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New Zealand needs guidelines for the safe and responsible inclusion of pregnant women in medical research

Angela Ballantyne

Pregnant women continued to be excluded from nearly all clinical research, without justification, for their own safety. But this is dangerous for pregnant women and foetuses because it means there is a lack of evidence to guide their clinical care. When pregnant women get sick they end up taking medicines off label. This is not good medical practice and it is not fair. One barrier to including pregnant women in medical research in New Zealand is the lack of research ethics guidance. New Zealand needs specific ethical advice to guide researchers and research ethics committees in ensuring that pregnant women are safely and responsibly included in medical research.

Auckland City Hospital's Ortho-Geriatric Service: an audit of patients aged over 65 with fractured neck of femur

Bodhi Wimalasena, Roger Harris

This is an audit looking at hip fracture care for patients aged over 65 at Auckland City Hospital in 2013. We collected the Minimum Data Set outlined by the Australia New Zealand Hip Fracture Registry which has recently been launched. We have looked at how our data compares to Auckland City Hospital audit data from 2007, as well as established international guidelines for hip fracture care. Emergency department waiting time and the rate of provision of timely surgery have improved since 2007. Deep vein thrombosis prophylaxis coverage and osteoporosis management are areas in need of improvement.

Treatment of uncomplicated cystitis: analysis of prescribing in New Zealand

Natalie J Gauld, Irene SL Zeng, Rosemary B Ikram, Mark G Thomas, Stephen A Buetow

Antibiotic prescribing should follow national guidelines to help limit resistance. We analysed prescribing for women with suspected urinary tract infections in New Zealand. While most prescribers used first-line antibiotics for suspected cystitis without complicating features, the dose or duration prescribed often differed from the BPAC Antibiotics Guide. This provides a useful snapshot of antibiotic use and potential areas for improvement.

Impact of PET-CT scan on management in upper gastrointestinal malignancy

Aditya Sharma, Michael Young

Cancer of the upper gastrointestinal system (oesophagus, stomach, pancreas and bile duct system) is associated with poor prognosis and curative treatments for their diseases are generally not offered if the cancer is advanced and has spread to other areas of body as the treatments come with significant risks. PET-CT scan is a technology that utilises chemical activity of cancer and can detect cancers elsewhere in the body that can be missed on the traditional CT scan. Our study showed that PET-CT scan showed that cancer has already spread in more than 20% of patients when a CT scan has shown that there was no spread of disease. These patients would have traditionally proceeded to have an invasive surgery with poor prognosis.

Incidence and type of bleeding complications early and late after acute coronary syndrome admission in a New Zealand cohort (ANZACS-QI-7)

WB Voss, M Lee, G Devlin, AJ Kerr on behalf of the All New Zealand Acute Coronary Syndromes Quality Improvement (ANZACS-QI) Investigators

Use of blood thinning (anti-thrombotic) drugs prevents further heart attacks and strokes in patients coming to hospital with heart attacks and unstable angina (acute coronary syndromes (ACS)), but these benefits are balanced against the increased risk of bleeding. It would be useful to be able to routinely identify and report these bleeding events to improve patient care. Our aim was to develop a consistent methodology to do this using a combination of All New Zealand Acute Coronary Syndrome Quality Improvement (ANZACS-QI) cohort which records information on heart attack patients across NZ and the routinely collected national datasets which can identify readmissions to hospital with bleeding events. We found that one in ten patients experienced a significant bleeding event, mostly gastrointestinal, within two years. The use of this method for identifying bleeding events in national ACS cohorts will facilitate the study of bleeding event incidence and type over time and between geographical regions, both nationally and internationally, and the impact of changes in anti-thrombotic therapy and interventional practice

Are ethnic inequalities in 30-day ischaemic stroke survival emerging as treatment becomes more effective?

Peter Sandiford, Vanessa Selak, Mazin Ghafel

We report data showing that the chance of surviving a stroke caused by a blood clot is lower for Māori, Pacific and Asian patients compared with Europeans and that the difference for Pacific and Asian has emerged only in the last 10 years. These inequalities have not been noted in previous studies, perhaps because they have not taken into account the differences in age at which different ethnic groups develop stroke. We do not fully understand the reason for these differences but it may be because of changes in the type and severity of the stroke, or alternatively because Europeans are getting better access to the increasing effective urgent treatments for stroke.

Development and initial outcomes of an upper gastrointestinal multi-disciplinary clinic

Anna Brown, Neil Wylie, Michael Rodgers, Jonathan Casement, Neil McIlree, Lindsay Gray, Glenn Mulholland, Vicki Volkova, Erna van der Watt, Michael Booth, Jonathan B Koea

Historically patients needing input from multiple medical services prior to complex upper gastrointestinal surgery (eg removal of the stomach or pancreas) were required to attend multiple different individual outpatient appointments. This slowed their treatment progression and relied on prompt interservice communication. In 2014 Waitemata District Health Board started a single clinic to see complex upper gastrointestinal surgery patients. This clinic includes surgeons, anaesthetists, intensive care specialists, dietitians, social workers, psychologists, nurse specialists and physiotherapists. The results of the clinics first year of function show a high degree of patient and staff satisfaction, improved functioning of the multidisciplinary team looking after patients and a sense that care is more comprehensive. There is improved compliance with Ministry of Health Faster Cancer Treatment targets.

Ethnic inequalities in stroke: improvements not fast enough for everyone

John Fink

The good news for New Zealand Europeans is that ischaemic stroke case fatality rates (CFR) are falling for them. In their study based on analysis of data from the hospital discharge coding National Minimum Dataset and the National Mortality Collection, Peter Sandiford and his colleagues have shown that age-sex standardised 30-day ischaemic stroke CFR for New Zealand Europeans fell from 13.4% in 2000–2004 to 10.7% in 2010–2014.[1] This good news likely reflects the improvements in stroke care in general in New Zealand over the same period. There is overwhelming evidence that stroke unit care significantly reduces death and disability after stroke compared with generic medical care.[2] Over the study period, there has been sustained effort to implement organised stroke unit care in New Zealand. A survey of stroke services in 2007 identified improvements in provision of organised acute inpatient stroke care since 2001, although gaps still remained.[3] The effort to improve the standard and standardisation of stroke care throughout New Zealand continues through regional and national stroke networks, supported by the Ministry of Health.

The news that despite these efforts, case fatality rates have not improved significantly in ethnic groups other than New Zealand European is bad news indeed. Sandiford's study shows clearly that other ethnic groups in New Zealand have a higher ischaemic stroke CFR than do NZ Europeans and that this difference appears to be increasing. While CFR for Māori was at least trending in the right direction over the last decade (down to 16.2% from 18.2%), this improvement was not statistically significant and the rate of any improvement is slower than for Europeans. The CFR for Māori remains significantly worse in absolute terms than for other ethnicities.

Not all the news for ethnic trends in stroke is bad. There are some positive signs of improvement in stroke outcomes from other sources, most notably the Auckland Regional Community Stroke (ARCOS) studies. Thirty-year trends in incidence and outcome of stroke in the Auckland region were published last year.[4] Age-standardised stroke mortality rates, a measure which includes stroke incidence and case-fatality rates, have fallen significantly in the last 30 years across all ethnicities. The positive trend has continued in the most recent ARCOS study period: 2002–3 compared with 2011–12. But the ARCOS data do also show ethnic disparities within these improvements: the 30-year trend for age-standardised stroke incidence is reducing for New Zealand Europeans, but not in other ethnic groups in Auckland (New Zealand European change from 153/100,000/year in 1982 to 122 in 2012, Māori 134 to 156, Pacific 147 to 197).[4]

The age at stroke onset is increasing in most ethnic groups—a good thing—but age remains a glaring indication of the inequalities in stroke in New Zealand: average age at stroke onset in Auckland in 2012 was 75.3 years in New Zealand Europeans (up from 72.2 in 1982), compared with 59.6 in Māori (56.7), 61.6 in Pacific (55.8) and 67.5 (down from 72.1) in Asian/other ethnic groups.

One cannot avoid the conclusion that public health efforts to prevent stroke and in-hospital efforts to treat stroke once it has occurred are showing good benefit for the New Zealand European population, but they don't appear to be working nearly as well, if at all, for others.

Why the disparities? As Sandiford and his colleagues discuss, the major possible

explanations for disparity in CFR could be differences in severity of stroke at presentation, or that there are differences in access to acute hospital stroke services. If non-European New Zealanders present with more severe stroke, this is most likely due to reduced rate of presentation with milder stroke, rather than a major biological difference in stroke type. Failure to diagnose mild stroke is important as it results in a missed opportunity to implement appropriate treatments that might prevent a more severe stroke later. There is a need to increase public awareness of the signs of stroke and the associated need to seek medical attention. If there are differences in access to life-saving acute hospital services, then timeliness of access may be an important factor. If patients present to hospital later after stroke they miss the opportunity for acute stroke treatments, including stroke thrombolysis and thrombectomy. However, while stroke thrombolysis reduces disability, it hasn't been shown to reduce mortality, and thrombectomy wasn't available during the period studied. The other aspects of stroke unit care to avoid complications and provide early rehabilitation may be more important. Regardless, there is a need to increase public awareness of the signs of stroke and the associated need to seek medical attention—fast.

This need to improve public awareness of stroke, its early signs, and the need to seek urgent medical attention, has been recognised by the Ministry of Health, which has funded a public awareness campaign using the "FAST" message (Face-Arm-Speech-Time), currently in progress nationally after an initial successful pilot in the Waikato. I hope that readers are indeed aware of this campaign's existence. But, studies like Sandiford's that show the severity of ethnic differences in stroke outcome in New Zealand mean that more questions need to be asked and we need to be aware that signs of overall improvement do not mean that all are improving. What are the details of geographic and ethnic variation in stroke care access, and what are the barriers that we can target to overcome? Will the "FAST" campaign be effective in raising awareness of stroke for all New Zealanders, or some ethnicities more than others? We need to ask, and answer these questions then act on them—fast.

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Are ethnic inequalities in 30-day ischaemic stroke survival emerging as treatment becomes more effective?

Peter Sandiford, Vanessa Selak, Mazin Ghafel

ABSTRACT

AIM: Studies of ethnic differences in stroke survival have produced inconsistent findings. As treatment becomes more effective, inequalities may increase. We examine time trends in ischaemic stroke case fatality in New Zealand.

METHOD: The 30-day case fatality rate (CFR) of ischaemic stroke in New Zealand was calculated from routinely collected data for two 5-year periods (2000–2004 and 2010–2014) in Māori, Pacific, Asian and European people. A Poisson regression model tested ethnic inequalities between Europeans and people of other ethnicities in each time period.

RESULTS: From 2000–2004 to 2010–2014, the age-sex standardised CFR in Europeans fell from 13.4% (95% CI 13.0 to 13.9%) to 10.7% (10.3 to 11.1%). In Pacific and Asian people, the CFR rose between the two periods, and in Māori there was a drop from 18.2% to 16.2%; neither of these differences were statistically significant. After controlling for socio-demographic variables, service factors and comorbidities, the CFR was higher for Māori than Europeans in 2000–2004, and for all ethnic groups compared with Europeans in 2010–2014.

CFR ethnic inequality rose over that time—the change being statistically significant for Pacific (p=0.033) and Asian (p=0.010), and of borderline significance for Māori (p=0.053).

CONCLUSIONS: Ethnic inequalities in 30-day ischaemic stroke survival have increased significantly in the last 10 years. This may be due to differences in severity at presentation, or in access and utilisation of the increasingly effective acute and hyper-acute stroke interventions.

Ethnic differences in incidence and mortality from ischaemic stroke have been well documented both in New Zealand[1-4] and elsewhere.[5-7] Some of this excess can be explained by a higher prevalence of cerebrovascular risk factors, including obesity, diabetes, and hypertension.[8] There is little evidence, however, that socially-disadvantaged ethnic groups have worse stroke survival or functional outcomes.[9] In the US, case fatality rates (CFRs) for stroke in blacks are similar to those in whites.[10]

The evidence for ethnic differences in stroke survival is mixed and inconclusive for New Zealand. Results from prospective studies conducted in Auckland in 1981–82, 1991–92, 2002–03 and 2011–12 have noted that ethnic-specific 28-day stroke CFRs have declined over time in all ethnic groups.[1] A previous report from the Auckland Regional Community Stroke (ARCOS) studies found that CFRs were similar for Māori, Pacific, and European people, but noted that Māori were the only ethnic group with no significant trend in CFR reduction over time.[11] Other analyses of these studies reported higher CFRs for Māori at 28 days,[12] and at 9 months,[13] but the differences were not statistically significant.

Here we analyse routinely collected data from the whole of New Zealand to

Table 1: Ischaemic stroke mortality outcomes in New Zealand by ethnicity for 2000–2004 and 2010–2014.

	Ethnicity	Deaths	Total strokes	Crude		Age-sex-standardised	
				CFR (95% C.I.)	Rate ratio† (95% C.I.)	CFR (95% C.I.)	Rate ratio† (95% C.I.)
2000–2004	Māori	197	1,462	13.5 (11.7–15.2)	0.91 (0.80–1.04)	18.2 (15.4–21.1)	1.36 (1.13–1.63)
	Pacific	94	852	11.0 (8.9–13.1)	0.75 (0.63–0.88)	14.1 (10.9–17.2)	1.05 (0.83–1.32)
	Asian	45	571	7.9 (5.7–10.1)	0.53 (0.43–0.65)	9.5 (6.6–12.4)	0.71 (0.54–0.92)
	Other+	2,902	19,616	14.8 (14.3–15.3)	-	13.4 (13.0–13.9)	-
2010–2014	Māori	273	2,154	12.7 (11.3–14.1)	1.0 (0.89–1.12)	16.2 (14.0–18.4)	1.51 (1.28–1.79)
	Pacific	131	1,109	11.8 (9.9–13.7)	0.93 (0.79–1.09)	15.2 (12.6–17.9)	1.42 (1.15–1.75)
	Asian	109	1,020	10.7 (8.8–12.6)	0.84 (0.71–0.99)	13.5 (11.1–15.9)	1.26 (1.03–1.53)
	Other+	2,696	21,231	12.7 (12.3–13.1)	-	10.7 (10.3–11.1)	-

CFR=case fatality rate, CI=confidence interval, +'Other' ethnicity is predominately European, †'Other' is the reference for rate ratio calculations

assess the magnitude and trend of ethnic inequalities in the 30-day CFR in two 5-year periods, separated by a gap of 10 years.

Methods

Data from the National Minimum Dataset (NMDS), which records all publicly-funded hospital inpatient events in New Zealand, were linked by anonymised identifier to the National Mortality Collection, which records all deaths in New Zealand. The vast majority of acute hospital inpatient events are included in the NMDS database, and although it may not be perfect, the quality of clinical coding is carefully controlled by regular internal and external audits. Patients were classified into one of four ethnicity groups: Māori; Pacific; Asian; or European/other. Patients were classified by 'prioritised ethnicity' as recorded in their hospital record. This assigns a single ethnicity to individuals who have recorded multiple ethnicities, based on a ranking specified in the national ethnicity standards.[14] Thus, those with Māori as any of their ethnicities are assigned Māori as their prioritised ethnicity. Similarly, those with any Pacific ethnicity code are classed as Pacific, unless they also have a Māori response.

Two 5-year periods were studied: 2000–2004 and 2010–2014, with eligibility based on the date of discharge. The methods for calculating CFR followed that defined by the Organisation for Economic Cooperation and Development (OECD) for the ischaemic patient-based in and out of hospital 30-day CFR.[15,16] Accordingly, the denominator comprises the number of patients in a given year with a primary discharge diagnosis ICD-10 code of I63 or I64 (ischaemic or non-specified stroke). The numerator is the number of patients that died (in hospital, or in the community) within 30 days of their first acute admission with ischaemic stroke in that calendar year. The numerator and denominator were both the sum of the numbers in each individual year in the 5-year period. Patients under 45 were excluded, and the CFRs were standardised by age and sex to the 2010 OECD stroke population, with 95% confidence limits calculated assuming a binomial distribution. Poisson regression analysis was used to examine the extent to which ethnic differences in CFR could be explained by a range of potential confounders, and whether there had been a significant change in ethnic inequalities between the two time periods. Comorbidities

Table 2: Relative risk of death within 30 days of an ischaemic stroke for Māori, Pacific, and Asian, compared with European/Other.

MODEL	Mortality relative risk (95% confidence limits)					
	2000–2004			2010–2014		
	Māori	Pacific	Asian	Māori	Pacific	Asian
Constant only	0.91 (0.80–1.04)	0.75 (0.61–0.91)	0.53 (0.40–0.71)	1.00 (0.89–1.12)	0.93 (0.79–1.10)	0.84 (0.70–1.01)
+ age and sex	1.50 (1.31–1.71)	1.14 (0.94–1.38)	0.74 (0.56–0.99)	1.76 (1.56–1.99)	1.51 (1.29–1.79)	1.20 (1.01–1.43)
+ deprivation	1.45 (1.27–1.67)	1.10 (0.91–1.34)	0.75 (0.56–0.99)	1.63 (1.44–1.84)	1.37 (1.16–1.63)	1.20 (1.00–1.43)
+ hospital, district & weekend admission	1.39 (1.21–1.60)	1.15 (0.95–1.41)	0.77 (0.58–1.02)	1.63 (1.44–1.85)	1.46 (1.23–1.74)	1.23 (1.03–1.48)
+ Elixhauser comorbidities	1.29 (1.12–1.49)	1.14 (0.94–1.39)	0.80 (0.60–1.06)	1.60 (1.41–1.81)	1.49 (1.25–1.77)	1.26 (1.05–1.51)

were controlled for using the Elixhauser comorbidity index, using coded diagnoses from the NMDS.[17] Area deprivation was controlled for using the New Zealand Deprivation Index 2006 data derived from patient domicile codes recorded in the NMDS.[18] Separate Poisson regression models were produced for each of the two periods to calculate the magnitude of ethnic inequality within each. Data from both periods was then combined in a fully parameterised Poisson regression model, controlling for the period, with an interaction term to test for statistical significance of the changes in ethnic inequalities in CFR between 2000–4 and 2010–14.

Results

Table 1 shows the crude and age-sex standardised 30-day case fatality rates for ischaemic stroke by ethnicity. A strong degree of confounding by age and sex is evident, with non-significant crude rate ratios for Māori versus European/Other becoming significant in both time periods when standardised. For Pacific, age-sex standardisation made a significantly lower CFR non-significant in 2000–2004; for the period 2010–2014, a CFR lower than for European/Other became significantly higher after standardisation.

Table 2 presents the results of Poisson regression analyses. Again, confounding by age and sex can be seen which was attenuated somewhat in Māori and Pacific after controlling for area deprivation. Controlling for service-related variables (hospital, District Health Board, and weekend admission) had only a small impact on the relative risks, despite all of these being significantly associated with CFR themselves. Although Elixhauser co-morbidity risk adjustment reduced the relative risks in each period for Māori, they remained statistically significant, and it made little difference to them for Pacific and Asian.

Ethnic inequalities have worsened in the 10 years separating the two cohorts. In 2000–2004, only Māori had a significantly higher CFR than European/Other, but by 2010–2014, all three ethnic groups had higher CFRs. Both absolute and relative inequalities have deteriorated for Māori compared with European/Other. The absolute difference in standardised CFR between Māori and European/Other increased from 4.8% in 2000–2004, to 5.5% during 2010–2014. The interaction term (ethnicity with period) in the full Poisson regression model was significant (p=0.003), and the relative risk changes were individually significant for both Pacific (p=0.033) and Asian (p=0.010), while for Māori the increase was of borderline statistical significance (p=0.053).

Discussion

This retrospective cohort study has documented a significant increase in ethnic inequalities in stroke. These findings are at odds with those recently published from the ARCOS IV study.[1] A plausible reason for this is that the published ARCOS IV 28 day CFRs do not appear to have controlled for age. As table 1 shows, age is a major confounder because it is related to both 30

day survival (younger patients tend to have better survival), and to ethnicity (Māori and Pacific suffer stroke at a younger average age).[1,19] Furthermore, in the ARCOS IV study, younger patients (15–64 years) increased from 52% to 62% of the total in Māori and Pacific between 2002/3 and 2011/12 ($p<0.05$), while the proportion of Europeans in this age group barely changed (21% to 22%, not significant). This significant increase in the proportion of younger Māori and Pacific stroke patients could have concealed the growing ethnic inequality in CFR in an analysis uncontrolled for age. Also, the figures in the ARCOS IV study combine ischaemic stroke with haemorrhagic stroke, which may dilute ethnic inequality if it exists only in the former subtype. The fact that our analysis includes stroke from across the whole of New Zealand, while the ARCOS IV study was confined to the greater Auckland region, is unlikely to explain the discrepancy since we obtained similar results when confining the analysis to Auckland and Waitemata Districts (results not shown).

How do we explain the growing ethnic inequality in ischaemic stroke survival? Two possible explanations warrant consideration: that there are (growing) differences in severity at presentation that could be due either to differences in the type of stroke, or differences in health-seeking behaviour that make non-European ethnicities less likely to present with milder strokes; or that there are ethnic differences in access to and use of the (increasingly) life-saving hospital and/or community services for acute stroke patients.

Growing differences in severity at presentation should first be examined as a possible explanation for the increasing inequalities in stroke survival. If combined with age, severity at presentation accurately predicts survival and functional outcome from stroke.[20] Failure of Māori, Pacific, and Asian people to obtain appropriate treatment in primary care for transient ischaemic attacks of very mild stroke might increase the probability of subsequent more severe stroke. Asians, but not Māori and Pacific people, are less likely to have visited a GP in the preceding 12 months than Europeans, but this statistic does not take into account the higher health needs of Māori and Pacific.[21]

With regard to etiologic risk factors and type of stroke, ARCOS IV data have shown that the pattern of risk factors in stroke patients has changed significantly over time, but to varying extents for the different ethnicities. In 2011/12, compared with 2002/3, there was a substantial increase in the prevalence of smoking, but only among Pacific patients; hypertension prevalence rose in European and Asian patients, but not in Māori or Pacific; a history of myocardial infarction increased by about 50% in Māori, Pacific and Asian patients, but more than doubled in European; the prevalence of diabetes rose in European, Pacific and Asian patients, but fell among Māori; and atrial fibrillation increased significantly in Europeans, but not in other ethnicities. By 2011/12, Māori and Pacific patients had a much higher prevalence of smoking and diabetes, and a lower prevalence of prior myocardial infarction than European patients. There was also a higher prevalence of diabetes in Asian.

Several studies have found short-term survival (1–3 months) to be better or no different in diabetics,[22-26] while others have found it to be significantly worse.[27-30] Similarly, smoking, hypertension, and previous myocardial infarction, have not been consistently associated with either higher severity or worse survival.[23,26,30-32] Atrial fibrillation has more often been significantly associated with higher in-hospital[33] and 30-day CFR,[26,31,32] but in ARCOS IV this risk factor only increased significantly in Europeans from 2002/3 to 2011/12,[1] which would tend to reduce any ethnic disparity in CFR.

The other possibility is that improvements in care have reduced CFRs in Europeans, but not Māori and Pacific, because of differences in access and uptake of these services. Higher levels of health literacy may give Europeans advantages in attaining time-dependent services such as thrombolysis, and they may have shorter travelling times to the hospitals that provide these. Europeans may also have advantages in complying with treatments to avoid life-threatening complications from stroke (eg, fewer language barriers). Post-acute rehabilitative services may not adequately cater to cultural diversity, reducing their potential benefit to non-Europeans. There is evidence of ethnic inequalities in hospital care

generally in New Zealand,[34] although the ARCOS IV study did not identify as significant any ethnic differences in a limited range of indicators of stroke management (admission to a hospital within 28 days of stroke onset, admission to an acute stroke unit, and neuroimaging).[1] Clearly, more in-depth research would be needed to explore the possibility of ethnic disparities in the type and quality of acute stroke care.

The significant decline in CFR documented here in Europeans, but not Māori, Pacific, or Asians, is consistent with the declines reported from Denmark[35] and France.[36] Similarly, the median stroke CFR for 10 OECD countries dropped from 11.65% to 10.35% between 2004/5 and 2010/11.[37] It would seem reasonable to suggest that these declines can be attributed to improvements in quality and access to acute stroke services, such as thrombolysis, neurological imaging, dedicated stroke units, and rehabilitation. Therefore, we should not be surprised to see socioeconomic and ethnic CFR inequalities emerging in other countries where there is variation in access and uptake of these services.

The strengths of this study—a large national sample—are to some extent offset by the limitation of only including patients who were admitted to hospital. Further, we may not have fully controlled for differences in pre-existing patient comorbidity, since the Elixhauser comorbidity index relies entirely on complete hospital documentation and accurate coding.

Based on these findings, we can no longer accept that ethnic-specific CFRs are similar for Europeans, Māori, Pacific, and Asians. Whether this is due to ethnic differences in severity at presentation, the type of stroke and the distribution of prognostic risk factors, or to differences in quality and uptake acute care remains to be elucidated. If it is the latter, then we expect that socioeconomic and ethnic inequalities in ischaemic stroke CFRs will soon emerge in other countries, especially those with disparities in other health outcomes.

Competing interests:
Nil

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Auckland City Hospital's Ortho-Geriatric Service: an audit of patients aged over 65 with fractured neck of femur

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ABSTRACT

AIMS: The aims of this audit were to collect the Minimum Data Set outlined by the Australia New Zealand Hip Fracture Registry (ANZHFR), assess patient characteristics, analyse process of care, and evaluate how this compares to NICE guidelines for hip fracture care, as well as to Auckland Hospital data from 2007.

METHOD: Retrospective case record audit of patients with fractured neck of femur aged 65 years and over admitted under Orthopaedics over a 4-month period in 2013.

RESULTS: Ninety-one patients were audited; mean age was 83 years, 68% were female. Both inpatient and 30-day mortality was 5%. 120-day mortality was 15%. Seventy-six percent of patients were admitted from ED within the national health target prescribed period of 6 hours. Only one patient was treated non-surgically. Eighty-six percent had surgery within 48 hours of admission. Eighty-two percent of patients had rehabilitation and treatment by Older People's Health. Of those living at home pre-fracture, 76% returned home on discharge. Thirty-seven percent of patients were able to walk unaided prior to hip fracture, but only 1% on discharge. Average overall length of stay was 22 days. Bisphosphonates were prescribed for 56% of patients.

CONCLUSIONS: Compared to 2007, Auckland City Hospital has demonstrated a significant improvement in the rate of provision of timely surgery for hip fracture patients. Most patients are receiving the guideline recommended fracture-specific surgical interventions. The assessment and treatment of osteoporosis needs further attention.

Hip fracture incidence is high, with significant associated mortality and morbidity. It was estimated that there were 3,803 hip fractures among New Zealanders in 2007, and the projected number of hip fractures for 2013 and 2020 were 4,535 and 5,350, respectively.[1] Mortality following hip fracture approaches 20–25% at 1 year.[2] Of those who survive for 12 months, only 50% are expected to reach their pre-fracture level of mobility and function.[3] The economic burden of hip fractures is equally significant. The total cost of treating one hip fracture case was estimated to be $23,859 in 2007.[1] Previous studies have reported that 8% of hip fractures result in first-time admission to a long-term residential facility, and this also contributes to the economic burden.[1]

UK hospitals have been auditing hip fracture care in relation to best practice guidelines since 2007 through the National Hip Fracture Database (NHFD). This system has led to observable improvements in outcomes for people with hip fractures. For example, the NHFD has demonstrated a decrease in 30-day mortality from 9.6% in 2008, to 8.9% in 2013.[4] Australia and New Zealand have decided to adopt a similar approach through the Australia New Zealand Hip Fracture Registry (ANZHFR) with the view of developing local standards of care and ensuring an ongoing centralised audit process to evaluate quality of hip fracture care. The Minimum Date Set (MDS) for ANZHFR first version was available in December 2012. The ANZHFR website was launched in 2014, and the New Zealand Hip Fracture Registry is currently being piloted in the Northern Region District Health Boards (DHBs).

