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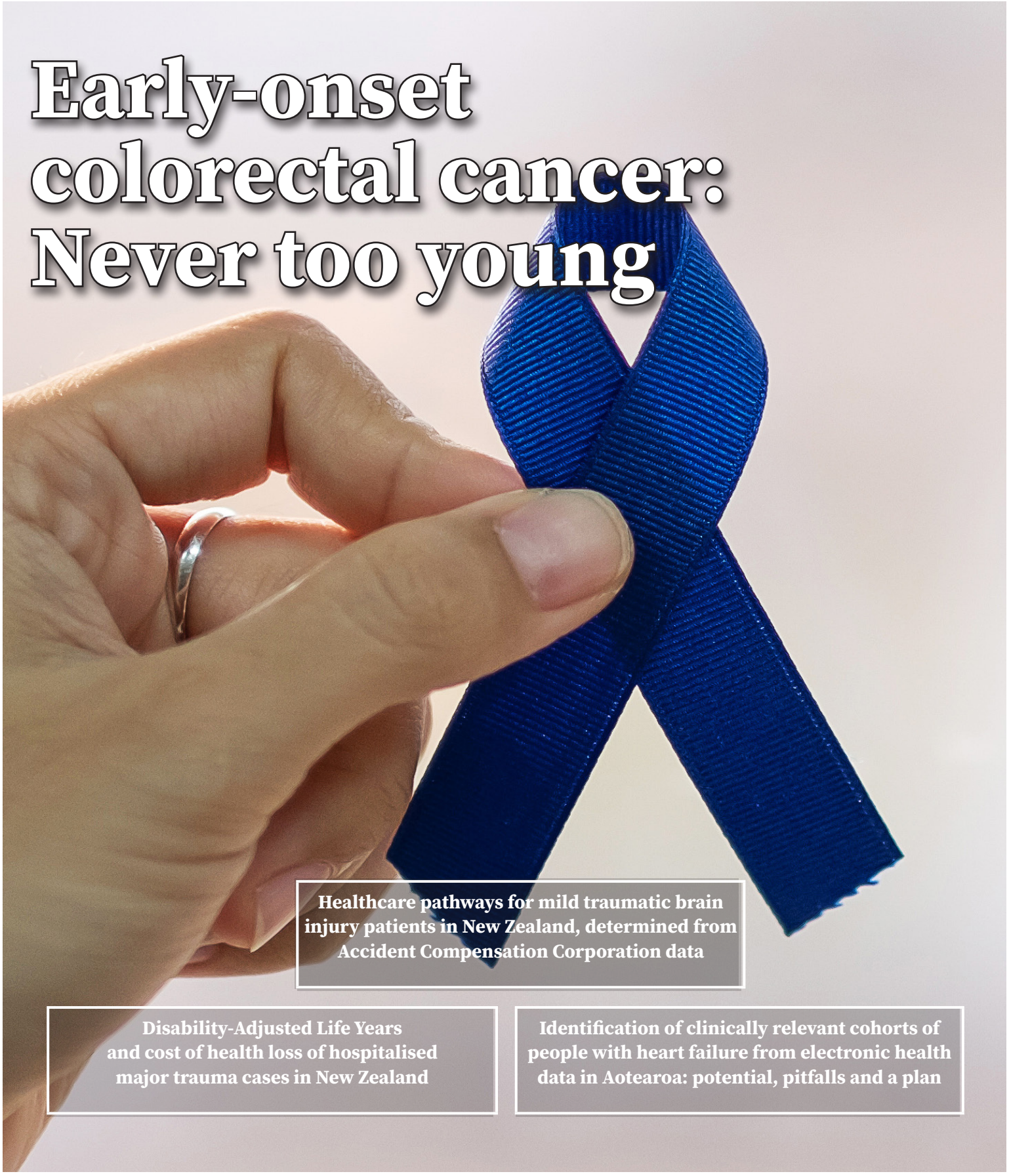
Early-onset colorectal cancer: Never too young



Healthcare pathways for mild traumatic brain injury patients in New Zealand, determined from Accident Compensation Corporation data

Disability-Adjusted Life Years and cost of health loss of hospitalised major trauma cases in New Zealand

Identification of clinically relevant cohorts of people with heart failure from electronic health data in Aotearoa: potential, pitfalls and a plan

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Summaries

A nurse-led and medically supported outpatient follow-up model following an acute coronary syndrome is as safe and effective as medical follow-up alone (ANZACS-QI 69)

Andrew McLachlan, Andrew Kerr, Mildred Lee

Heart attacks impact a large number of people every day and can leave people feeling stressed and anxious in the weeks following discharge from hospital. Cardiac rehabilitation offers support for people as they resume their lives, however, many do not take up this evidenced-based support for a variety of reasons. Most people, however, do attend the outpatient follow up review in traditionally medical clinics. This is the first study to prove that suitably qualified and supported nurses can provide effective and timely outpatient care, as safely as their medical colleagues.

Sources of healthcare-associated *Staphylococcus aureus* bacteraemia in New Zealand acute hospitals

Ruth Barratt, Grace Clendon, Barbara Gibson, Sally A Roberts

Staphylococcus aureus is a bacterium that is often found on the skin. It can cause infections, especially if there is an opportunity for the bacteria to enter the body. A bloodstream infection with *S. aureus* is very serious. This study looked at how people acquired *S. aureus* bloodstream infections while receiving healthcare. One of the common sources of these healthcare-associated infections (HAI) was having a line into a vein for medication. Improving care around these lines will help reduce these infections. The recent national healthcare associated infection point prevalence survey published on the Health Quality & Safety Commission website identified that 66% of all inpatients had a medical device in situ, of which vascular access devices were the most common medical device in use. *S. aureus* was the most common pathogen causing HAI and 13% of patients with HAI had a blood stream infection. One quarter, 25%, of these events were due to vascular access devices.

Healthcare pathways for mild traumatic brain injury patients in New Zealand, determined from Accident Compensation Corporation data

Renata Bastos Gottgtroy, Patria Hume, Alice Theadom

Efficient concussion care is important for quick recovery and positive patient and whānau experience. Our analysis of 55,494 patients showed that while concussion healthcare pathways in New Zealand were efficient for most patients, two out of three patients did not receive follow up care. Administrative delays affected thousands of patients every year. One quarter of patients waited more than two months to be seen at a concussion clinic. Patient pathways could be improved by facilitating concussion diagnosis, improving patient follow-up rates and reducing unnecessary administrative processes.

Bleeding risk of oral anticoagulants in liver cirrhosis

Oriana Munevar Aquite, Michael Hayes, Kebede Beyene, Amy Hai Yan Chan, Cameron Schauer, Henry Wei, Jiayi Gong

In New Zealand, two common blood thinners taken via the mouth are routinely used to manage diseases involving blood clots and irregular heart rhythms. However, the safety of one blood thinner called dabigatran or Pradaxa has not been routinely studied in patients with liver disease. Our research was aimed at comparing the risk of bleed that may occur if patients were treated with either Pradaxa or the usual warfarin. We found no different in bleeding risk between the two treatments but as our study was small with modest number of patients, we cannot be completely certain that this finding was by chance.

Disability-Adjusted Life Years and cost of health loss of hospitalised major trauma patients in New Zealand

Belinda J Gabbe, Siobhan Isles, Paul McBride, Ian Civil

Injury is one of the leading causes of death in New Zealand, and survivors of injury can experience substantial impacts of injury including lost health-related quality of life and disability. Disability Adjusted Life Years (DALYs) provide a way of measuring the health loss associated with conditions such as injury, as well as the cost of that health loss, across populations. In this study, we measured the DALYs lost due to major trauma in New Zealand from July 2017 to June 2020. Each year, an average of 7,573 DALYs were lost at an estimated cost of $341 million, highlighting the substantial impact serious injury has on the lives of New Zealanders.

Revascularisation and outcomes after acute coronary syndromes in patients with prior coronary artery bypass grafting—ANZACS-QI 67

Danting Wei, Jithendra B Somaratne, Mildred Lee, Andrew Kerr

In patients presenting with a heart attack, a prior history of coronary artery bypass surgery was associated with a high burden of comorbidities when compared with patients without prior bypass. Prior bypass surgery patients had higher rates of death as well as non-fatal outcomes. Despite accounting for a growing proportion of patients presenting to hospital, deciding treatment modalities for this subgroup is still a complex and challenging process. Further trials are needed to study the management strategies to improve prognosis in this high-risk group.

Prevalence of frailty and frailty outcomes within the inpatient rehabilitation setting: use of routinely collected electronic health information

Himali Aickin, Katherine Bloomfield, Zhenqiang Wu, Martin J Connolly

Frailty refers to a syndrome that is associated with poor health outcomes such as falls, hospital admissions and entry to aged residential care. We developed a tool to measure frailty in older adults admitted for a period of inpatient rehabilitation at Te Whatu Ora Waitematā using data that was recorded electronically as part of the normal admission process. Over 90% of patients were identified as frail and therefore at risk of future adverse health outcomes. Those with high frailty scores had significantly higher risks of being readmitted to hospital or dying in one year. Identifying such high risk patients should be used to deliver appropriate patient-centred individualised care.

Identification of clinically relevant cohorts of people with heart failure from electronic health data in Aotearoa: potential, pitfalls and a plan

Vanessa Selak, Katrina Poppe, Daniel Chan, Corina Grey, Matire Harwood, Shanthi Ameratunga, Sandra Hanchard, Sue Wells, Andrew Kerr, Mayanna Lund, Rob Doughty

Heart failure is a long-term condition in which the heart doesn't pump blood, or relax, as well as it should. Despite being treatable, heart failure continues to be associated with low quality of life and premature death as well as substantial cost to individuals, families and our health system, with the effects of heart failure more pronounced among Māori and Pasifika than other groups in Aotearoa. Health services need to be able to identify people with heart failure and their type of heart failure to ensure that all patients are receiving the right care. Some of the necessary information is available, but key aspects are missing and/or not easily accessible. We provide a number of recommendations to address these gaps.

