clostridium difficile*, *Campylobacter* spp. and *Cryptosporidium* spp. were identified in three outbreaks. The pathogen(s) were unidentified in 41 outbreaks.

Gastroenteritis outbreaks were mostly notified from aged care (n=98), followed by ECE (n=50). The rest of the outbreaks were reported from hospital (n=26) and defence facility (n=1). Multiple outbreaks were notified from 36 facilities. The largest number of outbreaks per facility was 21 and these were notified from a hospital.

Investigation of seasonality and trend

No evidence of cyclicity was observed in periodograms of gastroenteritis and norovirus outbreaks (not shown). In monthly boxplots there is a suggestion of higher counts of cases and increased variability in case numbers in the spring and autumn months (Figure 1). The non-parametric bootstrapped Spearman-test gave the value (ρ) of 0.23 (p=0.013), confirming the overall increasing significant trend in number of gastroenteritis outbreaks over the study period (1 January 2009–31 December 2014), whereas the value (ρ) of norovirus outbreak was 0.14 (p=0.099) over the same study period.

Figure 1: Raw monthly boxplot of gastroenteritis outbreak data (a) and norovirus outbreak data (b).



Modelling the duration of outbreaks

In the bivariate analysis (Table 2), covariates associated with the duration of outbreaks ($p \leq 0.20$) were time to notify, pathogen, type of facility and total cases. Covariates significant at $p \leq 0.05$ in the multivariable model (Table 3) were time to notify and pathogen. Compared with the baseline time to notify (0–1 day), the duration of outbreaks was longer by 1.2 days, 1.5 days and 3.4 days when the time to notify was respectively 2–3 days, 4–6 days and ≥7 days. These estimates were adjusted for pathogen and facility.

Modelling the size of outbreaks

In the bivariate analysis (Table 4), covariates associated with the log size (IR) of outbreaks ($p \leq 0.20$) were time to notify, pathogen, type of facility, duration of outbreak, year and sequence of outbreak. Covariates significant at $p \leq 0.05$ in the multivariable model (Table 5) were time to notify and pathogen. Compared with the baseline (0–1 day), the IR was larger by 1.1 times, 1.1 times and 1.6 times when the time to notify was respectively 2–3 days, 4–6 days and ≥7 days. These estimates were adjusted for pathogen and facility.

Table 2: Bivariate analysis: putative risk factors and statistical parameters for duration of gastroenteritis outbreaks (n=175) in facilities in PHS 2009 to 2014.

Variable	Category	N	exp(coef)	95% CI		*p* value
Time to notify PHS	0–1 day	64	ref			
	2–3 days	46	1.230	0.933	1.527	0.1729
	4–6 days	29	1.742	1.398	2.086	0.0019
	≥7 days	36	3.501	3.181	3.821	0.0000
Pathogen	Norovirus	108	ref			
	Unknown	41	0.455	0.159	0.751	0.0000
	Rotavirus	14	1.530	1.071	1.989	0.0711
	Sapovirus	9	0.823	0.263	1.384	0.4973
	Other	3	0.241	-0.705	1.186	0.0036
Type of facility	Aged care	98	ref			
	ECE	50	1.662	1.360	1.963	0.0012
	Other	27	1.030	0.652	1.407	0.8799
Total cases[a]		175	1.146	1.109	1.183	0.0000
Population at risk		141	1.000	0.999	1.001	0.5170
Year	2009	31	ref			
	2010	14	8.037	7.715	8.359	0.1970
	2011	32	1.464	0.887	2.040	0.9940
	2012	28	0.998	0.547	1.450	0.6300
	2013	18	0.891	0.424	1.358	0.8890
	2014	52	0.963	0.432	1.494	0.7020
Outbreak sequence	1	58	ref			
	2	36	0.899	0.519	1.279	0.5830
	3	24	0.893	0.458	1.328	0.6120
	≥4	57	0.836	0.502	1.170	0.2950

coef=coefficient; ref=reference categories.

Table 3: Multivariable analysis: risk factors and statistical parameters for duration of gastroenteritis outbreaks (n=175) in facilities in PHS 2009 to 2014.

Variable	Category	N	exp(coef)	95% CI		p value
Fixed effects:						
Time to notify PHS	0–1 day	64	ref			
	2–3 days	46	1.168	0.898	1.437	0.2616
	4–6 days	29	1.527	1.212	1.843	0.0097
	≥7 days	36	3.364	3.051	3.677	0.0000
Pathogen	Norovirus	108	ref			
	Unknown	41	2.309	2.057	2.561	0.0000
	Rotavirus	14	1.080	0.660	1.500	0.7203
	Sapovirus	9	1.457	0.974	1.939	0.1294
	Other	3	3.276	2.464	4.088	0.0050
Random effects:						
Facility (58 facilities, 175 observations)						
Variance	0.1689					
SD	0.6861					

coef=coefficient; ref=reference categories; AIC=400.49; BIC=431.67; log likelihood= -190.24.

Table 4: Bivariate analysis: putative risk factors and statistical parameters for size of gastroenteritis outbreaks (n=141) in facilities in PHS 2009 to 2014.

Variable	Category	N	IRR	95% CI		*p* value
Time to notify PHS	0–1 day	50	ref			
	2–3 days	38	0.956	0.816	1.096	0.5333
	4–6 days	25	1.177	1.020	1.334	0.0414
	≥7 days	28	1.160	1.007	1.313	0.0567
Pathogen	Norovirus	84	ref			
	Unknown	34	0.351	0.238	0.464	0.0000
	Rotavirus	13	0.634	0.477	0.791	0.0000
	Sapovirus	8	0.425	0.219	0.630	0.0000
	Other	2	0.317	-0.082	0.716	0.0000
Type of facility	Aged care	88	ref			
	ECE	43	0.777	0.656	0.897	0.0000
	Other	10	0.671	0.450	0.891	0.0004
Duration of outbreak		141	1.041	1.035	1.046	0.0000
Year	2009	21	ref			
	2010	12	0.831	0.602	1.061	0.1150
	2011	24	0.690	0.500	0.881	0.0001
	2012	23	0.628	0.436	0.820	0.0000
	2013	13	0.931	0.707	1.154	0.5281
	2014	48	0.881	0.718	1.043	0.1257
Outbreak sequence	1	49	ref			
	2	30	0.793	0.642	0.943	0.0025
	3	22	0.773	0.607	0.939	0.0023
	≥4	40	0.864	0.727	1.001	0.0359

IRR= incidence risk-ratio; ref=reference categories.

Table 5: Multivariable analysis: risk factors and statistical parameters for size of gastroenteritis outbreaks (n=141) in facilities in PHS 2009 to 2014.

Variable	Category	N	IRR	95% CI		*p* value
Fixed effects:						
Time to notify PHS	0–1 day	50	ref			
	2–3 days	38	1.137	0.900	1.437	0.2823
	4–6 days	25	1.104	0.838	1.454	0.4817
	≥7 days	28	1.559	1.189	2.043	0.0013
Pathogen	Norovirus	84	ref			
	Unknown	34	2.248	1.780	2.840	0.0000
	Rotavirus	13	1.842	1.308	2.594	0.0005
	Sapovirus	8	2.155	1.419	3.272	0.0003
	Other	2	3.015	1.323	6.870	0.0087
Random effects:						
Facility (56 facilities, 141 observations)						
Variance	6.74					
SD	0.0008					

IRR=incidence risk-ratio; ref=reference categories; AIC=1062.60; log likelihood= -521.29; ϑ (negative binomial dispersion parameter)=4.27; SE=0.61.

Model diagnostics

In both models (duration and size models), the random effects were normally distributed. The absolute value of the random effects for each facility was relatively low but some facilities had larger random effects than others.

Discussion

In our analysis of institutional gastroenteritis outbreaks norovirus was the most common pathogen and aged care was the most common institutional setting. A significant increasing trend in the number of institutional gastroenteritis outbreaks was observed over the study period. The model built to quantify the association between the main covariate, time to notify the PHS, and the main outcomes, duration and size of outbreaks identified that a shorter notification time to the PHS was significantly associated with shorter duration and smaller size of outbreaks.

Norovirus was identified as the most common pathogen in 61.7% (108/175) of the institutional outbreaks in MCPHS, which is similar to the 68% (39/60) of norovirus-attributable gastroenteritis found in an Australian study.[23] Norovirus was also the most common pathogen in New Zealand annual outbreak surveillance reporting (eg, 37.3% (322/863) in 2014).[10] Facilities such as aged care mostly consist of frail individuals who are more vulnerable to norovirus infection, so this may explain the difference in percentages between the New Zealand annual percentage and the rate in institutions.

Aged care and ECE were the most common settings of gastroenteritis outbreaks, comprising respectively 56.6% (99/175) and 28.6% (50/175) of outbreaks. Aged care was also the most common setting in New Zealand (2006–2014), and constituted about half of gastroenteritis outbreaks annually.[10] Aged care is occupied by frail individuals who are more vulnerable to infections, thus it is reasonable to expect that a higher percentage of notified gastroenteritis outbreaks is reported from aged care facilities. In a 2013/14 UK and Ireland study of norovirus outbreaks in care settings, hospital (71.3%, 383/537) and aged care (21.4%, 115/537) were the most common settings.[24]

The results from the time-series plots of gastroenteritis outbreaks confirmed a significant increasing trend in the number of notified outbreaks. The increasing trend was also seen nationally in New Zealand (2005–2014)[10] and in a study of gastroenteritis outbreaks in hospitals in the US (1996–2007).[25] The increased ageing population (accompanied by a presumed rise in the number of people in residential aged care), the funded 20 hours ECE, the introduction of national guidelines of norovirus management in hospital and aged care on 2 January 2009 and the emergence of the virulent Sydney GII.4 strain of norovirus[27] could have contributed to this increasing trend.

Although the time series analysis of our study showed no statistical evidence of a seasonal pattern, a trend was seen for more outbreaks in the Spring and Autumn. Previous research in the Northwest Territories of Canada[28] and US[29] reported seasonal patterns in gastroenteritis outbreaks. Gastroenteritis outbreaks peaked in spring and autumn in the Canadian study from community health facilities and this was suggested to be due to environmental and social factors such as higher temperatures, frequent travelling and surface water consumption.[26] Other studies performed in hospitals in the US (1996–2007)[25] and (2001–2009)[27] reported that gastroenteritis outbreaks mostly happened in winter. Temporal patterns are likely associated with the health-seeking behaviour peculiar to each country and some infections which are community- and not hospital-acquired. It may also reflect how the surveillance data are managed and the notification of outbreaks.