A number of guidelines of best practice in hip fracture care have been developed. The timely delivery of definitive treatment to hip fracture patients is one key quality standard of interest. The National Institute for Health and Care Excellence (NICE) guidelines and standards of care state that people with hip fracture should have surgery on the day of, or the day after, admission.[5] The ANZ guideline makes a similar recommendation. The orthopaedic department at Auckland Hospital has made a continued effort to try and reduce waiting times for surgery over the years. There are also standards of care with regards to the type of hip fracture repair surgery that should be performed depending on the type of hip fracture.

There has also been a significant focus on reducing waiting times in Emergency Department (ED) at Auckland Hospital. This is related to one of the six national health targets since 1 July 2009, that 95% of patients will be admitted, discharged or transferred from an ED within 6 hours. One would expect that hip fracture patients in particular would be a priority group in terms of the emergency department assessment and care pathways. One of the aims of this audit was to see if and how the 'Shorter Stays in ED' policy had affected the ED waiting times for hip fracture patients in particular.

Treatment of underlying osteoporosis with vitamin D and bisphosphonate therapy has been shown to reduce future fracture risk.[6] Hence, we would expect both some admissions and most discharges to be on bone protection medications. However, studies to date show that prescription rates for bisphosphonates is lower than expected.[7,8]

A shared care approach between the orthopaedic surgeons and geriatricians for patients with hip fracture is being increasingly utilised in medical institutions. The aims of such an integrated approach is to optimise pre-operative medical assessment, perioperative patient care and ensure that there are comprehensive falls and bone health assessments. There is data supporting this shared care approach with positive outcomes with regards to traditional outcomes, such as in-patient and 1-year mortality, and length of stay.[9] However, presently there is a lack of data with regards to other practical outcomes, such as functional recovery and quality of life.

At Auckland City Hospital, Orthopaedic patients aged 65 and over receive medical input from a geriatrician or Older People's Health (OPH) registrar by way of twice-weekly ward rounds, and they also attend weekly Ortho-Geriatric Interdisciplinary Team Meetings. In 2006 a new initiative was introduced, where selected hip fracture patients are 'fast-tracked' to one particular OPH ward as soon as possible post-operatively. There are four acute-funded beds in one OPH ward, and when a bed is empty this allows another patient to be taken over. The decision to 'fast-track' is initiated by the charge nurse of the OPH ward receiving the patient, when a bed is available. Those not 'fast-tracked' can still be placed on the OPH waiting list for rehabilitation as appropriate.

One of the recommendations in the NICE guideline is that patients are operated with the aim of allowing them to fully weight-bear in the immediate post-operative period. The Interim Care Scheme will be mentioned in this audit. This is an initiative that allows those patients that are deemed to require a period of non-weight-bearing after an orthopaedic injury to be cared for at a private hospital (high-level residential care facility) until their orthopaedic surgeon allows them to weight-bear. They usually return to Auckland City Hospital for rehabilitation under Older Peoples Health, although some receive rehabilitation in the community.

One of the aims of this audit was to assess the baseline characteristics of hip fracture patients, including their demographics and baseline functional and cognitive levels. We were interested in looking at process and outcome measures, and compared this information with previous data from Auckland Hospital, an audit performed in 2007. This allowed us to evaluate how our local practice has progressed over the last 6 years. Another aim of this audit was to compare our local practice with the global standards of care and try and identify areas in need of improvement.

Methods

A retrospective case notes audit was undertaken of all patients aged 65 and over with hip fracture admitted under the Orthopaedic service at Auckland City Hospital over a 4-month period from 12 January to

Table 1: American Society of Anaesthesiology (ASA) scores of hip fracture patients.

ASA score	Number	Percentage
1	3	3%
2	14	16%
3	56	62%
4	17	19%
5	0	0
Total	90*	100%

*1 person did not have an operation

Table 2: Analysis of bisphosphonate use on admission.

	Previous fragility fracture or other indication for bisphosphonate		
On bisphosphonate	Yes	No	Total
Yes	17	0	17 (19%)
No	17	57	74
Total	34	57	91 (100%)

25 May, 2013. The audit was restricted to this time period to ensure it was achievable as an advanced trainee project. Patients were identified at the weekly Ortho-Geriatric Interdisciplinary meeting and by the Orthopaedic ward and 'fast-track OPH ward' charge nurses and house officers. A diagnosis-related group (DRG) code based search for hip fracture events was also performed to ensure there was complete coverage.

A data collection form was designed to collect the required patient information. This was in accordance with the Minimum Data Set (MDS) outlined in the ANZHFR data collection form. Clinical notes and electronic records were reviewed manually by the principal investigator. Data was entered into a secure Microsoft Excel spreadsheet. The data was analysed and compared to the data from the Auckland City Hospital hip fracture audit from 2007.

It was confirmed that this study did not require HDEC (Health and Disability Ethics Committee) review.

Results

Group demographics

Ninety-one patients aged 65 and over were admitted with a hip fracture during the 4-month audit period. The median age was 85 years (range 65–97), which was the same as for the 2007 audit. There were 62 women (68%) and 29 men (32%). The mean age for male patients was 82 and for females was 84 years.

Clinical characteristics

ASA scores

The American Society of Anaesthesiology physical status classification (ASA) score prior to injury was recorded. Fifty-six patients (62%) were classified as ASA 3, indicating severe systemic disturbance which is not incapacitating or acutely life-threatening (Table 1). Of all the patients, 81% had significant medical co-morbidities (ASA ≥3). The 2007 audit showed a similar distribution of ASA scores.

Pre-operative cognitive status

Data on pre-operative cognition was collected from the admission notes, as well as previous clinical documentation (eg, clinical letters, discharge summaries). At least 54% of patients had impaired cognition or dementia on admission. This information was not collected in the 2007 audit.

Bone protection on admission

Table 2 summarises bisphosphonate use on admission. Nineteen percent of patients were on a bisphosphonate on admission. Of those who had a previous fragility fracture or other indication for bisphosphonate use, 17 (50%) were not on a bisphosphonate on admission.

Fracture characteristics

Table 3 summarises the anatomical distribution of hip fractures versus the type of surgical intervention performed.

The NICE guidelines for hip fracture care has an evidence-based recommendation to perform replacement arthroplasty (hemiarthroplasty or total hip replacement) in patients with a displaced intra-capsular fracture. All patients with a displaced intra-capsular fracture in our audit went on to have the recommended surgery.

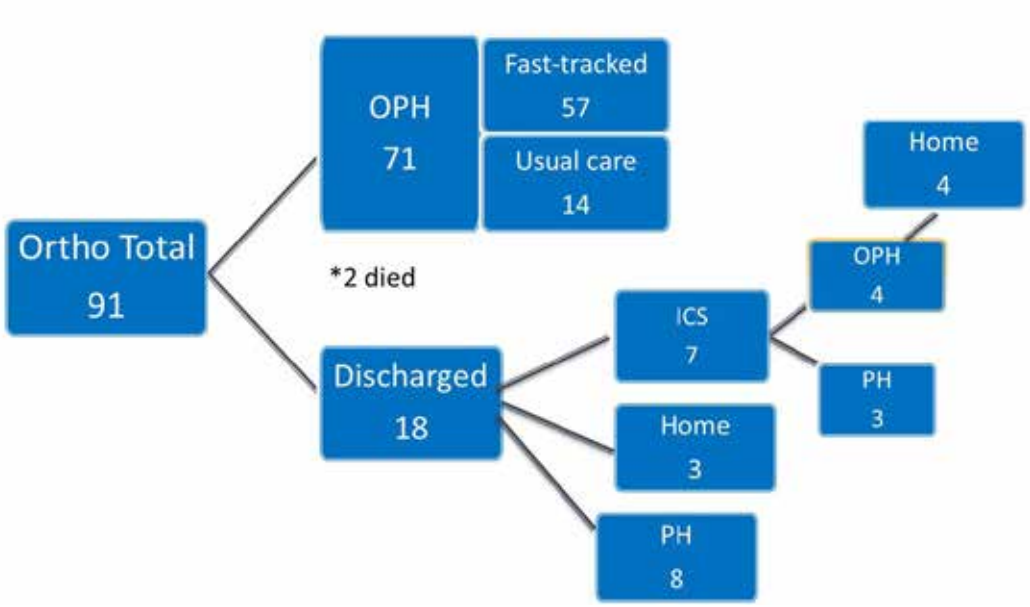
The NICE guideline recommends the use of extra-medullary implants, such as a sliding hip screw, in preference to an intramedullary nail in patients with trochanteric

Table 3: Anatomical distribution of hip fractures and types of surgical intervention.

	Type of surgery						
Type of fracture	**Cannulated screw**	**Dynamic hip screw**	**IM nails -long**	**Hemi-arthroplasty -cemented**	**Total hip joint replacement - cemented**	**Other**	**Total**
Intracapsular -undisplaced	1	15		2		1	19
Intracapsular -displaced				37	5		42
Extra-capsular -intertrochanteric		15	8	1			24
Extracapsular -subtrochanteric			5				5
Total	1	30	13	40	5	1	90*

* One person did not have an operation.

Figure 1: Pathways of care.



fractures above and including the lesser trochanter. Fifteen of 24 (63%) patients with per/intertrochanteric fractures had the recommended surgery.

There is an evidence-based recommendation for the use of intramedullary (IM) nails to treat patients with a sub-trochanteric fracture. All 5 of the patients with this type of fracture underwent IM nail surgery.

Type of anaesthesia

General anaesthesia was used in 72% of patients, and spinal anaesthesia was used in 28% of patients.

Pathways of care

Figure 1 summarises the pathways of care for the patients in this audit.

Ninety-one patients were included in this audit. Seventy-one (78%) patients were transferred from the orthopaedic ward to the Older Peoples Health ward after surgery. Out of these 71 patients, 57 (80%) were 'fast-tracked', while the remaining 14 were placed on an OPH waiting list and went through the 'usual care' process. The average time taken to be placed on the wait list was 4 days, and patients spent an average of 3 days on the wait list. Eleven patients were discharged directly from Orthopaedics (3 to home and 8 to private hospital). Two patients died while under the care of Orthopaedics. Seven patients went from Orthopaedics to the interim care scheme, and four later returned to have rehabilitation under Older Peoples Health. Therefore, a total of 75 (82%) of the audited group had rehabilitation and treatment by Older Peoples Health. The 2007 audit showed that 84% of patients received rehabilitation under Older Peoples Health.

Table 4: Time spent in ED.

	2007 (n=113)	2013 (n=88)
% that spent <6 hours in ED	27%	76%
Average time in ED	10.3 hours	6.4 hours *
Median time in ED	8.1 hours	5.6 hours

*There was a significant difference in the average time in ED for 2007 versus 2013 (p<0.0001).

Table 5: Time from admission to surgery.

	Time from admission to surgery		
	<24 hours	<36 hours	<48 hours
Patients who received surgery (n)	49	70	77
% of total (90*)	54%	78%	86%
Patients who did not receive surgery within the time frame (n)	41	20	13
Reasons for surgery delay	**n (%)**	**n (%)**	**n (%)**
Medically unfit	20 (49%)	12 (60%)	8 (62%)
Awaiting orthopaedic diagnosis	5 (12%)	4 (20%)	4 (31%)
Awaiting theatre availability	16 (39%)	4 (20%)	1 (7%)

*One patient was managed non-surgically

Process of care measures

Time from fracture to admission

Apart from 7 patients, all presented to hospital within 48 hours of injury. Out of these 7 patients, 4 were living alone, 1 was living at home with others and 2 were from residential care. One patient sustained her injury as far back as 6 months prior. Of the 7 patients, 3 were stated to have normal cognition, 2 had dementia, 1 had cognitive impairment and 1 had unknown state of cognition.

Time in ED

The majority of patients (97%) were admitted via the ED, while the remaining 3% came through the Admission and Planning Unit (APU). One of the 6 national health targets introduced 1 July 2009, shorter stays in emergency departments, is defined as "95% of patients will be admitted, discharged or transferred from an emergency department within 6 hours". We compared the time spent in ED in our audited group for 2013 with the data from 2007 (Table 4).[10]

Orthopaedic consultant presence during surgery

According to the theatre records, the orthopaedic consultant was present in theatre for 17% of cases. This may be an under-representation of the actual level of consultant supervision due to the fact that the consultants may have attended partway through some of the cases, leading to the omission of their names from the theatre records at times.

Time to surgery

Table 5 summarises data regarding time from admission to surgery based on commonly used time criteria. It also summarises the main reasons for delay.

Reasons for delay to surgery at 24 hours were both medical and theatre availability. At 48 hours, medical reasons predominated and most of them were cardiac issues

The 2007 audit showed that 24% of patients received surgery within 24 hours of admission, and 59% of patients received surgery within 48 hours of admission.

Medical assessments

Thirty-eight patients (42%) had a medical review pre-operatively from one or more of the following services: anaesthetics; older people's health; cardiology; and/or general medicine. A medical review was considered to be an assessment by anyone other than the orthopaedic house officer or registrar. Fifteen patients (16%) were reviewed pre-operatively by a geriatrician/registrar. A total of 21 patients had a pre-operative anaesthetic review.

Table 6: Length of stay (average days).

Orthopaedic discharge destination	Number of patients	Average Length of stay (LOS) (days)			
		Orthopaedic ward	OPH ward	ICS	Total
Home direct-alone	1	5.6	-	-	5.6
Home direct-with others	2	3.5	-	-	3.5
Residential care -direct	8	12.3	-	-	12.3
OPH-fast-tracked	57	2.7	20.8	-	23.8
OPH-not fast-tracked	14	9.0	17.0	-	26.2
Average for all above groups					22.0
Interim care scheme	7	13.0	30.5 (n=4)	32.9	63.5

Ninety-eight percent were seen by a geriatric medicine consultant or registrar at some point during their admission. The average time taken to be seen by geriatric medicine from the time of admission was 2 days.

Length of stay (LOS)

The average length of stay is summarised in Table 6. Patients have been sub-grouped into those who were discharged directly from the orthopaedic ward, those who were fast-tracked to OPH, those who went to OPH through the wait-list and those who went to interim care.

Three patients were discharged home directly from the orthopaedic ward. These were all patients who had sustained un-displaced intra-capsular fractures and were treated with DHS. Patients who were from a private hospital returned when deemed medically stable.

In terms of the patients transferred to OPH, there was a small difference in LOS between the fast-tracked group and the others. The average total LOS, excluding the interim care patients, was 22.0 days, compared to 28.1 days in the 2007 audit. In terms of the patients who went onto the Interim Care Scheme, it took approximately 9 weeks before they were re-settled.

Outcome measures

Mortality

There were 5 inpatient deaths (5%), 2 in the Orthopaedic ward and 3 in the Older Peoples Health ward. 30-day mortality was 5%. 120-day mortality was 15%. The inpatient mortality for the 2007 audit was 5% as well.

Complications

Table 7 shows the main post-operative complications. Fifty percent of patients had more than one complication. The rate of diagnosis of delirium was similar to the audit in 2007, where 23% of patients were documented to have delirium.[10] In this audit, of the 38 patients who were noted to have normal cognition on admission, two developed post-operative delirium.

Living situation

Table 8 shows the living situation of hip fracture patients on admission and at discharge.

Prior to admission, 56% of patients were living at home, and 76% of this group were able to return home on discharge. Of the whole group, 10% went into residential care for the first time. Of the 25 patients originally living in rest homes, 72% were discharged to private hospital after their hip fracture. In comparison, the 2007 audit showed that 61% of

Table 7: Complications.

Complication	Percentage
Delirium	22%
Urinary tract infection	22%
Anaemia	21%
Perioperative hypotension	21%
Pneumonia/LRTI	16%
Electrolyte disturbance	13%
Constipation	10%
Arrhythmia	10%
Heart failure	9%
Worsening renal function	9%
Urine retention/incontinence	9%

Table 8: Living situation on admission and on discharge following hip fracture.

Living situation on admission (number patients)		Living situation on discharge (number patients)			
		Home	Rest Home	Private Hospital	Deceased
Home	51 (56%)	39 (76%)	2	7	3
RH	25	-	5 (20%)	18 (72%)	2
PH	15	-	-	15	-
Total	91	39	7	40	5 (5%)

Table 9: Walking aids on admission and on discharge.

Walking aid	Admission	Discharge
No aids	32 (37%)	1 (1%)
1 aid	11 (13%)	3 (3%)
2 aids/frame	38 (44%)	67 (78%)
Wheelchair	3 (3%)	1 (1%)
Bed-bound	-	14 (16%)
Not known	2 (2%)	
Total	86*	86*

*Excluded deceased patients

Table 10: DVT prophylaxis measures.

DVT prophylaxis	Number	Percentage
None	14	15%
Pre-op aspirin continued	28	31%
Aspirin (new)	11	12%
Enoxaparin	52	57%
Warfarin	2	2%
Foot pumps	21	23%

patients were living at home prior to admission, and 70% of this group were able to return home on discharge.

Mobility

Table 9 shows patients' requirements for walking aids before hip fracture and on discharge.

There is a significant reduction in independent mobility at discharge. The numbers requiring a frame on discharge almost doubles, and 16% are bed-bound on discharge. The 2007 audit showed that 44% of patients were able to mobilise unaided prior to admission, but only 1% were able to mobilise unaided on discharge.

Post-operative weight-bearing status

Patients are encouraged to weight-bear as soon as able after surgery. In this audit, 90% of patients were allowed to fully weight-bear, but 10% of patients were recommended restricted weight-bearing by the orthopaedic teams.

Prescriptions for prevention

DVT prophylaxis

Table 10 summarises the DVT prophylaxis measures taken. A variety of measures were used for DVT prophylaxis, and 35% of patients received more than one type of prophylaxis measure. However, according to the clinical records, 15% of patients did not receive any form of DVT prophylaxis.

Osteoporosis management

Table 11 shows that a bisphosphonate was started or continued in 56% of patients. The 2007 audit showed that 63% of patients were on a bisphosphonate on discharge. Our audit showed that intravenous bisphosphonates were more commonly prescribed than oral bisphosphonates. Intravenous bisphosphonate usage is likely to be higher than in 2007, though this specific data was not collected in the 2007 audit. There was no assessment/explanation given for the omission of bisphosphonates in 20% of patients. An explanation was given for 24% of patients, and the most common reasons for bisphosphonates being withheld were clinical context (52%), renal impairment (24%) and patient declination (19%).

Comparison of 'fast-tracked' with 'usual care' patients

Seventy-one patients were transferred from the orthopaedic ward to the Older

Table 11: Osteoporosis management.

Osteoporosis management plan	Number	Percentage
Bisphosphonate started/continued	48	56%
Oral bisphosphonate	11	13%
IV bisphosphonate	37	43%
Explanation for no bisphosphonate	21	24%
No assessment /explanation	17	20%
Total	86	100%

*Note: Excluded deceased patients

Table 12: Comparison of home versus residential care.

	Usual residence		
	Home (n=51)	**Residential care (n=40)**	**Total (n=91)**
Age (mean years)	82	85	83
Gender (% women)	75%	60%	68%
Walking aid on admission*			
No aids 1 aid 2 aids/frame Wheel-chair Not known	58% 10% 29% 0% 2%	11% 16% 63% 8% 3%	37% 13% 44% 3% 2%
ASA Score			
ASA score 1 ASA score 2 ASA score 3 ASA score 4	6% 25% 57% 12%	0% 3% 69% 28%	3% 16% 62% 19%
Pre-operative cognitive status			
Normal Impaired Dementia Not known	69% 20% 8% 4%	8% 18% 70% 4%	42% 19% 35% 4%
Time spent in ED (average)	6 hrs 19 mins	6 hrs 46 mins	6 hrs 31 mins
% surgery <24 hours from admission	51%	58%	54%
Post-op weight-bearing status			
Full weight-bearing Restricted	86% 14%	95% 5%	90% 10%
Total LOS (days)	23.0	19.2	21.3
Walking aid on discharge*			
No aids 1 aid 2 aids/frame Wheel-chair Bed-bound	2% 6% 90% 0% 2%	0% 0% 63% 3% 34%	1% 3% 78% 1% 16%
Mortality	3 (6%)	2 (5%)	5 (5%)

*Excluding deceased patients

Table 13: Comparative data—Auckland City Hospital.

Patients ≥65 years with hip fracture	2007 (n=115)	2013 (n=91)
Living at home pre-fracture %	61	56
Transfer to OPH %	84	82
Mean wait time for OPH (days)	1	2
Mean LOS Orthopaedics (days)	9	5
Mean LOS total (days)	28	22
Mean waiting time in ED	20hrs 40mins	6hrs 31 mins
% Surgery <24 hours from admission	24	54
% Surgery <48 hours from admission	59	86
Home returning home %	70	76

Peoples Health ward after surgery. Of these 71 patients, 57 (80%) were fast-tracked, as opposed to going through the usual wait list process. Given the small numbers of patients, a valid comparison between the two groups could not be made. The 2007 audit showed that of all the patients transferred from the orthopaedic ward to the Older Peoples Health ward, 43% were fast-tracked.

Comparison of patients admitted from home versus residential care

Table 12 shows the baseline characteristics, process of care measures and outcome measures for patients admitted from home versus residential care. This shows that the group from residential care tended to be more dependent for their mobility and were more likely to have some compromise of their physical, as well as cognitive, status. The percentage that received surgery within 24 hours for the two groups was similar and potentially shows that there was no bias in their treatment.

Comparative data for the 2007 and 2013 audits at Auckland City Hospital

Table 13 summarises the findings from the 2007 audit and the current 2013 audit.

Discussion

This audit of hip fracture care at Auckland City Hospital was conducted around the time of the launch of the ANZHFR, and this provides much of the backbone to the data collection, as well as the forthcoming discussion. The initiation of the ANZHFR marks an exciting, and hopefully constructive, time ahead in our ventures to improve hip fracture care for patients in this region. Having a centralised audit process is expected to illuminate areas in need of improvement, thus encouraging hospitals to strive for best practise care for this vulnerable group of patients.

The Auckland City Hospital 2007 audit provided a valuable set of data for comparison. We noted that in 2007, only 24% of patients were undergoing surgery within 24 hours of admission. Lack of operating resources was noted to be a significant contributor at the time. It was postulated that changes in operating theatre access as a result of completion of the new Auckland City Hospital in late 2003 lead to increased delays for older patients with hip fractures.[10] It is reassuring to see that the proportion receiving surgery within 24 hours of admission has recovered (54% in this audit).

There has been ongoing debate regarding what is actually the most reasonable time frame to aim for in hip fracture surgery. Observational studies have suggested that operative delay beyond 48 hours after admission may increase the odds of 30-day all-cause mortality by 41%, and of one-year all-cause mortality by 32%.[11] However, there is also evidence that mortality is increased with night-time emergency treatment.[12] It is understood that surgery may need to be delayed to treat and stabilise certain medical conditions in our older population. Hence a time frame of 48 hours appears within reason, and this is what the ANZ guideline has decided on as well.

The UK NHFD is a well-established hip fracture registry, and it has noted improvements in a variety of hip fracture care measures and patient outcomes over the

years. The NHFD 2013 report quoted 86% of patients received operative management within 48 hours. It was reassuring to see the percentage receiving surgery within 48 hours at Auckland City Hospital is comparable to this.

This study showed that a high proportion of patients (82%) are transferred to OPH for rehabilitation, and this is similar to 2007. The mean length of hospital stay at Auckland City Hospital appears to have reduced since 2007 (from 28 days to 22 days). The NHFD 2013 report notes a mean LOS of 20 days. It is difficult to comment on what an optimal LOS is, as it would involve a fine balance between the significant costs involved with hospital stays and the potential to achieve some functional recovery, and the avoidance of a move into residential care for those living at home prior to the fracture. In this audited population, 10% moved into residential care for the first time, which is similar to the rates reported in previous studies.[1] Overall, 30% of patients went to a higher level of care on discharge. Rest home residents in particular appeared to make a relatively poor recovery, with 72% being discharged to private hospital level of care. This may be explained by the increasing dependency levels of people in residential care in the Auckland region.[13]

It was noted that the rate of fast-tracking is higher than in 2007. In 2007, 43% of patients were fast-tracked, whereas the current data shows that 80% were fast-tracked. The small numbers of patients in this audit made it difficult to compare outcomes for the fast-tracked patients versus the non-fast-tracked patients.

In terms of the baseline features of our patient population, we note that the age and gender distribution was in keeping with other publications. Inpatient mortality was 5%, which was the same as in 2007. The 30-day mortality was 5% in this audit. The NHFD 2013 report noted a case mixed adjusted 30-day mortality of 8.2%.

Times spent in ED have significantly improved since 2007, and the introduction of the national health target of 'Shorter Stays in ED' in 2009 likely contributed to this change. There has been a nation-wide focus on this target. However, this audit shows that with regards to the hip fracture patients at least, we are still not meeting the national health target. This highlights the problem that hip fractures are not yet being treated as an 'emergency' in the ED. We know that the ED protocols/pathways for ST elevation myocardial infarctions (STEMI) and acute stroke have led to positive changes in the form of timely assessment and treatment of these serious health-care problems. We would postulate that developing a similar ED-based protocol/pathway for hip fracture patients at Auckland City Hospital could lead to better outcomes for this group of vulnerable patients as well.

There is a strong evidence base behind the institution of secondary prophylaxis measures for osteoporotic fractures, such as hip fractures. Bisphosphonates and vitamin D are currently the mainstays of bone protection therapy in New Zealand. Bisphosphonates are much more accessible now as PHARMAC currently allows funding for alendronate and zoledronic acid for any patient with a history of at least one fragility fracture and age of over 75. Dual energy x-ray densitometry (DEXA) scans are also much more accessible nowadays. In this audit, 56% of patients were prescribed a bisphosphonate on discharge after their hip fracture. The NHFD 2013 report noted a bisphosphonate prescription rate of 69%. One of the main concerns raised in this audit is that 20% of patients did not appear to have any assessment with regards to osteoporosis management. This may be partly explained by a lack of clinical documentation around this topic. For instance, osteoporosis management may have been addressed on a ward round but not been documented in the clinical notes by the junior staff. Therefore, we would recommend that the junior staff are educated in the importance of documentation of osteoporosis management in the clinical notes, as well as in the discharge summaries. It is also possible that these patients did not receive any assessment at all, which is concerning. Protocols have been shown to be effective in improving bone protection prescribing,[14] and another strategy could include a discharge check-list. These are potential interventions we would consider introducing at Auckland City Hospital to try and improve bone protection assessments.