Early-onset colorectal cancer: Never too young

Oliver Waddell, Jacqueline Keenan, Frank Frizelle

Colorectal cancer (CRC) is the second most common cancer in Aotearoa New Zealand, second only behind prostate cancer in men and breast cancer in woman. It is the second highest cause of cancer death behind lung cancer, with approximately the same death rate as prostate and breast cancer combined.[1] In 2019, there were 3,318 colorectal cancers diagnosed in New Zealand[1] and, while the overall the rate is slowly declining, early-onset colorectal cancer (EOCRC), defined as CRC in adults under the age of 50, is on the rise.[2] From 1995 to 2012, early-onset rectal cancer in New Zealand men increased by 18%, and by 13% in New Zealand women.[2] This pattern is not confined to New Zealand, with increases reported in at least 18 other countries; however, New Zealand is seeing the second fastest increase in incidence in the world.[3] Moreover, the increase in EOCRC is occurring independently of late-onset CRC (LOCRC)[3,5] and, if current trends continue, it has been estimated that by 2030 1 in 4 rectal cancers diagnosed will be in patients under 50.[4]

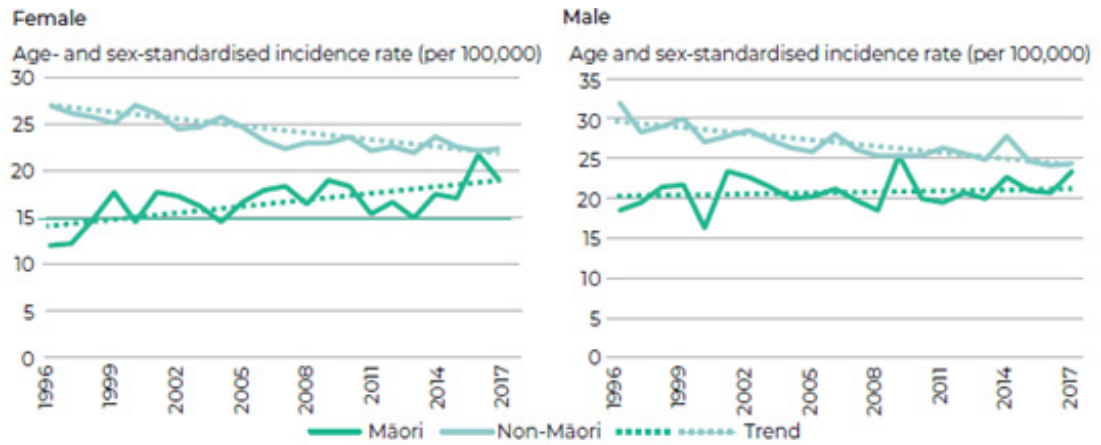
Clinical characteristics

EOCRC usually presents in the distal colon (sigmoid) or rectum and, compared to LOCRC, it has several distinct clinical and pathological characteristics. The vast majority (up to 95%) of EOCRC cases present with symptoms,[6] the most common being rectal bleeding, change in bowel habit and abdominal pain. These cancers are thought to show more aggressive histopathological characteristics with higher rates of mucinous or signet ring histology and poorly differentiated cancers.[7] EOCRC patients are more likely to present with advanced (stage 3 or 4) disease.[8]

Delays to diagnosis are reportedly more common in younger patients, ranging from a median time of 217 to 239 days in USA and New Zealand studies, respectively.[11,12] In contrast, these studies also report a median time from symptom onset to diagnosis in older patients as 29 and 122 days, respectively.[11,12] Moreover, this effect is likely to be larger if under 50s are subdivided out from the under 60s. That young people tend to not seek help when symptoms arise likely contributes to this delay, but another factor is when healthcare professionals do not adequately investigate symptoms in younger patients because they believe they are "too young" to have cancer. This can result in general practitioners (GPs) not referring young patients who are symptomatic, or in those referrals not been accepted by public hospitals despite evidence of rectal bleeding. Delays to CRC diagnosis made up the highest proportion of cancer-related complaints in a Health and Disability Commissioner (HDC) review in 2015, comprising nearly a third of delayed cancer diagnosis complaints.[9]

Optimal treatment for EOCRC remains unclear, and current major guidelines do not recommend any different management based on age alone.[10] However, studies show EOCRC patients receive

Figure 1: Colorectal cancer incidence in Aotearoa New Zealand, 1996–2017.[5]



more aggressive chemotherapy and radiation therapy regimes at every stage of disease, often without any matched survival benefit. This, in turn, raises concerns that some may be being overtreated, and at risk of harm from unnecessary treatment.[13,14,16,17]

The psychosocial impact of EOCRC is also different compared to that of LOCRC. Younger patients are at a different stage of their lives and have different concerns to older patients. This leads to a greater impact on quality of life and concerns around career, financial problems, sexual functioning, family functioning and emotional distress.[18–22] This needs to be considered when clinicians are looking after EOCRC patients, routinely enquiring about these issues, with early referral for supports when needed.

What could be driving the increasing incidence of EOCRC?

The exact reason behind the increasing incidence is not known, and it is likely multifactorial. While EOCRC patients do have a higher proportion of germline mutations than commonly seen in older patients, the majority (75–84%) of EOCRC are sporadic.[23] A recent study from the Memorial Sloan Kettering Cancer Center found no differences in survival, concluding that "while EOCRC are more commonly left sided…[they] are otherwise clinically and genomically indistinguishable from LOCRC".[24]

The risk factors for LOCRC such as obesity, alcohol, processed meat, sugary drinks, and the "Western diet" (high fat, high meat, and low fibre) may or may not contribute to EOCRC.[15,30–35] An individual's gut microbiome may also play a role. Several bacterial species have already been implicated in adenoma or CRC development.[25,26] While data specific to EOCRC are lacking, recent studies suggest the microbiome in patients with EOCRC is different compared that found in patients with LOCRC and healthy controls.[27,28] These differences may reflect early-life events and/or ongoing environmental factors, many of which emerged over the past several decades. These include caesarean delivery,[29] formula feeding,[36] antibiotic use,[37] changing diet, synthetic food dyes, MSG high-fructose corn syrup, or perhaps even microplastics.[38]

What should be done?

The biggest predictor of survival is the stage of disease at diagnosis; therefore, early detection of EOCRC is crucial.[8] The first step to reducing delays to diagnosis is to increase public awareness of symptoms, as exemplified by a recent study where one third of men were unable to name a single symptom of bowel cancer.[39] However, while the "Never Too Young" campaign recently run by Bowel Cancer New Zealand (https://bowelcancernz.org.nz/never-too-young) is helping to increase public awareness of significance symptoms of this disease, there also needs to be timely and adequate investigation once patients present to their GPs seeking help.

New Zealand recently introduced the national bowel cancer screening programme (NBSP), but the 25-year delay to establish this program is considered by many as an embarrassment rather than a success. This program currently only includes individuals over the age of 60, although this is being lowered to 50 for Māori patients to address the inequity caused with a higher proportion of Māori patients with bowel cancer presenting before the age of 60.[40] While this is a very welcome move, New Zealand is still behind many other Organisation for Economic Co-operation and Development (OECD) countries with the British National Health Service (NHS),[41] Australia,[42] Canada[43] and Germany,[44] all offering bowel screening from the age of 50. Germany has been doing this for the past 20 years.[44] The USA preventative task force guidelines for bowel cancer screening have recently recommended to reduce screening age to 45.[45,46]

Alongside lowering the screening age, timely access to colonoscopy for symptomatic young patients needs to be improved. In the future, as our technology and knowledge of drivers for EOCRC improves, we may be able to selectively screen higher-risk patients based on faecal testing, polygenic risk scores and presence of known risk factors.

There is concern that our already struggling health system cannot accommodate increasing demand for colonoscopy and New Zealand has a shortage of colonoscopists, gastroenterologists[47,48] and surgeons. However, failure to recognise the changing epidemiology of the disease, the impact this will have on changing our clinical behaviour, and the need to incorporate this impact into health planning will only make matters worse.

COMPETING INTERESTS
Nil.

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A nurse-led and medically supported outpatient follow-up model following an acute coronary syndrome is as safe and effective as medical follow-up alone (ANZACS-QI 69)

Andrew McLachlan, Andrew Kerr, Mildred Lee

ABSTRACT

BACKGROUND: At Middlemore Hospital, acute coronary syndrome (ACS) patients are admitted under the care of one of seven cardiologists working on a weekly rotation. Between 2010 and 2018 patients under the care of three of the cardiologists were followed up in a "medical only" post-ACS follow-up clinic model where the cardiologist or registrar saw all patients. Those admitted under the other four cardiologists were seen in a "nurse-led, cardiologist-supported" follow-up model where the majority of patients were seen by a nurse specialist. The study aim was to compare quality of care and outcomes between patients managed under these two follow-up clinic models.

METHOD: The ANZACS-QI registry was used to identify all ACS admissions, 2010 to 2018. The ANZACS-QI records for 5296 patients, discharged alive, were anonymously linked with hospital clinic follow-up and national administrative datasets. Time to follow-up, medication dispensation and titration and one-year clinical outcomes were compared for the two follow-up models.

RESULTS: Characteristics of patients managed under each model were similar. 4395 patients attended follow up, 74% in the nurse-led model. At one year there were no differences between the medical- and nurse-led cohorts in all-cause mortality (4.6% vs 3.9, p=0.29), rehospitalisations for myocardial infarction (MI) (9.2% vs 8.3%, p=0.31), stroke (1.2% vs 1.4% p=0.71), heart failure (5.7% vs 6.9%, p=0.15) or a combined endpoint of all-cause mortality and/or rehospitalisation for MI/stroke/HF (15.2% vs 14.8%, p=0.71). Patients were seen earlier post-discharge in the nurse-led model, (mean 83 vs 101 days). Medication dispensation one year post-discharge was similar for both models of care.

CONCLUSION: The nurse-led model is associated with earlier access to follow-up, was equally as effective at maintaining secondary prevention pharmacotherapy and associated with similar survival and readmission with non-fatal ACS/stroke/heart failure.

Despite effective evidenced-based therapies, acute coronary syndrome (ACS) and its complications remains one of the leading causes of mortality, morbidity and healthcare expenditure worldwide. ACS has a significant impact on families and communities with approximately 12,000 patients admitted to New Zealand hospitals every year.[1] Of those who survive, a third suffer a second cardiovascular event in the first year with approximately 50% of all major coronary events occurring in those with a previous diagnosis of cardiovascular disease.[2]

The mortality rates from ischaemic heart disease (IHD) have been declining steadily in New Zealand, due to a systematic focus on the prevention and management of cardiovascular disease.[3] These interventions include reductions in cholesterol and smoking prevalence, improvements in blood pressure control and timely revascularisation in the treatment of ACS.[4] While quality improvement initiatives have improved many facets of ACS interventional and medical management, less attention has been focussed on the long-term disease process that requires a lifelong and structured approach to care.[5]

The early recovery period following ACS is important, with a higher risk of mortality and recurrent events requiring a focus on prevention, including primary care follow-up, cardiac rehabilitation,[6] support around lifestyle change and evidence-based pharmacological interventions.[7] However, it's clear that much more can be achieved as guideline targets for secondary prevention interventions, following the transition from in-hospital to outpatient care, remain sub-optimal.[8] This may be partly due to increasing patient volumes with complex health needs and a lack of medical resources, including inconsistent funding for primary care involvement.[9]

Despite a focus on system improvements over the years, in our own department, timely access to cardiologist outpatient care remains an issue and new models of care have been introduced. These include a number of interventions led by clinical nurse specialists (CNS) and nurse practitioners (NP)[10–12] to support patients to better understand and manage their cardiac condition, address service gaps due to high demand or workforce shortages[13] and support patient outcomes following discharge.[14] These interventions are aligned with evidence-based cardiology best practice and include a focus on patient self-management[15] and cardiac rehabilitation/exercise promotion.[11] In these models the nurses work closely with the cardiologists.

Local audits[16–17] have identified that patients managed in the nurse-led clinics are more likely to be prescribed preventative therapies and individualised lifestyle advice e.g., smoking cessation support, exercise guidance and dietary advice, compared to usual care.[18] However, it is important that we demonstrate these interventions deliver outcomes that are as effective as medical-only models of care, before we promote nurse-led models more widely.

The aim of this study is to compare the quality of care and outcomes between patients referred for follow-up after an ACS via a traditional medical model to those with a nurse-led and cardiologist-supported follow-up model. Clinical outcomes studied include time to clinic review, medication dispensation, mortality and cardiac rehospitalisation.