The present study reported that 36.6% (64/175) outbreaks were notified to PHS within one day after the onset of symptoms of the second case, while 20.6% (36/175) outbreaks were notified later (≥7 days). In a similar study in residential care facilities (RCFs) in Queensland, Australia in 2008, 40% (24/60) were notified to the PHS within one day, and the latest notification was 18 days.[23] The range of notification was 0 to 37 days in a similar study in nursing homes in Alsace, France[6]. Approximately one of four persons at risk became cases in both this and Australian studies, and one of three persons

at risk became cases in the French study.[6,23] The duration of each outbreak as notified to the PHS in the current study was 1–55 days while in the Australian and French study the duration were 0–42 days and 2–26 days, respectively, of which Australian and French studies each had different definition of outbreak duration.[6,23] In the current study, the start of the gastroenteritis outbreaks was calculated based on the onset of symptoms of the second case recorded by the PHS.

Shorter notification time was associated with shorter duration and smaller size (IR) of gastroenteritis outbreaks. For example, after adjusting for pathogen and facility, the duration of outbreaks was 3.4 days (p=0.001, 95% CI=3.1–3.7) longer than baseline (0–1 day), when time to notify was ≥7 days. Further, there is an association between the outcome variables (duration and size of outbreaks) as displayed in Figure 3. Modelling both duration and size of outbreaks via a single composite outcome variable could be a useful next step in investigating the association between notification to the PHS and the impact of the outbreak.

The finding of an association between shorter notification time to PHS and shorter duration of outbreaks is similar to the Australian study, which reported that shorter notification time was associated with shorter duration of outbreaks. However, different from this current study, the Australian study found that shorter notification was not associated with smaller size of outbreaks.[23] The number of outbreaks notified in the Australian study was smaller (n=60)[23] than in this study (n=175). A lack of statistical power might explain this lack of association.

The limitation of this study is the possibility that some cases were unreported, eg, in New Zealand, aged care has a better notification system than other facility types. Aged care institutions are likely to have their own health professional staff, have systems of recording illness, and to audit outbreak management procedures. This is unlike ECEs where a child can be absent without definite reason. It is more difficult in ECEs to ascertain smaller outbreaks and cases. In ECEs children and staff members do not reside in the facilities and attendance is only during school or working hours. These facilities usually do not have their own health professional staff, and their population is larger and mobile so outbreak management procedures are more difficult to implement. Therefore, more unreported cases were expected to come from ECE. This might be attributed with the length and size of the outbreaks. In the multivariate analysis, type of facility was not significantly associated with outbreak duration and size. The characteristics of each pathogen, eg, incubation period, might also become a confounder in the duration and size of outbreak. Furthermore, not enough information about the characteristics of each facility could be obtained from the dataset, eg, whether a staff member of a facility was more skilled and experienced than other staff that could contribute to their acts responding to the outbreak. Staff experienced with managing previous outbreaks are more likely to put in effective control measures and notify the PHS earlier than those inexperienced with outbreak management.

Prompt notification to the PHS appears to be one of the factors associated with reduced outbreak duration and size. The act of notification to PHS *per se* will help reduce the impact of the outbreaks more effectively if the facility's procedures for controlling outbreaks have oversight by a regulatory authority.

If a facility notifies early then the PHS is able to provide earlier access to advice and action that support the facility's procedures for controlling outbreaks, including support with implementing the Ministry of Health (MoH) Norovirus guidelines. This PHS actions include assigning a health protection officer to the outbreak; daily oversight of the case logs and epidemic curves to monitor outbreak progress; support and advice regarding control measures and identification of likely source; procedural reviews of controls and site visits if required; identification of the pathogens (through samples collection and laboratory submission); advice to reduce further transmission of the current outbreak; and prevention of outbreaks occurring again in the future through outbreak management training workshops based on MoH guidelines.

Conclusion

The models built to quantify the association between the main explanatory factor, time to notify the PHS, and the main outcomes of interest, duration and size of outbreaks identified that a shorter notification to the PHS was significantly associated with shorter duration and smaller size of outbreaks. Future studies should consider more complex modelling of the association between time to notify the PHS, the duration and the size of the outbreak. This should be combined with an investigation of the sensitivity of the definition of the start of the outbreak. For this analysis we chose the date of onset of the second case. Identification and modelling of a composite outcome variable that captures the shape of the epidemic curve (both size and duration of outbreak) is beyond the scope of this study but an important next step in better understanding the effect of time to notify the PHS.

Better data capture, both laboratory and epidemiological (eg, clear staff role identifications and days off work due to illness) is important: the former to provide pathogen specific interventions and the latter to more clearly estimate the cost of the outbreak. Improved identification of associated cases beyond the staff and residents/attendees (for example family members of staff and residents/attendees, visitors to the institutions) will help more clearly define the extent of the burden associated with institutional outbreaks.

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Pregabalin misuse: preventing potential problems in New Zealand

Rhys Ponton

ABSTRACT

AIMS: Pregabalin has not been used widely in New Zealand to this point as it has not been funded, but from May 2018 it will be available fully subsidised. This paper intends to highlight the issue of pregabalin misuse, a concern that will be unfamiliar to most clinicians in New Zealand.

METHODS: A review of the literature of papers documenting the misuse of gabapentin and pregabalin was conducted with a specific focus on pregabalin.

RESULTS: There is a growing body of evidence regarding the potential of misuse of pregabalin. It produces a range of sensations, including euphoria, sedation and dissociation. It is commonly used in conjunction with other drugs, most notably sedatives and opioids, which leads to an additive effect. Although generally safe when taken alone, pregabalin is a growing feature of drug-related deaths.

CONCLUSIONS: Prescribers need to be alert to the potential of pregabalin misuse. This should be achieved through prescribing with great care (not prescribing to new or unknown patients; not in response to direct patient requests for it by name; supplying in limited quantities), regular review of patients and stopping treatment, by slow withdrawal, when lack of efficacy is seen.

In October last year, PHARMAC opened a consultation on the funding of pregabalin in New Zealand.[1] Up until now, pregabalin has not been subsidised for use in New Zealand. Now, from 1 May 2018, pregabalin will be available fully subsidised with no restrictions on prescribing.

Throughout history, the medical profession has played a significant role in the misuse and dependence on drugs, including the barbiturates, the benzodiazepines and more recently, oxycodone.

This paper intends to highlight the issue of pregabalin misuse, a concern that will be unfamiliar to most clinicians in New Zealand.

Pregabalin

Pregabalin is a drug of the gabapentinoid class, a group that also includes gabapentin, a drug most New Zealand prescribers will be familiar with.

Pregabalin, (S)-(+)-3-isobutylgaba (marketed under the brand name Lyrica®) is a gamma-butyric acid analogue that has a novel mechanism of action shared only by gabapentin.[2] Despite the close resemblance of these drugs to gamma-amino butyric acid (GABA), their pharmacological action is unrelated and, although the precise mechanism of action is unclear, is understood to occur through binding to calcium channels in the central nervous system.[2,3]

Gabapentin (Neurontin®) was initially developed as an antiepileptic drug in the mid-1980s[4] before its action as an 'antihyperalgesic' agent was identified.[5] In Europe, pregabalin was initially authorised for the treatment of peripheral neuropathic pain and epilepsy in 2004[3] with extensions to add generalised anxiety disorder in January 2006, and central neuropathic pain in July 2006.

In New Zealand, the NZ Formulary (NZF) and data sheet currently list pregabalin as indicated for neuropathic pain and adjunctive therapy for focal seizures with or without secondary generalisation.[6,7] The NZF also lists it for generalised anxiety disorder, although this is an unapproved indication.

Pregabalin is more rapidly absorbed than gabapentin, and it has a higher bioavailability.[8] The maximum plasma level of pregabalin is reached within one hour of taking a dose; gabapentin takes 3–4 hours to reach maximum plasma concentration. Pregabalin may have a higher addiction potential than gabapentin due to its rapid absorption and faster onset of action.[9]

The history of pregabalin licensing and the first discussions of misuse

Pregabalin was introduced in 2004. Prior to this, pregabalin had not been available in any form, so no experience of its use existed.

When pregabalin was approved for use in the US on 31 December 2004,the Food and Drug Administration (FDA) recommended the drug was controlled in Schedule V of the Controlled Substances Act.[10] A key paper in this decision making was the Abuse Liability Study '098'. Using this, the FDA determined that the drug was liable to misuse.[10] The FDA pointed out that 3.7% of patients taking pregabalin during studies experienced euphoria, compared to only 0.5% of patients who were administered a placebo. This euphoria continues for a 'considerable time' after initiation of treatment (median duration seven days) but diminishes on continued use. The same report stated that the FDA considers euphoria to be an uncommon adverse event for approved drug treatments.

In addition, withdrawal of pregabalin was noted to result in a discontinuation syndrome, however this was considered to be reported at rates lower than for a drug with a 'classic discontinuation syndrome'. The Abuse Liability Study concluded that a low dose of pregabalin (200mg) was similar in profile to a 15mg dose of diazepam, that is, patients identified it as a sedative. A 450mg dose of pregabalin was more 'stimulant-like' than a control of high-dose diazepam, but it resembled diazepam in what the author termed 'drug-taking behaviour' with comments including "Good drug effect" and "High". In contrast, the pregabalin licensing application to the European Medicines Agency (EMA) in 2005 considered misuse as a special safety issue, but dismissed it stating:

"Abuse potential: The abuse potential of pregabalin was studied in a separate study (098) versus diazepam and placebo. Pregabalin did not have the profile of a prototypic drug of abuse when compared with diazepam."[3]

Post-launch gabapentinoid misuse

Misuse of gabapentin was documented prior to the approval of pregabalin[10–12] and recreational misuse of pregabalin was predictable.

In the last five years, pregabalin misuse has become established with growing reports in the literature, and more recently in the general press in countries such as the UK.

A paper by Schifano et al in 2011[13] was the first to raise the misuse of pregabalin. As this paper documents, awareness of the recreational potential of pregabalin and gabapentin was already abundant on websites, internet forums and YouTube. One of the key papers first highlighting misuse to the medical community was the written by Des Spence in the *British Medical Journal* in November 2013.[14] Since these early papers, the evidence of misuse has grown in a large number of reports, including systematic reviews[15,16] and also in popular press reports.