In this audit, 10% of patients were prescribed restricted weight-bearing and arguably this is still too may. The aim should be that everyone can fully weight-bear in the immediate post-operative period. We also note that patients who go onto the Interim Care Scheme inevitably have a very prolonged recovery process, and it can take up to an average of 9 weeks before they know where they stand in terms of their mobility, functional status and living situation. The sharing of this data with the orthopaedic department will hopefully lead to some positive changes with regards to the surgical treatment and the post-operative weight-bearing status prescription.

There is a lack of evidence to help determine the optimal anaesthetic technique for hip fracture surgery. However, guidelines generally advocate for greater use of regional anaesthesia, as opposed to general anaesthesia.[15,16] Spinal anaesthesia was utilised in 28% of this cohort. The NHFD 2013 report noted that 47% of patients had spinal anaesthesia. Sharing our data with the orthopaedic and anaesthetic departments will hopefully lead to a review around this topic, and perhaps we will see more spinal anaesthesia being used in the future.

Auckland City Hospital orthopaedic department has a DVT prophylaxis policy. The NICE and ANZ guidelines do not include DVT prophylaxis recommendations, and they defer to other comprehensive guidelines. The Auckland City Hospital guideline summarises the guideline recommendations and defers to surgeon interpretation, and the decision to be made on a case-by-case basis. According to this audit, 15% of patients did not receive any form of DVT prophylaxis, and this is worth looking at closely alongside the orthopaedic department.

Conclusion

There have been some notable improvements in hip fracture care at Auckland City Hospital since 2007. ED waiting times are significantly better, though we are still not meeting the national health target. Also, the drop in the number receiving early surgery in 2007 appears to have recovered. The current rate of provision of early surgery at Auckland City Hospital compares well with hospitals in the UK. There has been a reduction in LOS at Auckland City Hospital since 2007. There is a growing demand for rehabilitation services, with 82% of hip fracture patients requiring a period of time on the rehabilitation ward.

There are certainly several areas in need of improvement. We would like to aim for having fewer patients with restricted post-operative weight-bearing status. DVT prophylaxis coverage, as well as osteoporosis management, need to be looked at as well.

There is obviously significant room for improvement in terms of hip fracture care at a national level. The ANZHFR will allow benchmarking within New Zealand, and with Australia and the UK. This will increase the attention and priority given to this vulnerable group of patients. The NHFD has shown improvements over the years, and we would hope for similar outcomes in Australia and New Zealand once the ANZHFR is established.

Competing interests:
Nil

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Incidence and type of bleeding complications early and late after acute coronary syndrome admission in a New Zealand cohort (ANZACS-QI-7)

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ABSTRACT

AIMS: Use of anti-thrombotic agents has reduced ischaemic events in acute coronary syndromes (ACS), but can increase the risk of bleeding. Identifying bleeding events using a consistent methodology from routinely collected national datasets would be useful. Our aims were to describe the incidence and types of bleeding in-hospital and post-discharge in the All New Zealand Acute Coronary Syndrome Quality Improvement (ANZACS-QI) cohort.

METHODS: 3,666 consecutive patients admitted with ACS (2007–2010) were identified within the ANZACS-QI registry. A set of International Classification of Disease 10 (ICD-10) codes that identified bleeding events was developed. Anonymised linkage to national mortality and hospitalisation datasets was used to identify these bleeding events at the index admission and post-discharge.

RESULTS: Three hundred and ninety-nine (10.8%) out of 3,666 patients had at least one bleeding event during a mean follow-up of 1.94 years. One hundred and sixty-one (4.4%) had a bleeding event during their index admission, and 271 (7.4%) patients were re-hospitalised with bleeding during follow-up. Sixty-one patients (37.9%) were transfused for bleeding in the index admission cohort, and 59 patients (21.8%) at a subsequent admission. Procedural bleeding was the most common event during the index admission, whereas gastrointestinal bleeding was the most common delayed bleeding presentation.

CONCLUSION: One in ten ACS patients experienced a significant bleeding event within 2 years. The use of this ICD-10 bleeding definition in national ACS cohorts will facilitate the study of bleeding event incidence and type over time and between geographical regions, both nationally and internationally, and the impact of changes in anti-thrombotic therapy and interventional practice.

The use of antithrombotic and antiplatelet agents in conjunction with an early invasive strategy has improved ischaemic outcomes in patients presenting with acute coronary syndromes (ACS). However, the paradox of treatment lies in the increased risk of bleeding. Bleeding events and need for blood transfusion are independent predictors of mortality and adverse outcomes in ACS patients.[1-5] Minimisation of bleeding events is, therefore, an important therapeutic target.

The All New Zealand Acute Coronary Syndrome Quality Improvement (ANZACS-QI) registry captures data in all New Zealand patients with ACS undergoing revascularisation by percutaneous coronary intervention (PCI) and/or coronary artery bypass grafting (CABG). The outcomes of patients in this registry are tracked by using anonymised linkage to national datasets. With its national implementation, there is an opportunity to better understand and track the incidence of bleeding after ACS in a large contemporary cohort.

Several bleeding scores have been developed to define bleeding events in the clinical trial setting.[6-8] While these scores provide the most definitive approach to identification of bleeding events, they may be less reliable in a national registry where clinical users rather than dedicated research staff are entering data. Furthermore, to obtain information about post-discharge events requires costly and time-consuming individual patient follow-up. An alternative approach is to track bleeding events using ICD-10 codes. This methodology has been used and reported in other international studies, such as in a Danish ACS cohort.[9] In New Zealand, ICD-10 codes are recorded in national datasets using standardised definitions for every public hospital admission.

This study aims to describe the incidence and types of bleeding in-hospital and post-discharge in the ANZACS-QI cohort using ICD-10 codes.

Methods

Cohort and data collection

Consecutive patients from Middlemore, Taranaki Base and Waikato Hospitals admitted with an ACS between 2007 and 2010 were included. Data was prospectively collected and electronically recorded in the ANZACS-QI registry (formerly known as Acute PREDICT) by trained clinical staff. The ANZACS-QI registry is a web-based electronic database which captures a mandatory in-hospital dataset in ACS patients which includes patient demographics, admission ACS risk stratification using the GRACE score, cardiovascular risk factors, investigations, management, inpatient outcomes and medications at discharge.

Details of data collected have previously been reported.[10,11] Some risk factor data is incomplete as it was non-mandatory (haemoglobin, white cell count), or was sourced from the paired Cardiovascular Disease and Diabetes Mellitus (CVDDM) Predict dataset collected predominantly at Middlemore Hospital (LDL cholesterol, BMI). History of congestive heart failure prior to the index acute event was not collected in the ANZACS-QI registry, but was identified from the national hospitalisation data sets using the relevant ICD-10 codes (I110, I130, I132, I500, I501, I509). History of prior bleeding was similarly identified using the ICD-10 bleeding code set developed for this study and described below.

All New Zealander's have a unique National Health Identifier (NHI) number. We used an encrypted version of the NHI to anonymously link in-hospital ANZACS-QI patient records to subsequent outcomes captured in national public hospitalisation and mortality datasets. The encryption and linkage methodology has been described previously.[10] Ethics approval was obtained from the National Multi Region Ethics Committee (MEC/07/19/EXP).

Identification of bleeding events

Bleeding events were identified using the World Health Organization (WHO) ICD-10 codes. Relevant ICD-10 code sets used by other investigators to identify bleeding events were reviewed.[9,12-14] The process followed to derive the final set of bleeding codes is shown in Figure 1.

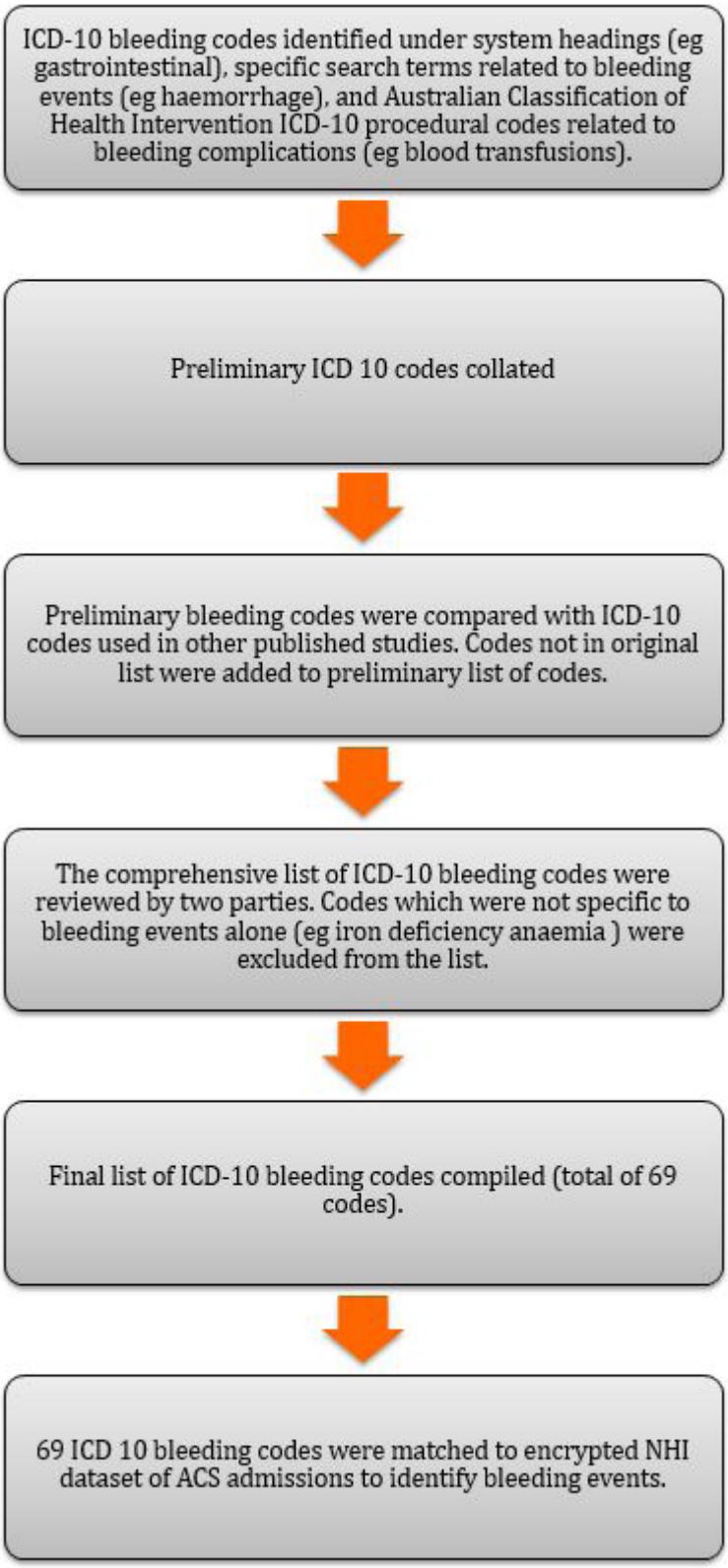
A total of 69 ICD-10 bleeding codes were selected for this study. (Appendix 1)

The encrypted linkage to national mortality and hospitalisation data sets was then used to identify patients with ICD-10 bleeding codes at the index ACS admission and after discharge. These codes were divided into bleeding sub-types: procedure related (PCI or CABG); gastrointestinal; respiratory; intra-cranial; intra-ocular; urogenital; and other. Bleeds were also divided into those associated with a fatal or a non-fatal outcome. A fatal bleeding-related outcome was any death within 28 days of admission in a patient with at least one bleeding code for that admission. Those patients with multiple bleeding codes during their index and or in subsequent hospital admissions were individually adjudicated. In these cases, the bleeding codes were prioritised and only the most serious one was reported. The prioritisation hierarchy was as follows: fatal bleed; intracerebral bleed; bleed requiring transfusion; gastrointestinal bleed; and other cause. Transfusion was only counted as a complication if it was paired with a bleeding event code.

Statistical analysis

Descriptive statistics for continuous variables were summarised as mean with

Figure 1: Process followed to derive the final set of bleeding codes.



standard deviation, and median with interquartile range. Categorical data were reported by frequency and percentage. For continuous variables, comparisons between groups were performed by the non-parametric Mann-Whitney U test due to all data being non-normally distributed. For categorical variables, the Chi-squared test or Fisher's exact test were used where appropriate. All p-values reported were two-tailed. A p-value <0.05 was considered significant. Data was analysed using SAS statistical package, version 9.4 (SAS Institute, Cary, NC).

Table 1: Cohort demographics and risk factors.

Variables	All (n=3,666)
Age (years)	
Mean ± SD	63.7 ± 13.1
Gender, n (%)	
Males	2,512 (68.5)
Females	1,154 (31.5)
Ethnicity, n (%)	
Māori	367 (10.0)
Pacific	422 (11.5)
Indian	298 (8.1)
Other Asian	80 (2.2)
European / Other	2,499 (68.2)
Current smoker, n (%)	554 (27.6)
Diabetes, n (%)	532 (26.5)
BMI	
n	1,840
Median (IQR)	28.44 (15.11–32.60)
Fasting LDL*	
n	2,011
Mean ± SD	2.7 ± 1.1
Previous CVD, n (%)	1,495 (40.8)
Previous MI, n (%)	865 (23.6)
Previous heart failure	348 (9.5)
Previous bleeding	342 (9.3)
Type of ACS, n (%)	
USA	663 (18.0)
NSTEMI	2,205 (60.2)
STEMI	798 (21.8)
Creatinine on admission	
n	3,666
Median (IQR)	89 (75–106)
Range	23–1,660
Haemoglobin (g/L)	
n	2,748
Mean ± SD	138.3 ± 18.1
WCC (x 109)	
n	3,170
Mean ± SD	9.16 ± 3.47

*Denominator = patients with complete CVDDM Predict records (n=2,011 for total, 82 for those who had bleeding and 1,929 for those who had no bleeding). CVDDM = cardiovascular disease and diabetes mellitus, LDL = low density lipoprotein, MI = myocardial infarction, USA = unstable angina, NSTEMI = non ST-elevation MI, STEMI = ST-elevation MI, WCC = white cell count

Table 2: Investigation and management.

Variables	All (n=3,666)
Heparin / Clexane, n (%)	2,689 (73.4)
GPIIbIIIa, n (%)	96 (2.6)
Angiogram, n (%)	2,729 (74.4)
PCI this admission, n (%)	1,546 (42.2)
Referral for CABG, n (%)	
Inpatient	350 (9.6)
Outpatient	92 (2.1)
None	3,224 (87.9)
Treatment at discharge alive, n (%)	
n=3,596	
Aspirin	3,520 (97.9)
Clopidogrel	2,498 (69.5)
ACE inhibitors or ARBs	2,366 (65.8)
Beta blockers	3,064 (85.3)
Statin	3,400 (94.6)

GPIIbIIIa = glycoprotein IIbIIIa, PCI = percutaneous coronary intervention, CABG = coronary artery bypass grafting

Results

Patient population and follow-up

3,666 ACS patients (2,210 from Middlemore Hospital, 1,459 from Waikato and Taranaki Base Hospitals) were identified from the ANZACS-QI registry between the years of 2007 and 2010. The mean follow-up was 1.94 years.

Demographics and clinical characteristics of patients in the ANZACS-QI registry are shown in Table 1.

In-hospital management and medications on discharge of patients in the ANZACS-QI registry are shown in Table 2.

Incidence of bleeding events and blood transfusions (Tables 3 and 4)

There were 399 (10.8%) out of 3,666 patients who had at least one bleeding event during a mean follow-up of 1.94 years. Of these, 161 (4.4%) patients bled during their index ACS admission and 271 patients (7.4%) were re-hospitalised with at least one bleeding event. Of these 271 patients, 33 patients (12.2%) had a bleeding event during their index ACS admission. The majority (n=206) had just one re-admission for a bleeding event, 51 patients had two subsequent admissions, and 14 patients had three or more admissions for bleeding events. There were 12 bleeding-related deaths at the index admission, and 51 on subsequent first readmissions.

Table 3: Types of bleeding at the index ACS admission.

Bleeding events	**Index admission**			
	Overall (n=161)	**Death = No (n=149)**	**Death = Yes (n=12)**	**Transfusion (n=61)**
Procedural n *Inpatient CABG* *PCI* *No PCI/CABG*	79 (49.1%) *28/79 (35.4%)* *44/79 (55.7%)* *7/79 (8.9%)*	77 (51.7%) *26/77 (33.8%)* *44/77 (57.1%)* *7/77 (9.1%)*	2 (16.7%) *2/2 (100%)* *0 (0%)* *0 (0%)*	34 (55.7%) *26/34 (76.5%)* *5/34 (14.7%)* *3/34 (8.8%)*
Gastrointestinal	25 (15.5%)	23 (15.4%)	2 (16.7%)	11 (18.0%)
Respiratory	19 (11.8%)	17 (11.4%)	2 (16.7%)	7 (11.5%)
Intracranial	10 (6.2%)	7 (4.7%)	3 (25.0%)	2 (3.3%)
Intraocular	5 (3.1%)	5 (3.4%)	0 (0%)	0 (0%)
Urogenital	18 (11.2%)	16 (10.7%)	2 (16.7%)	5 (8.2%)
Others	5 (3.1%)	4 (2.7%)	1 (8.3%)	2 (3.3%)

PCI = Percutaneous coronary intervention. CABG = Coronary Artery Bypass Grafts. Others = ICD-10 Codes R58 "Haemorrhage, not elsewhere classified", M25.06 "Haemarthrosis, lower leg" and K66.1 "Haemoperitoneum".

Table 4: Types of bleeding after index ACS admission.

Bleeding events	**First re-admission with associated bleeding n=271**			
	Overall (n=271)	**Death = No (n=220)**	**Death = Yes (n=51)**	**Transfusion (n=59)**
Procedural *n* *CABG*	54 (19.9%) *6/54 (11.1%)*	49 (22.3%) *5/49 (10.2%)*	5 (9.8%) *1/5 (20.0%)*	11 (18.6%) *1/11 (9.1%)*
Gastrointestinal	128 (47.2%)	100 (45.5%)	28 (54.9%)	40 (67.8%)
Respiratory	32 (11.8%)	25 (11.4%)	7 (13.7%)	4 (6.8%)
Intracranial	15 (5.5%)	11 (5.0%)	4 (7.8%)	1 (1.7%)
Intraocular	7 (2.6%)	6 (2.7%)	1 (2.0%)	1 (1.7%)
Urogenital	28 (10.3%)	23 (10.5%)	5 (9.8%)	1 (1.7%)
Others	7 (2.6%)	6 (2.7%)	1 (2.0%)	1 (1.7%)

Others = ICD 10 Codes R58 "Haemorrhage, not elsewhere classified", M25.06 "Haemarthrosis, lower leg" and K66.1 "Haemoperitoneum".

The rates of blood transfusion were higher in the group who bled during their index admission than those who bled during their subsequent admissions (37.9% vs 21.8%). This was largely accounted for by blood transfusions required for CABG and, to a lesser extent, PCI-related bleeding. Most procedures (PCI or CABG) occurred during the index admission.

Types of bleeding events (Tables 3 and 4)

The most common bleeding event during the index ACS admission was procedure related (49.1%), followed by gastrointestinal bleeding (15.5%). The reverse was seen in subsequent admissions, with gastrointestinal bleeding making up 47.2% of the bleeding events. The occurrence of respiratory, intra-cranial, intra-ocular, urogenital and other types of bleeding were similar for both index and subsequent admissions.

Discussion

In this study, we were able to describe the incidence and types of bleeding events in New Zealand ACS patients using a set of

ICD-10 bleeding codes. This study demonstrates that bleeding events in the ACS population are common, with approximately one in ten patients having a bleeding event during a mean follow-up of 1.94 years. Only 40% of the first bleeding events occurred during the index ACS admission. Transfusions were required in just over a third of those who bled during their index admission, predominantly CABG related, and in approximately a fifth of patients who bled during a subsequent admission. The most common types of bleeding events during the index ACS admission were procedure related, followed by gastrointestinal bleeding. In contrast, gastrointestinal bleeding was the most common in subsequent readmissions.

Methodological issues in identification of bleeding events and severity

Several studies have used ICD codes to define bleeding in atrial fibrillation[12,15] and PCI cohorts.[13,16] There are also prior studies using this methodology in a large cohort of ACS patients, the largest being the Danish registry studies.[9,12] There was substantial concordance between our ICD-10 bleeding codes with the two Danish studies of Sørensen et al[9] and Lamberts.[12] However, in the Danish studies, codes for intraocular and musculoskeletal bleeding were not included. Conversely, Sørensen et al[9] included the ICD-10 code for haemothorax (J94.2), which we excluded as we did not wish to include patients coded for a haemothorax from causes such as infection or malignancy. Additionally, both the Sørensen[9] and Lamberts[12] studies included codes for anaemia, whereas we excluded these codes as we were concerned that anaemia from a chronic bleed might predate the ACS event. To our knowledge, ours is the first study to outline the process in which the ICD-10 list of bleeding events was collated in the ACS population.

The incidence of 'severe' or 'major' bleeding in the context of ACS and PCI reported in prior studies range between approximately one and ten percent.[17] Comparison between studies is difficult due to a number of methodological variables. These include cohort differences, in particular registry compared with clinical trial populations, and variation in follow-up time (eg, in-hospital versus longer-term events). The bleeding definitions used have also varied widely, ranging across several clinical trial or registry and administrative dataset derived bleeding definitions.[6,9]

Clinical trial and registry bleeding definitions

The two most commonly used clinical trial bleeding definitions in ACS registries and randomised trials are the TIMI and GUSTO definitions.[7,8] These definitions were developed in the era of fibrinolysis. The TIMI and GUSTO definitions for major bleeding are well defined. However, there is only a modest concordance in grading bleeding severity between the definitions. They are also insensitive for more minor, but potentially clinically significant, bleeding and so may underestimate the true incidence of bleeding. The Bleeding Academic Research Consortium (BARC), taking into account the strengths and weaknesses of the prior bleeding definitions, recently proposed standardised definitions for bleeding end-points for use in cardiovascular clinical trials with the aim of improving uniformity in adjudicating the clinical impact of bleeding.[6] These various bleeding definitions vary in the way they record bleeding cause (eg, procedure versus non procedural related), bleeding site and severity of bleeding. Assessment of bleeding severity in these definitions also includes a combination of clinical and laboratory criteria.

Comparison of ICD-10 bleeding definition with BARC criteria

The BARC investigators identified several challenges in developing a bleeding definition, including a requirement to capture information regarding cause, site and severity of bleeding, correlation with prognosis and standardisation of the definition. They also emphasised the need for it to be practical and easy to use.

In the current study we have developed and explored the use of an ICD-10 bleeding code set as an alternative approach to using clinical trial definitions. This method has advantages and disadvantages compared with using the clinical trial derived definitions. The most important advantages relate

to these codes being routinely recorded by hospital clinical coders for all hospital admissions in New Zealand using standardised ICD-10 definitions from 2001 on. The use of ICD-10 bleeding codes have been validated against clinical records both locally[14] and internationally.[9] This means that bleeding events can be identified even in cohorts where the data needed for a specific bleeding definition (eg, BARC) is not available. It potentially facilitates the comparison of bleeding event trends both over time and between different geographical regions.

Using ICD-10 coding we are able to identify bleeding cause, for example bleeding related to CABG or PCI is captured by a specific ICD-10 code. However, this definition of procedure-related bleeding would not be as precise as the BARC definition, which requires the volume of transfusion received and chest drain loss.

The site of bleeding is also identified using ICD-10 codes and usefully divided into subtypes. The BARC definition separates out CABG and intra-cerebral/intraocular bleeding from other bleeding sites, but does not otherwise divide bleeding sites further.

Using ICD-10 codes, the severity of bleeding can be assessed by classifying into fatal versus non-fatal, intracerebral versus other, and transfusion requiring bleeding events. It is, however, not possible to identify the number of units transfused, or a drop in haemoglobin, which are included in the BARC criteria. The BARC criteria divide more minor bleeding according to whether medical intervention was required. This is not possible using the ICD-10 coding approach. While there is good evidence[17,18] that more severe TIMI and GUSTO bleeding portend a worse prognosis, a similar analysis has not been performed using an ICD derived definition of severity.

Other limitations of the ICD coding bleeding definition is that it is dependent on patients being hospitalised or dying for event ascertainment. Any more minor bleed in the community not requiring hospitalisation would be missed. A related issue is that it is not always possible to tell whether a bleeding-related admission was due to the bleeding event, or whether the bleed was an incidental problem. Use of primary versus secondary codes may be useful to distinguish these.

Incidence of bleeding

In this study, 10.8% of patients had a bleeding event during their index ACS or subsequent admissions to hospital, with 40% having their first bleed at the index admission and the remainder on a subsequent readmission. As discussed above, it is difficult to compare this figure with other studies due to methodological differences.

As a local comparison, this figure (4.4% index admission bleeding) is lower than the Dunedin group who reported TIMI bleeding in 10.5% of a 2005 ACS sub-group of non-ST elevation ACS (NSTEACS) patients exposed to enoxaparin, which excluded CABG-related bleeding.[14] In the 2005 Danish cohort[9] using a similar ICD-10 bleeding code set, the incidence of bleeding post-discharge was 4.6% in a mean follow-up period of 18 months. This compares with 7.4% post-discharge bleeding in nearly 2 years in our cohort. They did not, however, report index admission bleeding rates.

Types of bleeding

Procedure-related bleeding accounted for the majority of index admission bleeding (49%). As expected, an important proportion of the procedural bleeding events were related to CABG (35%). In some prior studies, CABG-related bleeding was excluded. Our rationale for including it was that CABG-related bleeding is common—10% of our ACS cohort underwent in-patient CABG, and 20% of the total index admission bleeds occurred in these patients. The mechanism and clinical implications of CABG-related bleeding may be different from those with non-procedural causes and depending on the research question, it may be appropriate to either include or exclude these patients.

In subsequent admissions, the most common type of bleeding was gastrointestinal bleeding (47% of readmissions). This is likely to reflect the association between long-term exposure to anti-platelet agents, and the development of gastrointestinal ulceration. Similar to our study, Ko et al also found that gastrointestinal bleeding was the most common cause for late bleeding post discharge after percutaneous coronary

intervention (56% of bleeders).[13] The higher incidence in Ko's study compared to our study may have related to the older population studied (age >65 years).

Strengths and limitations

There were several limitations in this study. As previously described, this study involved the retrospective extraction of data from a registry that was then linked to national routine health datasets, so it has the inherent limitations of such datasets. Some patients had more than one bleeding event per admission and it was necessary to prioritise severity. Furthermore, several codes appeared to code for the same bleeding event within an admission. As only one bleeding event per admission was counted, this did not affect our incidence data. However, it is possible we might have underestimated the incidence of bleeding events when more than one separate event occurred during an admission. The timing of bleeding events during a patient's admission could also be helpful in improving our understanding of those who bleed and the precipitants of bleeding. Due to the reliance on encrypted datasets, the timing of bleeding events could not be determined. For example, it was not possible to determine whether a gastrointestinal bleed occurred before or after an intervention. Furthermore, our analysis did not differentiate between a bleeding event being the primary or secondary cause for readmission.

Future directions

Further analysis on the incidence of bleeding and types of bleeding is required to reflect more current practices. This dataset includes patients between the years of 2007 and 2010. Since this time, there has been a greater move towards a radial approach to angiography, which has been associated with fewer bleeding complications than femoral access.[20,21] Additionally, the use of newer and more potent antiplatelet agents, such as ticagrelor, and novel oral anti-coagulation, may influence the incidence and types of bleeding seen in the ACS population.