Methods

This study used a retrospective cohort study design based on the ANZACS-QI registry and linked Middlemore Hospital, based in the Counties Manukau District Health Board (CMDHB), electronic health records. The ANZACS-QI registry is a web-based electronic database, which captures a mandatory dataset for all patients admitted with an acute coronary syndrome (ACS), and is used by the Middlemore Hospital Coronary Care Unit. Data collected includes patient demographics, admission ACS risk stratification, cardiovascular risk factors, investigations and management, inpatient outcomes and medications prescribed at discharge. Details regarding this data collection have previously been reported.[19] The Middlemore Hospital ACS cohort was identified from ANZACS-QI and encrypted National Health Index (NHI) numbers linked this cohort with corresponding CMDHB hospital coding data to identify patients who were followed by the nurse-led and medical-only services. The cohort was also anonymously linked to national health datasets including hospitalisations, mortality and drug dispensing.

At CMDHB, patients with ACS are admitted to the Cardiology team in Coronary Care Unit, and are cared for by one of seven cardiologists working on a weekly rotation. Follow-up of each patient is then under one of the seven cardiologist's clinics. Before 2010, all patients at discharge after ACS were followed up by a consultant cardiologist or consultant supervised registrar, designating a medical-only follow-up clinic model. Increasing demand and long waiting times for outpatient review led to funding for a nurse-led post-ACS follow-up clinic model, designated a nurse-led follow-up clinic model. The nurses leading this service were experienced in cardiology, cardiac rehabilitation and long-term condition support; they were mentored by a senior cardiologist.

During the period of this study, 1 January 2010 to 31 December 2018, four of the cardiologist clinics transitioned to the nurse-led clinic model, where the majority of patients were seen by a nurse but with a small proportion of patients still seen by the consultant or the registrar. The decision regarding which patient would see a cardiologist vs the nurse in these clinics was at the discretion of medical staff at hospital discharge. The nurse-led model progressively expanded as additional nurses were trained and credentials were certified using a locally designed mentorship and competency process.

Overall, ACS care after discharge is based on established and agreed guidelines and protocols, and substantial variation in practice between cardiologists is unlikely and this care has been largely unchanged over the study time period. Guidelines recommend, following ACS, the scheduling of a timely follow-up appointment.[20] At the follow-up visit, a clinician obtains a history of any interval symptoms of ischemia, heart failure and/or arrhythmias and performs a focused cardiovascular examination. Management and interventions are implemented as required. The nurse-led process provides 30-minute appointments to facilitate an additional structured exploration of self-management, psychological coping, adherence and optimisation of the pharmacotherapy regimen to meet secondary prevention targets, when applicable. Support is offered, where appropriate, on stress management, medications adherence, diet, exercise and smoking cessation. All patients are

offered referral to the "Healthy Hearts" cardiac rehabilitation/exercise program.[16] The cardiologists work alongside the nurse-led clinics and are available to review and advise. Standard medical follow-up appointments were 20 minutes.

Ethics review

ANZACS-QI is part of the wider Health Research Council (HRC) and National Heart Foundation (NHF) funded Vascular Informatics using Epidemiology and the Web (VIEW) research programme based at the University of Auckland. The VIEW research team oversees the use and governance of any audit or research use of the national routine information datasets. As all ANZACS-QI registry data and national Routine data is anonymised before being sent to the VIEW researchers; individual patient consent is not required by ethics committees. The VIEW study was approved by the Northern Region Ethics Committee Y in 2003 (AKY/03/12/314), with subsequent amendments to include the ANZACS-QI registries, and with annual approvals by the National Multi-Region Ethics Committee since 2007 (MEC07/19/EXP). Approval was also granted by the Middlemore Hospital research department (#442).

Statistical analysis

The main outcomes of interest were rehospitalisation for myocardial infarction, stroke, and heart failure in the year after discharge, mortality in the year after discharge and the proportion of patients dispensed guideline-recommended medication.

The cohort is described in relation to summary data for patients followed in the nurse-led compared to medical-only follow-up models where continuous variables were reported as mean and standard deviation (SD) and/or median and inter-quartile range (IQR), and categorical variables were reported as counts and proportions were expressed as percentages. Comparison between groups was done using Chi-squared test for categorical data, and for the continuous data comparison between groups was done using non-parametric Mann–Whitney U tests, Kruskal–Wallis tests, student's T-tests or ANOVA tests where appropriate. All patients had at least one year of available follow-up time. Cox proportional hazard regression models were constructed to estimate the hazard ratios and 95% confidence interval for the one-year all-cause mortality, each rehospitalisation outcome and the composite of one-year all-cause mortality and rehospitalisation MI/stroke/HF outcomes to compare outcomes between the two models of care ("medical only" and "nurse led"). The results of univariate and multivariable adjusted models are presented. Variables adjusted for were for age, sex, ethnicity, ACS type, GRACE score, LV function, revascularisation and admission year from 2010 to 2018, after ensuring that the assumption of proportional hazards was met. Survival curves are shown using Kaplan–Meier estimates.

All p-values reported were two tailed and a p-value <0.05 was considered significant. No adjustment is made for multiple statistical testing. Data was analysed using SAS statistical package, version 9.4 (SAS Institute, Cary, NC). The survival curves were plotted using RStudio version 1.2.1335.

Results

Between 2010 to 2018, we identified 5296 New Zealand residents, eligible for outpatient follow-up, who were discharged alive following a first ACS event. Of these 4395 (83%) had a follow-up with a clinician, of whom 1,161 (26%) had their first follow-up via a medical model, and 3234 (74%) used the nurse-led model (Figure 1). The proportion of patients seen in the nurse-led follow-up clinics was stable over the time period.

Baseline characteristics (Table 1)

There were some differences between the two cohorts: compared with the medical cohort the nurse-led cohort were slightly younger (62 years vs 63.5 years, p=0.001), had experienced more ST Elevation myocardial infarctions (17.8% vs 14.4%, p=0.002) with more moderate or severe left ventricular impairment (16.3% vs 11.9%, p=0.001). The nurse-led cohort were more likely to require coronary artery bypass referral (18.2% vs 17.8%, p=0.002). Ethnicity, socio-economic measures, risk factors, risk scores and comorbid conditions were similar.

Time to follow-up (Figure 2)

The recommended time to follow up is six to 12 weeks in our service. Patients followed up under the nurse-led model were seen earlier than the medical model (mean (SD) 83.2 days (50.1) vs 101 days (76.5), p<0.001).

Outcomes (Table 2, Figures 3 & 4)

In the year post-discharge there were no differences between the two cohorts in all-cause

mortality, rehospitalisation for MI, stroke, heart failure or a composite endpoint of all-cause mortality and/or rehospitalisation for MI/stroke/HF. Compared with the reference medical only model the multivariable adjusted hazard ratios for the nurse-led model did not differ significantly for either all-cause mortality (HR 0.80, 95% CIs 0.58 to 1.10) or the composite outcomes (HR 0.93, 95% CIs 0.78 to 1.11).

Medication dispensed (Table 3)

The dispensing of important secondary prevention pharmacotherapies was high at discharge, with no important differences between patients at discharge followed up in the medical or the nurse-led model of care. Dispensing of ACE inhibitors (ACEi)/angiotensin receptor blockers (ARB) by one-year was slightly higher in the nurse-led follow-up (68.3% vs 63.9%) but this difference had been present early post-discharge, before any follow-up visits.

Dispensing of HF pharmacotherapy post-ACS with LVEF <40% at one year following discharge (Table 4)

Beta blockers and ACE I/ARB, at the doses used in clinical trials, are consistently recommended by all guidelines for patients with a reduced left ventricular ejection fraction (LVEF <40%).[21] We identified 594 patients who met these criteria and identified no significant differences in the rates of dispensing of these important medications between the cohorts.

Figure 1: Patients seen in nurse-led and medical follow-up clinics over time.

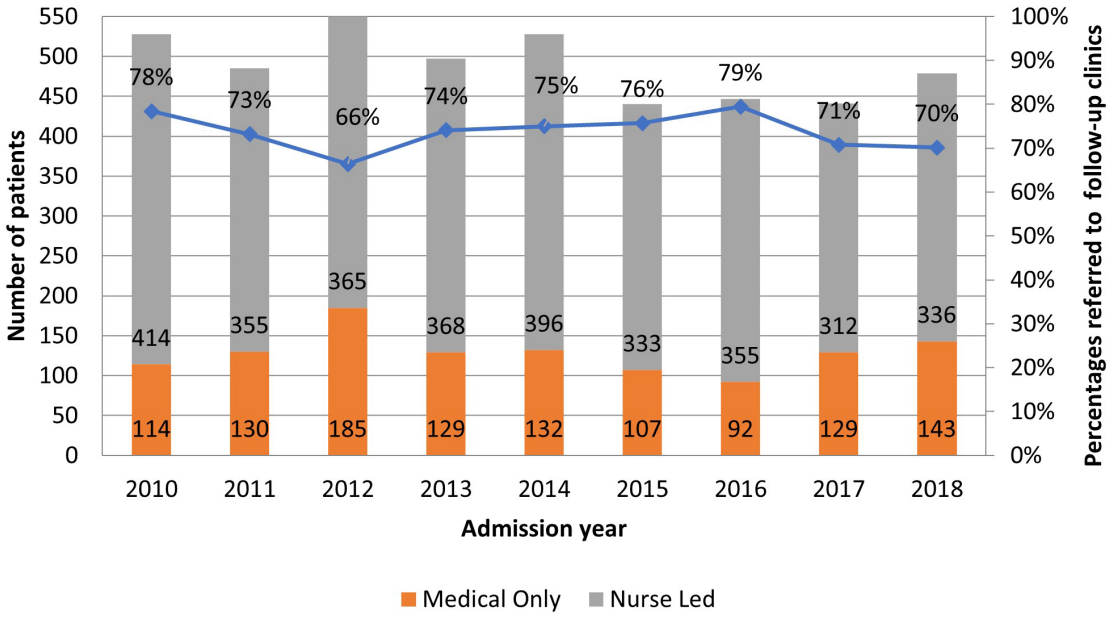

Table 1: Baseline characteristics.