Effects

The effects that pregabalin produces when misused can be considered in two ways. Firstly, the drug may be taken to experience the effects induced by the drug itself. Secondly, it may be taken in combination with other drugs, particularly sedatives and opioids, to produce a synergistic effect. When taken, particularly at high dose, the effects are described as a mixture of sedative, psychedelic, dissociative and euphoric.[13]

Deaths

Gabapentin and pregabalin safety has been extensively studied both prior to launch and continues to be monitored. The safety of pregabalin in overdose has been shown in overdoses, with doses of up to 15 grams producing no unexpected adverse effects.[6] The concurrent use of CNS depressants is a well-known risk. The data sheet acknowledges an additive effect with alcohol, benzodiazepines and opioids, and these are drugs that are typically used alongside pregabalin in a polydrug use scenario. Baird et al[17] describe the use of pregabalin to potentiate the effects of methadone, and a recent paper outlines the risk to heroin users from concurrent gabapentinoid misuse.[18]

In the New Zealand data sheet, Pfizer state that there have been recent ('post-marketing') reports of respiratory failure and coma in patients taking pregabalin with other CNS depressant medications.

In the UK, concern has grown over the number of deaths where pregabalin was mentioned on the death certificate. Table 1 shows data from the Office for National Statistics[19] with clear increases in both pregabalin and gabapentin.

Table 1: Number of drug-related deaths where pregabalin and gabapentin were mentioned on the death certificate, deaths registered in England and Wales 2012–2016 (from UK Office for National Statistics).

	2012	2013	2014	2015	2016
Pregabalin	4	33	38	90	111
Gabapentin	8	9	26	49	59

Concerns surrounding the role of gabapentinoids in opioid overdose deaths were first raised in 2013.[20] In a recent work, Elliott et al[21] describe a series of cases of deaths involving pregabalin and in every case, pregabalin had been consumed alongside other drugs, either prescribed and/or illicit, as well as alcohol in some of the cases. The presence of other drugs is expected given the reported safety of pregabalin alone[6] and most importantly it demonstrates that pregabalin is frequently taken as part of a poly-drug cocktail. Similar toxicological examinations conducted earlier by Häkkinen et al[9] found no fatalities from pregabalin or gabapentin alone.

In 2016, the increase in deaths in the UK linked to the gabapentinoids prompted the ACMD (Advisory Council on the Misuse of Drugs) to recommend they be controlled under UK law.[22] Control of pregabalin in the UK would bring it into line with other jurisdictions including the US. At the current time, pregabalin is classed as a prescription medicine in New Zealand, and not as a controlled drug.

How to approach prescribing

When prescribing pregabalin, practitioners are suggested to use the same cautions that are applied to any drug of misuse, such as opioids or benzodiazepines.

The decision to initiate treatment using pregabalin should only be taken with the considerations typical to any drug, namely suitability for the condition and the evidence for efficacy. Treatment guidelines should be adhered to and other agents tried prior to trialing pregabalin, if appropriate.

Prescribers should exercise caution in the use of pregabalin in any patients with a history of alcohol or drug misuse. The New Zealand data sheet specifies patients should be carefully evaluated for a history of substance abuse and observed for signs of pregabalin misuse or abuse (eg, development of tolerance, increase in dose, drug-seeking behaviour) during treatment.[6] Prescribers should be aware of patients who increase their dose as this has been linked to patients at high risk of addiction.[23] Prescribers should ensure that patients prescribed pregabalin take it as prescribed and be alert to potential binge use of large doses for pleasure.

Patients who specifically request pregabalin, particularly new or unknown patients, should be treated with extreme caution. Furthermore, it must be remembered that those seeking drugs may not be taking the drug themselves but supplying others on the illicit market—this is especially true for New Zealand, where many drugs are diverted pharmaceuticals due to the limited importation of other drugs.[24]

It is important that pregabalin (and gabapentin) are not simply used to avoid the use of opioids,[25] particularly in patients of concern in respect of potential, or documented, opioid misuse. These drugs may themselves become misused.

Interactions with other sedative medicines as discussed above mean that prescribers need to take additional care when choosing to prescribe this drug. Potential prescribers are reminded of the similar situation with respect to benzodiazepines, which when used alone are generally safe, but when taken in combination with other sedative drugs can potentiate CNS depression.

Review, review, review: Most importantly, any treatment with pregabalin should be subject to regular review. In the treatment of neuropathic pain in particular, the efficacy should be assessed on a regular basis, particularly early on into treatment. Cautious

up-titration of dosage is recommended, but the possibility of treatment failure should be considered if there is a lack of benefit after two to four weeks. Pain relief should be seen in the first few days of treatment with an effective dose, it is not an effect that takes time to develop.[26,27] Furthermore, a Cochrane systematic review suggests that 18–28% of patients will need to stop treatment due to adverse events.[28]

The decision to stop pregabalin treatment should be made carefully (including specialist input then used for seizure disorder) as abrupt cessation can lead to a discontinuation syndrome. Effects seen are predictable and the opposite in action to those of the drug; each of the following has been reported: insomnia, headache, nausea, anxiety, diarrhoea, flu syndrome, nervousness, depression, pain, convulsion, hyperhidrosis and dizziness.[29] Seizures have also been reported. The severity of withdrawal effects will be related to the dose and the time the drug has been taken. Pregabalin should be gradually tapered down to minimise these. The taper should extend for a minimum of one week.[6,30]

Pregabalin is not an opioid drug, however existing guidance, particularly that pertaining to opioids, can be of relevance to its use. Readers are referred to the 2005 paper by Gourlay et al,[31] which discusses many of the salient points in chronic pain prescribing, including the assessment of the risk of potential substance use disorder, pre- and post-intervention assessment of pain and pre- and post-intervention assessment of function.

In summary

Large-scale medical use of pregabalin in other countries during the last decade provides a significant amount of insight into potential misuse. New Zealand has been fortunate to avoid similar problems due to restricted use. The approval for funding means that potential prescribers need to be acutely aware of the risk of pregabalin misuse.

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New Zealand transplant patients and organ transplantation in China: some ethical considerations

Phillipa Malpas

ABSTRACT

In this viewpoint article we consider the situation of organ procurement from China, and address some of the ethical aspects arising for health professionals when New Zealand transplant patients contemplate traveling to China for an organ. We also consider some of the challenges facing health professionals involved in providing care to such patients.

The ability to successfully transplant organs has restored to health many patients who would have faced an early, inevitable death.[1] High success and survival rates have fuelled the demand for organs, leading to shortages in almost every country in the world. Yet alongside such successes lie a number of ethical and legal concerns. One of the most disturbing is the trafficking of persons for the explicit purpose of organ removal. Despite international condemnation,[2] the trade continues in many countries and has been widely reported in the academic literature.[3–5] It is estimated that up to 10% of all transplants rely on organs that have been illegally acquired.[6]

A further disturbing aspect of the organ trade was first published 26 years ago in a report by Guttmann when he addressed the acquisition of organs from executed prisoners in China.[7] Guttmann advocated that transplant professionals "*not become involved in procurement activities for organs and tissues from executed prisoners*". In a letter to the editor in the *New Zealand Medical Journal* three years later, Miles[8] gave further evidence of how organs were sourced from executed prisoners in China, adding to a growing body of international literature in this area.[9,10]

Knowledge that China uses executed prisoners' organs is not in doubt.[11–13] In 2008, Huang Jiefu (then Vice Minister of Health, Beijing) disclosed in the Lancet[14] that *"more than 90% of transplanted organs are obtained from executed prisoners"*, a fact he had earlier stated in 2007.[15] The term 'executed prisoner' includes prisoners of conscience who are executed for their organs without due process, as well as death-sentence prisoners whose organs may be removed following judicial execution.

While concerns about the origin of organs used in transplantation in China are not new, the landscape has recently changed. Critical appraisal of available data concludes that transplant organs in China are taken from executed prisoners of conscience with official sanction from the Communist Party in collusion with the health system, transplant professionals and hospitals,[16–18] on an industrial scale. Evidence exists that Falun Gong members, and to a lesser extent, Uyghurs, Tibetans and House Christians are intentionally killed for their organs.[19]

Although organ procurement abuses are known to occur elsewhere in the world, in no other country are the state and medical profession acting so complicity in the retrieval and transplantation of organs

from executed prisoners and prisoners of conscience. For instance, Dr Zheng Shusen, a leading liver transplant surgeon at Zhejiang University's First Affiliated Hospital, is also chairman of the Zhejiang Provincial Anti-Cult Association, which is an organisation responsible for directing anti-Falun Gong propaganda. *"It worked closely with the 610 Office, a Gestapo-like organisation that oversees the persecution of Falun Gong members"*.[20]

Despite assurances from Chinese officials that organs would not be taken from executed prisoners from 1 January 2015,[21] serious doubts exist as to the legitimacy of such claims.[22,23] The Chinese Government has not initiated any legislative changes to regulations permitting organ procurement from executed prisoners, and there is no transparency in the current organ allocation system about where organs have been sourced. This has led some commentators to conclude that *"it is not possible to verify the veracity of the announced changes, and it thus remains premature to include China as an ethical partner in the international transplant community"*.[24]

Recently the prestigious medical journal, *Liver International*, retracted a paper by Yu et al.[25] This eventuated after serious allegations were made to the journal concerning questions about the provenance of transplanted organs retrieved from organ donation after cardiac death (DCD) in China.[26] Yu et al were given the opportunity by the journal to provide evidence that China had implemented legislative change. Although the authors stated no organs were obtained from executed prisoners, Rogers et al disputed this.[27] Evidence from China shows that during the stated period of the paper, executed prisoners remained the primary source of organs for all transplants in China.

Given the strong likelihood that a small number of patients from New Zealand (and Australia) may travel to China each year to receive an organ, the implications of China's transplantation industry have ethical and legal ramifications for transplant patients and health professionals in New Zealand. In the following discussion, we consider how viewing this issue through an ethical lens has relevance for patients considering traveling to China for a transplant, and the questions that arise for New Zealand health practitioners.

Organ transplantation in New Zealand

The central force driving organ transplantation is a desperate need for organs compounded by a limited supply. Quite simply, demand exceeds supply in almost every country in the world, including New Zealand. For instance, there are currently more than 500 people waiting for an organ or tissue transplant in New Zealand;[28] most are waiting for a kidney. Faced with waiting and possibly dying on a transplant register, some patients may consider travelling overseas to procure an organ for a fee.