Understanding the incidence and types of bleeding is only the first step in understanding those vulnerable to this complication of treatment. Our next step is to develop a multivariate bleeding risk score relevant to the real world population of ACS patients.

Conclusions

One in ten ACS patients in this New Zealand cohort experienced a significant bleeding event within 2 years. Using an ICD code-based approach to identifying bleeding events within national ACS cohorts will enable the study of bleeding event incidence and type over time, facilitate comparison between geographic regions both nationally and internationally, and allow us to assess the impact of changes in anti-thrombotic therapy and interventional practice on bleeding rates.

Appendix

System	ICD 10 AM	Description
Gastrointestinal	1850	Oesophageal varices with bleeding
	K226	Gastro-oesophageal laceration-haemorrhage syndrome (Mallory-Weiss syndrome)
	K250	Gastric ulcer, acute with haemorrhage
	K252	Gastric ulcer, acute with both haemorrhage and perforation
	K254	Gastric ulcer, chronic or unspecified with haemorrhage
	K256	Gastric ulcer, chronic or unspecified with both haemorrhage and perforation
	K260	Duodenal ulcer, acute with haemorrhage
	K262	Duodenal ulcer, acute with both haemorrhage and perforation
	K264	Duodenal ulcer, chronic or unspecified with haemorrhage
	K266	Duodenal ulcer, chronic or unspecified with both haemorrhage and perforation
	K270	Peptic ulcer, acute with haemorrhage
	K272	Peptic ulcer, acute with both haemorrhage and perforation
	K274	Peptic ulcer, chronic or unspecified with haemorrhage
	K276	Peptic ulcer, chronic or unspecified with both haemorrhage and perforation
	K280	Gastrojeju nal ulcer, acute with haemorrhage
	K282	Gastrojejunal ulcer, acute with both haemorrhage and perforation
	K284	Gastrojeju nal ulcer, chronic or unspecified with haemorrhage
	K286	Gastrojeju nal ulcer, chronic or unspecified with both haemorrhage and perforation
	K290	Acute haemorrhagic gastritis
	K625	Haemorrhage of anus and rectum
	K661	Haemoperitoneum
	K920	Haematemesis
	K921	Melaena
	K922	Gastrointestinal haemorrhage, unspecified
lntraocular	H356	Retinal haemorrhage
	H431	Vitreous haemorrhage
lntracranial	1600	Subarachnoid haemorrhage from carotid siphon and bifurcation
	1601	Subarachnoid haemorrhage from middle cerebral artery
	1602	Subarachnoid haemorrhage from anterior communicating artery
	1603	Subarachnoid haemorrhage from posterior communicating artery
	1604	Subarachnoid haemorrhage from basilar artery
	1605	Subarachnoid haemorrhage from vertebral artery
	1606	Subarachnoid haemorrhage from other intracranial arteries
	1607	Subarachnoid haemorrhage from intracranial artery, unspecified
	1608	Other subarachnoid haemorrhage
	1609	Subarachnoid haemorrhage, unspecified
	1610	Intracerebral haemorrhage in hemisphere, subcortical
	1611	Intracerebral haemorrhage in hemisphere, cortical
	1612	Intracerebral haemorrhage in hemisphere, unspecified
	1613	Intracerebral haemorrhage in brain stem
	1614	Intracerebral haemorrhage in cerebellum
	1615	Intracerebral haemorrhage, intraventricular
	1616	Intracerebral haemorrhage, multiple localised
	1618	Other intracerebral haemorrhage
	1619	Intracerebral haemorrhage, unspecified

Intracranial (cont)	1620	Subdural haemorrhage (acute)(nontraumatic)
	1621	Nontraumatic extradural haemorrhage
	1629	Intracranial haemorrhage (nontraumatic), unspecified
	S064	Epidural haemorrhage
	S065	Traumatic subdural haemorrhage
	S066	Traumatic subarachnoid haemorrhage
Respiratory	R040	Epistaxis
	R041	Haemorrhage from throat
	R042	Haemoptysis
	R048	Haemorrhage from other sitesin respiratory passages
	R049	Haemorrhage from re.spiratory passages, unspecified
Urogenital	R31	Unspecified haematuria
Procedural	T810	Haemorrhage and haematoma complicating a procedure, not elsewhere classified
Haematology (Others)	RS8	Haemorrhage, not elsewhere classified
Musculoskeletal (Others)	M2500	Haemarthrosis, multiple sites
	M2501	Haemarthrosis, shoulder region
	M2502	Haemarthrosis, upper arm
	M2503	Haemarthrosis, forearm
	M2504	Haemarthrosis, hand
	M2505	Haemarthrosis, pelvic region and thigh
	M2506	Haemarthrosis, lower leg
	M2507	Haemarthrosis, ankle and foot
	M2508	Haemarthrosis, other site
	M2509	Haemarthrosis, siteunspecified

Competing interests:
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Impact of PET-CT scan on management in upper gastrointestinal malignancy

Aditya Sharma, Michael Young

ABSTRACT

INTRODUCTION: Curative treatments of upper gastrointestinal (UGI) cancers carry significant morbidity and mortality. Therefore, accurate pre-treatment staging is important. PET-CT scan is an expensive modality, and not readily available in New Zealand. The aim of this study was to describe how PET-CT scan influences management in UGI cancer.

METHODS: This retrospective descriptive study included patients with UGI cancer with no evidence of metastatic disease on IV contrast CT scan, and those medically fit for curative treatment. Patients then underwent PET-CT scan. We defined influence or change in management if PET-CT showed metastatic disease or other lesions requiring further investigation.

RESULTS: Seventy-nine patients were identified for the purposes of this study. Fifty-nine (74.7%) had CT scan showing no evidence of metastatic disease. Of these, PET-CT scan influenced management in 14 patients (23.7%) and found distant metastasis in eight patients (13.6%). The remaining 20 of 79 patients (25.3%) had CT scan showing indeterminate lesions. Of these, PET-CT scan influenced management in eight patients (40%), with metastatic disease seen in seven patients (35%).

CONCLUSION: Our study confirms the value of PET-CT scan in pre-operative staging of UGI cancer. It had a greater impact on patients with intermediate lesions on staging CT.

Background

Upper gastrointestinal (UGI) malignancy in the western world differs from other forms of cancer in that it often presents at an advanced stage.[1] Curative treatment, in almost all cases, is only possible if there is no distant metastatic disease (Stage I–III), although there are several palliative management options. Such treatment with curative intent often involves multi-modality therapies with significant morbidity and mortality. Although accurate determination of tumour size, depth of tumour invasion, and involvement of lymph nodes is important in providing prognostic information and tailoring treatment to the individual patient, the detection of metastatic disease is more important to select out those patients who would not benefit from aggressive treatments with curative intent.

Increasingly, accurate pre-treatment staging is possible based on newer imaging and surgical techniques, such as positron emission tomography (PET), laparoscopy, thoracoscopy, laparoscopic ultrasound, and endoscopic ultrasound (EUS).[2]

Traditional imaging methods, including IV contrast computed tomography (CT) scan and/or ultrasound scan (USS), utilise anatomical anomalies for determining staging. PET scan utilises physiological differences between normal tissues and those of neoplastic cells, which may precede detectable structural changes. The glucose analogue 18F-fluorodeoxyglucose (FDG) is commonly used, as it highlights differential in glucose uptake between normal and adjacent abnormally active tissues, including neoplasia.[3] PET scan could therefore detect small or indistinct metastasis, metachronous neoplasms, or primary neoplasms affecting a different organ system, which may not be detected by IV contrast CT or USS. However, it has limited usefulness in assessing tumour size, depth of invasion and loco-regional

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nodal involvement.[1] PET scan is commonly combined with a CT scan (PET-CT scan), which allows for representation of lesions anatomically and physiologically.[4]

Due to the costs and logistics of providing radioactive substrates with a short half-life, and the limited availability of PET-CT scanners in New Zealand, we undertook this study to determine the impact of PET-CT scan on the management of upper gastrointestinal cancer in our MidCentral Health District Health Board Regional Cancer Treatment Service (RCTS).

Objective

A retrospective study to ascertain how PET-CT scan influenced management of upper gastrointestinal cancer in our MidCentral District Health Board RCTS.

Methods

Data was retrieved from the patient database of the MidCentral Health RCTS multi-disciplinary forum for gastro-intestinal and intra-abdominal cancer, to which a vast majority of elective patients with UGI (oesophago-gastric and hepato-biliary/ pancreatic) tumours/cancers are referred for imaging, pathology review, and management planning. A significant number of such patients are referred from outside the domicile boundaries of the MidCentral Health District Health Board (Wanganui, Taranaki, Hawkes Bay, and Wairarapa District Health Boards [DHBs]), but whose cancer management falls within the auspices of the MidCentral Health RCTS. Paradoxically however, not all patients with such cancers who live in these other DHBs are referred for management discussion to this forum.

Most referred patients have already undergone IV contrast CT body scan. Such referred patients are nearly always discussed at this multi-disciplinary forum for gastro-intestinal and intra-abdominal cancer, prior to PET-CT scan principally as a means of avoiding unnecessary or inappropriate ordering of PET-CT scans. Although oesophageal, gastro-oesophageal junction (GOJ), and hepato-biliary cancers have a streamlined administrative approval mechanism for PET-CT scan requests, other UGI malignancies (gastric and pancreatic) do not enjoy such a streamlined process. None of the patients recommended to undergo PET-CT scan by this forum were declined funding or the scan itself.

The IV contrast CT scan, typically arterial and delayed portal venous phase CT scan chest and abdomen with oral contrast, was mostly performed and reported in the hospital of the patient's domicile DBH. PET-CT scan was almost always performed and reported by Pacific Radiology, 98 Churchill Ave, Crofton Downs, Wellington. All images were separately reviewed by our radiologists at the MidCentral Health multi-disciplinary forum for gastro-intestinal and intra-abdominal cancer.

An unquantified, but minority, of patients with upper GI cancer/tumours were referred to another DHB/RCTS without prior discussion here (anecdotal).

Participants

We included patients with UGI tumours/ cancers who were discussed in the MidCentral Health multi-disciplinary forum for gastro-intestinal and intra-abdominal cancer between June 2004 and June 2014. The following patients were excluded from the study:

- Patients with definite evidence of distant metastatic disease on IV contrast CT scan
- Patients who were not medically fit for curative treatment
- Patients referred with recurrent cancer.

Baseline characteristics

Baseline patient characteristics collected included: age, sex, site of malignancy, and histopathology.

Determining how PET scan influenced management

To determine how PET-CT scan influenced management, we initially described what the management algorithm would be if PET-CT scan was not available. Medically fit patients with confirmed UGI cancer would undergo IV contrast CT scan +/- staging laparoscopy (the latter at the discretion of the treating surgeon). If there was no evidence of distant metastatic disease, the patient would undergo treatment with curative intent. If IV contrast CT showed indeterminate lesions that were unable to be biopsied, the patient would

Figure 1: Management of UGI cancer without PET-CT scan.

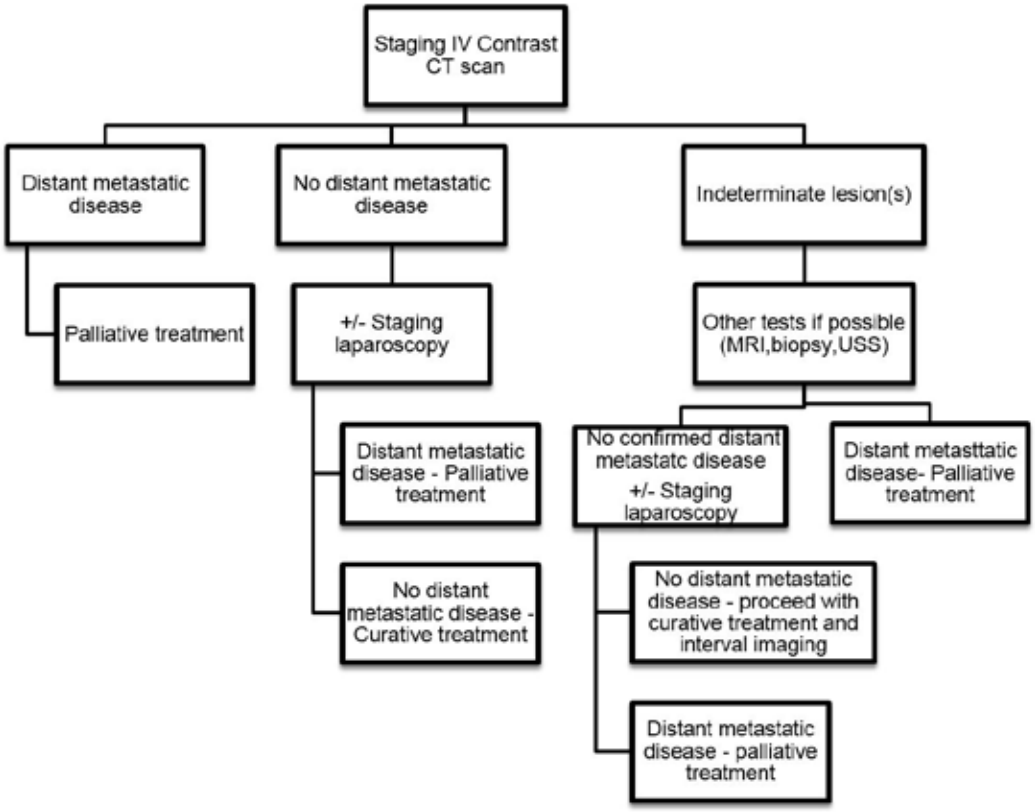

Figure 2: Management of UGI cancer with addition of PET-CT scan.

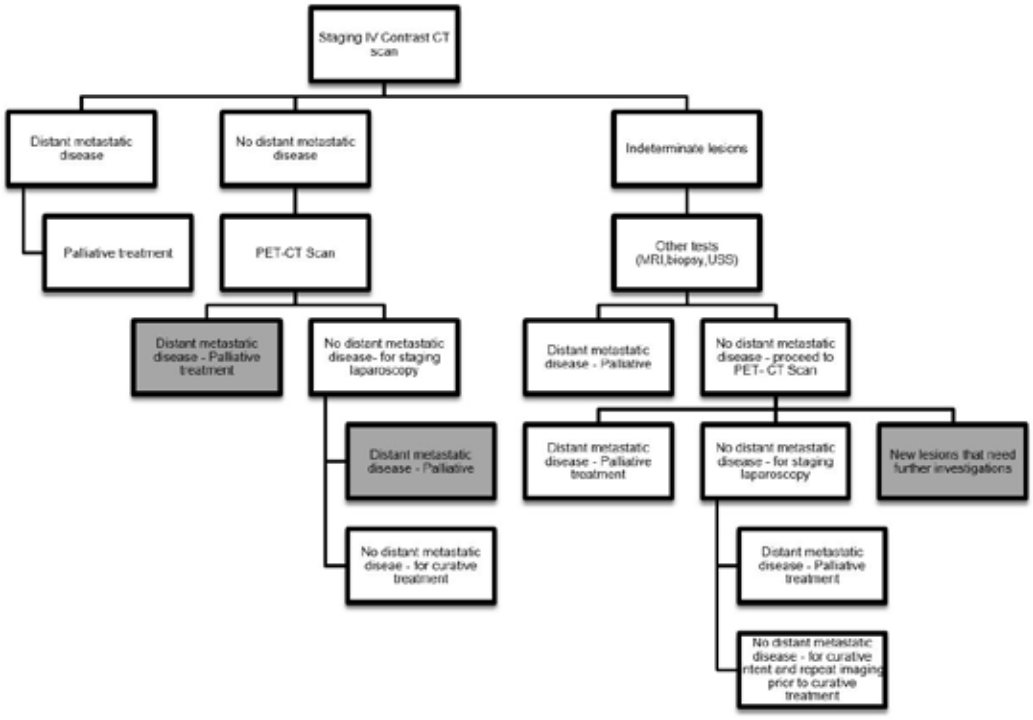

Table 1: Showing baseline characteristics of patients.

Characteristic	Number (%)
Sex	
Male	56 (70.1)
Female	23 (29.1)
Mean age at diagnosis (years)	68 (42–87)
Location	
Oesophagus	57 (72.2)
Upper	4 (5.1)
Middle	5 (6.3)
Lower	48 (60.8)
Gastroesophageal junction (GOJ)	4 (5.0)
Stomach	8 (10.1)
Pancreas	8 (10.1)
Biliary tree	1 (1.3)
Gall bladder	1 (1.3)
Pathology	
Adenocarcinoma	55 (69.6)
Squamous cell carcinoma	21 (26.6)
Lymphoma	1 (1.3)
Not available	2 (2.5)

be given the benefit of doubt and would undergo treatment with curative intent, with interval CT scan for reassessment. If multi-modality treatment was undertaken, interval imaging typically occurred prior to surgery. If interval CT scan was indicative of distant metastatic disease, treatment intent would change to palliative.

Any deviation from this algorithm because of the PET-CT scan result would be considered a change in management. These included:

- PET-CT scan showing abnormal avid areas indicating distant metastatic disease
- PET-CT scan showing other abnormal avid area(s) aside from the known primary tumour site and not typical for metastatic disease from that primary site, requiring further investigation thus interrupting the intended management pathway.

This is illustrated in Figures 1 and 2. In Figure 2, patients in pathway marked grey would be considered as change in management.

Ethics

No ethical committee approval was required as this study was a retrospective data audit.

Results

There were 79 patients included for our study. Baseline characteristics are shown in Table 1. Male: female ratio was 2.43:1, mean age 68 years at the time of diagnosis. Oesophageal cancer was the most common pathological site (72.2%), followed by pancreatic and gastric cancer (10.1% each). GOJ cancers, cholangiocarcinoma and gall bladder cancers were a small minority. Adenocarcinoma (69.6%) and squamous cell carcinoma (26.6%) formed the vast majority of histodiagnosis. Histology was not available in two patients, both of whom had pancreatic cancer.

PET-CT influencing management

Figure 3 shows the influence of PET-CT scan on patient management. Of the 79 patients, 59 (74.7%) had no evidence of distant disease or indeterminate lesions on IV contrast CT scan. Fourteen of this group of 59 patients (23.7%) had PET-CT scans that influenced management, and eight (13.6%) patients had PET-CT showing metastatic disease. The remaining 20 of 79 patients (25.3%) had indeterminate lesions on IV contrast CT scans that were unable to be further characterised. Of this group of 20 patients, eight (40%) had a PET-CT scan result that changed their management, with seven patients (35%) having metastatic disease. Thus, PET-CT scan influenced management in a total of 22 patients out of 79 (27.8%) and showed metastatic disease not seen on CT scan in 18 out of 79 patients (22.8%).

Analysis of patients where PET-CT scan influenced management

Table 2 details the patients where PET-CT scan influenced management.

Figure 3: How often PET-CT scan influenced patient management.

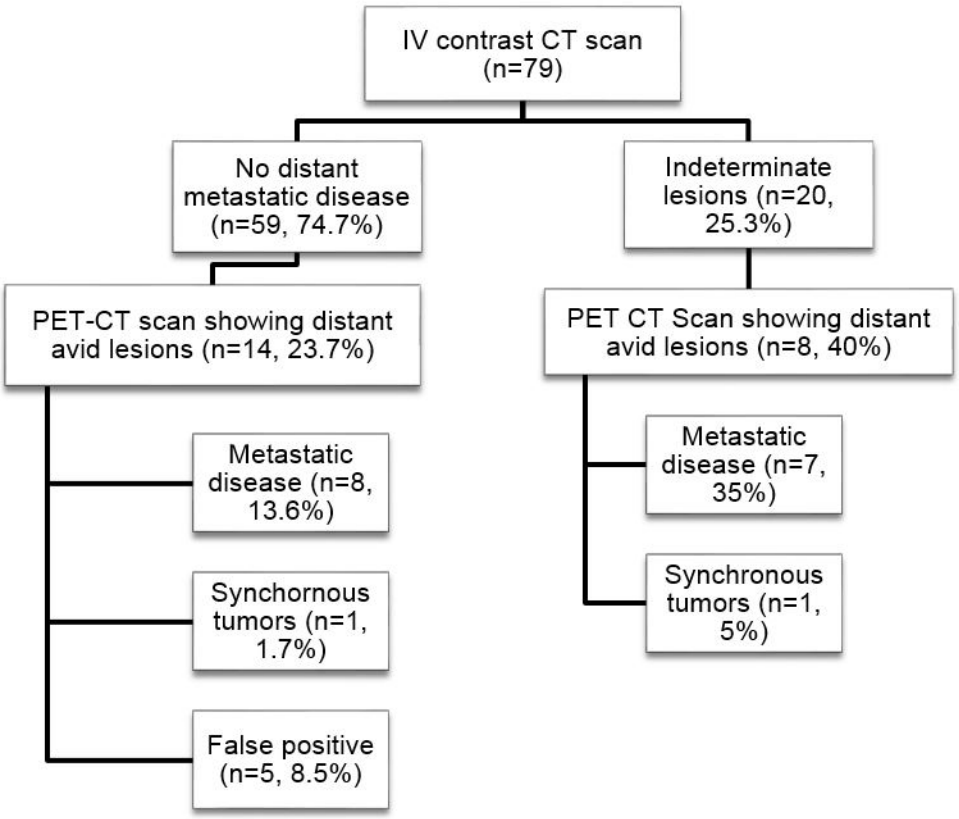

Table 2: Detailing the distant metastatic disease seen on PET-CT scan.

Location of distant disease on PET-CT scan	Number (%)	Location of indeterminate lesion on IV contrast CT scan
IV Contrast CT showing no distant disease		
Liver lesions Skeletal lesions Distant lymph node Stomach lesion Adrenal lesion Gluteal lesion Bowel lesions Total	4 (6.8) 2 (3.4) 2 (3.4) 1 (1.7) 1 (1.7) 1 (1.7) 3 (5.1) **14 (23.7)**	NIL
IV Contrast CT showing indeterminate lesions		
Skeletal metastasis (T1) Retroportal lymph node Left Gastric node Lung metastasis Coeliac lymph node involvement Root of neck Sigmoid lesion Vocal cord metastasis Total	1 (5) 1 (5) 1 (5) 1 (5) 1 (5) 1 (5) 1 (5) 1 (5) **8 (40)**	Retrothyroid nodes Retrocural and coeliac lymph node Left gastric node Lung Lung and Liver Left gastric node and left adrenal Left kidney and Left adrenal Left gastric node and left adrenal

Table 3: Detailing lesions on PET-CT scan requiring further investigation.

Lesions needing further investigation	Final diagnosis	Number (%)
Caecal lesion	**Normal colonoscopy**	1
Sigmoid lesion	**Low grade tubulovillous adenoma**	1
Sigmoid lesion	**Sigmoid adenocarcinoma**	1
Sigmoid lesion	**Intramucosal adenocarcinoma**	1
Hepatic lesion	**Hepatic haemangioma**	1
Adrenal lesion	**Benign lymph node**	1
Retroportal lymph node	**Granulomatous lymphadenitis**	1
Total		**7 (8.9%)**

Table 4: Shows how often PET-CT scan influenced management based on location of tumour.

Location	Number where PET-CT influenced management (%)	Number where PET-CT showed metastatic disease (%)
Oesophagus	18 (31.6)	12 (21.1)
GOJ	1 (25)	1 (25)
Pancreas	1 (12.5)	1 (12.5)
Stomach	2 (25)	1 (12.5)
Cholangiocarcinoma	0 (0)	0 (0)
Gallbladder	0 (0)	0 (0)

When IV contrast CT scan showed no evidence of distant metastatic disease (59 patients), four (6.8%) had liver lesions. Skeletal lesions and distant lymph node involvement (eg, para-aortic lymphadenopathy) were seen in a four patients (6.8%) each. Stomach (one patient, 1.7%) and adrenal metastasis (one patient, 1.7%) was also seen. There were three patients (5.1%) who had avid lesions in the bowel (one caecal lesion and two sigmoid lesions) needing colonoscopies.

When IV contrast CT showed indeterminate lesions (20 patients), one (5%) had skeletal metastases (T1 vertebral body). Lung metastases was seen in one patient (5%). Distant lymph node involvement was seen in three (15%) patients (left gastric node, retroportal node, coeliac node), while one patient (5%) had a vocal cord metastasis. One patient (5%) had a sigmoid colon lesion and underwent sigmoidoscopy. The last patient (5%) had a lesion in the root of the neck and underwent palliative treatment. Of these eight patients, only two patients had PET-CT lesions which corresponded to those on IV contrast CT scans.

Table 3 details patients with other organ lesions highlighted by PET-CT scan that required further investigation/management. It shows that four patients (5.1%) had large bowel lesions that required colonoscopy. Of these, one had a focal avid caecal area but a subsequent normal colonoscopy, one had a large sigmoid tubulovillous adenoma with low-grade dysplasia removed at colonoscopy, one had an intramucosal adenocarcinoma and underwent endoscopic resection with surveillance colonoscopies, and the final patient had a sigmoid adenocarcinoma and underwent an anterior resection prior to oesophagectomy. The remaining three patients had benign lesions. Patient with hepatic haemangioma had a primary gastric cancer, while the remaining six patients had a primary oesophageal cancer.

Abnormal PET-CT scan influencing management according to primary cancer site

Table 4 shows that management was changed in 31.6% of patients with oesophageal cancer, 25% with GOJ cancer, 12.5% with pancreatic cancer, 25% with gastric cancer, and in none of the patients with cholangiocarcinoma or gallbladder cancer.

Discussion

Upper GI cancer in the western world often presents at an advanced stage that precludes treatment with curative intent. The prevalence of hepatic metastasis at initial diagnosis is 50% for oesophageal cancer, and 12% for gastric cancer.[8] Furthermore, curative intent treatment is frequently multi-modal and carries significant morbidity and mortality. Therefore, it is important to undergo comprehensive pre-treatment staging particularly to exclude distant metastatic disease, where the management will almost always be palliative.

IV contrast CT scan has accuracy in predicting tumour respectability of 60%.[5,6,14-16] It has shown to be very useful in detecting hepatic, pulmonary and adrenal metastasis, but less so in assessing local disease and lymph node involvement in upper GI cancer.[1] It is particularly less effective in distal third of oesophagus due to motion artefact from surrounding heart, diaphragm and lungs. It is also limited in assessing the depth of tumour invasion.[6]

Compared to structural changes seen in most imaging modalities like IV contrast CT scan, MRI scan or EUS, PET-CT scan using FDG utilises physiological variance seen with neoplasms where there is increased glucose uptake compared to normal tissues.[1] There have been limited studies published on the impact of PET-CT scan in the management of upper GI cancer. Indeed, not all centres utilise routine PET-CT scan as part of the staging of UGI cancer.

Our baseline participants are comparable to a UK study by Blencowe et al.[7] In our study, PET-CT scan influenced management in 27.8% of patients. Blencowe et al, in a dataset combining oesophageal and gastric cancers, found that PET-CT scan influenced management in 38% of patients, but their database did not include pancreatic, biliary and gall bladder carcinomas.

In our study of 79 patients, 75% had an IV contrast CT scan that did not show any evidence of distant metastatic disease or other abnormal areas of concern. Despite this, PET-CT scan showed lesions in over 23% that needed further investigation, with 14% showing metastatic disease, which is comparable to Blencowe et al (18%).