	Medical (n=1161)	Nurse-led (n=3234)	P-value
Demographic			
Age, mean (SD)	63.5 (12.1)	62.0 (12.1)	0.001
Female	313 (27.0)	926 (28.6)	0.277
Ethnicity			
Māori	136 (11.7)	392 (12.1)	0.373
Pasifika	200 (17.2)	636 (19.7)	
Indian	163 (14.0)	442 (13.7)	
Other Asian	61 (5.3)	148 (4.6)	
NZ European/other	601 (51.8)	1,616 (50.0)	
NZDep13 9–10	502 (43.2)	1,437 (44.4)	0.482
Risk factors and medical history			
Current smoker*	275/1,069 (25.7)	798/2,886 (27.7)	0.226
Diabetes*	345/1,069 (32.3)	990/2,886 (34.3)	0.230
BMI			
<18.5 underweight	7 (0.6)	22 (0.7)	0.387
18.5<25 normal	210 (18.1)	518 (16.0)	
25<30 overweight	362 (31.2)	975 (30.2)	
30+ obese	382 (32.9)	1,118 (34.6)	
Missing	200 (17.2)	601 (18.6)	
Prior CVD	359 (30.9)	901 (27.9)	0.048
COPD	107 (9.2)	279 (8.6)	0.543
Creatinine (median, IQR)	86 (72 to 105)	86 (73 to 103)	0.493
Systolic BP (median, IQR)	139 (124 to 155)	138 (122 to 156)	0.568
LDL (n)	1,059	2,865	0.912
Median (IQR)	2.6 (1.8 to 3.4)	2.6 (1.9 to 3.4)	
Clinical presentation			
Type of ACS			
USA	175 (15.1)	383 (11.8)	0.002
NSTEMI	819 (70.5)	2,276 (70.4)	
STEMI	167 (14.4)	575 (17.8)	
Clinical presentation			
Killip Class			
I	1,032 (88.9)	2,833 (87.6)	0.248
II-IV	129 (11.1)	401 (12.4)	
GRACE risk score			
<1%	252 (21.7)	748 (23.1)	0.266
1<3%	404 (34.8)	1,166 (36.1)	
≥3%	505 (43.5)	1,319 (40.8)	
Missing	0 (0)	1 (0.03)	

Table 1 (continued): Baseline characteristics.

	Medical (n=1161)	Nurse-led (n=3234)	P-value
Investigations and management			
LVEF Normal (≥50%) Mild (40 to 49%) Moderate or severe (<40%) Not quantified	 662 (57.0) 141 (12.1) 138 (11.9) 220 (19.0)	 1,681 (52.0) 429 (13.3) 527 (16.3) 597 (18.5)	0.001
Angiogram	1,066 (91.8)	2,966 (91.7)	0.912
Angiogram results No obstructive CAD Single/double VD (>50%) Three VD and/or LMS >50%	 111 (10.4) 600 (56.3) 355 (33.3)	 355 (12.0) 1,642 (55.4) 969 (32.7)	0.395
PCI	599 (51.6)	1,587 (49.1)	0.395
CABG referral	207 (17.8)	587 (18.2)	0.002
Revascularisation	797 (68.7)	2,159 (66.8)	0.240

Abbreviations: BMI = Body Mass Index; CVD = Cardiovascular Disease; COPD = Chronic Obstructive Pulmonary Disease; BP = Blood Pressure; LDL = Low Density Lipoprotein; ACS = Acute Coronary Syndrome; USA = Unstable Angina; NSTEMI = Non ST Elevation Myocardial Infarction; STEMI = ST Elevation Myocardial Infarction; LVEF = Left Ventricular Ejection Fraction; CAD = Coronary Artery disease; VD = Vessel disease; PCI = Percutaneous Coronary Intervention; CABG =Coronary Artery Bypass Graft surgery.
*No smoking or diabetes data pre-2011.

Figure 2: The cumulative percentage of patients followed up after ACS for the nurse-led and medical models.

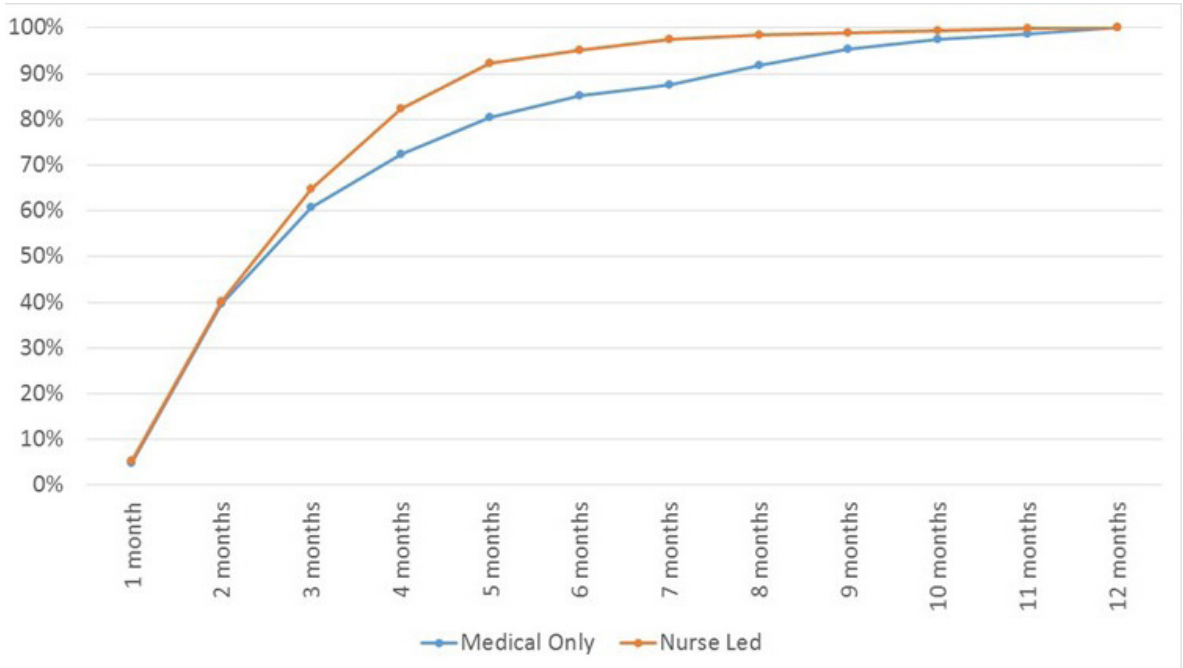

Table 2: Outcomes.

Outcome	Event/N (%)	Univariate Cox Regression		*Multivariate Cox Regression	
		HR (95% CI)	P-value	HR (95% CI)	P-value
One-year all-cause mortality					
Medical only	53/1161 (4.6%)	Ref	0.294	Ref	0.172
Nurse led	125/3234 (3.9%)	0.84 (0.61–1.16)		0.80 (0.58–1.10)	
One-year rehospitalisation MI					
Medical only	107/1161 (9.2%)	Ref	0.313	Ref	0.198
Nurse led	268/3234 (8.3%)	0.89 (0.71–1.12)		0.86 (0.69–1.08)	
One-year rehospitalisation stroke					
Medical only	14/1161 (1.2%)	Ref	0.708	Ref	0.827
Nurse led	44/3234 (1.4%)	1.12 (0.62–2.05)		1.07 (0.58–1.97)	
One-year rehospitalisation HF					
Medical only	66/1161 (5.7%)	Ref	0.150	Ref	0.185
Nurse led	224/3234 (6.9%)	1.22 (0.93–1.61)		1.21 (0.91–1.60)	
One-year all-cause mortality and rehospitalisation MI/stroke/HF					
Medical only	177/1161 (15.2%)	Ref	0.707	Ref	0.409
Nurse led	479/3234 (14.8%)	0.97 (0.81–1.15)		0.93 (0.78–1.11)	

* Adjusted by age, sex, ethnicity, ACS type, GRACE score, LV function, revascularisation and admission year from 2010 to 2018.

Figure 3: Outcome–one-year all-cause mortality.

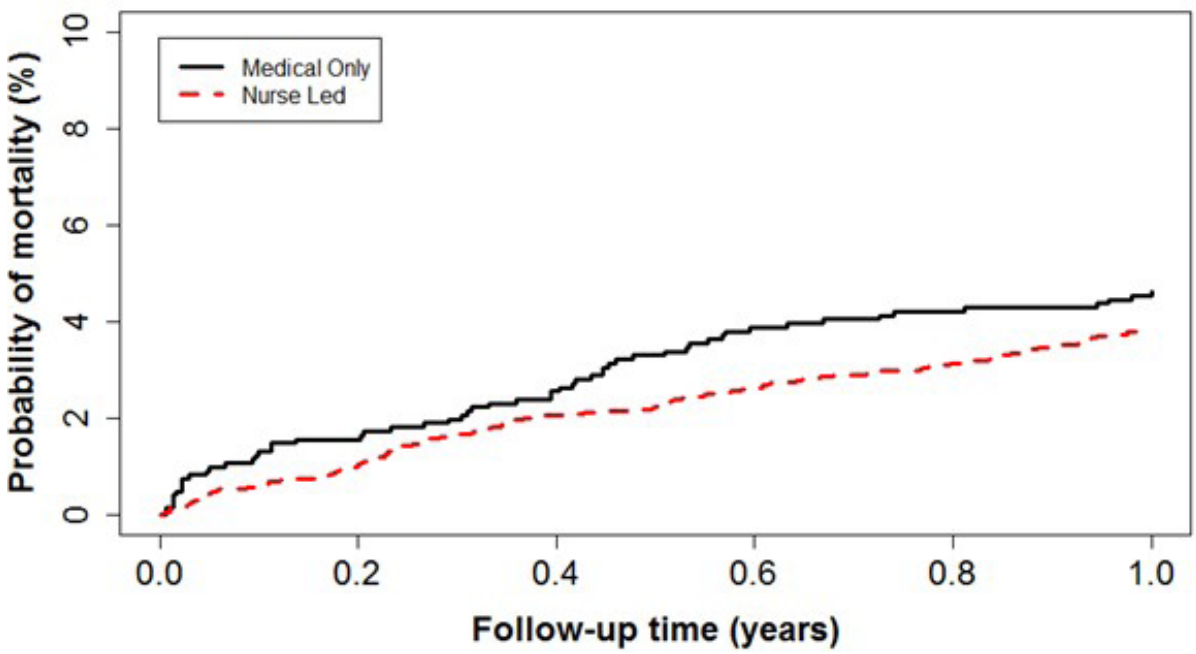

Figure 4: Outcome–rehospitalisations.

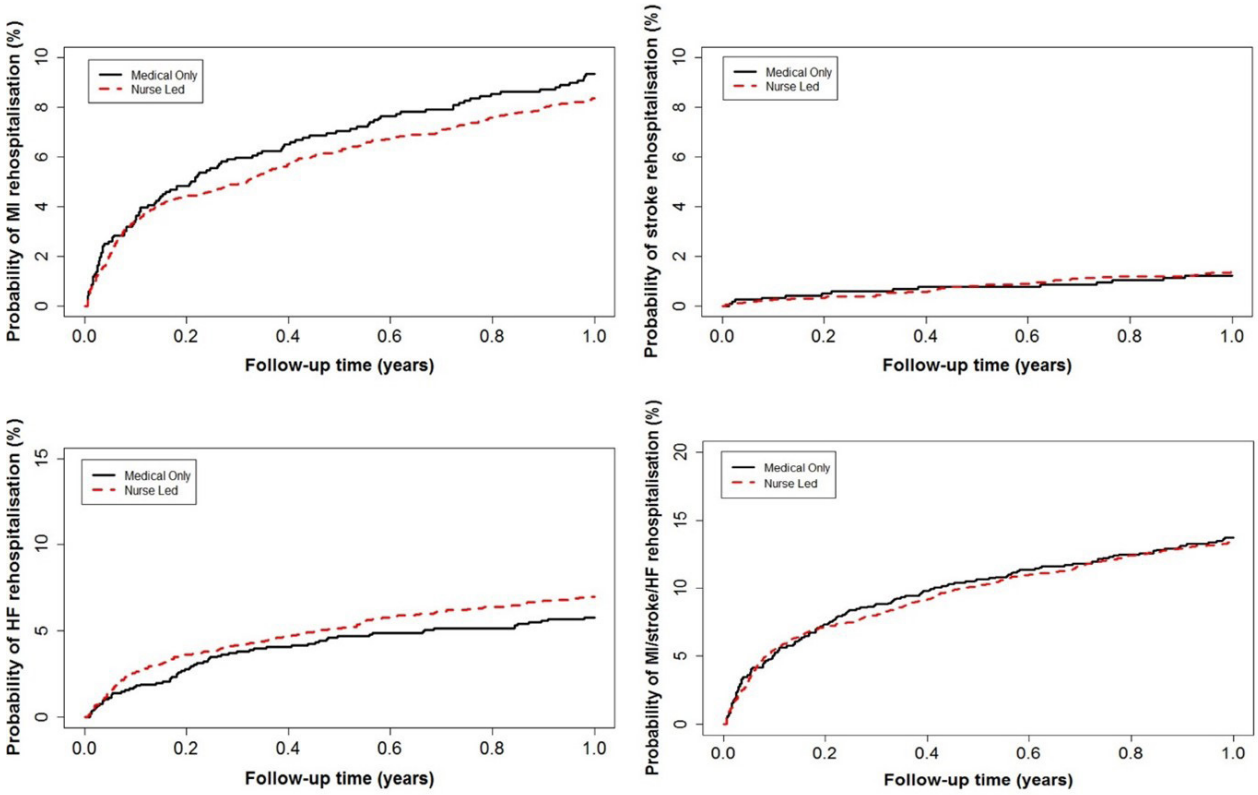

Table 3: Dispensed medication post-discharge and at one year.