Although numbers are small, each year New Zealand and Australian dialysis patients travel overseas for a kidney transplant.[29] These transplants may be performed ethically and legally. During the period 2000–2015, 27 Australians and 5 New Zealanders underwent a kidney transplant outside of their home country. The ANZDATA Registry report for 2016 notes that it is "*possible that these numbers are an underestimate of the true number, since some patients may not return to Australia/New Zealand and hence be reported to ANZDATA as lost to follow-up"*.[29] The number of New Zealand patients traveling internationally for other organs and tissues such as livers, hearts, corneas, etc are unknown, as are the countries the organs originated from.

It is likely many of those who travel internationally for an organ such as a kidney, travel to China because of their availability. Some of those travellers may be New Zealanders and Australians. The recent documentary *Human Harvest*[16] documents a number of international transplant tourists who travelled to China to purchase an organ, some of them knowing in advance the day their surgery would take place. There are also anecdotal reports confirming the existence of such knowledge[30] (the cases discussed in the cited article are, in some cases, more than 10 years old). Australian Senator Derryn Hinch was alleged to have been told that if he had $150,000 he could travel to Shanghai to secure a liver within a week.[31]

Ethical concerns and their relevance for New Zealand

For the procurement of an organ transplant to proceed in New Zealand, consent must be given by the individual in the case of living donation, while in the case of a deceased donation, the consent of a family member will be sought with consultation from a health professional. Informed consent is evidence of intent, understanding and autonomy and affirms the organ was given freely without coercion: it was the individual's choice. Knowing that the organ one receives from a donor (whether living or deceased) has been procured ethically assures one is not complicit in any harms inflicted on the donor.

Although there has been rigorous debate about whether prisoners can truly give informed consent to donate,[32,33] condemned prisoners in China may include those who stole a car, hold certain beliefs, discharged a firearm or were the perpetrators of corruption or embezzlement.[10] If such crimes in China justify capital punishment, it is doubtful consent would be sought to use their organs, and were consent to be granted, its legitimacy and validity must be questioned.[34] The World Medical Association is clear in its policy that in jurisdictions that permit the death penalty, *"executed prisoners must not be considered as organ and/or tissue donors"* because *"it is impossible to put in place adequate safeguards to protect against coercion in all cases"*.[35] But even if one could defend the use of organs taken from executed prisoners who had faced a fair trial and given their consent for their organs to be used (for instance, as some kind of atonement for their crimes), it is stretching the bounds of credibility to accept the legitimacy of the consent from executed prisoners of conscience who are killed extra-judicially. To be the recipient of an organ sourced from China may render one complicit in that person's killing, and thus to be morally blameworthy.

As noted earlier, anguish and desperation fuel the demand for organs. Yet knowing that one's own death may result from a lack of available organs does not trump the intentional killing of another person, nor the taking of their organs without their consent. No reason can justify the forced procurement of organs from individuals detained by the state, regardless of their criminal status or their beliefs.[36]

Ethical concerns for health professionals

A number of ethical tensions arise for New Zealand health professionals if they suspect or know their patient is considering procuring an organ from China, or if their patient returns to New Zealand with a transplanted organ. In regards to pre-travel, do health professionals have a duty to assist a patient with any pre-surgical testing prior to going to China; furthermore, is there a duty to warn such travellers of the use of executed Chinese prisoner's organs so that they can make informed choices?

In answering the first question, one could argue that patients have a legal and moral right to access their medical record and their request for it should not be obstructed. Yet, as Caulfield et al claim, despite the obligation to provide medical records, doctors *"have no obligation to take any actions that would facilitate an illegal transplant, such as providing a patient with a summary of the medical file or a letter for the surgeon that is going to perform the transplant"*.[2] This is because providing medical records for the purposes of ensuring transplant surgery proceeds is likely to directly contribute to the victim's death, thus, there is absolutely no moral duty to provide such support.

The answer to the second question is surely, yes! Patients who consider purchasing an organ from China should be warned that organs are still obtained from executed prisoners who have not given their informed consent. Patients should also know that there are increased rates of morbidity and mortality with internationally sourced transplants.

In regards to providing care post-operatively, do health professionals have a duty to provide medical care to their transplant patients; and is there an obligation for health professionals to disclose such information to New Zealand authorities (when they suspect or know that transplant surgery has occurred in China)? Some health professionals may feel conflicted about their duty to provide medical treatment and care, with their personal views on the patient's decision to pursue an organ from China.

When patients return from China with a transplanted organ, there is an obligation on health professionals to provide appropriate medical care to them, although some may choose to transfer the care of the patient to another health professional. Punishing returning patients seems inappropriate, may create injustice issues[37] and is probably not effective at deterring others from heading to China for an organ transplant.

Complicating the landscape is evidence that generally patients who *"return from a commercial transplant overseas commonly do not tell their transplant professional how the organ was obtained".*[38] Moreover, if a patient was required to disclose information about where they were looking to source an organ, or provide details of where their transplantation surgery took place, they may avoid seeking medical care post-surgery. The potential for harm is implied.

Implications for practice

Until independent transparent verification confirms forced organ procurement in China has ended, it is recommended that:

- New Zealand medical practitioners should strongly dissuade their patients from traveling to China for the purpose of receiving an organ transplant. Informing patients of the ethical, medical, psychosocial and legal aspects of buying an organ from China is recommended and is consistent with rights 4(2), 5(1,2), 6(1b,e, 2,3 and 4) of the Code of Health and Disability Services Consumers' Rights.[37] The Declaration of Istanbul Custodian Group has developed material that can assist practitioners in discussions with their patients.[34]
- New Zealand medical practitioners are justified in exercising their duty to elect to transfer the care of their patient (who intends to travel to China to receive an organ, or a patient who returns from China with a transplanted organ) to another practitioner as long as such a referral does not jeopardise the health of one's patient.[39] Yet such a suggestion is not without challenge, given the fact that a health professional may be either working alone in a small centre, working in a small group, or an alternative clinician is simply unavailable or unwilling to assume the care of such patients. For instance, where a patient returns with a transplanted liver, the fact that New Zealand has only one liver transplant service may result in a clinician having little choice but to continue to care for a patient whose actions one deeply opposes. Similar ethical challenges arise for health professionals who have a conscientious objection to providing abortion, sterilisation and contraception services to patients. In such situations, the duty to treat one's patient trumps the interest one has in transferring their care to another colleague as the choices available to patients are severely limited.
- Transplant surgeons from China who intend to continue their training and practice at home should not be permitted to further their transplant training in New Zealand. Prohibiting the continued medical education of Chinese transplant practitioners in New Zealand sends a strong message to China that New Zealand will not be complicit in their organ transplant industry.

Furthermore, it is recommended that professional medical bodies provide formal guidance for health professionals engaged with patients who are organ transplant candidates.

Conclusions

The ability of an individual living in one country to procure an organ from another country has changed organ transplantation surgery. A person in New Zealand with financial means can contact agents in China via the web and confirm transplant surgery before they leave the country. Organs can include, hearts, kidneys, livers and tissue.

Despite allegations surfacing almost 25 years ago in New Zealand, little, if anything, has been done to address the ethical implications such transactions have for medical practitioners caring for patients who require transplant surgery. Neither has much been done to address the obligations medical educators may have when Chinese transplant doctors, who intend to return to China, come to New Zealand to further their transplant training.

In 2016, Rogers et al wrote *"...why does the international community, including transplant doctors, medical ethicists and journal editors remain complicit in this silence?"*[36]

There are doubtless many reasons why the international community remains silent on the issue of forced organ procurement in China: apathy, a concern about jeopardising trade relationships, disbelief that such atrocities can occur, or the mistaken belief that the organs of executed prisoners no longer fulfil the demand for organs. Yet these can become excuses not to act when documented and verified evidence is confirmed. The words of Martin Luther King Jr seem especially poignant in this context: *"He who passively accepts evil is as much involved in it as he who helps to perpetrate it. He who accepts evil without protesting against it is really cooperating with it"*[40]

We have a moral obligation not to remain complicit in this silence.

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Phillipa Malpas is a member of the group, End Transplant Abuse in China (ETAC).

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Traumatic haemorrhagic lumbar synovial facet cyst presenting as bilateral foot drop: a case report

Caitlin Bodian, Jordan Davis, Alastair Hadlow

Lumbar synovial cysts are extradural lesions that arise from degenerative lumbar facet joints.[1,2,7] They most commonly arise at the L4/5 level.[2] Patients are typically male and present between the 5th and 8th decades of life.[1] Cyst haemorrhage is rare, but is important to identify as it can cause abrupt volume expansion and nerve compression. Trauma is a well-recognised cause of haemorrhagic synovial cysts and typically produces unilateral neurological symptoms.[6] To our knowledge we present the first case of a haemorrhagic facet joint cyst secondary to trauma causing acute bilateral foot drop.

Case report

A 77-year-old man normally well and independently mobile presented with a 12-day history of lumbar back pain and severe bilateral foot drop after a direct blow from a shopping cart. At the time of injury he collapsed due to leg weakness. He had no previous spinal injuries or operations. He was on aspirin for ischaemic heart disease. On examination he was unable to walk independently. He had bilateral grade 4 hip abduction, grade 0 ankle eversion, grade 2 toe dorsiflexion and grade 3 ankle plantar flexion. Normal perianal sensation and sphincter function. MRI reported multilevel critical stenosis at L3/4 and L4/5 second to a diffuse annular bulge with facet joint hypertrophy and epidural fat compressing the thecal sac. (Figures 1 and 2) The patient underwent emergent posterior decompression of L3 to L5. Intraoperative findings demonstrated a large haemorrhagic cyst at the L4/5 facet joint compressing the cauda equina, which was confirmed by histology. Post-operatively the patient's neurological function improved immediately. At six-week follow-up he had a full neurological recovery.

Figure 1: Sagittal MR of the patient's lumbar spine. T2 on the left and T1 on the right.