Of the 25% of patients in our study with indeterminate lesions, 40% had change in management due to PET-CT scan, with 35% of patients showing metastatic disease. This suggests that PET-CT scan is more crucial in the presence of intermediate lesions on IV Contrast CT scan. Of the eight patients with intermediate lesions on IV contrast CT scan, six had PET-CT showing distant disease which did not correspond to the lesions seen on the IV contrast CT scan.

In our series, oesophageal cancer formed the largest histopathologic diagnostic group (57 out of 79, 72%), of which over 60% were in the lower oesophagus. PET-CT scan influenced management in these patients in 31.6%, with metastatic disease in 21%. This is comparable to previous studies suggesting 14–25%.[8,9]

PET-CT influenced gastric cancer patients in 25%, with 12.5% showing distant disease not seen on IV contrast CT scan. Use of PET-CT in gastric cancer remains controversial with limited evidence on its usefulness. A study by Hur et al compared 142 patients with PET-CT scan and their surgical diagnosis to predict curability of the disease. A further study by Mukai et al, with 62 gastric cancer patients, investigated tumour size and nodal involvement. However, these studies did not comment on the proportions of positive PET-CT with a negative IV contrast CT scan. Similar influence of PET-CT was seen on pancreatic cancer, where one patient (12.5%) had metastatic disease with IV contrast CT showing no evidence of distant disease. Our database only included four GOJ cancers, one gallbladder cancer, and one cholangiocarcinoma, so no conclusions can be drawn regarding the impact of PET CT scan for these diagnoses.

Of our patients with PET-CT scan suspicious of distant metastatic disease, two patients deserve special mention. One patient had a focal avid area in the vocal cord, while another had a right gluteal avid lesion (the latter was subsequently shown to be metastatic adenocarcinoma on percutaneous core biopsy). These lesions would have been out of the conventional IV contrast CT 'scanning zone'. This illustrates the rare distant metastatic sites that PET-CT scan can detect.

There were four patients (5.1%) where IV contrast CT scan showed no definite distant

metastatic disease, but PET-CT showed large bowel lesions needing colonoscopies. Even though two of these patients had a benign process, we included them as a change in management because scheduling of the colonoscopy interrupted the conventional management pathway for the upper GI cancer. Furthermore, two of the patients had an asymptomatic sigmoid adenocarcinoma, which would have been undetected without the PET-CT scan, until it presented clinically.

There were three other patients that had other lesions requiring further investigations. One patient had a PET-CT scan suspicious of a hepatic metastasis. He underwent an MRI scan and a laparoscopy, with a final diagnosis of hepatic haemangioma. One patient had a PET-CT scan suggesting an adrenal lesion. Subsequent MRI scan showed an abnormal lymph node corresponding to the lesion on PET-CT scan. This was resected during the oesophagectomy with the final histology not showing any evidence of malignancy. The final patient had a PET-CT scan showing an avid retroportal lymph node. Subsequent laparoscopic lymph node excision showed granulomatous lymphadenitis. The presence of granulomatous changes causing a false positive PET-CT scan has been previously described.[1,12,13] Our false positives included five patients with benign processes out of the 22 patients (22.8%), with PET-CT suggesting distant disease. This is slightly higher compared to previous studies suggesting false positive rates of 10–18%.[1,7,8]

There were two patients in our series who had IV contrast CT and PET-CT scan that showed no evidence of distant metastatic disease. These patients underwent a staging laparoscopy which showed biopsy confirmed hepatic metastasis. Thus, we had a false negative rate for distant metastatic disease of 4.4%. Previous studies have shown variable sensitivities with PET-CT to be ranging between 72–100%.[1,8,14,15]

Our study has several limitations. Our patient numbers are small, as with most studies on this subject. Statistical analysis was not possible as this is a descriptive study. Our definition of 'influencing management' was different to that of other studies, and our 'without PET-CT scan' management plan may differ from that of other cancer centres. We included synchronous tumours and benign processes (false positives) in 'influencing management' group as they have resulted in investigations and treatments delaying curative surgery of the UGI cancer. Even though it may have not changed management of the UGI cancer, it has influenced the management of the patient. We have, however, also provided the proportions of patients with PET-CT showing distant disease, which would be more clinically relevant to some clinicians. Oesophageal cancer formed the majority of our patients followed by gastric and pancreatic cancer. Therefore our results would be best applied to these patients and extrapolation to other malignancies should be made with caution.

Use of PET-CT in gastric and pancreatic cancer remains controversial due to limited evidence, as was the case in our our study due to small numbers. An unquantifiable number of patients with obstructive gastric cancers were not referred for PET-CT scan and underwent acute surgical resections. Therefore, our database is potentially an underestimate of the true incidence of gastric cancer in our treatment area.

Conclusion

PET-CT scan influences management in over one-quarter (27.8%) of patients with UGI cancer and shows distant disease not seen on IV contrast CT scan in 22.8%. PET-CT has a larger effect when IV contrast CT scan shows indeterminate lesions (from 27.8% to 40%). Our study confirms the value of PET-CT scan in the treatment staging of oesophageal cancer. There is some evidence of its usefulness in gastric and pancreatic cancer, but more numbers are required to shed light on this. We cannot comment on the usefulness of PET-CT scan in gallbladder cancer and cholangiocarcinoma as our study database had very few patients with this diagnosis.

Competing interests:
Nil

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Development and initial outcomes of an upper gastrointestinal multi-disciplinary clinic

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ABSTRACT

INTRODUCTION: Patients with upper gastrointestinal cancer are often comorbid and require complex surgical treatments for their cancers, meaning that their preoperative assessment can be based around numerous outpatient assessments with multiple services. A multidisciplinary clinic (MDC) was developed for the assessment of patients with confirmed or suspected upper gastrointestinal cancers.

METHODS: Face-to-face meetings were held between stakeholder services at Waitemata District Health Board, and clinic resource allocated. Significant IT modification of existing clinic booking software was required.

RESULTS: Between September 2014, and September 2015, there were a total of 165 new patient, and 710 follow-up appointments. All new patients were seen by a surgeon and then other specialties. Of the 165 new patient appointments, 146 (88%) patients had a definitive treatment plan in place and were cleared by anaesthesia and intensive care at the end of the clinic. Staff and patients report high levels of satisfaction for the clinic.

CONCLUSION: A dedicated MDC has provided a single forum where complex patients can be reviewed, and a definitive treatment plan formulated in nearly 90% of patients, even when this involves multiple medical and paramedical specialties with high levels of patient and clinician satisfaction.

The upper gastrointestinal unit at Waitemata District Health Board (WDHB) manages patients with surgical conditions (both benign and malignant) affecting the oesophagus, stomach, pancreas, duodenum, liver, gallbladder and bile ducts. The unit serves the WDHB catchment population of 597,500, and also provides specialist service support to Northland District Health Board (population 169,000). Annually, the unit is referred approximately 500 complex patients, and of these, half have a diagnosis of, or high suspicion of upper gastrointestinal cancer.

The assessment, staging and treatment of patients with upper gastrointestinal cancer presents several challenges.[1-3] A tissue diagnosis may be difficult to confirm due to technical difficulties associated with biopsy,[1,2] treatment must encompass a large area of field change,[2] cancer incidence peaks in the 7th and 8th decades meaning the patients are usually elderly and comorbid, requiring multiple diagnostic and staging investigations and sequential multidisciplinary review.[3] In addition, there is an increasing role for neoadjuvant therapy in a number of tumours, in addition to surgical therapy with significant perioperative risk, requiring patients to be in optimum condition pre-operation and prepared for significant postoperative rehabilitation.

From a patients perspective, the prevailing outpatient model requires multiple outpatient appointments and review by many specialties. This results in prolonged periods of pre-operative workup as assessments and investigations are done in a sequential, linear fashion, input from other specialty areas, in particular Intensive Care Medicine, was missing,

meaning that the opportunity for combined decision making was compromised. Inter-disciplinary communication relied on dictated letters, which take time to become available, or e-mails that are not accessible to all healthcare providers.

The current faster cancer treatment (FCT) guidelines for District Health Boards (DHBs) mandate that at least 85% of cancer patients receive their first treatment within 62 days of referral,[4] and encourage an efficient, patient-friendly process for diagnosis, staging and treatment. Multidisciplinary clinics (MDC) for the assessment of cancer patients have been previously described in the management of patients with breast,[5] gynaecological,[6] lung,[7] skin,[8] head and neck,[9] and prostate cancer,[10] while in the upper gastrointestinal tract specialist MDC have been described in the management of pancreatic[11,12] and liver tumours.[13] Based on these reports, MDC have been shown to be less stressful and more convenient for patients, facilitate care coordination, improve clinical team satisfaction and may lead to faster delivery of care.[5-13] Patients are also better prepared to assume an active role in their care and report feeling part of the team.[14] MDC also have the potential to improve quality of life by providing the opportunity to include other services, such as palliative care for symptom management, and psychologists and social workers for psychosocial support. However, MDC are resource intensive and often require significant rescheduling and change in practice by care providers.[13]

In response to a significant referral load, a realisation that the average journey for an upper gastrointestinal cancer patient had become convoluted and prolonged, as well as a commitment to meeting the 62-day FCT target, a MDC for upper gastrointestinal cancer patients was established in September 2014 at North Shore Hospital. This paper outlines the experience and results of the first 12 months of this clinic's function.

Methods and process

The decision to proceed with developing an upper gastrointestinal MDC was made 6 months prior to its introduction. One surgeon changed his usual acute surgical call commitment to Monday from Tuesday to ensure that he was consistently available to attend the MDC on a Wednesday morning. Separate clinics were developed to provide opportunity for separate assessment and treatment of patients with non-specialist general surgical conditions and to free-up clinic space for assessment of patients with upper gastrointestinal cancers.

Scheduling

Formal meetings were held with the Departments of Anaesthesia, Intensive Care, Palliative Car, Physiotherapy, Interventional Radiology and Nutrition Services to define their resource requirements. Physiotherapy were initially unable to attend the clinic, however a clinical trial investigating the benefits of pre-operative education on post-operative respiratory complications provided interim physiotherapy input for trial patients. The MDC is also supported by interventional radiology who run an adjacent fortnightly concurrent clinic facilitating cross-referral and assessment. A palliative care consultant was able to attend on a case by case basis. Time allocations for each service appointment are presented in Table 1.

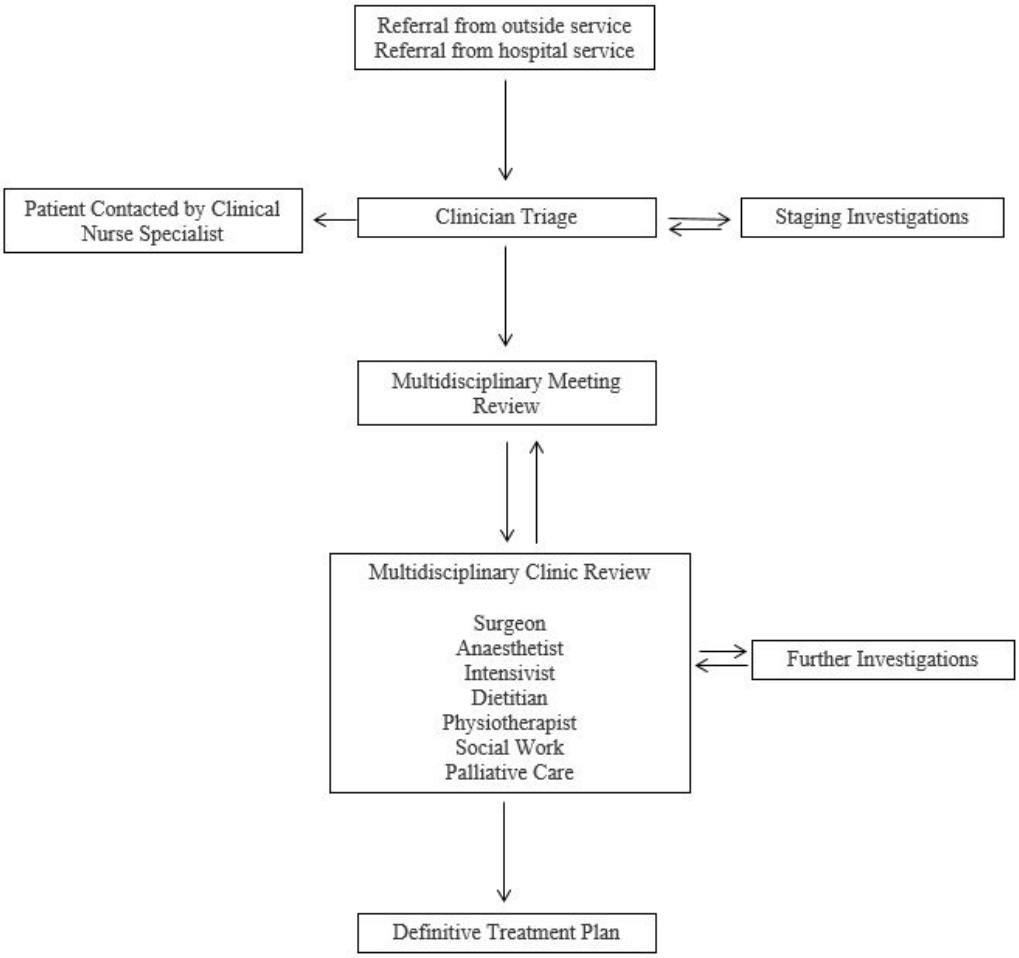
Patient pathway

New patient referrals are received by the booking and scheduling service at WDHB and triaged by one of the upper gastrointestinal surgeons. Investigations (eg, staging CT scans) are booked at the time of triage with the aim of seeing patients for a definitive first specialist assessment (FSA) within 14 days of the receipt of the referral. The Clinical Nurse Specialist (CNS) then contacts the patient to inform them their referral has been received and to warn of any pending investigations. Patients who receive their cancer diagnosis at their FSA will see only the surgeon so they are not overwhelmed by an MDT assessment on the day of their diagnosis, although patients with dysphagia, or other significant nutritional issues, will also see the dietitian at their FSA. Radiology and pathological findings were reviewed in a multidisciplinary meeting (MDM) prior to the first specialist appointment. Following the MDM, a decision is made regarding who will be the lead surgical clinician for that patient and what other services should also be involved in their assessment and treatment.

Table 1: Time allocation chart.

Clinician time allocation	FSA appointment	MDT appointment	Follow-up appointment
Surgeon	20 mins	20 mins	20 mins
Clinical Nurse Specialist	20 mins	20 mins	20 mins
Dietician	40 mins	20 mins	20 mins
Intensive Care		20 mins	
Anaesthetics		40 mins	20 mins

Figure 1: Summary of patient pathway from referral, triage to multidisciplinary review.



Multidisciplinary Clinic appointment

New patients are initially seen by a specialist upper gastrointestinal surgeon with discussion of the results of MDM review and the proposed treatment plan. Other services are then involved. Anaesthetic assessment occurs at the beginning of the patients' treatment journey, prior to neo-adjuvant chemotherapy, which allows extra time for optimisation and, if required, a pre-habilitation programme with the physiotherapist. Each clinician sees the patient individually and documents the outcome separately. There is opportunity for cross service discussions. A dedicated clinic letter template was developed with a 24 hour turnaround on transcription to ensure all healthcare providers have timely access to the clinic outcome. The lead clinician also fills out a MDC outcome form and any other relevant documentation, such as a surgical booking form. The CNS then sees the patient to review the visit,

treatment plan and any remaining questions. The time allocations for each service are presented in Table 1.

Time allocation for each service in multidisciplinary clinic. Intensive care require only new patient appointments. It was initially thought that anaesthesia would only require one new patient appointment, however, subsequent reviews are often done after the completion of neo-adjuvant chemotherapy or following additional assessments with other specialists such as cardiology or respiratory specialists. (FSA: first specialist assessment, MDT: multidisciplinary team).

Resourcing and coding

WDHB uses iPMS (Patient Information Management System, Department of Veterans Affairs, US) to book outpatient clinic appointments. This system requires the appointments to be booked under an individual staff member name rather than under a service or similar entity.

Clinic profiles for surgeons with session codes built within them enabled other specialties to be added to the appointment.

The MDC was initially named the multidisciplinary team clinic, but this created the expectation among both staff and patients that all patients would be seen by everyone. Patient text reminders for the clinic were adjusted to just one text rather than the patient receiving separate texts for 3–5 appointments. Clinic profiles were also sent to Information Consultant Decision Support for review and approval from a Purchase Unit level and new clinic letters were written for MDC appointments describing the process and the need for up to 3 hours of clinic attendance.

Specific information system support was then involved to create a clinic profile that:

- enabled clinic appointments for between 1 to 5 clinicians
- permitted individual clinicians to access their patient lists
- enabled clinical records to send records to all clinics
- charged the Ministry of Health accurately
- captured the work being done (both for funding as well as operational reasons. In particular the dietitian and anaesthetists needed to accurately capture the numbers of patients seen for resource and staffing justifications).

This resulted in a separate clinic list sent to the out-patient department for each clinician, the work done is captured by each department and the funding requirement from the Ministry of Health is clear and transparent.

Clinic outcomes

The desired outcomes of the MDC were:

- numbers of patients receiving a definitive treatment plan by the completion of their MDC appointment
- patient satisfaction measures and numbers of complaints received
- staff satisfaction measures
- impact on FCT compliance.

Results

Between September 2014, and September 2015, there was a total of 165 new patient appointments, and 710 follow-up appointments. Of the new patient appointments, all 165 were initially reviewed by a surgeon, a further 33 were reviewed by anaesthesia alone, and 38 were reviewed by anaesthesia and intensive care prior to defining a surgical plan. Sixty-three patients were formally reviewed by the upper gastrointestinal clinical nurse specialist, and 67 were assessed and reviewed by a dietitian with respect to nutritional optimisation prior to surgery. In total, the assessments by anaesthesia, intensive care, nurse specialists and dietitians amounted to 238 discrete appointments. For the new patients, formal review of radiology and pathology was undertaken at a multidisciplinary meeting prior to the clinic appointment in 121 patients, although the proportion improved from 42 (35%) in the first 6 months to 79 (65%) in the second 6 months as coordination improved.

Of the 165 new patient appointments, 77 were for liver or biliary disease (primary hepatic tumours = 7, metastatic tumours of the liver = 52, tumours of the gallbladder = 12, tumours of the bile ducts = 6), 51 were for pancreatic disease (primary pancreatic cancer = 34, pancreatic cysts = 17), and 44 for gastro-oesophageal disease (gastric cancer = 18, oesophageal cancer

= 26). Patients planned for pancreatic or gastro-oesophageal resections were more likely to see both an anaesthetist (20 of 33 anaesthetic appointments) and an intensivist (21 of 38 combined anaesthetic and intensive care appointments) than patients being assessed for hepatectomy.

Of the 165 new patient appointments, 146 patients had a definitive treatment plan in place and were cleared by anaesthesia and intensive care at the end of the clinic appointment. Of these, 67 were consented and booked for surgical resection or percutaneous tumour ablation, 31 were referred to medical oncology for systemic chemotherapy, 16 to radiation oncology, 20 were assessed by palliative services for palliative care only, 8 were planned for follow-up imaging alone, and 4 were referred for percutaneous tumour biopsy to confirm disseminated disease. Of the 19 patients who did not have a definitive treatment plan in place, 13 were referred for further diagnostic imaging and 6 for biopsy to confirm benign disease.

Between September 2014 and September 2015, no patient complaints were received regarding the MDC, and staff (both medical and nursing) reported high levels of satisfaction (>90% completely satisfied). Faster cancer treatment parameters for upper gastrointestinal surgery also improved over this time, with 62-day treatment compliance increasing from 58% in September 2014, to 80% in September 2015, and 31-day compliance increasing from 72% to 93% over the same period.

Discussion

This investigation describes our experience in developing and implementing a multi-disciplinary management clinic for patients with confirmed or suspected upper gastrointestinal cancers. The drivers for this were a desire to create a more patient-friendly method of assessment and eliminate the need for multiple clinic appointments for review by multiple specialties, to assemble the multidisciplinary team in a single site to assess patients in real time, to include intensive care medicine at the beginning of the patient journey, to encourage direct clinician to clinician communication and decision making, and to improve the efficiency of our patient assessments in line with the Ministry of Health's FCT targets.

We were conscious of a number of potential problems that may affect the ability of the MDC to function efficiently. The MDC requires patients to spend a half day in hospital and they receive a large amount of complex information in a short space of time. However, patient feedback was very positive and emphasises that, after clinic, they have a clear management plan in place, often with a confirmed date for surgery, have completed anaesthetic pre-assessment, personally met all their clinicians and their questions have been addressed. A further anticipated barrier was the question whether several services could work together and function effectively making decisions in a relatively short space of time. Staff satisfaction levels with the clinic are very high, primarily because patients are seen, assessed, and a definitive treatment plan is decided on by the end of clinic and future schedules are established. The Intensive Care Medicine specialists report the benefit of having met the patient and family prior to postoperative admission. The CNS is better placed to facilitate and coordinate any further investigations, procedures and referrals as a result of the enhanced inter-disciplinary communication.

In the clinics first year of operation, we were able to decide on a definitive treatment for 88% of new patients at a single clinic appointment. In the majority of patients, their clinic appointment was proceeded by MDM review prior to their appointment. However, this was not always possible due to scheduling or limited availability of MDM resource (currently capped at 20 patients per 60 minute weekly meeting), although coordination of MDC and MDM review improved over the year. We plan to begin a second weekly MDM immediately prior to the clinic to review radiology on clinic patients and make initial decisions around multidisciplinary care and treatment. We hope that this will mean all patients (both new and follow-up) will have radiology formally reviewed in MDM prior to assessment.

Most previously described MDC concentrate on managing the interplay between surgery, medical oncology, and radiation

oncology in the various tumour types.[5-13] Our clinic currently differs from these in that we have initially concentrated on the multidisciplinary assessment of patients with upper gastrointestinal malignancies, and placed an emphasis on preoperative and pretreatment assessment and optimisation in an often highly comorbid group of patients. Currently, patients who require medical or radiation oncology review and treatment are discussed in MDM, reviewed in MDC and then referred directly to oncology services at Auckland City Hospital. Following treatment (either neoadjuvant, adjuvant or palliative) they are referred back to the MDC for surgical management or ongoing follow-up. However as part of the development of a local oncology service at WDHB, the intention is to expand the scope of the clinic to include medical oncology assessment by on-site oncology staff with their treatment planning facilitated by MDM review immediately prior to the clinic. Specialist clinical psychologists have also been appointed and will also begin to see referrals in the MDC in early 2016 and it is anticipated that a research nurse will also be available to discuss clinical protocols and biobanking with clinic patients.

Review of the first year of function of a specialist upper gastrointestinal MDC has shown that it is provides a single forum where patients can be reviewed and a definitive treatment plan formulated in nearly 90% of patients, even when this involves multiple medical and paramedical specialties. The clinic results in high levels of patient and clinician satisfaction.

Competing interests:
Nil

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Treatment of uncomplicated cystitis: analysis of prescribing in New Zealand

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ABSTRACT

AIMS: To describe prescribing for women with suspected urinary tract infections, including suspected uncomplicated cystitis, in New Zealand.

METHODS: Randomly selected community pharmacies participated in the study. Women attending the pharmacy in a 2-week period in 2012 for prescribed or non-prescription treatment of symptoms suggesting a urinary tract infection, or prophylaxis of a urinary tract infection, were invited to self-complete a questionnaire. Analysis focused on prescribing for women with symptoms of cystitis without complicating features.

RESULTS: Valid questionnaires arising from a prescription treatment were received from 789 patients from 139 pharmacies. Questionnaire data indicated that 17% of women had symptoms of cystitis without complicating features. Most prescribing was for a first-line agent, trimethoprim (59%) or nitrofurantoin (14%), but norfloxacin was also common (21%). Women with self-reported antibiotic use for suspected cystitis in the past 6 months were more likely to be prescribed norfloxacin than those with no such use. Many prescriptions were for a dose or duration outside those recommended in New Zealand guidelines.

CONCLUSIONS: While use of first-line agents is generally high, norfloxacin use could be reduced further. There is scope to understand clinical practice that deviates from guideline use regarding dose and duration.

One of the most common reasons for medical visits by young women is acute lower urinary tract infection (UTI), or cystitis.[1] UTIs occur in 30–50%[1,2] of women at least once in their lifetime,[1,2] and suspected cystitis is the second most common reason for empirical antimicrobial treatment.[1] Therefore, appropriate treatment of women with suspected UTIs is important for women's health and antimicrobial stewardship. The 2011 and 2013 Best Practice Advocacy Centre (BPAC) guidelines for treating uncomplicated cystitis in non-pregnant women, recommend treatment with trimethoprim 300 mg once daily for 3 days, or nitrofurantoin 50 mg four-times-daily for 5 days first-line, with norfloxacin second-line.[3,4] In pregnant women, trimethoprim (except first trimester) or nitrofurantoin (except from week 36) have the same dosing but for 7 days, and norfloxacin is avoided. BPAC reported increasing use of ciprofloxacin and high use of norfloxacin in New Zealand, despite "very few situations in general practice where a quinolone would be considered first-line treatment".[5] Recent studies show cystitis in women is commonly treated with fluoroquinolones in France,[6] and with nitrofurantoin in the Netherlands.[7] General practice prescribing of trimethoprim for cystitis in England is commonly for longer than the recommended duration.[8] While adhering to guidelines on drug, dose and duration for infections benefit antimicrobial stewardship,[9,10] and potentially aids effectiveness and limit adverse effects, it is unknown how well New Zealand prescribers adhere to local guidelines for many infections including cystitis, and how often quinolone antibiotics (norfloxacin and ciprofloxacin in New Zealand) are used in suspected cystitis without complicating features. Additionally, although antimicrobial resistance for some agents including trimethoprim increases with recent prescribing of antibiotics,[11,12]

whether and how previous antibiotic use affects prescribing is unknown.

In November 2012, trimethoprim became available from specially trained pharmacists for women aged 16–65 years with symptoms of cystitis without any complicating features (such as pregnancy, treatment failure, frequent infections, or antibiotic use in the past 6 months). Therefore, this study aimed to provide information on prescribing and pharmacy supplies for UTIs in New Zealand before and after pharmacist supply. Changes in overall supply of antimicrobials are reported elsewhere. This paper focuses on prescribing in UTIs, specifically: 1. What treatment was prescribed to women presenting in a pharmacy with a prescription to treat a possible UTI or for prophylaxis of a UTI? 2. What treatment was prescribed to women with symptoms of cystitis without complicating features? 3. What treatment was prescribed to women with symptoms of cystitis without complicating features who self-report antibiotic use in the last 6 months. 4. What treatment was prescribed to pregnant women with presumed UTI?

Given the greater quantity of data in the baseline phase (2012), and minimal change in prescribing from the baseline phase to the second phase, this paper reports the 2012 data.

Patients and methods

Ethics committee approval was not required because the study was an observational investigation collecting no identifiable patient details, with written confirmation provided in the on-line process by the Health and Disability Ethics Committee (4 September 2012).

Questionnaire data and observational data were collected over a 14-day period (24 September to 7 October 2012) before pharmacists could supply trimethoprim without a prescription.