Medication dispensed 0–3 months ***Includes only 3 months survivors**	**Medical only (n=1161)**	**Nurse led (n=3234)**	**P-value**
Aspirin	1,080 (94.6)	3,054 (95.8)	0.087
Second anti-platelet	822 (72.0)	2,304 (72.3)	0.850
DAPT	753 (65.9)	2,160 (67.8)	0.262
Statin	1,084 (94.9)	3,056 (95.9)	0.184
High dose statin	919 (80.5)	2,578 (80.9)	0.773
ACEI/ARB	835 (73.1)	2431 (76.3)	0.035
Beta-blocker	934 (81.8)	2,684 (84.2)	0.060
Medication dispensed 9–12 months ***Includes only one-year survivors**	**Medical only (n=1108)**	**Nurse led (n=3109)**	**P-value**
Aspirin	928 (83.8)	2,535 (81.5)	0.098
Second anti-platelet	477 (43.1)	1,406 (45.2)	0.212
DAPT	415 (37.5)	1,212 (39.0)	0.369
Statin	933 (84.2)	2,623 (84.4)	0.899
High dose statin	769 (69.4)	2,184 (70.3)	0.599
ACEI/ARB	708 (63.9)	2,122 (68.3)	0.008
Beta-blocker	810 (73.1)	2,278 (73.3)	0.914

Abbreviations: DAPT = Dual Antiplatelet Treatment; ACEi = Angiotensin Converting Enzyme Inhibitor; ARB = Angiotensin Receptor Blocker.
The dispensing rate for all preventive medications reduced similarly for both cohorts by one year.

Table 4: Dispensing of HF medication one-year post-ACS in patients with LVEF <40%.

	All (n=594)	**Medical only (n=119)**	**Nurse led (n=475)**	**P-value**
ACEI/ARB				
<50% target dose	159 (26.8)	35 (29.4)	124 (26.1)	0.381
≥50% target dose	168 (28.3)	30 (25.2)	138 (29.1)	
Target dose	157 (26.4)	27 (22.7)	130 (27.4)	
No ACEI/ARB	110 (18.5)	27 (22.7)	83 (17.5)	
Beta-blocker				
<50% target dose	262 (44.1)	60 (50.4)	202 (42.5)	0.133
≥50% target dose	173 (29.1)	36 (30.3)	137 (28.8)	
Target dose	53 (8.9)	4 (3.4)	49 (10.3)	
Other beta-blocker	1 (0.2)	0 (0)	1 (0.2)	
No beta-blocker	105 (17.7)	19 (16.0)	86 (18.1)	

Discussion

This is the first study to compare hard clinical outcomes between a traditional medical model and a nurse-led model of care post-ACS. Patients managed under the nurse-led model had one-year clinical outcomes and medical management, which were as good as those managed under a traditional medical model. They also had timelier access to outpatient review.

The nurse-led model of care is not novel and examples have been reported overseas, but implementation has been slow to develop in New Zealand. A frequent impediment to developing new nurse clinics is that the growing body of nurse-led literature is often classed as low-level evidence[22] with a highly selected patient cohort[23] and a heterogenous evidence base.[24,25] Despite this, many studies describe successful implementation[26,27] and report a positive impact on risk factors,[28,27] patient satisfaction,[29] access to care,[14,30] timely and more frequent monitoring of high-risk post-MI patients[31] with mixed results on cost-effectiveness.[29,32]

The evidence supporting nurse-led models post-ACS in the context of care co-ordination, rehabilitation programmes and IHD secondary prevention is also increasing. Some of these models involve nurses triaging whether a cardiologist medical review appointment is necessary[33,34] and most report nurse-led clinical follow-ups are feasible[13] and useful in freeing up clinical resources. To date, we have no evidence that nurse-led ACS clinics improve clinical outcomes, such as survival. However, a small UK audit of a nurse follow-up clinic in patients with ACS reported a reduction in six-month readmission rate (from 28.5% to 14.2%). The clinic provided early follow-up to patients classified as a higher risk based on TIMI scores: the nurses reviewed diagnosis, management plan and any symptoms in a 30-minute appointment. Cardiac rehabilitation was offered to all patients, and all patients were discussed with a consultant cardiologist.[34]

Guidelines[35] now recommend follow-up at 2–6 weeks depending on risk status of the patient, however, this has been difficult to achieve due to high patient demand. Our service recommends seeing a primary care clinician in one week and then cardiology clinic review in six to 12 weeks. The cardiac rehabilitation team contact the patient within two weeks and offer further support as required. Patients with impaired heart function are seen earlier with an aim of 2–6 weeks.

Reducing delay in seeking care for the initial presentation of ACS has been a successful quality improvement focus across the globe[36] and in New Zealand.[37] Delays to outpatient review has been less of a focus but delays are associated with worse outcomes compared to earlier follow-up[38] with reports of increased hospitalisation and worse short-term and long-term medication adherence.[39] The recovery period following ACS is stressful and impacts on patient's work, family situation and both physical and psychological health.[40] A significant number of patients continue to experience emotional symptoms that may impair their daily functioning.[41] It is important to provide early access to answer questions, correct misconceptions and identify and address significant issues affecting recovery. While cardiac rehabilitation has an important role in providing support, many patients choose or are unable to partake in these programmes. The nurse-led clinic model meant we were able to bring patients in for review earlier and address barriers to recovery and encourage engagement with their primary care team.

There appears to be a lot of variation in different healthcare systems about the ongoing relationship and responsibilities of outpatient and primary care. Goddard[42] describes a protocol for a four-week post-ACS practice nurse appointment in primary care. This appointment is timed to ensure recommended treatments and medication changes are implemented appropriately, as well as advice on lifestyle changes and assessment of psychosocial health. In New Zealand, lifelong secondary prevention following ACS is usually managed in primary care, although structured care is inconsistently delivered and has not been a focus of primary care targets in recent years. It is important that health systems support patients following ACS not just in the acute and early recovery period but for life. In New Zealand, who provides this ongoing care is usually the general practitioner; however, little is known about the level of management provided.[9] Nurse practitioner or practice nurse involvement has not been well described in post-ACS care. However, for many patients, successful, lifelong secondary prevention requires a structured and holistic approach, that nurses have shown they can provide.[43]

Non-adherence following ACS is associated with increased risks of mortality and hospital readmissions. Medication dispensing is a useful way to measure adherence, and we identified a decline in important secondary prevention med-

ication usage at one year. A New Zealand study investigated high dose statin use and reported that 21% of the cohort were not on a statin at one year.[1] More work is required to understand the best approach to supporting long-term medication usage and will require more collaboration between the patient and whānau, the cardiology team, primary care and community pharmacists.

Limitations

There are several limitations in this paper. This was a retrospective observational study, so patients were not formally randomised to follow-up under medical vs nurse-led models. Nevertheless, patients were effectively randomised because ACS admissions are not planned, and the only determinant of which model of follow-up they received was the week in which they were admitted to hospital—patients admitted in a week when a consultant with medical only follow-up was on-call were managed under the medical model and those admitted in a week where a consultant had a nurse-led follow up model were managed under the nurse-led model. There were only a small number of differences identified between the two groups and some of these may have been due to the multiple statistical comparisons performed (Type I error). However, the observed group difference in age, distribution of ACS type and of LV ejection fraction were potentially clinically significant and may have been a source of bias. Multivariable regression modelling was therefore performed as an additional check that any differences between the cohorts did not impact on the study conclusions. The study is limited by the number of patients who presented with ACS during the study period and it is possible that with a larger study population differences in outcomes between the cohorts might be apparent. The development and growth of the nurse-led process was non-linear and started as a purely educational adjunct to standard cardiology care and grew as the nurses gained clinic experience to take on a more hybrid nurse/medical focus. The main goals of the clinic remain engrained in nursing philosophy and offer an experience that is different to standard medical practice. However, it is difficult to adjust for improving clinical experience and diagnostic skills, nurse prescribing and eventually nurse practitioner preparedness, which will all have had impacts on outcomes. There were also a number of other processes that we could not account fully for, including access and contact with cardiac rehabilitation, involvement of the heart failure up-titration clinics and the likelihood of patients having multiple admissions and crossing over from the nurse-led process to the medical-only process and vice versa. Data collection in cardiac rehabilitation and the community HF clinics have improved over the last few years and we now have robust data bases, but for the majority of this study we could not account for additional nurse input.

There is very little information on patient experience, however, qualitative research with patients is planned and will provide further insight into accessibility and acceptability of the different models, particularly for our diverse local populations.

Conclusion

This is a large New Zealand cohort study that reports on the safety of the addition of a nurse-led model of care to usual cardiologist-only care and is associated with earlier access to follow-up. The nurse-led model is as effective at maintaining secondary prevention pharmacotherapy as the gold standard medical model with no difference in clinical outcomes.

Further studies examining cost effectiveness and patient experience have the potential to support the implementation of this model across New Zealand.

COMPETING INTERESTS
Nil.

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Appendices

Appendix 1: Deaths at three months and 12 months post-ACS discharge.

	All (n=5296)	Medical (n=1161)	Nurse-led (n=3234)	No follow-up (n=901)	P-value (medical vs nurse- led)	P-value (all)
Died in the first three months post ACS	85 (1.6)	19 (1.6)	46 (1.4)	20 (2.2)	0.604	0.241
Died in the first year post-ACS	225 (4.2)	53 (4.6)	125 (3.9)	47 (5.2)	0.299	0.171

Appendix 2: Baseline characteristics.