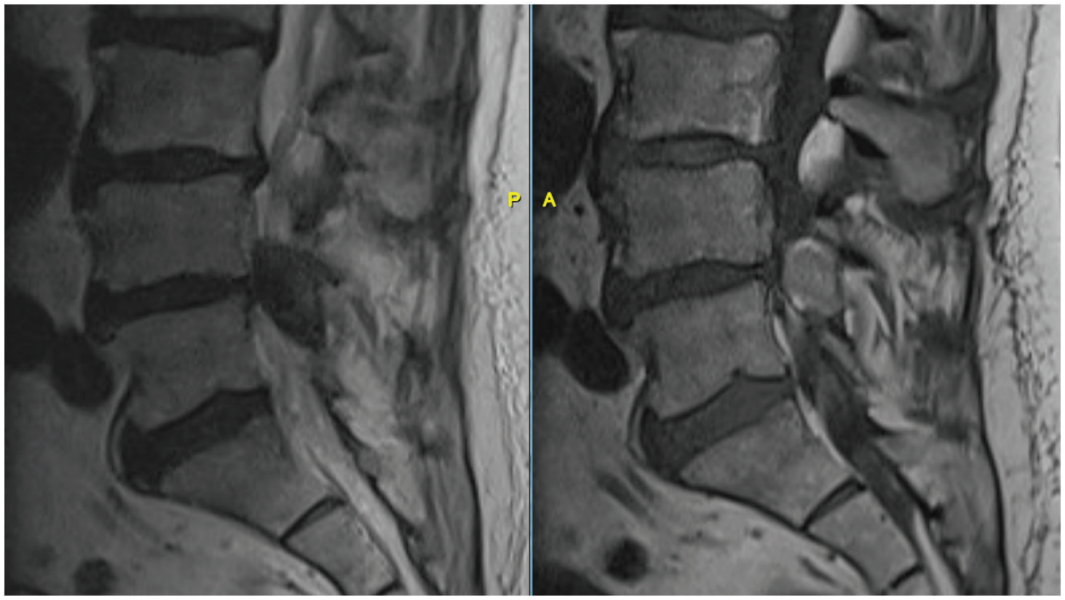
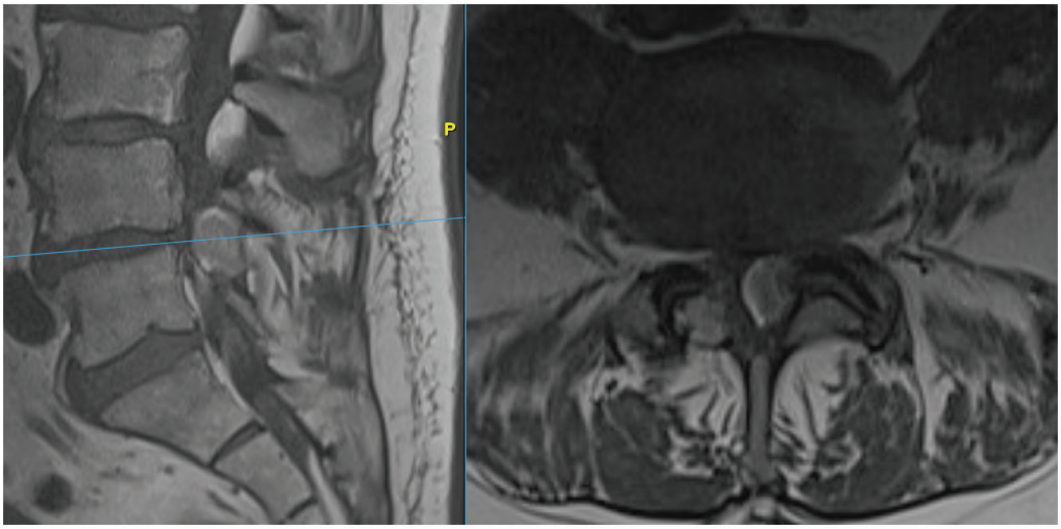


Figure 2: T1 sagittal and transverse images of haemorrhagic cyst at L4/5 spinal level.



Discussion

Trauma is an important cause of synovial cyst haemorrhage and is attributed to approximately one-quarter of the documented cases.[2,3–5] Other risk factors include anticoagulation, underlying vascular abnormalities and co-existing disc herniation.[1] Bleeding occurs from the cyst's neoangiogenic vessels and leads to volume expansion within the spinal canal leading to neurological symptoms.[2,6] These neurological findings have previously been reported as unilateral. The most common findings are paraesthesia and weakness.[9] Gait disturbances and cauda equina are rare. [8,9]

MRI is the preferred modality for diagnosis of cyst haemorrhage with 90% sensitivity.[4] Appearance of cystic haemorrhage on MRI is variable as it depends of the acuity of bleeding. Acute haemorrhage will appear hyperintense on T1 and on T2, whereas subacute haemorrhage will be hyperintense on T1 and heterogeneous on T2 due to the presence of hemosiderin.[4]

Nearly all haemorrhagic cysts are treated with spinal decompression and cyst excision.[1] Emergent surgical intervention is often required due to intractable pain and acute neurological decline and produces excellent results. Forty of the published cases detailed post-operative outcomes, in which 75% experienced complete resolution of symptoms and 25% experienced significantly improved symptoms.[10] Our patient experienced a complete recovery of neurological function post-operatively.

The histology of synovial cysts demonstrates a viscid fluid filled sac with a lining of epithelium-like cuboid cells.[4] Ganglion cysts are also found in the lumbar region and can haemorrhage in a similar manner requiring identical treatment. Diagnosis between synovial and ganglionic cysts can only be done though histopathological examination.[10]

Conclusion

Trauma is a well-established cause of haemorrhagic synovial lumbar cysts. They can cause significant lower limb neurology, which is almost always unilateral. We describe a patient who experienced a clear traumatic event to the lumbar spine which led to a symptomatic haemorrhagic facet joint cyst and acute bilateral foot drop. The treatment for nearly all cases is emergent surgical decompression and cyst resection and outcomes are highly favourable.

Competing interests:
Nil.

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Applying the Reason Model to enhance health record research in the age of 'big data'

Rajan Ragupathy, Vithya Yogarajan

There is considerable international interest in applying powerful data research techniques ('big data') to health records.[1] This will become increasingly viable in New Zealand as previously siloed records held by private primary providers and public secondary institutions become accessible at the regional level—such as through the Midland Clinical Portal—and perhaps eventually even at the national level. Such research could, for instance, uncover the real-world safety and effectiveness of new health technologies, identify health disparities or optimise application of international guidelines in New Zealand.

However, such research opportunities will only be viable if the public can trust that patient confidentiality will be protected. Similarly, providers would rightly be wary of making records available for research if doing so might breach legal and ethical obligations, such as those in the Health and Disability Consumers' Code of Rights and the Health Information Privacy Code. We propose here a framework—drawing from patient safety methods in healthcare and 'big data' safeguards already in use in New Zealand—for protecting the confidentiality of health records in research.

Many health professionals will be familiar with the Reason Model of patient safety. This model posits that any safeguard against patient harm will inevitably have holes in it, due to system design limitations and human factors. These holes are constantly opening and closing, creating opportunities for an error to bypass the safeguard. It is therefore necessary to have multiple adaptive safeguards and continuous learning to prevent an error reaching the patient.[2]

Health professionals may be less familiar with the safeguards used by Statistics New Zealand's Integrated Data Infrastructure (IDI).[3] The IDI allows 'big data' techniques to be applied to linked datasets that contain information about (among other things) New Zealanders' income, certain health interventions, educational outcomes, housing, use of Government benefits and social services, and interactions with the criminal justice system. Multiple safeguards—known as 'the five safes'—protect the confidentiality of this information.[4] Each of the 'safes' are detailed below, along with their applicability to protecting confidentiality in health record research.

Safe people

Researchers are referee checked and must sign a declaration of secrecy under the Statistics Act 1975 before accessing data in the IDI.[4] This can be replicated in the health sector through confidentiality agreements, employment contracts and professional codes of practice. However, as cases of health professionals inappropriately accessing patient records ('employee browsing') have shown, such measures may not fully protect against human nature.[5]

Safe projects

Statistics New Zealand requires the Government Statistician (or a delegated person) to sign off all research projects as being in the public interest, and not compromising individual privacy.[4] However, there is currently no single standardised pathway for signing off data research projects in the health sector. The National Ethics Advisory Committee's Ethical Guidelines for Observational Studies provide guidance for investigators and institutional review boards, but allow considerable scope for determining whether projects needs to be reviewed by the Health and Disability Ethics Committee (HDEC).[6] It has also been argued

that the current HDEC review process is tailored for interventional research, and may not be ideal for considering the risks of data research.[7] Institutional review boards such as those at universities or DHBs may face similar or even greater limitations. We strongly endorse calls to strengthen the review process with expertise in data science, a public registry of projects and a detailed pathway for approval.[7]

Safe settings

Statistics New Zealand uses a secure Data Lab environment to release data to researchers, with designated non-networked computers from which Statistics New Zealand staff control the release.[4] It may not be financially or logistically feasible to replicate this in the health sector. However, a corresponding safeguard may include a set of universally agreed encryption and cyber-security protocols that researchers must be validated against before accessing health records. (Encryption keys should be kept secure and regularly updated to conform to current encryption best practices). If data is to be stored 'in the cloud' at any point in this process, there should be transparency about where the cloud servers are located, who else may be accessing the data and (in cases where the servers or cloud providers are based overseas) which nations may be able to assert jurisdiction.

Safe data

Statistics New Zealand de-identifies data before releasing it to researchers. However, de-identification of health records may be more challenging due to the wealth of potentially identifying information in health records, especially those of a longitudinal nature. The United States Health Insurance Portability and Accountability Act (HIPPA) Privacy Rule sets what is arguably the gold standard in health record de-identification, and lists 18 different categories of personal information that must be removed before a record is considered de-identified.[8] The HIPPA requirements could be considered equivalent to the standard in the Health Information Privacy Code that information does not identify an individual.[9] This makes the de-identification of records in New Zealand equally challenging. Manual de-identification of health records requires specially trained staff who also have medical knowledge, is laborious and is potentially very expensive. Automated de-identification is still an unsolved problem and has not yet achieved the 95% threshold needed (across all 18 HIPPA categories) for a record to be considered de-identified.[10,11]

Safe outputs

Statistics New Zealand sets standards for research outputs to ensure individuals cannot be identified. This could be replicated by universally agreed standards for outputs that researchers must agree to before gaining access to the data. It is important here to consider not just the final outputs (such as reports and publications) but also intermediate outputs (such as data collated into a spreadsheet for analysis). The accidental release of such a document could result in a major privacy breach.[12]

In summary, there are a number of potential hurdles to be overcome to fully unlock the potential of health record research in New Zealand. Instead of either putting such research in the 'too-hard' basket, or alternatively allowing a set of ad-hoc and potentially variable standards to develop, we urge cautious progress through a set of universally agreed safeguards that benefit patients, providers and researchers. These also concord with proposed ethical frameworks for data research: public interest, trust and transparency.[7]

Competing interests:
Nil.

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On-call goes with the territory!

Stephen Main

A plan is needed to sustain the provision of GP after-hours urgent/emergency care in New Zealand.

I worry about the future of general medical practice in New Zealand.