Following a 1-week pilot phase in 10 pharmacies, 170 community pharmacies were randomly selected and invited to participate in the study. Random numbers were generated using Stat Trek (stattrek.com) for the 947 New Zealand community pharmacies listed in the Pharmacy Guild's directory (October 2010). Pharmacy staff provided eligible women with written information explaining the study, and invited them to self-complete a two-page questionnaire in the pharmacy.

Women were considered eligible to enter the study if they were: aged 16 years or over and had been dispensed a prescribed treatment for a suspected UTI (including an antibiotic and/or a urinary alkaliniser); had purchased a relevant non-prescription remedy (including urinary alkaliniser, cranberry or methenamine hippurate); or had consulted a pharmacy staff member about a suspected UTI. Women living in a rest home were excluded. No patient identifying information was collected, other than the patient initials to match questionnaire data with the dispensing recording sheet (see below). Questionnaire completion was taken as consent to participate.

Pharmacy staff were asked to record all dispensings for norfloxacin, ciprofloxacin, nitrofurantoin or trimethoprim (regardless of reason for use), or other prescribed treatments possibly for a suspected UTI (from patient discussion). In this 'dispensing log', staff recorded the date, patient initials, medicine, quantity dispensed, whether the questionnaire was completed, and reasons for non-supply of the questionnaire (ie, male, age under 16 years, use for an indication other than a UTI, or living in a residential care home). The dispensing log indicated the proportion of supplies without a questionnaire, and reasons for non-completion (including ineligibility). This log also aided questionnaire accuracy with respect to medicine and quantity, where the study team matched the dispensing log and questionnaire by date and patient initials.

Women were asked about their symptoms, medical history, treatment received that day, previous treatment for this current infection, and demographics. They were instructed to ask the pharmacist for help if necessary. Pharmacy staff had been asked by the researchers to help the participant list the medication prescribed.

Women were considered to have suspected cystitis if they reported in the questionnaire: burning or pain on urination; pain in the lower abdomen just above the genital area; and/or the need to urinate often or urgently.

Table 1: Demographic and presenting features of the participants.

	All women who provided questionnaires (%)
Total	949
Ethnicity*	
European	745 (78.5)
Māori	118 (12.4)
Pacific	53 (5.6)
Indian	22 (2.3)
Chinese	15 (1.6)
Other	41 (4.3)
Unknown	19 (2.0)
Age	
16–20	86 (9.1)
21–30	164 (17.3)
31–40	130 (13.7)
41–50	149 (15.7)
51–60	138 (14.5)
61–65	57 (6.0)
>65	195 (20.5)
unknown	30 (3.2)

* respondents could indicate multiple ethnicities so total proportion is more than 100%.

Women were excluded from the suspected cystitis group if they had possible symptoms of pyelonephritis, defined as: pain in the lower back or kidney area, or fever, or chills. Suspected cystitis was considered to have no complicating features if the woman reported none of the following: having an abnormal urinary tract; previous kidney problems other than an infection; recent presence of a urinary catheter; being pregnant or diabetic; having had more than three UTIs in the past 12 months; failure of an antibiotic for their current suspected UTI; a hospital admission in the preceding month; treatment with an antibiotic in the previous 6 months; or age under 16 years or over 65 years.

Pharmacies and women participating in the study received no payment, but $1(NZD) was donated from the study funds to the Women's Refuge for each questionnaire completed.

Questionnaire data were entered into Excel spreadsheets, and analysis was conducted using Statistical Analysis System (SAS) 9.3, SAS Institute, Cary, NC, US.

The Chi-squared test (χ^2), or Fisher exact test, was used to assess associations between categorical variables; the Kolmogorov-Smirnov two-sample test was used to test the cumulative distribution of continuous variables between groups. A non-linear mixed effect model was used for nominal survey responses for medicines supplied. A covariance test was used for the prescriptions in a nonlinear mixed-effect model. In the analysis of women eligible for pharmacist supply of trimethoprim, cluster analysis was not used because the observations for most pharmacies numbered less than three. Showing no statistically significant variation in severity or duration of symptoms between pharmacies, the analysis from the complete data set was computed at the patient level.

Results

Completed materials were returned to the study centre by 139 pharmacies, 81.8% of those invited to participate. Prescription data recorded by pharmacy staff dispensing

Table 2: Prescribed treatment in respondents, and the subgroup of women aged 16–65 years with suspected cystitis without complicating features.

Medicine	All respondents receiving a prescription (%)	Prescription management in participants with suspected cystitis without complicating features (%)
Trimethoprim	418 (53.0)	74 (58.7)
Norfloxacin	194 (24.6)	26 (20.6)
Nitrofurantoin	129 (16.3)	17 (13.5)
Ciprofloxacin	14 (1.8)	0 (0.0)
Co-trimoxazole	9 (1.1)	4 (3.2)
Amoxicillin + clavulanic acid	8 (1.0)	1 (0.8)
Cefaclor	6 (0.8)	1 (0.8)
Other/unspecified antibiotic	9 (1.1)	2 (1.6)
Non-antibiotic treatment	21 (1.8)	1 (0.8)
Total number of questionnaires*	789†	126

* Where two antibiotics were supplied, both are counted; †missing data four questionnaires

logs during the study period comprised 1,783 patient entries. Four hundred and forty-four (24.9%) met the exclusion criteria for the study (eg, male, child, rest home patient, or indication other than UTI). Of the 1,339 patients eligible or possibly eligible for the study, the 789 valid questionnaires arising from prescription supply represented a 55.6% response rate, assuming the dispensing logs were accurate. Questionnaires from 958 patients were returned, and after nine exclusions, 949 were included in the study. An average of 6.8 questionnaires per pharmacy (range 0–32), were available for analysis.

Demographic and presenting features for women respondents

Most women were of European ethnicity, with approximately 12% Māori, and Pacific peoples and other ethnicities providing a small minority of those surveyed (Table 1).

Of the valid questionnaires, most (789, 82.1%) arose from prescription dispensing. The most commonly-prescribed treatments to all participants receiving a prescription were trimethoprim, norfloxacin and nitrofurantoin (Table 2). Women aged 16–65 years with suspected cystitis without complicating features also were most likely to receive these same three medicines.

Prescription supplies in women with symptoms of cystitis without complicating features

Approximately one-in-six (16%) of 789 participants reported symptoms of cystitis and did not report any complicating features. In suspected cystitis with no complicating features, most prescriptions dispensed were for the first-line agents: trimethoprim or nitrofurantoin (n=91, 72.2% of questionnaires arising from prescriptions). A minority of prescriptions for this subgroup of women used the recommended dose and duration of a first-line agent in the New Zealand guidelines (20.6%).

Around one-third of trimethoprim dispensings (35.1%) appeared to use the recommended duration of 3 days (Figure 1). Most trimethoprim treatments appeared longer than recommended with a median of five trimethoprim tablets prescribed. No nitrofurantoin supplies complied with the recommended dose and duration, with considerable variation observed (Figure 2). Norfloxacin was mostly prescribed in quantities of six tablets (consistent with recommended dosing of twice-daily dosing for 3 days, 72%), with 20% prescribed 10 tablets.

Previous antibiotic use was associated with some differences in antibiotics used (Table 3). Previous antibiotic use (for cystitis or for other uses) did not appear to affect the frequency with which nitrofurantoin was prescribed (12.8–15.8%). However, norfloxacin usage increased significantly in women who reported having cystitis in the last 6 months (33.3% vs 20.6%, respectively; χ^2=4.95, df=1, p=0.026).

Figure 1: Trimethoprim quantity prescribed to women with suspected cystitis without complicating features.

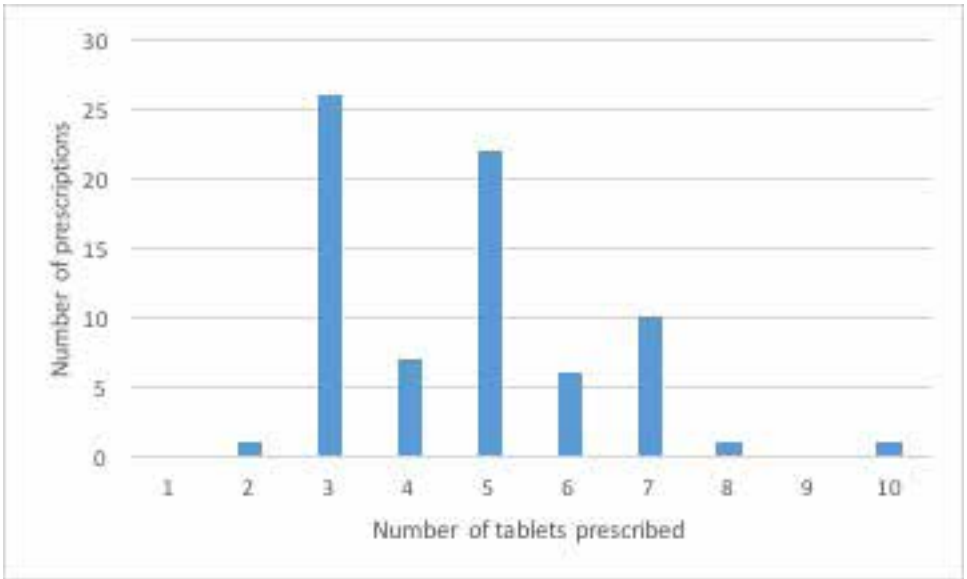

Figure 2: Nitrofurantoin strength and quantity prescribed to women with suspected cystitis without complicating features.

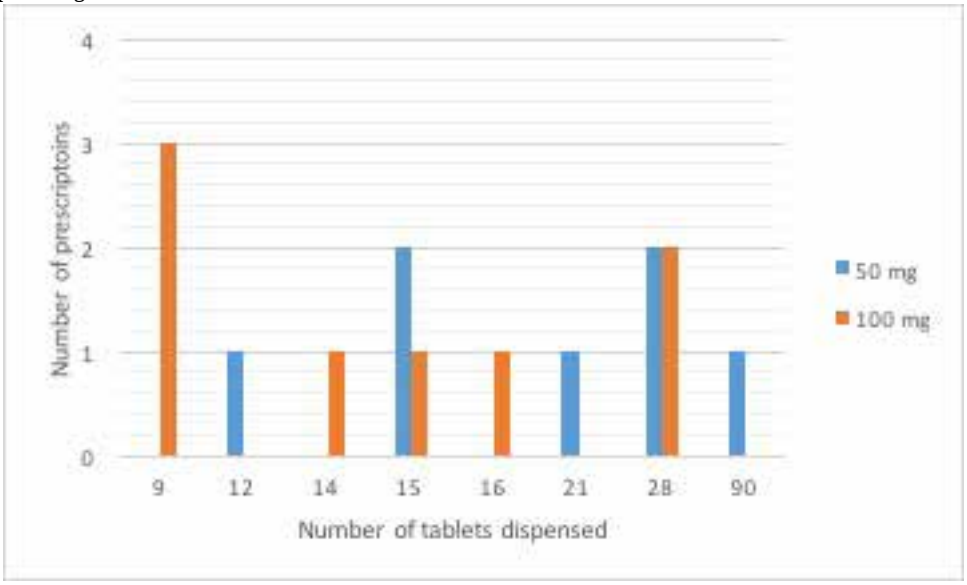

Table 3: Antibiotic prescribing in women with suspected cystitis without complicating features, according to previous antibiotic use.

	Subgroup except no self-reported antibiotic use in the last 6 months	Antibiotics for cystitis in last 6 months but otherwise matching subgroup criteria	Antibiotics for reasons other than cystitis in last 6 months but otherwise matching subgroup criteria
Trimethoprim	74 (58.7%)	27 (50.0%)	27 (69.2%)
Nitrofurantoin	17 (13.5%)	8 (15.8%)	5 (12.8%)
Norfloxacin	26 (20.6%)	18 (33.3%)	5 (12.8%)
Other antibiotic	8 (6.4%)	1 (1.9%)	2 (5.2%)
Totals	125	54	39

Pregnant women with symptoms of cystitis also had variable antibiotic prescribing. Most received nitrofurantoin (n=16), or trimethoprim (n=6), with one woman receiving amoxicillin-clavulanic acid. Half of the women received a quantity indicative of the recommended 7-day treatment (although not always at the recommended strength for nitrofurantoin). Most other women received fewer tablets than recommended, eg, 3–6 trimethoprim tablets.

Discussion

This study provides insight into prescribing for suspected UTIs prior to pharmacist supply of trimethoprim. The paper concentrates specifically on women with symptoms of cystitis without any complicating features, for which guideline-adherent treatment would usually be appropriate. These prescribers would have been doctors in all or almost all cases, as few nurses have prescribing rights.[13] For pregnant women with symptoms of cystitis, prescribers were midwives or doctors.

Most women with suspected UTIs were prescribed medicines recommended in New Zealand guidelines as first-line for cystitis (trimethoprim and nitrofurantoin). For women with symptoms of cystitis and no complicating features, nearly three-quarters were prescribed a first-line agent according to New Zealand guidelines, mainly trimethoprim. In 2011, New Zealand's BPAC expressed concern about ciprofloxacin and norfloxacin use.[5] We found a low level of ciprofloxacin use by women with UTIs, and no ciprofloxacin use in women without complicating features, but about one-fifth of such women treated through prescription received norfloxacin. This quinolone usage is considerably lower than in France[6] and Switzerland,[14] but higher than the Netherlands.[7] In New Zealand, fosfomycin and pivmecillinam are not licenced, or generally funded on prescription.

Further research over an extended period would reveal change over time, and whether national messages on antibiotic use are working. In 2014, funding restrictions on norfloxacin were implemented to reduce first-line use, so a repeat survey may be warranted to ascertain the effect of this policy. Additionally, the reclassification of trimethoprim may alter prescribing in the long-term. A repeat of this survey would indicate further changes.

Nitrofurantoin had low use, despite being recommended first-line in New Zealand for suspected cystitis,[4] and having low rates of resistance.[15,16] The variable dosing we found could contribute to treatment failure from insufficient dosing or duration, or expose the patient and commensal bacteria to a longer duration than necessary. Some countries have higher nitrofurantoin use in uncomplicated cystitis, eg, the Netherlands (56–67%)[7] and Canada (27%).[17] In New Zealand, the four-times-daily dosing may be discouraging for prescribers (and patients), hard for prescribers to remember, or may be deliberately ignored given the inconvenience or difficulty of four-times-a-day dosing. A slow-release formulation (currently not available in New Zealand) with twice-daily dosing may simplify dosing, improving guideline adherence. It is unclear whether guideline non-adherence reflects lack of knowledge of the guidelines, lack of confidence in the guidelines, or a decision responding to individual patient circumstances. The guidelines differ from manufacturer product information for nitrofurantoin, which may create confusion. New Zealand guidelines could be reviewed to aid simplicity; for example, Scottish[18] and Belgian[19] guidelines recommend nitrofurantoin for 3 days in uncomplicated cystitis, which may limit adverse effects and aid compliance, although Dutch guidelines are for 5 days' treatment.[20]

With the low resistance profile for *Escherichia coli* to nitrofurantoin, we expected greater use of nitrofurantoin in women with previous antibiotic use, but it did not occur. Women who reported using antibiotics for cystitis in the last 6 months were more likely to get norfloxacin, a second-line agent. Why this shift occurred is unknown; possibly it arises from patient demand by women who regularly get these infections. Education may be required on resistance patterns with previous antibiotic use.

To reduce resistance, antibiotic prescribing should provide the "right drug at the right time at the right dose for the right duration".[10,21] Additionally, prescribing should be according to national guidelines, avoiding broad-spectrum agents, and using the shortest antibiotic course

likely to be effective.[10] We found prescribed trimethoprim use was often longer than the recommended 3 days for uncomplicated cystitis, nitrofurantoin dosing was highly variable, and some broad-spectrum agent use occurred. Duration is not often reported, but our results are consistent with data from England published in 2007, which indicated that most trimethoprim supplies exceeded the recommended duration.[8] In a later, small Scottish study, 56% of general practice prescriptions for cystitis were for the recommended duration.[22]

Other New Zealand research has found higher consumption of antimicrobials, and lower usage of narrow-spectrum penicillin than in some other countries.[9] Further research is required to investigate why antimicrobial prescribing in New Zealand is not more reflective of national guidelines or in-line with countries elsewhere. Routine laboratory urine data on rates of bacterial resistance may differ from rates of bacterial resistance in women with uncomplicated infections.[23] Therefore ongoing surveillance is needed to show bacterial resistance in such women to help inform local prescribing decisions and show what, if any, changes are associated with policy changes.

Strengths and limitations

Our research relied on self-reported information, with potential for recall errors. Diagnosis of cystitis typically relies on self-reported symptoms, but medical examination might have been more accurate. For example, low back pain may occur with cystitis,[24] and not indicate pyelonephritis. Around one-third of our questionnaires had possible symptoms of pyelonephritis (data not shown). This prevalence is likely to be an over-estimation, given that in adult women in primary care, cystitis is over 20 times more frequent than pyelonephritis.[25] Women who reported kidney problems were all considered 'complicated', but some might not have been. We could not identify whether women who reported having had kidney stones had them currently, and therefore we did not include such women in the complicated group. The limited medical history we asked excluded some history, such as medication intolerance, non-response with a medication, or immunosuppression, which may alter prescribing. Accuracy of medication recorded on the questionnaire was likely given the pharmacist's help in some cases, and the research team used the dispensing log for medication and quantity where necessary.

Entries in the dispensing log might have been missed, although checks against dispensary computer records often occurred to minimise missing data. Checks were indicated by the provision of computer records in some cases, how the pharmacy recorded the information, or anecdotal feedback when questioned about possible missing data. Thus, our denominator data may be under-stated. However, we have concentrated primarily on the questionnaire data, and prescribing data from the Ministry of Health indicates that our prescription questionnaires reflected around 40% of the expected prescriptions for trimethoprim. Women can receive trimethoprim and co-trimoxazole directly from their medical clinic, family planning, or sexual health clinics, under practitioner supply orders for emergency supply, but this is likely to be a small proportion of overall usage of these agents.

Usage of broad-spectrum agents other than norfloxacin and ciprofloxacin might have been under represented, as pharmacy staff were specifically asked to enquire on all trimethoprim, nitrofurantoin, norfloxacin and ciprofloxacin supplies, and where other antibiotics were used for a suspected UTI. Pharmacy staff therefore might have focused on the named agents.

We did not collect the exact prescribing information for the antibiotics, but used the quantity prescribed to ascertain compliance with guidelines.

The response rate shows that nearly half of eligible women did not complete the questionnaire. This finding could reflect a staff member forgetting the study, or lack of awareness of the study by a locum. However, it is possible that women with more severe symptoms did not participate, feeling too unwell to participate in the survey or attend the pharmacy in person. Minority ethnic groups might have been under-represented, possibly because of cultural sensitivity or language barriers,

precluding detection of variation by ethnicity. We do not know the ethnicity of those who did not participate.

The strengths of the research included the random selection of pharmacies and the high participation rate by pharmacies. Using the pharmacy meant that prescribers were probably unaware of the study. Dispensing logs helped to ensure the accuracy of the medicine/s supplied and their strengths and quantities, rather than rely on participant self-report.

Conclusion

This research provides a baseline of New Zealand prescribing for women with suspected UTIs, and particularly women with suspected cystitis without complicating features. Further research is required to ascertain long-term effects on prescribing from policy changes, and understand reasons for deviation from guidelines in treating cystitis.

Competing interests:
Natalie Gauld received funding from Pharmacybrands Ltd (now Green Cross Health) for work on the trimethoprim reclassification. Rosemary Ikram received funding for training and input into the trimethoprim reclassification. The other authors have no conflicts to report.

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New Zealand needs guidelines for the safe and responsible inclusion of pregnant women in medical research

Angela Ballantyne

ABSTRACT

Pregnancy is a crucial window of time that influences long-term population health. As a matter of justice, pregnant woman are entitled to high quality, evidenced-based care. As a matter of population health, we need to better understand foetal development, particularly the impact of lifestyle, stress, chronic conditions and clinical treatment during pregnancy. Pregnancy continues to be dominated by the precautionary principle, advocating for the routine exclusion of pregnant women from medical research, particularly intervention studies, on the grounds of foetal vulnerability. But this stance simply shifts the risk into the community. Due to a lack of evidence-based data, many pregnant women are refused medically important drugs, are subject to dangerous delays in getting drugs, or are prescribed drugs that are thought 'safe', despite evidence of possible teratogenicity. I argue that New Zealand needs to shift to a default position of inclusion of pregnant women in research; and to develop guidelines to facilitate their safe and responsible inclusion. The uniqueness of pregnancy gives rise to specific questions regarding research ethics. These questions warrant focused debate and the answers cannot simply be deduced from the general principles of research ethics we currently have in New Zealand.

Clinical research with pregnant women is limited; and that which does occur tends to focus on obstetric practice, and foetal safety. We need to broaden the research agenda to include a much wider range of health conditions, and study both short and long-term maternal and foetal outcomes. For example, this could include research on mental health, asthma, oral health and hypertension during pregnancy.

Pregnancy is a crucial window of time that influences long-term population health. Optimising health during pregnancy benefits the pregnant woman and her child, and can moderate future levels of chronic disease. During foetal development epigenetic programming occurs. This can have significant and long-lasting effects on mental and physical health through the course of the child's life.[1] Health, diet, drug use, exercise, sleep and stress can all have profound effects on the growing foetus. For example, domestic violence triggers stress in pregnant women that changes the cortisol receptors of offspring observed during adolescence.[2] Epigenetic effects can extend across generations through impact on germ cells.[3]

Significant advances have been made in the last century in understanding what constitutes best health during pregnancy, resulting in vast improvements in both maternal and infant mortality and morbidity in developed countries such as New Zealand.[4] Despite these advances, pregnant women remain one of the most underserved populations in clinical research.[5] Much healthcare for pregnant women, especially drug prescription, is not evidence-based because pregnant women are routinely excluded from participating in clinical trials. Some pregnant women face serious medical conditions, such as heart disease, diabetes, lupus, and cancer.

But medicines for these conditions are prescribed off-label for pregnant women. There are only 12 medicines approved by the FDA for use in pregnancy, and those are used to prevent premature labour or treat labour pains.[6] There is no equivalent empirical research regarding prescribing during pregnancy in New Zealand.

The use of medication during pregnancy and lactation is one of the least-developed areas of clinical pharmacology and drug research.[7] Due to a lack of evidence-based data, many pregnant women are refused medically important drugs, are subject to dangerous delays in getting drugs, or are prescribed drugs that are thought 'safe', despite evidence of possible teratogenicity.[8] Correct drug dosage, changes in pharmacokinetics during pregnancy, and compliance during pregnancy are not well understood. The teratogenic risk in pregnancy is unknown for 91% of medications.[9] Research shows that pregnant women continue to be prescribed drugs despite the lack of clinical research. The most common drugs provided to pregnant women are antiasthmatics, antibiotics, NSAIDS, anxiolytivcs, antidepressants and (inadvertently) oral contraceptives.[10] In Scotland, 85% of pregnant women are prescribed drugs via primary care services: many of the drugs are classified as high-risk, with one-fifth of women using FDA category C, D and X drugs during their pregnancy.[11] One study at Liverpool Women's Hospital in the UK found that 10% of total prescriptions for pregnant women were high-risk, off-label medicines.[12] In the US, 64% of pregnant women are prescribed one or more medications for the management of chronic or acute illness during pregnancy.[13] Adherence to treatment for chronic conditions (cardiovascular, rheumatic and bowel disorders, diabetes and epilepsy) during pregnancy remains low in Europe, North America and Australia; with women's views about the safety of drugs affecting their adherence.[14] We have a situation where the drugs are not tested, the risks are not well understood, drugs continue to be prescribed, and many pregnant women do not adhere to regimes—where all of these factors are related.

The exclusion of pregnant women from research is driven by liability concerns on the part of the manufacturer; restrictive regulatory environments; researchers' concerns about the vulnerability of pregnant women and their foetuses; ethical guidelines stating that research that can be undertaken in other populations should not be done in vulnerable populations; reluctance of health care providers to recruit pregnant women; and the risk aversion of pregnant women (and their families, and communities).[8]

Vulnerability and dangerous research

The split between research ethics and clinical ethics was driven by public outrage at cases of unethical research by clinicians. For example, in the US, the Tuskegee study prompted the National Research Act 1974, the establishment of institutional review boards, and the Belmont Report in 1979.[15] In New Zealand, the research ethics framework is based on Judge Cartwright's 1988 recommendations following investigation of cervical cancer research conducted at National Women's Hospital in Auckland.[16] As a result of this history, the field of research ethics is pervaded with a sense that research is dangerous rather than a social good.[17]

Research ethics guidelines have historically advocated for the protection of vulnerable groups from the potential harms of research. Vulnerable groups are generally deemed by international and national research ethics regulation to include: children, women of reproductive age, pregnant women, people in prison, people with cognitive impairment, and those highly dependent upon medical care.[18]

Pregnant women and their foetuses are physiologically vulnerable, and pregnant women may also be subject to social, cultural and economic pressures that constrain their freedoms and options.[8] But exclusion from research is not a simple answer to supposed vulnerability. Protective policies may have been motivated by concerns for the wellbeing of pregnant women and their foetuses, but the effect is unjust because the consequence of such exclusion is that pregnant women lack information about treatment options that would ordinarily be available to other non-pregnant patients.

The widespread exclusion of so called vulnerable groups from medical research

has resulted in a disproportionate body of evidence regarding the health of middle-aged white men.[19] Some clinical guidelines continue to be based on research that under-represents women, rather than actively selecting for studies that are more representative.[20] The last 40 years have seen a progressive effort to rebalance this perspective and to recognise that research participation is of value to both the individual and the population they represent. Recent policies have advocated for more medical research with women,[21] children,[22] and prisoners.[23] But pregnant women remain one of the last groups to be routinely excluded from research.[23] Why is this?

The precautionary principle and pregnancy

Pregnancy care is dominated by the precautionary principle;[25] which advocates action to reduce potential threats, before there is strong evidence of harm, in cases where the potential harm is serious or irreversible.[26] Two seminal cases of drug use during pregnancy changed the way we perceive risk and pregnancy. Ten thousand foetuses were affected by exposure to thalidomide, prescribed for morning sickness during the 1950s. And the daughters of women prescribed diethylstilbestrol (DES) were subsequently found to have a 40-fold increase in the risk of cancer later in life.[27]

The problem with the precautionary principle in relation to research is that it simply shifts the risk from the environment of a carefully controlled and monitored study, to inconsistent use of untested treatments and medicines off-label in the community. In other words, it is precautionary about one sort of risk, and blind to the other sort of risk that it itself thereby causes. The danger to pregnant women and their foetuses arises primarily from the lack of evidence about medical treatment during pregnancy, not from research itself. Untreated and under-treated disease can be dangerous for the foetus, and off-label prescription of untested drugs can be dangerous. A philosophy of absolute risk aversion may appear superficially lofty, but is actually impractical; it does not take account of the complex trade-offs that women make daily throughout their pregnancy.[28] If we are to take precautionality seriously—rather than myopically focusing on only one source of risk—we have to assess the risks and potential benefits of research versus treatment to determine which approach would be overall most precautionary. In some cases, this will call for the careful inclusion of pregnant women in well-designed studies.