	Medical (n=1161)	Nurse-led (n=3234)	No contacts (n=901)	P-value (medical vs nurse-led)	P-value (all)
Age group					
<50	163 (14.0)	532 (16.5)	151 (16.8)		
50–<60	289 (24.9)	844 (26.1)	222 (24.6)	0.021	0.023
60–<70	322 (27.7)	934 (28.9)	236 (26.2)	0.001	0.002
70–<80	271 (23.3)	672 (20.8)	197 (21.9)		
80+	116 (10.0)	252 (7.8)	95 (10.5)		
Mean (SD)	63.5 (12.1)	62.0 (12.1)	62.8 (13.2)		
Female	313 (27.0)	926 (28.6)	289 (32.1)	0.277	0.036
Ethnicity					
Māori	136 (11.7)	392 (12.1)	132 (14.7)		
Pasifika	200 (17.2)	636 (19.7)	176 (19.5)	0.373	0.268
Indian	163 (14.0)	442 (13.7)	118 (13.1)		
Other Asian	61 (5.3)	148 (4.6)	37 (4.1)		
NZ European/Other	601 (51.8)	1616 (50.0)	438 (48.6)		
NZDep13					
1–2	156 (13.4)	394 (12.2)	145 (16.1)		
3–4	166 (14.3)	500 (15.5)	112 (12.4)		
5–6	135 (11.6)	360 (11.1)	91 (10.1)	0.608	0.063
7–8	200 (17.2)	528 (16.3)	145 (16.1)		
9–10	502 (43.2)	1437 (44.4)	392 (43.5)		
Missing	2 (0.2)	15 (0.5)	16 (1.8)		
NZDep13 9–10	502 (43.2)	1437 (44.4)	392 (43.5)	0.482	0.738
Current smoker*	275/1069 (25.7)	798/2886 (27.7)	217/812 (26.7)	0.226	0.467
Diabetes*	345/1069 (32.3)	990/2886 (34.3)	273/812 (33.6)	0.230	0.486
BMI					
<18.5 underweight	7 (0.6)	22 (0.7)	4 (0.4)		
18.5–<25 normal	210 (18.1)	518 (16.0)	137 (15.2)	0.387	<0.001
25–<30 overweight	362 (31.2)	975 (30.2)	240 (26.6)		
30+ obese	382 (32.9)	1118 (34.6)	286 (31.7)		
Missing	200 (17.2)	601 (18.6)	234 (26.0)		

Appendix 2 (continued): Baseline characteristics.

	Medical (n=1161)	Nurse-led (n=3234)	No contacts (n=901)	P-value (medical vs nurse-led)	P-value (all)
Killip Class				0.248	0.167
I	1,032 (88.9)	2,833 (87.6)	776 (86.1)		
II-IV	129 (11.1)	401 (12.4)	125 (13.9)		
GRACE risk score				0.266	0.298
<1%	252 (21.7)	748 (23.1)	190 (21.1)		
1–<3%	404 (34.8)	1,166 (36.1)	314 (34.9)		
≥3%	505 (43.5)	1,319 (40.8)	397 (44.1)		
Missing	0 (0)	1 (0.03)	0 (0)		
Angiogram	1066 (91.8)	2966 (91.7)	717 (79.6)	0.912	<0.001
CAD >50% on angiogram				0.395	<0.001
No obstructive CAD	111 (10.4)	355 (12.0)	138 (19.2)		
Single/double VD	600 (56.3)	1,642 (55.4)	370 (51.6)		
Three VD and/or LMS >50%	355 (33.3)	969 (32.7)	209 (29.2)		
Type of ACS				0.002	<0.001
USA	175 (15.1)	383 (11.8)	108 (12.0)		
NSTEMI	819 (70.5)	2,276 (70.4)	680 (75.5)		
STEMI	167 (14.4)	575 (17.8)	113 (12.5)		
Prior CVD	359 (30.9)	901 (27.9)	361 (40.1)	0.048	<0.001
COPD	107 (9.2)	279 (8.6)	89 (9.9)	0.543	0.482
Serum creatinine				0.493	0.735
Median (IQR)	86 (72 to 105)	86 (73 to 103)	86 (72 to 106)		
Admission systolic BP				0.568	0.486
Mean (SD)	140.2 (24.4)	139.7 (25.2)	140.7 (25.8)		
Median (IQR)	139 (124 to 155)	138 (122 to 156)	140 (123 to 156)		
LDL				0.912	0.004
N	1,059	2,865	800		
Mean (SD)	2.67 (1.11)	2.71 (1.10)	2.57 (1.09)		
Median (IQR)	2.6 (1.8 to 3.4)	2.6 (1.9 to 3.4)	2.4 (1.8 to 3.2)		
PCI	599 (51.6)	1,587 (49.1)	336 (37.3)	0.395	<0.001
CABG referral	207 (17.8)	587 (18.2)	97 (10.8)	0.002	<0.001
Revascularisation	797 (68.7)	2,159 (66.8)	431 (47.8)	0.240	<0.001
LVEF				0.001	<0.001
Normal (≥50%)	662 (57.0)	1,681 (52.0)	377 (41.8)		
Mild (40 to 49%)	141 (12.1)	429 (13.3)	111 (12.3)		
Mod or Severe (<40%)	138 (11.9)	527 (16.3)	147 (16.3)		
No EF or not quantified	220 (19.0)	597 (18.5)	266 (29.5)		

* No 2010 smoking and diabetes data available

Appendix 3: Medications.

Medication at discharge	All (n=5296)	Medical only (n=1161)	Nurse-led (n=3234)	No follow-up (n=901)	P-value (Medical only vs nurse-led)	P-value (all)
Aspirin	5,120 (96.7)	1,123 (96.7)	3,146 (97.3)	851 (94.5)	0.334	<.001
Other antiplatelet	3,742 (70.7)	824 (71.0)	2,318 (71.7)	600 (66.6)	0.649	0.012
DAPT	3,665 (69.2)	810 (69.8)	2,273 (70.3)	582 (64.6)	0.741	0.004
Statin	5,104 (96.4)	1,117 (96.2)	3,142 (97.2)	845 (93.8)	0.111	<.001
Beta-blocker	4,358 (82.3)	950 (81.8)	2,684 (83.0)	724 (80.4)	0.367	0.167
ACEi/ARB	4,039 (76.3)	886 (76.3)	2,497 (77.2)	656 (72.8)	0.533	0.023
Medication dispensed 0–3 months *Includes only three-months survivors	**All* (n= 5211)**	**Medical only (n=1142)**	**Nurse-led (n=3188)**	**No follow-up (n=881)**	**P-value (Medical only vs nurse-led)**	**P-value (all)**
Aspirin	4,947 (94.9)	1,080 (94.6)	3,054 (95.8)	813 (92.3)	0.087	<.001
Second anti-platelet	3,725 (71.5)	822 (72.0)	2,304 (72.3)	599 (68.0)	0.850	0.041
DAPT	3,457 (66.3)	753 (65.9)	2,160 (67.8)	544 (61.8)	0.262	0.004
Statin	4,938 (94.8)	1,084 (94.9)	3,056 (95.9)	798 (90.6)	0.184	<.001
High dose statin	4,139 (79.4)	919 (80.5)	2,578 (80.9)	642 (72.9)	0.773	<.001
ACEI/ARB	3,903 (74.9)	835 (73.1)	2,431 (76.3)	637 (72.3)	0.035	0.017
Beta-blocker	4,332 (83.1)	934 (81.8)	2,684 (84.2)	714 (81.0)	0.060	0.034
Medication dispensed 9–12 months *Includes only one-year survivors	**All (n=5071)**	**Medical only (n=1108)**	**Nurse-led (n=3109)**	**No follow-up (n=854)**	**P-value (Medical only vs nurse-led)**	**P-value (all)**
Aspirin	4,117 (81.2)	928 (83.8)	2,535 (81.5)	654 (76.6)	0.098	<.001
Second anti-platelet	2,244 (44.3)	477 (43.1)	1,406 (45.2)	361 (42.3)	0.212	0.202
DAPT	1,927 (38.0)	415 (37.5)	1,212 (39.0)	300 (35.1)	0.369	0.111
Statin	4,223 (83.3)	933 (84.2)	2,623 (84.4)	667 (78.1)	0.899	<.001
High dose statin	3,486 (68.7)	769 (69.4)	2,184 (70.3)	533 (62.4)	0.599	<.001
ACEI/ARB	3,359 (66.2)	708 (63.9)	2,122 (68.3)	529 (61.9)	0.008	0.001
Beta-blocker	3,671 (72.4)	810 (73.1)	2,278 (73.3)	583 (68.3)	0.914	0.013

Sources of healthcare-associated *Staphylococcus aureus* bacteraemia in New Zealand acute hospitals

Ruth Barratt, Grace Clendon, Barbara Gibson, Sally A Roberts

ABSTRACT

AIM: The primary aim of this study was to identify the source of healthcare-associated *Staphylococcus aureus* bacteraemia (HA-SAB) in acute district health board (DHB) hospitals to inform future national quality improvement activities.

METHOD: De-identified HA-SAB event source information was submitted to the Commission from all DHBs for the period 1 January 2017 to 30 June 2021. Data was categorised and analysed to identify trends and significant sources of infection.

results: There were 1,867 HA-SAB events. Of the events where *S. aureus* susceptibility results were reported, 159 (10%) isolates were methicillin-resistant *S. aureus.* The principal sources of HA-SAB were medical devices (65%), surgical site infection (10%), and organ site (8%). Ninety-five percent of medical devices were for vascular access, primarily central venous catheters (50%) and peripheral intravenous catheters (45%).

CONCLUSION: This study has identified intravascular devices as significant sources of HA-SAB. Ongoing surveillance for HA-SAB source is required to identify the major risk factors and to support quality improvement activities targeting infection prevention measures and best practice related to intravascular and other medical devices.

Staphylococcus aureus is a common human commensal of the skin and upper respiratory tract, and is an important opportunistic pathogen.[1,2] It is a major cause of both community-acquired and healthcare-associated bacteraemia worldwide. It is associated with significant morbidity and mortality.[3–5] Key sources for healthcare-associated *S. aureus* bacteraemia (HA-SAB) infections include vascular access devices, medical procedures and surgical site infections (SSI).[6,7]

In Aotearoa New Zealand, the Health Quality and Safety Commission (the Commission) infection prevention and control (IPC) programme regards HA-SAB as an important measure of infection prevention practice. The Commission currently reports HA-SAB incidence data as an outcome measure for the Hand Hygiene New Zealand (HHNZ) programme and includes the HA-SAB incidence in quarterly Quality and Safety Marker (QSM) reporting. This provides important national data about this serious and potentially preventable infection and includes both hospital- and community-onset HA-SAB.[8]

Despite improvement in hand hygiene performance, there has not been an associated significant decrease in HA-SAB rate. Instead, the HA-SAB rate has increased steadily; the median quarterly HA-SAB rate rose from 0.11 to 0.13 HA-SAB events per 1,000 bed-days in late 2016 and increased again to 0.15 events per 1,000 bed-days in 2019. This increase prompted the Commission to investigate the source of HA-SAB events nationally, to identify any trends or other information that may inform future quality improvement activity to reduce the rate of HA-SAB in District Health Board (DHB) hospitals.