GPs in both urban and rural environments seem increasingly reluctant to provide urgent and out-of-hours cover for patients. Historically they have always organised 24/7 care for their practices. Some GPs, especially in rural areas, continue to offer a full rostered after-hours availability, but arrangements vary widely. Expectations of virtually infinite availability are no longer realistic but how urgent care is best organised so as to provide a satisfactory balance between patients' needs and doctors' working conditions is far from clear.

Both in urban and rural areas there is increasing reliance on hospital emergency departments for many problems that used to be the province of general practice. This is not popular with emergency physicians. It places undue extra pressure on already overworked hospital emergency departments.[1]

Assessment of urgent presentations by a local generalist doctor should make it easier to organise prompt definitive care and may reduce unnecessary ED visits.[1,4] Not all headaches are strokes, not all fevers are meningitis and not all chest pain is life-threatening coronary thrombosis, but it may take a doctor to spot the difference.

The situation is made worse, particularly in rural and high needs areas, by the higher GP co-payments paid "up front" for out-of-hours service. If you're trying to get by on a benefit, what are you going to do if you need medical care urgently or out of hours or both if the choice is between a free service at a hospital ED (with free investigation or admission if needed) or $50 or more to see a GP? Even a community services card doesn't cut that bill to zero! A&M urgent care centres are hardly the answer unless they offer a full overnight service—and they aren't cheap either.

Any practising GP should be able to deal competently with the initial assessment and treatment of potentially serious medical problems.

On call remains an inescapable part of community medical care and GPs can and should do it.

It all costs money but the whole point of an organised primary care system is the best use of all the capabilities of medicine for the population served. Strong primary care systems deliver better outcomes overall than pure specialist systems and probably more cheaply too.[2–4]

It is important that the commitment of GPs to urgent, emergency and out-of-hours care remains part of this.

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Evaluation of the rapid molecular diagnostic test for the New Zealand *Mycobacterium tuberculosis* Rangipo strain in a clinical setting

Claire V Mulholland, Duncan Thorpe, Ray T Cursons, Noel Karalus, Yang Fong, Vickery L Arcus, Gregory M Cook, Htin Lin Aung

Tuberculosis (TB) is a curable disease but claims over 1.7 million lives annually, and there were estimated to be 10.4 million new cases of TB worldwide in 2016.[1] Despite New Zealand being a low-TB burden country, there are disproportionately high rates of TB in socioeconomically disadvantaged populations of New Zealand. Māori, the indigenous people of New Zealand, have an approximately nine-fold higher rate of TB compared to New Zealand Europeans.[2]

Molecular typing of *Mycobacterium tuberculosis* (*M. tb*) isolates using the Mycobacterium interspersed repetitive units (MIRU) system has shown that approximately two-thirds of New Zealand-born TB notifications can be assigned to clusters of infection.[3] The largest *M. tb* cluster is known as the Rangipo cluster and has been the cause of ongoing outbreaks for at least the last 25 years.[3] This cluster is strongly associated with Māori, with nearly 90% of Rangipo TB cases reported in Māori in the last 10 years [personal communication with Dr Sherwood, ESR (The Institute of Environmental Science and Research)]. Anecdotal evidence and reports from previous outbreaks suggest the Rangipo strain may be highly transmissible and has high rates of progression to active disease relative to other circulating strains.[4,5] If this strain is indeed more virulent, close supervision to ensure treatment adherence and the broadening contact tracing networks may be necessary to ensure secondary cases are completely and quickly detected to prevent potential later reactivation and further spread. Therefore, it is of the utmost importance to timely diagnose this strain to control further transmission.

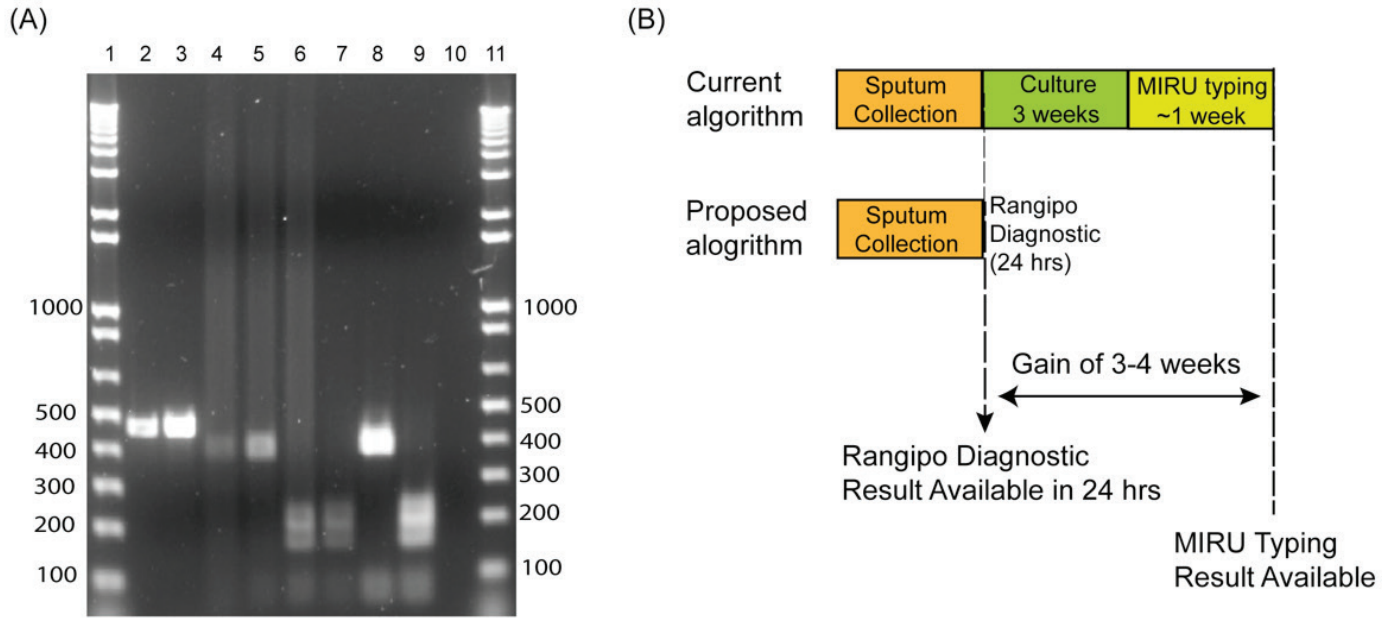
Recently, we developed a whole genome sequencing-directed, single nucleotide polymorphism (SNP)-based, polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) diagnostic for the rapid identification of Rangipo strain using DNA from cultured *M. tb*.[6] Our diagnostic was also shown to offer greater discriminatory power and higher resolution over conventional MIRU typing.[6] Here, we have applied this PCR-RFLP diagnostic in a clinical setting using culture-independent *M. tb* DNA from sputum as proof of concept that Rangipo can be differentiated from other *M. tb* strains directly from sputum for rapid diagnosis upon patient presentation.

In this study, four clinical sputum specimens received at the Waikato DHB Laboratory were subjected to the Rangipo PCR-RFLP diagnostic. Briefly, decontaminated sputum samples were heat inactivated at 95°C for 20 minutes and then spun down at 4,500rpm for 10 minutes. A PCR reaction was performed directly on 0.5µl of the supernatant to amplify a 455bp region of the *M. tb* Rv1821 gene (Figure 1A, lane 2 and

3). Using the G1380A SNP in Rv1821, which is only present in Rangipo as a molecular maker, digestion of amplified products with the MboI restriction enzyme produces cut fragments of 386 and 69 bp for Rangipo, and 215, 171 and 69bp for non-Rangipo samples (Figure 1A, lane 4–7). Results were produced within 24 hours and the banding patterns obtained from the diagnostic identified Sample 1 and 2 as Rangipo (Figure 1A, lane 4 and 5) and Sample 3 and 4 as non-Rangipo (Figure 1A, lane 6 and 7). The sputum samples were also sent to the Tuberculosis Reference Laboratory (LabPlus) in Auckland for routine strain identification, which involves a total of 3–4 weeks culturing and MIRU typing. Consistent with our diagnostic results, the MIRU typing identified Sample 1 and 2 as Rangipo (MIRU code 233325153324 341444223362) and Sample 3 and 4 as non-Rangipo (MIRU code 223325173533 445643423382). We have shown that our diagnostic produces the correct results from sputum specimens within 24 hours, substantially reducing the turnaround time of 3–4 weeks for strain typing (Figure 1B). Hence, this Rangipo diagnostic can be used as a standard and timely test upon patients' presentation in a clinical setting for effective intervention to prevent further transmission.

In short, this affordable, rapid and reliable diagnostic will serve as a valuable tool for the district health boards in New Zealand to control the spread of the Rangipo strain, the cause of a prolonged and sustained TB outbreak in New Zealand.

Figure 1: Rangipo PCR-RFLP diagnostic.



(A) PCR-RFLP assay results; lanes 1 and 11, 1 Kb Plus DNA Ladder, Invitrogen with 100, 200, 300, 400, 500 and 1000 base pair bands marked; 2, Rangipo control isolate before restriction digest; 3, Non-Rangipo control H37Rv laboratory strain before restriction digest; 4 and 5, clinical isolates diagnosed as Rangipo by this assay (samples 1 and 2); 6 and 7, clinical isolates diagnosed as non-Rangipo by this assay (samples 3 and 4); 8, Rangipo control isolate after restriction digest; 9, Non-Rangipo control H37Rv laboratory strain after restriction digest; and 10, PCR-negative control.
(B) Timelines for current algorithm and proposed Rangipo PCR-RFLP diagnostic-based algorithm, which could reduce turnaround time by 3-4 weeks. MIRU; Mycobacterium interspersed repetitive units.

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Poor female representation at surgical conference

Joy R Rudland

As the Director of the Educational Development and Staff Support at the University of Otago Medical School and also a partner of the female surgical trainee, I noted with interest the programme for the New Zealand Association for General Surgeons (NZAGS) held in March. There were 24 speakers advertised, all men. Of the surgeons, all but one were white.

It is an issue of concern that women were not represented. What we know is that the number of female surgeons in New Zealand is low and that generally females are promoted at a slower rate than male surgeons.[1] The lack of a female presence fails to give young female trainees aspiring role models important for career aspiration[2,3] or even legitimacy in the profession. The NZRAG conference's male-dominated presenter list certainly perpetuates the impression that the female is not valued.