International trends

Research ethics guidelines have a role to play in defining whether the default position is to include or exclude pregnant women from research. International guidelines tend to support inclusion. The Declaration of Helsinki, Item 5, notes that:

> *"Medical progress is based on research that ultimately must include studies involving human subjects. Populations that are underrepresented in medical research should be provided appropriate access to participation in research."*[29]

The Council for International Organizations of Medical Sciences (CIOMS) Guideline 17 asserts, "Pregnant women should be presumed to be eligible for participation in biomedical research."[30] The CIOMS guidelines are currently under revision and it is anticipated that the section on pregnant women will be significantly updated and revised.

In some jurisdictions, guidelines now advocate for limited and careful inclusion of pregnant women in research, subject to extra safeguards. In the US, pregnant women and their foetuses are categorised as a vulnerable research population and regulated under Subpart B of the Code of Federal Regulations (45 CFR 46).[31] These regulations are now thought to be overly restrictive and the categorisation of vulnerability is in tension with the views of the National Institutes of Health, which argue that pregnant women should be reconceptualised as 'complex' rather than 'vulnerable'.[32] The Australian *National Statement on Ethical Conduct in Human Research* has a chapter devoted to "Ethical considerations specific to participants",

which contains a section on pregnant women, along with other groups usually considered vulnerable. The *National Statement* requires that all research with pregnant women (including, for example, a questionnaire of dietary habits) is scrutinised by full Human Research Ethics Committee (HREC) review, rather than any expedited or alternative review pathways. Under these guidelines, interventional research with pregnant women must be limited to "therapeutic research".[33]

New Zealand guidelines

New Zealand does not have any research ethics regulation regarding the safe and responsible participation of pregnant women in research. In general terms, National Ethics Advisory Committee (NEAC) Ethical Guidelines for Interventional Studies state:

> *5.26 Investigators may not exclude participants on the basis of sex, ethnicity, national origin, religion, education or socioeconomic status, except where such exclusion or inclusion is essential to the purposes of the study.*
>
> *5.27 Inclusion and exclusion of participants affect the extent to which study findings can be generalised. To contribute to an equitable distribution of study benefits and burdens, investigators should, when practicable, consider including all those who may benefit from the study findings.*[34]

These general statements may be read to support the inclusion of pregnant women, because to routinely exclude them is not essential for the purposes of the research and discriminates against groups who could benefit from the knowledge gained from the research.

Paragraph 5.28 of the Guidelines identifies the following classes of vulnerable groups: children and young people, people with a mental illness, people with serious intellectual disability, people with English as a second language and/or a different cultural background to the investigators, people whose freedom to make independent choices is restricted (eg, prisoners, employees of a sponsoring company, or students) and people with serious illness.[34] From this list, the appendices include specific advice for research involving children, persons with an intellectual disability, unconscious patients, terminally ill patients, and older persons. Various sections of the guidelines discuss the need for special care to ensure that vulnerable participants are not subject to discrimination, abuse, undue inducement, coercion or exploitation.

One might assume that the general tone of New Zealand guidelines facilitates reasonable inclusion of pregnant women in New Zealand health research simply because they do not prescribe any specific limits on research with pregnant women (By New Zealand health research I mean research conducted with New Zealand residents in New Zealand, regardless of whether the sponsor is from New Zealand or overseas). In my experience, this is not the case. I have served on the Central Ethics Committee for 3 years, and in my view pregnant women are still routinely excluded from research without any justification. Often it is the case that pregnant women are excluded from studies for conditions known to affect them, where there is a high likelihood that they will be receiving treatment in the community off-label. Researchers rarely offer any justification for exclusion.

Specific guidelines

Health and Disability Ethics Committees, and researchers in New Zealand, need specific guidance about when and how to ethically include pregnant women in research. During pregnancy an entity of indeterminate moral status, with the potential to become a separate human being with legal identity and rights, exists inside a competent autonomous adult. The moral status of the foetus, and whether it is entitled to moral rights, is hotly contested. However, it is widely accepted, and reasonably so, that a wanted foetus which is likely to be carried to term, is a morally valuable entity worthy of care and protection. It is plausible to assume that the community has some duty of care to prevent irresponsible and unnecessary harm to the foetus. Does this duty extend to excluding pregnant women from trials that are relevant to their own health needs,

solely on the basis of potential risk to the foetus? Or would this unreasonably impede on the autonomy of the pregnant women?

Nor is pregnancy equivalent to the state of parenthood. A child is not located inside the mother, and its physiological health is not integrally linked to the health of the mother. The courts can independently assess the best interests of the child. During pregnancy, is it often difficult to disentangle the interests of the mother and the foetus, because the well-being and health of each is inter-dependent. We cannot therefore extrapolate from the research ethics guidelines regarding the inclusion of children in research. The uniqueness of pregnancy gives rise to specific questions regarding research ethics. These questions warrant focused debate, and the answers cannot simply be deduced from the general principles of research ethics we currently have in New Zealand. Research with children, unconscious patients, patients with a terminal illness, and prisoners also raise specific ethical issues, and all these populations receive focused attention and research related advice from NEAC. Pregnancy is mentioned nowhere in the NEAC guidelines for interventional or observational research or in the Operating Standards for ethics committees.

The US guidelines are generally thought to be overly restrictive. The Australian and CIOMS guidelines are currently under review, and the inclusion of pregnant women is expected to receive greater attention. In New Zealand, NEAC is reviewing their research ethics guidance in 2016–2017 and so this is a timely point to consider research ethics and pregnancy.

Questions for debate:

Research ethics guidance should include advice on the following topics:

- Should the foetus be conceived of as a separate patient or research participant?
- Who should assess the balance of risks versus potential benefits on behalf of the foetus? For example, should ethics committees reject applications on the grounds that they are too risky to the foetus, even if they represent some benefit to the woman? Or should the ethics committee's role be limited to ensuring that the risks and potential benefits are clearly explained in the informed consent process, leaving pregnant women to make the risk/potential benefit assessment themselves?
- Should the consent of the father or other nominated parent be required for research during pregnancy?
- Should the consent of the father or other nominated parent be required for the child's continued participation in the research or follow-up after birth?
- When assessing the risks of research, should ethics committees consider the relative risks to pregnant women of not participating in research (for example, undergoing untested 'treatment' in the community or remaining untreated)?
- Should pregnant women be classed as a separate sub-category of research participants within the study, subject to distinct data collection, safety monitoring and grounds for stopping the pregnancy-related arm of the trial?
- What rules should govern research in cases when the woman intends to abort the foetus?

Conclusion

For some, these questions may seem obscure, academic and uncomfortable. The default routine exclusion of pregnant women from research may appear safer and easier. We must remember that pregnancy is not simply a 9-month window; it is a crucial period affecting the long-term health of the future person. As a community we need to better understand health, disease, and medical treatment during pregnancy, and we can only achieve this by including pregnant women in health research. We have an ethical obligation to determine how to achieve this safely and responsibly.

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Doris Gordon: foundation of a legacy

Ronald W Jones
Doris Gordon Memorial Oration*

*Doris Gordon Memorial Oration delivered to RANZCOG Annual Meeting, Wellington, 2 October, 2015.

A journalist described 'Doctor Doris' (as she was always called) as "a severely handsome woman with a somewhat formidable manner which concealed—or sometimes cracked to reveal—a tender compassion which made her intensely and vulnerably feminine". The writer then went on to say that Doris used "her determination and intelligence…like a flail, a barb, a pitchfork, even a pistol, to force people to attend, and to agree, and to work, and to give, and to get things done".[1]

During a brief time as Director of Maternal and Infant Welfare, she was described as "highly unconventional and controversial…sweeping red tape out of pigeon-holes, humbug out of negotiation, cotton wool out of unwilling ears—like a young hurricane on rampage".[2] An obituarist said of her, "those who were privileged to see her at work described her as a spider in the middle of a web pulling strings to make everybody do what she wanted them to do" and "her achievements are fitting memorials to her restless spirit".[3]

Professor (later Sir) Bernard Dawson noted, "It is safe to say that no-one has contributed more to British obstetrics and the welfare of the women of New Zealand".[4] Her name and monumental contributions have almost been forgotten, although she was the catalyst in transforming largely primitive Victorian childbirth to mid-to-late twentieth century practice. She established the New Zealand Obstetrical Society in 1927, was its long-serving honorary secretary, and used the Society as the vehicle to create her visionary changes to maternal welfare. It is difficult for us today to comprehend how the vision, energy and commitment of a general practitioner from the backblocks of our country led to such enormous benefits for doctors, their women patients and families; we are standing on the foundations Doris Gordon established three-quarters of a century ago.

Doris was born in Australia in 1890 of a pioneering and missionary background. Following the financial crash in 1893, her family moved to a 'new start' in New Zealand where her father, a part-time lay preacher, continued his banking career, becoming a manager in Tapanui, Southland. She rebelled against attending the local high school and decided she should become an accomplished musician and make housework her livelihood. Doris's 'missionary' zeal is exemplified in her writings on the fly leaf of her Bible where, from a very young age, she professed her Christian principles and goals in life. "When I was utterly certain in my heart that I was doing right, I believed that God was my senior partner." Doris had a fragmented education until she decided to be a medical missionary and she was enrolled at Tapanui District High School from where she matriculated.

At university she wrestled with her creationist upbringing and the new Darwinian view of evolution. She was described as a "brilliant medical student", topping the class in medicine and surgery in her final year.[5] Later she claimed to be "probably the most poorly qualified entrant ever to cross the threshold" of the Otago Medical School.[6] She graduated in 1915 and, during house surgeon years in Dunedin, married a fellow medical graduate, Dr William Gordon, days before he left on overseas war service in 1917. She also became a university lecturer in microbiology under the tutelage of Professor Sydney Champtaloup, who was described as the "driving force" in the new medical laboratory, and who encouraged Doris to do a Diploma in Public Health. Her brief

placement in the head office of the Health Department led her to the realisation that bureaucrats "were frightened of newspaper publicity", an "awareness she later used to good effect in her campaign for maternity reform". "She zipped around Wellington in the sidecar of the health inspector's motor cycle" and "repacked samples of tinned foodstuffs obtained during factory visits to send to her new husband on the western front".[5] This experience provided Doris with a broader appreciation of 'community' health. It was during this time Doris was diagnosed with a 'spot on the lung' which resulted in her rejection for missionary work in India.

Following the war, she and her husband bought a country general practice in Stratford, Taranaki. She observed: "My Quaker-Puritan genes found an informal life in provincial Taranaki, great fun, I was well content to be the 'lady-doc' to the farmers as well as a mother or sister to their women folk".[6]

For the next 8 years her life was consumed with domestic responsibilities and the role of a busy general practitioner/obstetrician. An early enthusiast for pain relief in labour, Doris reported that cumulatively, she and her husband had 74 years of chloroform use without a single mishap, "in dentists' chairs, isolated farmhouses, in operating theatres warmed by roaring log fires, and in a hotel double bed where mine host wished his wife's affairs be kept quiet".[6] An early devotee of 'twilight sleep' led to her MD thesis titled *Scopolamine—Morphine Narcosis in Childbirth* in 1924. Her thesis was accepted by the London examiners 'with commendation'. Her busy life precluded the time and effort to complete the written part of the examination. A series of obstetric disasters caused her to consider the shortcomings in her own training in obstetrics and she "knew I should have a Fellowship of the Royal College of Surgeons of Edinburgh (FRCS Ed) so that if I was faced with another disaster, I would have the surgical standing to overrule the conservative 'wait and see'."[6] Together with her husband, Bill, she sailed to Britain where they both sat and passed the FRCS (Ed) in general surgery, obstetrics and gynaecology. Doris, who was second in the examination with another New Zealander, Dr Leslie Averill of Christchurch, was the first Australasian woman to gain the FRCS (Ed) qualification. After the examination, she made the acquaintance of a number of leading British obstetricians and gynaecologists, including Victor Bonney; Doris already understood the importance of networking. Following the establishment of the Royal College of Obstetricians and Gynaecologists (FRCOG) she became a founding member.

While Gordon is generally credited with the establishment of the chair in obstetrics and gynaecology in Dunedin, it was Henry Jellett from Christchurch (formerly Master of the Rotunda Hospital in Dublin), who first favoured the abandonment of 200 private New Zealand maternity 'homes' and their replacement with large teaching hospitals, and a chair in Dunedin. Professor Wayne Gillett has noted: "In 1921, James Parr, the Minister of Health, learned that more New Zealand women died in childbirth than in any developed country other than the United States of America." In 1920, it was 6.48 per 1,000 cases. He thought these figures would jeopardise New Zealand's public health reputation and appointed Truby King to identify the 'causes and cure' for maternal mortality.

There was a public outcry especially when they learned that the department had known about this for many years.

Truby King was a well-known eugenist, an authority in mental diseases and an internationally acclaimed infant health crusader. King met this challenge of the maternity mortality scare by intensifying the Plunket criticism against meddlesome midwifery. He travelled the country lecturing on the hazards of birth and babies damaged by forceps deliveries. "Fortunately a special committee on maternal mortality superseded King's propaganda and the direction of maternity care in New Zealand was ultimately changed by two individuals, Jellett and Gordon."[7]

In 1926, Gordon proposed a remit to the Napier Division of the British Medical Association (BMA) recommending the formation of a New Zealand Obstetrical Society, later New Zealand Obstetrical and Gynaecological Society (NZO&G Society), this was founded in Dunedin in 1927. The draft aim of the Society was "to correlate

the efforts of individual workers and to promote the scientific study of obstetrical matters in New Zealand…and to give the art of obstetrical practice the status it so rightly deserved, but at that time lacked", and "obstetrics seems to be very much the Cinderella among medical sciences".[8] Doris recognised that if this new Society was to achieve her long-term goals, she needed to have firm control over its destiny and, as she would later write, "the assemblage took for granted that my husband (Bill) would be the honorary treasurer and I would be the pen-driving honorary secretary".[6] She declined an honorarium.

The early minutes of the new Obstetrical Society provide a fascinating insight into the important issues of the day: the inadequate teaching of obstetrics in Dunedin; a remit to Otago University regarding the establishment of a chair of obstetrics; the possibility of a postgraduate school of obstetrics in New Zealand ("the time was not yet right");[9] the establishment of a resident obstetric training post for New Zealanders in Melbourne, and a supporting scholarship fund; the possible involvement of the National Council of Women (NCW) in fundraising; the possibility of a Māori obstetric hospital; and research into stillbirths, neonatal deaths and puerperal sepsis. The great Victor Bonney, whom Doris had recently visited in London, accepted her invitation to be present and speak to the New Zealand branch of the BMA following the foundation meeting of the Society.

Together with Dr Henry Jellett, Doris pursued her vision for the future of obstetrical education in New Zealand. The Dean of the Otago Medical School, Lindo Ferguson, wrote to Doris: "…some are insisting that midwifery and gynaecology…should have as much time as medicine and surgery…I shall have to keep out of the clutches of the obstetricians who are anxious to reform us so violently".[10]

The University of Otago accepted the O&G Society offer of a £25,000 endowment for the establishment of a chair in O&G together with an undertaking that the Otago Hospital Board would build a large, new maternity hospital suitable for training medical students. Doris relished the challenge of raising the necessary funds, and organised provincial committees. She enlisted the assistance of NCW; women in power—for instance, Lady Bledisloe, the wife of the Governor General, organised a supportive letter from Queen Mary, the Queen Mother; rich and poor women alike. Men's groups, in particular Rotary, were supportive; every member of the Auckland Savings Bank board was personally interviewed—resulting in a gift of £2,000. She proudly described the "press agitation" she achieved with the editors of all major newspapers, and the broadcasting service. While her husband ran both his own and his wife's practices, Doris criss-crossed the length and breadth of New Zealand—"midnight journeys"—addressing thousands of women—"prospecting". The six-month campaign raised £31,741 ($3,013,386 in 2016), of which £25,000 was presented to the University of Otago for a chair in O&G, and the remaining £6,000 was directed for two postgraduate travelling scholarships.[6]

Dr Bernard Dawson took up the Otago chair in 1932, impressing Doris with his "quick brain, military precision and eloquence".[6] He quickly established an harmonious relationship with her, aimed at improving obstetric practice in New Zealand. Later their relationship cooled when Doris promoted the development of a postgraduate department of obstetrics in Auckland, diminishing his sphere of influence.[11,12]

Doris Gordon's sterling work on behalf of the women of New Zealand led to the award of an MBE in 1935, and an Honorary Fellowship of the Royal College of Obstetricians and Gynaecologists in 1954. At the time she was the only woman outside royalty to be so honoured, and the only recipient in the southern hemisphere.

Barbara Brookes has noted that while "New Zealand had received acclaim for its ready acceptance of women's rights, in the central areas of private morality, birth control and abortion, New Zealand women have not been granted such ready recognition of their autonomy".[13] Doctors in the 1930s had little knowledge or training in contraceptive instruction and were reluctant to discuss birth control with their patients. At that time, New Zealand needed more, not fewer, births. The Obstetric and Gynaecological Society was prepared to give instruction in birth control where reasons of the health of the mother demanded

it, but only through hospital clinics. The Society was, however, concerned there was no restriction on the sale of contraceptives, including to minors, and felt it was "contrary to the public interest" for contraceptive knowledge to reach single men and women. During this time, illegal abortion was a major source of concern for the Society and women's groups, leading to the establishment of a commission of inquiry in 1936. During the previous year, 42 maternal deaths had been attributed to criminal abortion—the average number of children born to each of these women was eight.[14] In 1937, together with Dr FO Bennett from Christchurch (the first person outside Britain to be awarded a Hunterian Medal), Doris wrote a controversial polemic, *Gentlemen of the Jury*, in which they described their conservative views on contraception and the problem of illegal abortion.[15] While this book created controversy, it expressed the views held by most of the medical profession of the time. The book aroused parliamentary debate, one MP observing: "Tomorrow the Springboks play the All Blacks in Auckland. I wonder how many of the 55,000 people who will be present will realise that during the actual period of play, one child—perhaps a potential All Black—will have been wilfully destroyed in the womb of its mother."[13]

While Gordon was opposed to the state control of medicine, she did applaud the Labour government's introduction in 1939 of free general practitioner and specialist obstetrician maternity services, and 14 days' rest following childbirth.

If obstetric care was to progress in New Zealand, young, trained specialists were needed, and to this end the vision of Doris and the Society in providing scholarships for young doctors to gain postgraduate examinations and experience in obstetrics and gynaecology was far-sighted. The first scholarship was awarded in 1928, and from that time they were awarded annually. It soon became apparent that the young, newly-trained specialists were not returning to New Zealand, but remaining in Britain where better job opportunities existed—Dr Ken Pacey from Wellington was the only scholar among the first nine awardees to return to New Zealand. Doris noted: "…the only way to get the scholars [back] is to have a good obstetrics and gynaecology centre anywhere in the country…our hospital boards were badly advised by medical interests that did not want to see gynaecology exulted as a specialty".[6] Doris must have sensed she would not have received the necessary support for her nascent plans in New Zealand, and decided to enlist assistance from the powers-that-be in Britain; to this end she attended the RCOG meeting in Edinburgh in 1939. The College President, William Fletcher Shaw, was sympathetic to her plight and, together with previous scholars permanently resident in Britain—including Stallworthy and Hawksworth and anaesthetist, MacIntosh—they organised meetings in Manchester, Oxford and London. A decision was made to build a postgraduate obstetric and gynaecological hospital which would attract young specialists back to their country of birth. With British support, the O&G Society in New Zealand resolved: "The time has arisen for the establishment of a postgraduate centre for obstetrics and gynaecology".[16] It is noteworthy that Stallworthy, Doris Gordon, and others, made a strong case to recruit Hawksworth back to the foundation chair. Hawksworth's case for limited private practice (the funds to go to the departmental research fund) was the public basis for his rejection, but the real reason was personal jealousy by some senior members of the profession for his "right to private practice".[10] Hawksworth delivered the First Doris Gordon Memorial Oration in New Plymouth in 1963.[17] He recalled Doris was an examiner at his final oral medical examination, and he thought she was "a bit of a dragon". Doris Gordon's life extended beyond medicine: with husband Bill she raised four children of their own, sponsored 30 European refugees, ran a dairy farm and cared for her beloved garden and animals.

Around this time, a remarkable Auckland thoracic surgeon, Douglas Robb, wrote to Doris asking if he could become a member of the O&G Society. Doris described Robb as "an academic visionary who was always in hot water with the more myopic of his professional brethren".[6] Doris and Robb formed a powerful partnership, and teamed up with Stallworthy and Fletcher Shaw, to make a case for the establishment of a postgraduate

school of O&G in Auckland. Speaking at a Society meeting March 1941, Robb quoted the Rockefeller Foundation's lament: "'In the shadows that are deepening over Europe, the Lights of Learning are being extinguished one by one…more and more institutes of learning are being blotted out.' New Zealand has hitherto been content to send its doctors to Europe for higher training in obstetrics and gynaecology. Now that Europe is plunged into a scientific and cultural blackout it behoves New Zealand to 'light its own light of Science' and preserve (in the South) the learning we borrowed in happier years from the old world."[18] Once again, Doris's organisational skills came to the fore and with the assistance of businessmen, women's groups and the public at large, £104,594 ($7,618,760 in 2016) was raised to endow a postgraduate chair in obstetrics and gynaecology in a new women's hospital promised by the government.

Towards the end of the war, Doris invited one of New Zealand's most eminent sons, Charles Read, an obstetrician and gynaecologist soon to be knighted following his elevation to the presidency of the RCOG in London, to advise on matters related to the new postgraduate hospital in Auckland. Dawson, jealous of the projected new academic department, wrote to the college president in London expressing the opinion that "someone—not a New Zealander—should be sent in order to give a more detached view".[11,12] Fletcher Shaw came instead.

Doris Gordon died in her own hospital, Marire, Stratford, in 1956, and did not see the opening of the new National Women's Hospital in 1964. Following her death, the New Zealand O&G Society and the National Council of Women raised £4,793 to establish the Doris Gordon Trust, to "promote, sponsor, cooperate in, and otherwise further the study and/or practices of gynaecology and obstetrics". Her autobiography *Back-Blocks Baby Doctor* has been reprinted nine times, once as an e-book.[6]

Declining interest in general practitioner obstetrics in the 1980–90s, the increasing participation of midwives following the passage of the 1990 Section 88 legislation, and deaths of the Doris Gordon trustees, led to the demise of the O&G Society and the Trust. The lengthy failure of the Trust to submit IRD returns led to my accountant's request for assistance.

Following years of enquiries and considerable goodwill, a new Trust has been established between the NCW (an original trustee) and the New Zealand branch of the RANZCOG (*vis-á-vis* the O&G Society) with $130,000 from the original Trust and $160,000 from the defunct O&G Society establishing a financial base for education in women's health including an annual Doris Gordon Memorial Lecture.

In a memorial broadcast in 1957, Sir Douglas Robb remembered Doris: "No one who knew Doris Gordon, or at least no one who was being used by her for her high purposes, would remain long in doubt about her tenacities and inflexibilities in pursuit of her ends. A mere male, the ordinary peace-loving type, might even be a little afraid of her energy and the services she required. Fear was even, on occasions, known to develop into alarm as the pressure was put on and the chariot wheels revolved faster and faster. To be of any use to Dr Doris, you had to be ready to write letters, ring people up, try to put pressure on them, and generally leave your bed at any hour of the day or night. Nice work if you were pleasing her, but not so nice if you were dragging your feet, or getting her to change her mind. Some mere males have even been so peevish as to characterise her communications as unparliamentarily or even unscrupulous, but these persons take no account of Doris Gordon as a creative woman. Any person, male or female, who can cause to be endowed two medical chairs in the University of New Zealand, in addition to leading a full professional, business and family life, as Doris did, deserves our admiration and grateful thanks."[19]

Competing interests:
Nil

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Adult idiopathic hypertrophic pyloric stenosis

Simon Richards, Glenn Farrant, Gerard McCarthy

Case report

A 71-year-old female was referred by her general practitioner for an upper gastrointestinal endoscopy, with 3 months of progressively worsening dysphagia, epigastric pain, nausea and vomiting. She had concurrent weight loss. A trial of pantoprazole had made no improvement. Her symptoms were typically worse post-prandially. Her past medical history was significant for ischaemic heart disease, mild emphysema, rheumatoid arthritis, hypothyroidism and hypertension.

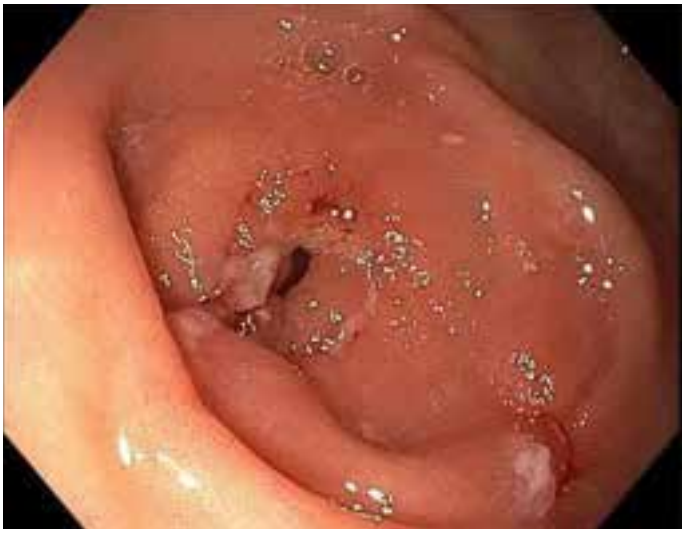
Upper gastrointestinal endoscopy showed a large amount of food residue in the stomach. The pylorus was scarred, stenosed and unable to be traversed (Figure 1). Biopsies showed no evidence of malignancy. As she was taking clopidogrel, dilatation was not attempted.

Her proton pump inhibitor dose was increased to 40 mg per day, and she had a repeat endoscopy at 6 weeks. Endoscopic findings were unchanged and biopsies again showed no malignancy. Dilatation was attempted but was unsuccessful. She proceeded to a CT scan of her abdomen, which showed circumferential pyloric wall thickening and small 9 mm gastrohepatic and mesenteric nodes, suspicious for a pyloric neoplasm (Figure 2).

She proceeded to surgery for a Billroth II subtotal gastrectomy. Operative findings were of a thickened isolated mass at the pylorus. There was no evidence of infiltrative changes nor of surrounding lymphadenopathy. A subtotal gastrectomy was performed. Her recovery was uncomplicated and post operatively, her symptoms were much improved.

The macroscopic pathological findings were of a 2 cm ill-defined submucosal mass at the level of the pylorus. The serosal and mucosal surfaces were unremarkable. Microscopic sections showed hyperplasia of the muscularis propria in the pyloric region (Figure 2). The presumptive diagnosis was of idiopathic hypertrophic pyloric stenosis.

Figure 1: Endoscopic view of the pylorus.



ISSN 1175-8716

Figure 2: Axial CT. Arrow: thickened pylorus.