Method

All 20 DHBs were asked to submit de-identified details of all HA-SAB events for the period 1 January 2017 to 30 June 2021. The definition of a HA-SAB event is as previously defined.[9]

Data was reported on a supplied Excel template or local spreadsheet. DHBs were asked to supply numbers of HA-SAB infections per month, and for each HA-SAB event, the clinical service providing clinical care, *S. aureus* susceptibility results, source and type of relevant medical device or medical/surgical procedure, if appropriate.

No standard definitions for the source data were provided, to allow DHBs to submit already collected data. For DHBs who omitted data for more than eight quarters, counts of HA-SAB infec-

tions for the omitted period were obtained from the HHNZ QSM data set.

HA-SAB sources were categorised into eight groups for analysis: medical device, neutropenic sepsis, organ site infection (not SSI), pneumonia, medical procedure, SSI, "other source" and "no source identified". The category "no source identified" included those HA-SAB events where the DHB reported the source as "unknown" or where the source category was left blank by the DHB. We interpreted the absence of data in the latter to mean that the source was not identified by the DHB team. Medical devices were further categorised by type.

The Commission collated and analysed the data. This study was approved by the Auckland Health Research Ethics Committee (Ref AH24626).

Results

DHBs provided monthly data sets for the source of HA-SAB events between 1 January 2017 and 30 June 2021 (54 months, 18 quarters). Three DHBs omitted data for more than eight quarters (292 events, 16%). In total, there were 1,867 HA-SAB events from all 20 DHBs.

The three DHBs with incomplete data sets were excluded from detailed source analysis. The remaining 17 DHBs provided HA-SAB data for 1,575 events (84% of total events).

The majority of DHBs returned their data using local data collection spreadsheets which had differences in the description of the source and amount of source detail provided. Notably, the type of surgery for which the HA-SAB infection was attributed to was often not reported, and clinical specialities were categorised differently. Consequently, these two variables were excluded from our analysis. Although descriptions varied for other data fields, the intended category was clear. Conversely, DHBs consistently provided HA-SAB source details attributed to intravascular devices.

S. aureus susceptibility

S. aureus susceptibility was available for all 1,575 of reported events from the 17 DHBs. There were 159 methicillin-resistant *S. aureus* (MRSA) HA-SAB (10%) events of which 114 (74%) were reported from Northern Region DHBs (Northland, Waitematā, Auckland and Counties Manukau DHBs). There was no significant increase in the MRSA percentage over time.

Sources of HA-SAB

Of the 17 DHBs which provided HA-SAB data, the source was recorded for 1,369 (73%) HA-SAB events (Table 1). The remaining 206 (13%) of these HA-SAB events did not have a source recorded.

Medical devices accounted for the majority of HA-SAB sources (65%) followed by SSI (10%) and organ site (8%). Other sources of HA-SAB included medical procedure (7%); neutropenic sepsis (4%); and pneumonia (2%). Variation in SSI data provided by individual DHB teams limited reporting by type of surgery or class of SSI.

HA-SAB sources were analysed as a percentage of reported HA-SAB events, where source was identified (Figure 1).

Table 1: Number of HA-SAB sources reported by DHBs, 2017–2021.

Year	Medical device	SSIa	Organ siteb	Medical procedurec	Neutropenic sepsis	Pneumonia	Other sourced	No source recorded	Total
2017	158	41	16	26	10	10	2	27	290
2018	165	45	18	20	3	10	5	26	292
2019	214	27	22	20	20	8	1	47	359
2020	235	34	33	17	10	5	0	64	398
2021e	124	23	20	16	6	5	0	42	236
All	896 (65%)	170 (12%)	109 (8%)	99 (7%)	49 (4%)	38 (2%)	8 (0.6%)	206(13%)	1,575

[a] Surgical site infection.[b] Non-surgical organ sites, e.g., liver, gastrointestinal tract, heart, skin and soft tissue, ear, nose and throat, reproductive system.[c] Includes insertion of pacing wires, interventional radiology, endoscopy, intracavity ultrasound.[d] "Other source" as reported by DHB but not specified.[e] First two quarters only reported for 2021.Source: DHB surveillance data.

Figure 1: HA-SAB sources as a percentage of total HA-SAB events by quarter, 2017–2021.

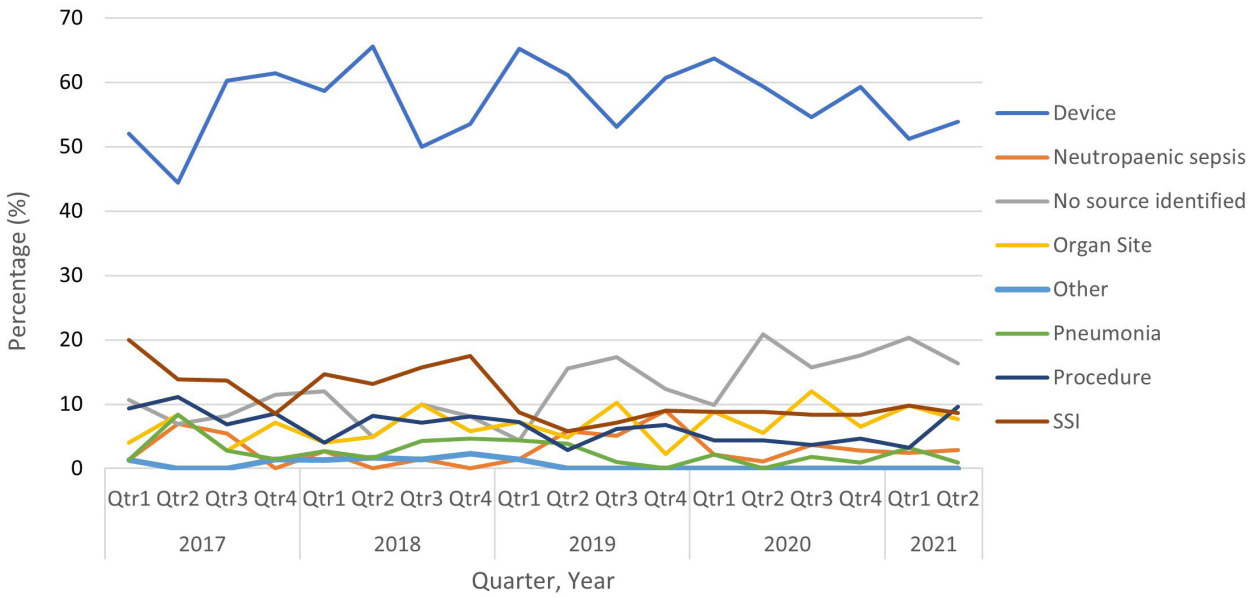
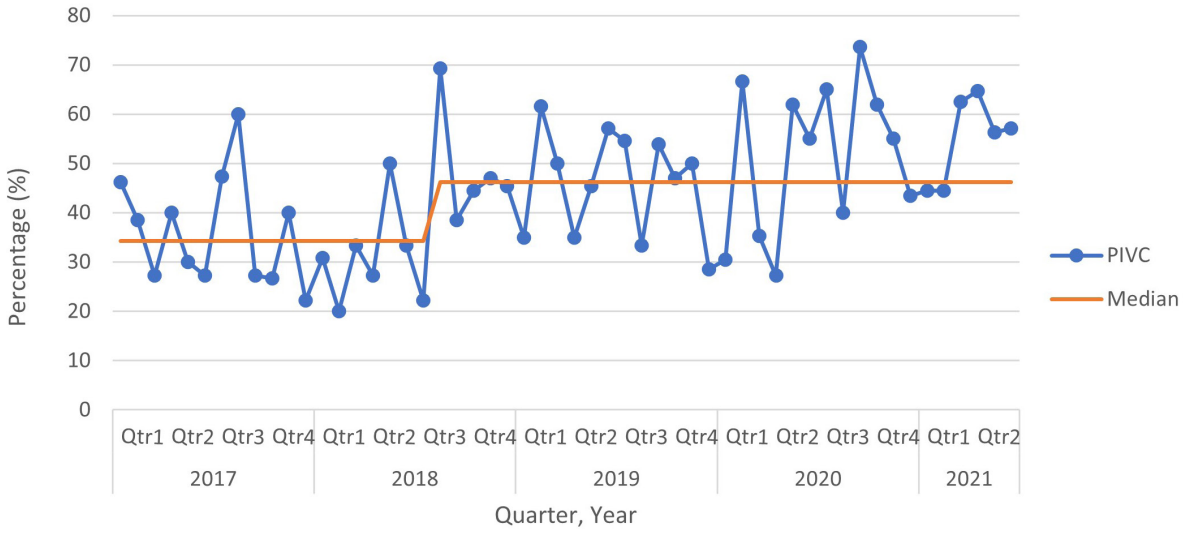


Table 2: Number of devices by type reported as HA-SAB sources by DHBs, 2017–2021.

Year	Type of device						
	CVC	PIVC	IDC	Arterial catheter	ETT	SPC	Total
2017	97	58	3				158
2018	96	65	4				165
2019	106	97	8	3			214
2020	101	121	7	2	2		233
2021	53	63	5		1	1	123
Total	453(50%)	404(45%)	27 (3%)	5 (0.6%)	3 (0.3%)	1	893

Abbreviations: CVC = central venous catheter; PIVC = peripheral intravenous catheter; IDC = in-dwelling urinary catheter; ETT = endotracheal tube; SPC = suprapubic catheter.
Source: DHB surveillance data.

Figure 2: PIVC-related HA-SAB as a percentage of total HA-SAB events by quarter, 2017–2021.



Abbreviation: PIVC = peripheral intravenous catheter.
Source: DHB surveillance data.

Medical device-related HA-SAB source

Medical devices were the most common source of HA-SAB events (Table 2).

The proportion of medical devices reported as a source of HA-SAB infection increased from 60% in 2017 to 70% in 2020 (p<0.02). Vascular access devices accounted for 95% of all medical devices, comprised of central venous catheters (CVC) for 50% and peripheral intravenous catheters (PIVC) for 45%.

Run chart analysis indicates a significant increase in HA-SAB events between 2017 to mid-2021 (34% to 46%, p<0.01) where a PIVC was identified as the source (Figure 2).

Discussion

This national descriptive study of the source for HA-SAB events has identified medical devices as the major contributor, accounting for 65% of all events. In general, international HA-SAB surveillance programmes do not report HA-SAB source data; however, our percentages of medical device-related HA-SAB is high compared to Scotland's at 23.1%.[10]

The source for 65% of all HA-SAB events was a medical device, of which 95% were vascular access devices. In New Zealand and Australia, vascular access devices have previously been identified as an important source of SAB. A one-year prospective observational study in 2009 reported 1994 SAB events from 27 independent or hospital pathology laboratories in Australia (24) and New Zealand (3), with 60.8% having onset in the community. 34% were due to medical devices with vascular access devices, accounting for 96% of the medical devices.[11]

A recent review of HA-SAB events across participating healthcare facilities in Victoria, Australia, identified CVCs as the source for 28% of all cases and 40% in a cohort of cancer patients. The proportion of intravascular device-related HA-SAB events was approximately twofold higher in the cancer cohort than the state-wide comparator.[12]

Fifty percent of all HA-SAB events in this study were associated with a CVC. CVCs are widely recognised as a significant source of bloodstream infection.[13,14] Quality improvement programmes and infection prevention interventions incorporating CVC bundles of care have been used successfully in high-risk settings to reduce CVC-related infections.[13–16] Similarly the Commission's Target CLAB Zero programme has been successful in reducing central line blood stream infections (CLABSI) in ICU.[17] However, in this present study, many of the CLABSI events reported by DHBs appeared to have occurred in patients outside of the ICU setting (results not reported), such as renal dialysis, haematology and oncology patients. CLABSI are an important source of morbidity and mortality in vulnerable populations, and are associated with high hospital costs.[18,19] Targeted surveillance for CLABSI in high-risk populations would be useful to monitor adherence to infection

prevention strategies but can be challenging due to the difficulty in capturing catheter days to support reporting as a rate per catheter days.