Although research indicates that there is a significantly reduced risk of dying after 30 days if treated by a female surgeon as opposed to a male surgeon,[4] female surgeons tend to get a bad deal. Female surgeons in America are paid on average 20% less than their male counterparts and are more harshly judged by male surgeons when mistakes are made with greater long-term effects;[5] men forgive mistakes made by their male but not their female colleagues. In America, 25% of women surgeons are single compared to 6% of men, and 60% of female surgeons have children compared to 92% of men. Seventy-six percent of female surgeons perceive that male surgeons are treated more favourably.[6] None of this seems equitable.

The surgical community needs to acknowledge and perhaps embrace the fact that research has identified differences in the way women and men behave. For example, when under stress women are inclined to 'tend and befriend'[7] and ideally with a female peer;[8] the men lean more to the 'fight and flight' stress response. Looking at attrition, a recent New Zealand study confirmed global findings that females were twice as likely to consider leaving surgical training as male trainees.[9] Poor lifestyle and lack of support were the main reasons cited but given the other discriminatory practices it may be surprising that the attrition rate is not higher.

I don't restrict my criticisms to male surgeons. Female surgeons may be as blinkered to discrimination against other women as the most hardened misogynistic man. The need for some women surgeons to be 'hardcore' and show masculine traits for legitimacy[10] is sad, but also undermines what women can bring. Women should not need to assimilate themselves into an unwelcoming alien environment. The culture needs to change, not the women, before a truly gender-neutral meritocracy can be established.

I appreciate (in both senses of the word) that there are many wonderful male surgeons leading change to ensure better representation of women with positive actions like the 'HeforShe movement'. In surgery, it will take these courageous men to make a difference. However, unless organisations like NZAGS feature female surgeons in a meaningful way it is all rather pointless. Perhaps next time when you, as the pale male, are asked to present at a conference, ask about female representation and suggest one of your talented, kind, diligent female colleagues. Conferences such NZAGS should be striving to promote women in surgery, not minimise their role. This is not just a New Zealand issue; in the UK, women represent 11% of surgeons but 58% of medical students.

While the Royal Australasian College of Surgeons have made laudable inroads into poor behaviour through 'Operating with Respect', the line-up of presenters at NZAGS is disrespectful and discriminatory. As a minimum, it may just be lazy falling back on the 'old boy' network, at worst it might be deliberate, but I am not prepared *to walk past* this blatant sexism.

Whakatū Wāhine

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Response to: Poor female representation at surgical conference

Julian Speight

At the very outset I'd like to state that the New Zealand Association of General Surgeons believes strongly in the concept of gender equality. It is unfortunate that this was not clearly reflected in the choice of speakers invited to talk at the recent Annual Scientific Meeting in Paihia.

It should be noted that there were female speakers within the programme. Four out of the total 12 speakers in the free-paper session were women surgeons, which equates to a third of the free papers. I recognise that these speakers were not visible in the provisional programme which advertised the scientific programme and the invited speakers. A further four female trainees had poster presentations. All the general surgeons in the Northland DHB surgical department, which includes two female surgeons, had a role in deciding the theme of the conference, including the invited speakers. The organising committee consisted of three surgeons, one of whom is a woman. I have spoken to all three of the conveners, and they all state that the speakers were chosen based on their expertise within their fields. At that point in time no thought was given to their gender. As the theme for the conference was the 'History of New Zealand Surgery', it transpired that most of the invited speakers were older surgeons. The conveners also extended invitations to other organisations to provide speakers. These included the Royal Australasian College of Surgeons, EGGNZ, CADENZA, Southern Cross Insurance and Health Workforce NZ. The speakers were provided by these organisations without input from the organising committee. Each of these speakers transpired to be men.

It is well recognised that in the past the majority of surgeons have been male. This reflects the cultural norm of a generation past. However, there has been a significant effort made in the last two decades to redress this balance, and this is reflected in the fact that currently 40% of our surgical trainees are female. Twenty-four percent of the new fellows qualifying in 2017 were female, and women make up nearly a quarter of the Royal Australasian College of Surgeons, Councilors and committee members. NZAGS has only recently become responsible for selecting surgical trainees, but the figures that I have access to between 2010 and 2016 show that there has been significant progress in gender equality. In this six-year time-period there have been 167 applicants to the New Zealand General Surgery Training Programme (102 male and 65 female). That equates to female applicants making up 39% of the total number applying. Fifty-six candidates have been selected in that six-year period, of which 59% were male and 41% female. This represents a success rate of 35.4 % overall for female candidates and a 32.4% success rate for male candidates. Allowing for the sample size, this would seem to suggest that male and female applicants have an equal chance of being selected. I think this should be seen as a very positive step towards the "truly gender-neutral meritocracy" that Ms Rudland is advocating for.

Ms Rudland's letter is quite wide-ranging, and touches on many aspects of gender equality in surgery. I note that only one of the papers referenced relates specifically to New Zealand. I am hopeful that New Zealand may have a better track record for working towards gender equality than perhaps some of the countries from which this research emanates. I am happy to report that the NZAGS CEO is a woman. In my position as President of NZAGS I can only reply to Ms Rudland's concerns regarding the lack of invited female speakers at

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our recent Annual Scientific Meeting. Ms Rudland described the choice of presenters as "disrespectful and discriminatory" and suggested that the conveners were at best lazily "falling back on the 'old boy' network" and that at worst this was "deliberate, blatant sexism". I am disappointed in the overall tone of the letter. The use of emotive terms such as "pale male" and "hardened misogynistic man" only serve to distract from what is otherwise an important issue. In defense of our organising committee, I would like to reiterate that there was no intent to exclude female speakers. Speakers were selected on their expertise, without thought given to gender or creed. But this is a timely reminder that future conference conveners need to make positive steps to ensure that there is gender parity. I am told by Philippa Mercer, the conference convener for the 2019 NZAGS ASM in Christchurch, that there are a good number of invited female speakers from across New Zealand on the programme.

The New Zealand Association of General Surgeons has many female members, and will continue to strive toward gender equality. Indeed, we support diversity and equality throughout our membership.

Nãku noa, nã

Competing interests:
Nil.

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Response to: A systematic review of leadership training for medical students

Dominic Jaikaransingh, Harry VM Spiers, Hugo Layard Horsfall

We read with interest the article by Lyons et al.[1] Their group assessed the efficacy of undergraduate medical leadership criteria and identified common features of effective curricula. They concluded that despite subjective effectiveness, there was limited objective evidence. Currently, management and leadership skills are formerly assessed in only 36% of UK medical schools,[2] confirming the need for research into the area. Another study[3] suggested that medical students in the UK saw the need for management and leadership training, and understood its importance in their future careers. They also found that medical students felt the little training they do receive in the area is generally poor.

Medicine in the UK follows a rigid hierarchical structure. As students advance through training they gain increasing levels of clinical responsibility, each with greater need to manage and lead teams. Performing these tasks effectively requires specific leadership skills and qualities. These qualities include communication, time management and allocation of resources, which are especially pertinent in the UK National Health Service (NHS), given it is a cash-strapped organisation under immense pressure. Considering the previously outlined lack of formal teaching around these skills, most doctors rely on learning these skills by observing their seniors and learning through experience. There are private courses offered in leadership, such as the one run by 'The Healthcare Leadership Academy'. However, courses like these are privately run and can be expensive and time consuming, requiring a lot of work and attention. This makes them unattractive to many medical students who cannot afford the time for extra-curricular activities.

The results and themes from the above discussion were corroborated by our group through a questionnaire assessment of undergraduate medical students at a single London medical school. Eighty-four clinical year medical students were surveyed with regards to whether they received any formal or informal teaching on management or leadership in their time at medical school. They were also asked whether they thought leadership should be taught formally as part of the curriculum. Of the 84 students surveyed, only two students (2.4%) had received formal leadership training through lectures, and only two students (2.4%) had received informal teaching by senior staff on placement. Thus 80 students (95.2%) had received no training in leadership and management, and when asked whether it should be taught formally as part of their medical school curriculum, 80 students (95.2%) said yes. Those students answering no were asked to explain their response; the recurring theme was that they felt leadership to not be relevant for medical students, and adding leadership teaching would overload an already saturated medical school curriculum. These results outline a significant gap between supply and demand for management and leadership teaching for students, as well as the need for medical student education regarding the importance of these skills.

We believe that formal leadership and management teaching should be integrated into medical school curricula, evidently an opinion shared by medical school students as demonstrated by Rouhani et al[2] and our own data. However, this may not be possible and so extra-curricular student-led societies should be utilised. Invited leaders, clinicians and guest speakers can provide educational workshops. This empowers students to take control of their own learning and careers, while promoting and delivering management and leadership education.

Competing interests:
Nil.

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Why did so many women develop cancer? Part 3

Ronald Jones

The editor has allowed Professor Bryder to reopen correspondence relating to her book *A History of the 'unfortunate experiment' at National Women's Hospital* on the mistaken basis of "important new information". Reluctantly, I must respond.[1]

Bryder's reasoning that the authors of a recent "systematic review and meta-analysis of the clinical course of untreated cervical intraepithelial neoplasia (CIN) 2 under active surveillance"… "support what Associate Professor Herbert Green suggested to the NWH Hospital Committee in 1966" is incorrect.[2] Whereas the meta-analysis was restricted to the study of CIN 2 mainly in women under 30 years, mainly for a few months, and with treatment either if CIN 2 persisted or if CIN 3 was diagnosed; Green, on the other hand, studied women who had CIN 3 (some for almost 20 years) or microinvasive cancer at the outset, he ignored age limitations and safeguards, aimed to follow women indefinitely and (clinically) invasive cancer was the endpoint at which treatment was given.[3,4]

Green was familiar with inter and intraobserver variation:[5,6] indeed, when some of his patients with histologically diagnosed CIN 3 later developed cancer he personally reviewed the original histology himself and determined the woman had invasive cancer at the outset and removed the case from his study.[7] At no time has HPV status been taken into account when managing CIN 3.

Bryder headed her letter *Primum non nocere*. Presumably Green intended to do no harm at the outset, but sadly he did great harm. As spelt out in the new paper she cites when women with CIN 2 were subject to active surveillance for up to five years, and treated if their disease progressed to CIN 3, only 0.5% developed invasive cancer.[2] By contrast the authors of the systematic review cite the re-examination of Green's study by McCredie et al of the women with CIN 3 followed without treatment for five years, of whom 17% developed invasive cancer.[8] This is 34 times higher. Why has Professor Bryder persistently refused to answer my question: why did so many women in Green's study develop cancer?[9,10] Until she answers this question her defence of Green is spurious.

Competing interests:
Nil.