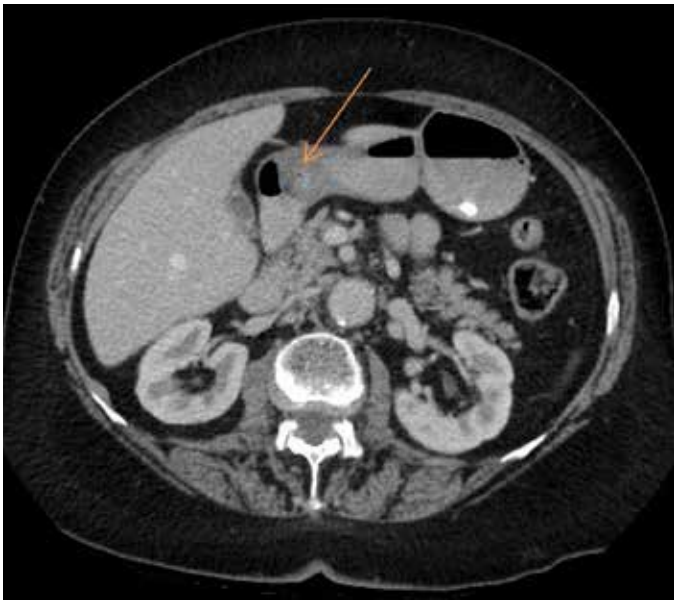
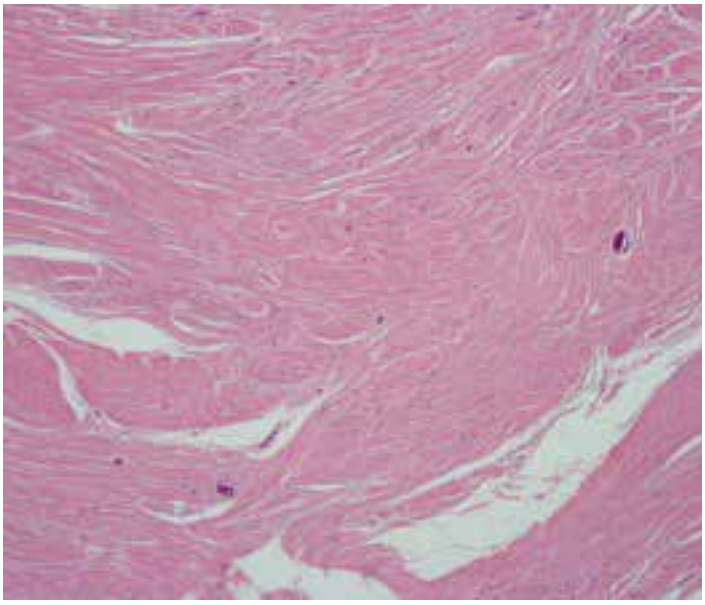


Figure 3: Microscopic view of the pylorus showing hyperplasia of the muscularis propria.



Discussion

Idiopathic hypertrophic pyloric stenosis (IHPS) is a disease usually seen in infants. Adult IHPS (AIHPS) is rare, and was first described by Jean Cruveilhier in 1835.[1] It is generally classified as either primary or secondary.

AIHPS presents in adult life without any apparent cause, and with no history of infantile vomiting, suggestive of pyloric stenosis of infancy. Microscopically, there is total or segmental hypertrophy of the smooth muscle of the pylorus, without any identifiable underlying disease.[2]

Secondary hypertrophic pyloric stenosis is as a result of other diseases of the upper gastrointestinal tract, such as peptic ulcer disease, malignancy and inflammatory diseases. Microscopically, there is localised replacement by fibrous tissue, and minimal or no hypertrophy of the muscularis propria.

The aetiology of AIHPS remains unknown. Most authors believe it is likely due to the persistence of a mild infantile form into adult life.[3] Infantile and adult IHPS have a similar anatomical and histological appearance.

Diagnosis is based upon history, clinical and radiological findings and endoscopic appearance. The predominant symptom is postprandial abdominal pain and distension. The discomfort tends to be relieved by vomiting. Weight loss and anorexia are common. Unlike infantile IHPS, an abdominal mass is not usually palpable. It may be mistaken radiologically and endoscopically for a gastric gastrointestinal stromal tumour, or a diffuse infiltrating adenocarcinoma given the normal overlying mucosa.

Endoscopically, the pylorus is fixed, narrowed and has a smooth border. Its appearance has been described as the "cervix sign" by Schuster and Smith[4]. Biopsies should always be taken, however they are frequently normal as the gastric mucosa is unaffected and therefore submucosal malignancies cannot be excluded. An endoscopic ultrasound and fine-needle aspirate or core biopsy may be performed, predominantly to exclude other submucosal tumours. Biopsies, however, may be inconclusive and currently there are no clear guidelines on their use. Dilatation can be performed, but results are usually temporary and recurrence high.

Surgery is indicated in the treatment of AIHPS. Partial gastrectomy, gastroenterostomy, pyloromyotomy and pyloroplasty have all been proposed as treatments.[2, 3, 5] In many cases, malignancy cannot be excluded, therefore gastric resection with either Billroth I or II reconstruction may be performed, and is preferred by most clinicians. Pyloroplasty is generally favoured over pyloromyotomy, due to the risk of mucosal laceration and subsequent diverticulum formation with pyloromyotomy. Pyloroplasty can be successfully performed laparoscopically.[5]

Conclusion

AIHPS is a rare condition with less than 300 case reports in the literature. Its aetiology is unclear, but may be an attenuated form of infantile pyloric stenosis. It may be treated endoscopically, however most patients proceed to surgery and a partial gastrectomy is preferred by most clinicians.

Competing interests:
Nil

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Intercalated degrees in New Zealand: a call for more undergraduate medical research training opportunities

Ibrahim S Al-Busaidi

The importance of medical student participation in research has been the subject of increasing scholarly research. Involvement in undergraduate medical research is associated with higher postgraduate research productivity, promotes interest in academic medicine as a career, and increases research outputs of medical institutions.[1] Two related trends have been observed worldwide: the low involvement in voluntary undergraduate medical research, and the declining number of clinician-scientists.[1] To combat these alarming trends, and produce a generation of capable clinical researchers, several strategies to increase student engagement in research have been established in New Zealand and abroad.[1-3] One of these is the introduction of intercalated research degrees.

Intercalated degrees are the most formal optional method of undergraduate medical research training in New Zealand.[2] Two degrees are on offer in New Zealand: the Bachelor of Medical Sciences with Honours (BMedSc(Hons)) and the Doctor of Philosophy (PhD). Intercalating students are required to take a year or two off their medical course to conduct a supervised research project, culminating in a thesis.

Despite the apparent benefits from medical student research,[1] intercalated degrees are unpopular research training opportunities in New Zealand. The mean uptake rates of BMedSc(Hons) degree at the Otago and Auckland Medical Schools are 7.7 and 1.5 per annum, respectively.[2,3] Allowing for differences in class number, medical students' interest in intercalated degrees is much higher in other Western countries. In Australia, the average number of intercalating students is approximately 10 per annum.[4] Furthermore, up to one-third of UK medical students combine their medical degree each year.[5] Reasons for the low rates in New Zealand have been scrutinised and include: a perceived lack of research training opportunities; poor support from faculty and supervisors; financial constraints; and delayed graduation time.[1,2]

While obstacles to intercalating ought to be addressed and rectified, alternative undergraduate research training opportunities need to be explored. Given the barriers posed by intercalated degrees, increasing mandatory curricular research activities seems to be a plausible alternative. Furthermore, summer studentships and independent/voluntary research involvement (such as research electives/selectives and clinical audits) are short-term endeavours which are arguably sufficient to provide interested students, unable to intercalate, with the necessary knowledge and skills to conduct research, pursue higher academic degrees and gain a foothold in academia.

New strategies to increase medical student involvement in research have been proposed. The concept of 'student research interest groups' have been introduced.[6] In these student-run research-focused groups, members exchange ideas and share their research-related workload, thereby increasing their research productivity. Furthermore, a recently implemented strategy is the introduction of formal

university administered student research bodies dedicated to facilitating medical students' engagement in research.[7,8] None of these strategies have been employed within New Zealand medical schools.

Despite the significance of, and benefits from undergraduate medical research,[1] New Zealand medical schools' efforts to engage students have come a long way, but are still suboptimal.[2,3] It is imperative to direct our attention to the low involvement of medical students in extracurricular research activities generally and intercalated degrees specifically. I call on the medical institutions in New Zealand to implement alternative innovative methods, compulsory or elective, to increase medical student research involvement and productivity.

Competing interests:
Nil

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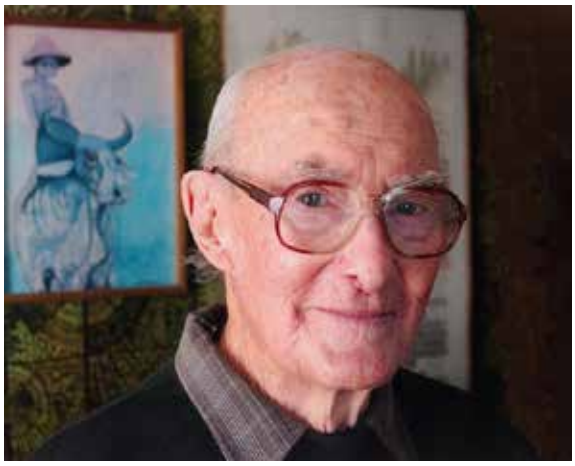
Douglas Paviour Short

17 March 1922 –20 May 2016
MB ChB, FRCS, MCCM, FFPHM RACP



Born in Auckland in 1922, Doug spent his early years in Remuera, attending primary school and two terms at Auckland Grammar. Completing his secondary education at Nelson College with a Fell Scholarship, he went on to study at the University of Otago, where he graduated in medicine with distinction in obstetrics and gynaecology in 1946 and won the Bachelor Memorial Prize and Medal.

Under the tutelage of the Medical Superintendent, Dr Percy Brunette, Doug began his working life at Nelson Hospital as a house surgeon. His interest in medical administration and ambition to become a surgeon were greatly influenced by Dr Brunette. In Edinburgh, he completed his postgraduate training as a Fellow of the Royal College of Surgeons in 1951.

On his return to New Zealand from 1952 –1953, Doug was Acting Medical Superintendent at Nelson Hospital, until his appointment as resident surgeon and Medical Superintendent at Dannevirke Hospital. It was here he honed his surgical skills, developed his ability as a medical administrator and began to pursue his lifelong interest in community health.

Again combining administration with surgical responsibilities, Doug took the position of Medical Superintendent at Tauranga Hospital in 1956 where he built on his Dannevirke reputation. His ability to envision what could be and to bring people together to achieve results that would improve health delivery for a community was a special quality.

In 1966, Doug interrupted this appointment to become leader of the New Zealand Surgical Team in Qhi Nhon, South Vietnam. Here, he further extended his surgical and administrative skills in a challenging 'Third World' wartime environment.

From Tauranga, Doug left the hospital service to take up a position with Tasman Vaccine Laboratories as it's Medical Director and Director of Special Projects Research.

Two years working in private industry saw a return to the hospital environment, firstly working as Senior Medical Officer, Accident & Emergency followed by Director of Medical Services at Wellington Hospital.

In 1976, Doug became Superintendent-in-Chief of the Bay of Plenty Hospital Board in Whakatāne. Here, he focused on several community projects funded by the beer and tobacco tax, and did some of his most inspiring work by bringing healthcare to the community—for example, the development of school-based health clinics and mobile ear caravans.

The next big step in Doug's involvement with community health care was his key role in the formation of the New Zealand College of Community Medicine (now the New

Zealand College of Public Health Medicine) in 1980, being its foundation president.

Finally, he returned to his roots in Nelson as Medical Superintendent of Nelson Hospital in 1983. Due to government policy at the time, he had to retire at 65, but still had considerable energy and enthusiasm for pursuing projects.

As the founding Chairperson of the Nelson Regional Hospice Trust, he was instrumental in setting up the hospice service in Nelson. He helped found Nelson's Health Action Trust, establishing a community-based health promotion initiative to help people with alcohol, drug and mental health issues, as well as working part-time as a Medical Advisor for the Accident Compensation Corporation (ACC) until he retired at 84.

Doug was a man of many talents; he loved music and was a skilled pianist. As a skilled watercolour painter, he gained great satisfaction from yet another outlet for his creative spirit.

Such was the foresight and commitment of Doug Short. He devoted his considerable intellect and vision to a lifelong service of making a difference in people's lives and will long be remembered with affection and thanks by his family, his many friends and colleagues and all those people who benefited from his wisdom and expertise.

He was a devoted husband to wife Marie, who predeceased in 2004. He is survived by three children, Jill, David and Judy, as well as six grandchildren, and at his death on 20 May 2016 after a major stroke was the proud great grandfather to three lovely great-grandchildren.

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Blood-pressure and cholesterol lowering in persons without cardiovascular disease

Elevated blood pressure and elevated low-density lipoprotein (LDL) cholesterol increase the risk of cardiovascular disease. Lowering both should reduce the risk of cardiovascular events substantially.

This proposition is examined in this randomised trial in which patients without cardiovascular disease were randomised to receive such treatments compared with placebos.

The combination of rosuvastatin (10mg per day), candesartan (16mg per day), and hydrochlorothiazide (12.5mg per day) was associated with a significantly lower rate of cardiovascular events than dual placebo among persons at intermediate risk who did not have cardiovascular disease. Muscle weakness and dizziness were more common in the combined therapy group, but the rate of discontinuation was similar in the two groups.

N Engl J Med 2016;374:2032-43

Antidepressant use and risk of cardiovascular outcomes in people aged 20 to 64

This report concerns a cohort study of 238,963 patients aged 20 to 64 years with a first diagnosis of depression.

Antidepressant class, dose and duration, and individual antidepressant drugs used were noted. Outcomes sought were myocardial infarction, stroke or transient ischaemic attack, and arrhythmia. The incidence of these outcomes were compared with a matched cohort of subjects not taking antidepressants.

No significant associations were seen between antidepressant class and myocardial infarction, stroke/transient ischaemic attack, or arrhythmia over 5 years' follow-up. Some indication of a reduced risk of myocardial infarction was noted in those taking selective serotonin reuptake inhibitors.

BMJ 2016; 352:i1350

Effictiveness of non-steroidal anti-inflammatory drugs for the treatment of pain in the knee and hip osteoarthritis

In this network meta-analysis, the researchers considered randomised trials comparing any of the following interventions: NSAIDs, paracetamol, or placebo, for the treatment of osteoarthritis pain.

Seventy-four randomised trials involving more than 58,000 patients were included in the analysis. The data suggests that paracetamol is ineffective, irrespective of the dose. Conversely, diclofenac at the minimum daily dose of 150mg/day is most effective for the treatment of pain and physical disability in osteoarthritis, and superior to the maximum dose of frequently used NSAIDs, including ibuprofen, naproxen, and celecoxib.

The researchers conclude that diclofenac 150mg/day is the most effective option for improving both pain and function in knee and hip osteoarthritis. They suggest that intermittent, short-term use is preferable to long-term fixed doses in view of the potential gastrointestinal and cardiovascular harms.

Lancet 2016;387:2093-105

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Lodges and Doctors

To the Editor of *The Press*, 1916

Sir,

The dispute between the British Medical Association of Wellington and the Friendly Societies has given certain members of Parliament an opportunity to talk in the House in a foolish manner. At that I am not surprised, but when Mr. Russell talks of applying an Act of Parliament or Ministerial pressure to coerce medical men into a course of conduct of which they do not approve, I am surprised indeed. Both parties, the ordinary members and the Minister, are talking to the gallery; in other words, are bidding for political favour and support.

It has always been a recognised rule that a doctor can decline to meet another medical man in consultation; this, instead of being a public disadvantage, has a contrary effect, and helps to maintain a proper standard of conduct. Mr. Russell would find that he is quite powerless to alter that rule, but there is not the slightest chance that he will try.

The medical men of Wellington are trying to obtain a more reasonable remuneration for their services to the members of the lodges, and, having agreed amongst themselves, they will decline to act with any doctor who contracts for attendance at the old rate, which has not been increased for many years. The workers of New Zealand from whom the Friendly Societies derive their members, have converted the Dominion, industrially, into a battlefield on which war is continually waged between themselves and their employers. They hedge round their work with all sorts of conditions as to rates of pay, hours of work, preference to unionists, and many particulars too numerous to mention, and in the final event are prepared to go on strike, and put the whole Dominion to great loss and inconvenience, by not only working themselves but endeavouring to prevent anyone else doing the work they decline, and have not hesitated to break the law and act with violence. Now, the Wellington doctors are not going to molest any doctor who chooses to undertake the medical treatment of members of the lodges on their own terms: they will simply decline to act with him or consult with him; but if any member of such lodges prefers any other doctor in Wellington, that doctor will willingly attend him as a private patient. I think the conduct of the Wellington doctors compares favourably with that of the trade unionists, who wish to coerce them into accepting rates of pay they consider very inadequate.

Yours, etc.

A DOCTOR.

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Health Practitioners Disciplinary Tribunal Notices

Med 14/299P

Charge

On 29 April 2015, the Health Practitioners Disciplinary Tribunal considered a charge laid by the Professional Conduct Committee against Dr Temalesi McCaig, a medical practitioner of Auckland (the Doctor).

The charge alleged that the Doctor forged and/or falsified documents provided to the Medical Council of New Zealand (MCNZ) for the purpose of gaining general registration.

Finding

The Tribunal found the charge established and agreed that it required disciplinary sanction. The Tribunal accepted that the Doctor had made a deliberate attempt to mislead the MCNZ into believing she had completed the intern requirements to support her application for general registration.

Penalty

The Tribunal censured the Doctor and suspended her from practice for a period of 1 month and imposed a $2,000 fine. The Tribunal ordered that on resumption of practice for a period of 3 years, the Doctor advise her current and future employers of the Tribunal's findings and penalty in this case, and within 12 months to attend an ethics course approved by the MCNZ. The Tribunal ordered costs be paid by the Doctor in the sum of $15,000 as a contribution to the costs of the Tribunal and the PCC.

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

The Doctor appealed the penalty imposed in regard to the period of suspension, the fine and the imposition of costs to the High Court on 04 December 2015. The High Court partially upheld the appeal noting that the suspension will be regarded as served given the period the Doctor was out of work as a medical practitioner. The censure, and the $2,000 fine remain, but the contribution to the costs was reduced to $5,940.

The full decision of the Tribunal can be viewed at http://www.hpdt.org.nz/Default.aspx?tabid=446

Med15/308P

Charge

On 5 May 2015, the Health Practitioners Disciplinary Tribunal considered charges laid by the Professional Conduct Committee against Dr Daniel Quistorff (the Doctor), medical practitioner of Auckland.

The first charge alleged that the Doctor was convicted for making false documents by issuing false medical certificates to students. The second charge alleged that the Doctor issued two referral letters while not holding a current practising certificate.

Finding

The hearing proceeded by way of an agreed summary of facts. The Tribunal was satisfied that the conviction charge was established and that the offence reflected adversely on the Doctor's professional obligation to act ethically, honestly and lawfully. The Tribunal found

the second charge amounted to professional misconduct, and that both charges required disciplinary sanction.

Penalty

When considering penalty, the Tribunal noted the Doctor's voluntary suspension from practice since December 2011, and the very real penalty he has already paid before the Court, financially, his prolonged suspension awaiting trial, and the distress he suffered as a result of the publicity his Court case attracted. The Tribunal censured the Doctor and imposed conditions on resumption of his practice and ordered that he pay a contribution of costs of $10,283 to the Tribunal and the PCC.

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

The full decision can be viewed at http://www.hpdt.org.nz/Default.aspx?Tabid=452

Med 15/316D

Charge

On 7 July 2015, the Health Practitioners Disciplinary Tribunal considered the charge laid by the Director of Proceedings against Dr Vijay Harypursat, medical practitioner of Whangarei (the Doctor).

The charge alleged that the Doctor failed to set and/or maintain appropriate professional boundaries with his 22-year-old patient with a history of serious mental health issues.

Finding

The hearing proceeded by way of an agreed summary of facts, and the Tribunal noted it had little difficulty in finding the charge established against the Doctor and disciplinary sanction was warranted.

The Tribunal noted that consideration of the seriousness of any given case necessitates consideration of far more than the type of relationship which eventuates. It involves considerations such as the extent to which the practitioner has subjugated his or her patient's interests to his or her own; the magnitude of the power imbalance in the case; the doctor's knowledge of these things; the scope of the breach of trust involved; the nature of the doctor's behaviour and in particular the extent to which he or she has manipulated or exploited the patient; the inherent dangers for the patient in the relationship; and the impact of the practitioner's misconduct for the patient.

Penalty

The Tribunal censured the Doctor and suspended his registration for a period of 9 months. Conditions were imposed on the Doctor on resumption of practice and he was ordered to pay 40% of costs of the hearing.

The Tribunal directed publication of its decision and a summary.

The full decision of the Tribunal can be viewed at: http://www.hpdt.org.nz/Default.aspx?Tabid=466

Med15/315P

Charge

On 14 and 15 September 2015, the Health Practitioners Disciplinary Tribunal considered the charge laid by the Professional Conduct Committee against Dr Ashley Hodgson, Medical Practitioner of Tauranga (the Doctor).

The charge relates to a conviction in the District Court in 2014 of 5 charges of dishonestly using a document with intent to obtain prescription medicines the Doctor was not entitled to, and that the conviction reflects adversely on the Doctor's fitness to practise.

The charge also alleges that the Doctor wrote prescriptions, obtained and consumed drugs without proper medical oversight, prescribed drugs to a patient in a manner which departed from usual prescribing practices, and that this conduct allegedly amounts to professional misconduct.

Finding

The hearing proceeded on an agreed summary of fact basis with the Doctor admitting the convictions and that they reflect adversely on his fitness to practise. The Doctor also admitted the other particulars as set out in the charge and they amount to professional misconduct.

The Tribunal was satisfied that all parts of the charge were established and disciplinary sanction was warranted.

Penalty

The Tribunal censured the Doctor, suspended him from practise for 3 months, and imposed conditions on resumption of practice. The Doctor was ordered to pay a contribution of 15%, or $9,725, towards the cost of the Tribunal and the PCC.

An application for permanent name suppression of the Doctor's name was declined.

The Tribunal directed publication of its decision and a summary.

The full decision of the Tribunal can be viewed at http://www.hpdt.org.nz/Default.aspx?Tabid=465

Med15/320P

Charge

On 3 and 4 November 2015, the Health Practitioners Disciplinary Tribunal considered the charge laid by the Professional Conduct Committee against Dr Gregory Thorne, Medical Practitioner of Hamilton (the Doctor).

The charge contained 14 particulars which fell into four categories of alleged offending: inappropriate prescribing of controlled drugs; failing to record prescriptions for drugs, including controlled drugs; inappropriately issuing medical certificates; and making false entries in medical records and/or medical certificates.

Finding

The hearing proceeded by way of an admission of charge by the Doctor. With the exception of particular 9 (obtaining excessive amounts of pethadine), the Tribunal found all other particulars of the charge established and was satisfied that disciplinary sanction was required.

The Tribunal noted that it is a serious abuse of the power and privilege that doctors are given to write prescriptions if they are not for the proper care of patients.

Penalty

The Tribunal censured the Doctor and suspended him from practice for 6 months; conditions were imposed on resumption of practise for 3 years. The Doctor was ordered to pay 35% of the total costs of the PCC and the Tribunal, a total of $43,096.

The Tribunal directed publication of the decision and a summary.

The Tribunal's full decision can be viewed on its website: http://www.hpdt.org.nz/Default.aspx?Tabid=470

Med15/310P

Charge

On 18 June 2015, the Tribunal considered two charges laid by a Professional Conduct Committee against Dr Y (the Doctor).

The first charge alleged the Doctor was guilty of professional misconduct as she wrote prescriptions for the supply of medicines and controlled drugs not for medical treatment of her patients, but to obtain drugs of dependency for her own use and she consumed some of those drugs without proper medical oversight.

The second charge alleged the Doctor was guilty of a conviction which reflected adversely on her fitness to practise. She was convicted of an offence of driving with excess breath alcohol (906 micrograms per litre) having previously been convicted of the same offence.

Finding

The charges were admitted by the Doctor and the Tribunal found both charges were established.

Penalty

The Tribunal found the charges were such that a suspension of 12 months was warranted. However, having regard to a period when the Doctor had not been practising from her own choice and receiving therapy it was treated that 9 months of that period had been met, leaving a net period of suspension of 3 months which operated from the date for hearing until 17 September 2015.

Various conditions were imposed on resumption of practice by the Doctor relating to:

- random breath testing and monthly blood and urine tests for 3 years
- monthly clinical supervision for 3 years
- prohibiting the prescription or supply of all controlled drugs for 2 years
- remaining abstinent from alcohol and non-prescription drugs of addiction for 3 years with the recommendation that this condition continue indefinitely
- engaging in an addiction support network for 3 years with the recommendation that this condition continue indefinitely
- the Doctor not work in sole practice as a medical practitioner for 3 years
- registration with and maintenance of a regular level of contact with a general practitioner for 3 years, and
- giving immediate advice to future employers of the Tribunal decision and orders.

The Doctor was ordered to pay a contribution of $17,250.00 to the costs of the hearing.

There was an order for permanent non-publication of the name and identifying details of the Doctor.

The Tribunal further ordered publication of the decision in the New Zealand Medical Journal and the HPDT website. The full decision can be found on the Tribunals website: http://hpdt.org.nz/Default.aspx?Tabid=456

Med15/317P

Charge

On 7 to 10 December 2015, the Tribunal considered three charges laid by a Professional Conduct Committee against Dr Christopher John Heron (the Doctor).

There were three Charges which, in summary, were:

- That the Doctor was engaged in a number of acts in relation to the 15-year-old complainant which were likely to bring discredit to the medical profession and therefore were misconduct under section 100(1)(b) of the Health Practitioners Competence Assurance Act (HPCA Act).
- That the Doctor had twice prescribed for the complainant oral contraceptives in circumstances amounting to malpractice or negligence.
- That the Doctor had on six occasions, including three involving the complainant, acted as a medical practitioner in writing prescriptions when he did not have a current practising certificate.

The Doctor admitted charges 2 and 3 but defended the first charge in regard to engaging in a number of acts in relation to the 15-year-old complainant.

Finding

The Tribunal found Charge 1 to be made out but that not all the particulars of that charge of themselves, warranted disciplinary sanction.

The Tribunal noted that to the extent that the particulars of Charge 1 are found to be made out, the behaviour is significantly inappropriate on the part of the Doctor and is likely to bring discredit to the medical profession. While at no time was the Doctor officially the

complainant's medical practitioner he was known to be a doctor and was trusted as such.

The medical profession must maintain its standards and the public require protection. Accordingly the Tribunal found that the particulars of Charge 1 taken cumulatively, were deserving of disciplinary sanction.

The Tribunal found Charge 2 to be established as misconduct, warranting disciplinary sanction.

The Tribunal found Charge 3 to breach the provision of the HPCA Act and again, warranted disciplinary sanction.

Penalty

The Tribunal censured the Doctor; ordered a fine of $5,000 in respect of Charge 2; and ordered that the Doctor contribute the sum of $30,000 towards the costs of the PCC and the Tribunal.

Had the Doctor been in practice, the Tribunal would have suspended him for a period of 12 months, but because there had been a period of time since the Doctor last practised, which would necessitate reassessment by the Medical Council of New Zealand, and because the evidence indicated the Doctor was unlikely to practice again, no order was made.

The Tribunal directed publication of its decision and a summary.

A full copy of the decision can be viewed at: http://hpdt.org.nz/Default.aspx?Tabid=467

URL:
www.nzma.org.nz/journal/read-the-journal/all-issues/2010-2019/2016/vol-129-no-1437-1-july-2016/6940