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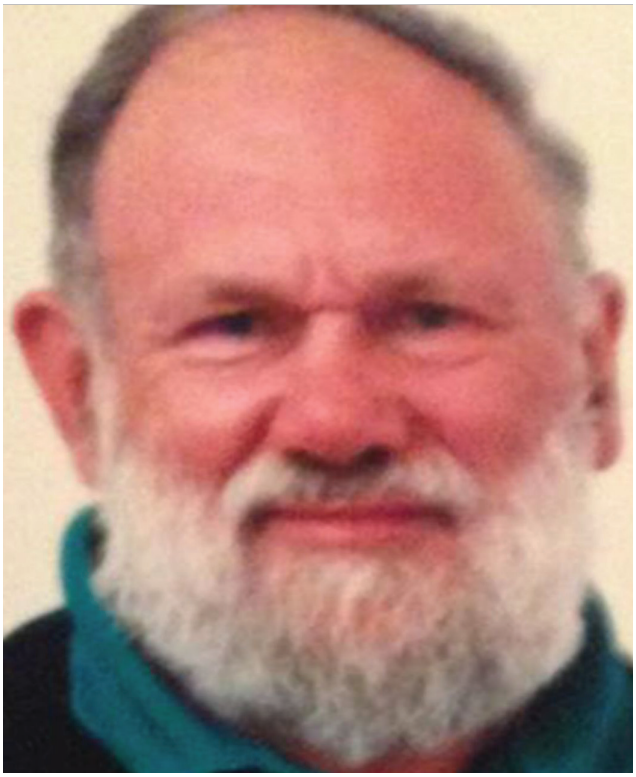
Alexander Leslie Florence

1927–26 March 2018



Alexander Leslie Florence was born in Aberdeenshire, Scotland. He was the first in his family to attend university, graduating from the University of Aberdeen in 1950. He served as a general practitioner in Turriff, Scotland until 1966, after which he and his family moved to Tawa, New Zealand, where he practised until he retired in 1998.

He was known and respected by patients as "Dr Florence—such a good GP," and his thoroughness and acumen were evident in a letter published in *The BMJ* on 31 December 1960. On the basis of his observations of the side effects of Distaval/thalidomide on his patients, he questioned the use of this drug by pregnant women. Nevertheless, the pharmaceutical company responsible for the latter's manufacture continued to produce this toxic "treatment." Persistent in his belief and supported by growing evidence of the drug's iatrogenic properties, Florence continued to contest its production and prescription. According to Michael Magazanik, an Australian journalist and lawyer, who wrote *Silent Shock: The Men behind the Thalidomide Scandal and an Australian Family's Long Road to Justice*, "Dr Leslie Florence became the first doctor to publish on the connection between thalidomide and nerve damage" (p 117). His putting pen to paper resulted in the US Food and Drug Administration's rejection of the pharmaceutical company's application to market thalidomide in the US.

"Grip fast," the motto of Florence's clan, Leslie, is a fitting description of his nature. Ever determined and curious, he moved through life in his own distinctive way. He was one of the few GPs whose beloved dog accompanied him to work—no questions asked. Through his commitment to learning and his love of travel and outdoor pursuits (including golf, skiing, and boating), he generously provided opportunities for his children to live good lives.

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Doing justice to the medical and personal contributions Florence offered throughout his life requires far more than an obituary word count allows. While his contribution to exposing the noxious effects of thalidomide are little known beyond those involved in the prioritising of profit over ethics, his words in 1960 made a difference in many lives then, and have reached far into the years beyond.

Alexander Leslie Florence died at Rotorua Hospital, New Zealand, in the early morning of Monday 26 March. He is remembered for his good heart and deeds by his three children, four grandchildren, and former wife.

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Prescribing inappropriate

Charge

At a hearing held on 25 October 2017 the Health Practitioner's Disciplinary Tribunal considered a charge laid by the Professional Conduct Committee (PCC) against Dr M, (the doctor) of Auckland.

The charge alleged that the doctor provided ongoing care to her husband by prescribing Class C controlled drugs to him without appropriate monitoring or oversight; she failed to keep accurate patient records of the treatment she provided to her husband and she compromised her husband's health and safety.

The hearing proceeded on an agreed summary of facts basis.

Findings

The Tribunal was satisfied that the charge was established and warranted disciplinary sanction.

Penalty

The Tribunal censured the doctor and fined her $5,000. Conditions were imposed on her practice and she was ordered to pay a total contribution of $12,000 towards the costs of the PCC and the Tribunal.

A full copy of the decision can be viewed at: http://www.hpdt.org.nz/ChargeDetails.aspx?file=Med17/382P

URL:
http://www.nzma.org.nz/journal/read-the-journal/all-issues/2010-2019/2018/vol-131-no-1478-13-july-2018/7632

Indecent assault

Charge

At a hearing held 9 March 2018 the Health Practitioner's Disciplinary Tribunal considered a charge laid by the Professional Conduct Committee (PCC) against David Lim (the doctor).

The charge alleged that the doctor had been convicted, following trial in the district court, of five charges of stupefaction without lawful justification and five charges of indecent assault.

These charges related to four separate victims. The doctor was sentenced to a total of five years imprisonment.

The hearing proceeded by way of an agreed summary of facts.

Findings

The Tribunal found the charge established and disciplinary sanction was necessary.

Penalty

The Tribunal censured the doctor; cancelled his registration as a medical practitioner and ordered him to pay a total contribution of $4,380 towards the costs of the PCC and the Tribunal.

A full copy of the decision can be viewed at: http://www.hpdt.org.nz/ChargeDetails.aspx?file=Med17/412P

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Indecent assault

Charge

On 21 February 2018 the Health Practitioners Disciplinary Tribunal heard a conviction charge laid by a Professional Conduct Committee appointed by the Medical Council of New Zealand against Dr Bruce James Spittle, consultant psychiatrist of Dunedin (the doctor).

The charge alleged that the doctor was convicted of two counts of indecent assault, which are offences under the Crimes Act being punishable by a term of imprisonment not exceeding seven years, and these convictions either separately or cumulatively reflect adversely on his fitness to practise.

Background

The victim of the doctor's indecent assault was a patient of the doctor and one of the indecent assaults occurred while the patient was in hospital.

The doctor maintained his denial of the conduct for which he was convicted but acknowledged that the Tribunal's role was not to review the conviction and accepted that the convictions reflected adversely on his fitness to practise.

The hearing proceeded by way of an agreed statement of facts.

Finding

The Tribunal was satisfied that the offences both separately and cumulatively, reflected adversely on the doctor's fitness to practise.

Penalty

The Tribunal cancelled the doctor's registration and censured the doctor to mark its disapproval. It also ordered the doctor to pay 25%, ($5,720) of the costs of and incidental to the PCC's investigation, prosecution and the Tribunal's hearing.

The Tribunal further directed publication of its decision and a summary.

A full copy of the decision can be viewed at: https://www.hpdt.org.nz/ChargeDetails.aspx?file=Med17/406P

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http://www.nzma.org.nz/journal/read-the-journal/all-issues/2010-2019/2018/vol-131-no-1478-13-july-2018/7634

Mortality and morbidity in acutely ill adults treated with liberal versus conservative oxygen therapy

Supplemental oxygen is often administered liberally to acutely ill adults, but the credibility of the evidence for this practise is unclear. In this paper the authors systematically reviewed the efficacy and safety of liberal versus conservative oxygen therapy in acutely ill adults.

Data from 25 randomised trials involving over 16,000 appropriate patients was reviewed. The liberal oxygen strategy was found to be associated with an increased in-hospital mortality (relative risk 1.21) and also an increased mortality risk at 30 days and at longest follow-up. Morbidity outcomes were similar in the two groups.

The authors conclude that "in acutely ill adults, high-quality evidence shows that liberal oxygen therapy increases mortality without improving other patient-important outcomes. Supplemental oxygen might become unfavourable above an Sp02 range of 94–96%. These results support the conservative administration of oxygen therapy".

***Lancet* 2018; 391:1693–705**

MRI-targeted or standard biopsy for prostate cancer diagnosis

Men with a clinical suspicion of prostate cancer on the basis of an elevated prostate-specific antigen (PSA) level or an abnormal digital rectal examination are typically offered a standard transrectal ultrasonography-guided biopsy of the prostate.

An MRI-targeted biopsy is a possible alternative and this is explored in this report. Five hundred men suspected to have prostate cancer were randomised to have MRI-targeted biopsy or standard transrectal ultrasonography-guided biopsy. Clinically significant cancer was detected in 38% of the MRI cohort compared with 26% in the standard group.

The researchers concluded that MRI-targeted biopsy was superior to standard transrectal ultrasonography-guided biopsy in men at clinical risk for prostate cancer who had not undergone biopsy previously.

N Engl J Med 2018; 378:1767–77

Urolithiasis is associated with an increased risk of stroke

Epidemiological studies have reported an association between urolithiasis and cardiovascular disease. However, studies examining the risks of ischaemic and haemorrhagic stroke in patients with urolithiasis are limited.

This issue is evaluated in this report. Using information obtained from a nationwide population database in Taiwan, the investigators have been able to confirm the hypothesis. Both ischaemic and haemorrhagic strokes were found to be significantly more common at five-year follow-up in the urolithiasis cohort. The findings were consistent in both men and women.

The present study detected an increased risk of both ischaemic and haemorrhagic stroke in patients with urolithiasis, particularly in those older than 40 years.

Internal Medicine Journal 2018; 48:445–450

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Fallopian Tube and Ovary in Hernia

By James Young, M. D.

I wish to report the following case because I think it is rare:—

C.B., female, age six months, healthy and well nourished at the breast. Soon after birth mother observed a small, hard, moveable lump in the right groin, about the size of a filbert and free from tenderness. This condition remained and the child gave no trouble till about 2nd May, when she seemed to suffer when the part was touched. On the 3rd of May the child was brought to me with the report that the lump had manifestly increased in the previous 24 hours, as it continued to do till the 6th May. There was no general sign of illness, the child being free from fever or any suffering unless when the swelling was handled, but the skin over the part had become red. On the 6th May I operated as usual for hernia and removed a tumour from a hernial sac, on which Dr. Drennan gives the following report: "The tissue consists of broad ligament with Fallopian tube and ovary. In these there is extensive haemorrhage, nothing but blood being seen over large areas. The vessels, especially the veins, are greatly engorged. In one part of broad ligament there is a collection of serum with a number of acute inflammatory cells. The appearances are those of acute strangulation of the broad ligament with ovary, due, as the history indicates, to involvement in the hernial sac. It is an interesting and unusual finding in a hernia."

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