There was a significant increase in the number of HA-SAB events associated with PIVC use over the time period; 34% to 46%, ($p<0.01$). Although prevention of CLABSI events has received attention with the introduction of bundles of care, PIVC infection rates are less well documented.[20] A systematic review of blood stream infections associated with PIVCs in the hospital setting revealed that PIVCs account for a mean of 38% (range 12%–64%) of intravascular device related HA-SAB.[21] A prospective observational study in Spain reported an increase in PIVC bacteraemia from 0.06 episodes/1,000 patient days in 1992 to 0.13 episodes/1,000 patient days in 2016.[22]

Recognising phlebitis as an indicator of localised PIVC infection is an important first step in reducing HA-SAB events. An international point prevalence study involving more than 40,000 patients with a PIVC revealed that one in 10 had symptoms of phlebitis.[23] A device point prevalence survey at Auckland DHB in 2018 reviewed 564 adult patients and 49.8% had one or more vascular access devices in situ. Five (1.7%) patients had evidence of phlebitis (personal communication, S. Muttaiyah). Canterbury DHB undertook a point prevalence survey for PIVC complications in 2019 and found that of the 212 patients with a PIVC in situ, 13% (n=27) had signs of phlebitis.[24]

Intervention programmes to reduce PIVC complications commonly use an insertion and maintenance care bundle which includes a PIVC assessment and decision-making tool to facilitate early identification of complications and the timely removal of the catheter.[20,25] In New Zealand, several DHB and private surgical hospitals are in the process of implementing an ACC-funded hospital-based programme called "Know Your IV Lines", which incorporates a care bundle to reduce PIVC complications.[26] Other DHBs use alternative PIVC monitoring tools.[24] The sustainability of these programmes is challenging and non-compliance with the bundles of care has been reported.[24,27]

The surveillance data collected by DHBs for HA-SAB source varies and was not standardised. Notably the source of HA-SAB was not known for 206 (13%) of events during the report period. The Scottish Antimicrobial Resistance and Healthcare-associated Infection (ARHAI) programme failed to identify a point of entry for 22.1% of all HA-SAB reported events.[10] A review of all HA-SAB events in 2019 at Auckland DHB found 15% had no identified source, however, upon further review of the medical records a source was identified for 60% of those events; the majority were due to vascular access devices.[28] In a study that examined the mortality of blood stream infections (BSI) acquired within the ICU, the rate of BSI of unknown source was 33.5% and was associated with a higher risk of death.[29]

A limitation of this study was that complete source data was not provided by all 20 DHBs. The three DHB who provided incomplete data were excluded from the source data analysis, however, the source data were incomplete for 206 (13%) patients from the other 17 DHB. Overall, source data were not known for 498 (27%) of all HA-SAB events; 292 events from three DHBs who provided no source data and 206 events from the remaining 17 DHBs. This may have skewed the data. However, the sample size—1,369—was large and while there was some variation in absolute number per source category over time, HA-SAB events related to medical devices were the most common source. The review at Auckland DHB identified that vascular access devices were the source for 60% of events where the source was not initially identified,[27] so it is unlikely that the absence of this data would have impacted on the overall finding.

To improve the quality of the data, the Commission has developed a standardised data collection tool for HA-SAB, using dropdown lists for source data fields. The tool will facilitate the reporting of HA-SAB data by the DHBs. Standardising the categorisation and details of HA-SAB source data will support the use of performance measures for national quality improvement programmes aimed at reducing these events.

Conclusion

HA-SAB events related to medical devices are not a new issue. Accurate and standardised surveillance is required to identify the major risk factors and to support quality improvement activities targeting infection prevention measures and best practice related to intravascular and other medical devices. There needs to be a concerted effort to reduce these largely preventable events; they can no longer be considered an acceptable consequence of healthcare.

COMPETING INTERESTS
Nil.

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Healthcare pathways for mild traumatic brain injury patients in New Zealand, determined from Accident Compensation Corporation data

Renata Bastos Gottgtroy, Patria Hume, Alice Theadom

ABSTRACT

AIMS: To describe healthcare pathways for mild traumatic brain injury (mTBI) patients in New Zealand and identify areas for improvement.

METHODS: A data science methodology was applied to mTBI ACC claims (children and adults) between 1 September 2016 and 1 September 2018, and payment and purchase order data until 1 September 2020. Frequency, median and interquartile ranges were used to describe the pathway.

RESULTS: Of the 55,494 claims and 63,642 referrals, >99% were accepted by ACC. Claim processing took more than a week for 7% (3,647) of claims and referral processing took more than three days for 33% (21,139) of referrals. One in four (25%) cases referred to a concussion clinic took >2 months to receive the service due to administrative delays. Of all patients, 36% (20,413) received more than the initial appointment, and their median time in the pathway was 49 days (IQR, 12–185). TBI diagnostic codes were not added at initial appointment in 6% (3,382) of cases.

CONCLUSIONS: Administrative claim and referral processes resulted in minimal delays in the pathway for most patients. However, the volume of claims meant delays affected thousands of New Zealanders every year. Pathways could be improved by facilitating mTBI diagnosis, improving follow-up rates and reducing unnecessary administrative processes.

Mild traumatic brain injuries (mTBI) affect 35,000 people every year in New Zealand.[1] When a person sustains a mTBI in New Zealand and seeks medical treatment from an Accident Compensation Corporation (ACC) registered health professional, the treatment provider lodges an ACC 45 injury claim form. An accepted claim covers compensation for a range of services that include approved medical treatment, income replacement, social and vocational rehabilitation and ancillary services (transportation and accommodation) as part of the patient's healthcare pathway.[2]

Whilst classified as being mild in severity, people affected by mTBI can go on to experience significant and enduring consequences that can last for months or years if left untreated.[3] A routine follow-up 7–10 days after injury is recommended to determine if the person has recovered or requires further treatment.[4,5] Multidisciplinary rehabilitation services often referred to as concussion clinics do improve recovery for those experiencing persistent difficulties after mTBI.[6] Early access to concussion clinics is associated with faster recovery and improved social, emotional and functional outcomes.[7,8] Conversely, delays in access to concussion clinics have been associated with worse symptoms and lower wellbeing.[9] In New Zealand, anyone can receive a referral to a concussion clinic if they have an accepted ACC claim for a medically diagnosed mild or moderate TBI or persisting concussion symptoms from an injury in the previous year.[10] However, there has been concern from patients and clinicians that the patient journey through ACC healthcare pathways are complex with delays in access to treatment.[11–13] Therefore, understanding of ACC mTBI healthcare pathway characteristics from a patient-centric perspective was needed to identify areas for improvement.

Methods

Ethical approval

The project was approved by ACC Ethics Committee (#426) and Auckland University of Technology Ethics Committee (AUTEC #20/21).

Methodology

The Cross-Industry Process for Data Mining (CRISP-DM) is a process model widely used in data science.[14,15] The first three phases of the CRISP-DM methodology were applied to ACC data to reliably map out the patient journey, provide a description of ACC mTBI healthcare pathways in New Zealand and identify areas for improvement. The first

phase (business understanding) involved understanding the application domain (ACC processes and mTBI care) and converting this knowledge into the study objectives. The second phase (data understanding) involved becoming familiar with the data, understanding how it relates to the processes outlined in the business understanding, identifying data quality problems and discovering initial insights. This information is used to direct the third data preparation phase to construct a data set (e.g., deriving new variables) that can be used to meet the study objectives. The remaining phases involve creating a data mining model, evaluating the model and reporting findings.[14] Following this systematic process allows reliable and representative analyses of real-world large data and produces novel, useful and understandable insights related to study objectives.[16]

Business and data understanding

To enable a comprehensive understanding of ACC processes, meetings with ACC, mTBI service providers and academics were held. Service schedules and operational guidelines of mTBI service contracts were used to understand the data within the wider clinical context and healthcare processes. Business Process Model Notation, a graphical notation that depicts the key players and their actions in a business process, was used to present the ACC mTBI healthcare pathway process.[17] Business and data understanding revealed that ACC's mTBI data definition did not capture all mTBIs. Therefore, a list of International Classification of Diseases Version 10 codes (ICD 10 codes) and readcodes were used to define TBI and mTBI in this study (see Appendix 1). Data quality reports were created to direct the data preparation phase.

ACC data stored in three data sets (claims, payments and purchase orders) were retrieved. The mTBI patient ACC claims data for all ages for 1 September 2016 and 1 September 2018, and corresponding payment and purchase order data until 1 September 2020, were selected. The claims data set included information on the patient, their injury diagnoses, claim processing times and lodgement claim provider (first treatment of the pathway). The purchase order data set contained items created by ACC which represent the referrals (to another provider or requests for more patient treatments) by treatment providers. A description of the referral, requesting provider and referral processing times are included. The payments data set contained payments generated for all services the patient received, retrieved from invoices sent to ACC. The service item (the service provided to the patient at the most detailed level), the provider, service date and cost were included.

Data preparation

The three data sets were merged, exclusion criterion applied (data outside study period, moderate and severe TBI, non-residents of New Zealand and declined claims), data cleaned and new variables derived. Service items were labelled with a type (treatment, administration for treatment, income maintenance, provider travel, patient travel, lump sum or other) based on item explanations found in ACC service schedules and operational guidelines. New variables were derived to answer research questions (e.g., time from injury to pathway exit). The final data set contained 55,494 unique claims, 696,800 unique payments and 63,642 unique referrals. Service dates, service types, date of mTBI code being added to the claim and treatment provider were used to determine common providers, follow-up rates, missed mTBI diagnoses and length of pathways. Injury, first treatment day and claim and referral processing dates were used to determine pathway delays. Data were combined to describe the healthcare pathway for each claim. Study definitions and details of data exclusion criterion are in Appendix 2 and Appendix 3.

Statistical analyses

All data in CSV files were analysed with Python (version 3.9.2). Data were highly skewed; therefore, results are reported as medians (Mdn), interquartile ranges (IQR), Fisher–Pearson coefficient of skewness (g_1) and Fisher's coefficient of kurtosis (g_2) with bias correction, frequencies and percentages. Some mean (M) and standard deviation (SD) values are reported for comparison with literature.

Results

Process model

Figure 1 outlines the process model for the ACC mTBI healthcare pathway (details in Appendix 4). Key events were patient injury, treatments with a treatment provider on the first day of treatment (where ACC 45 injury claim form was completed), claim lodgement to ACC, ACC claim registration, ACC claim acceptance or decline and second treatment day if claim was accepted, with treatment provider referral if needed. A referral required ACC approval: registration of referral (creation of purchase order) and ACC referral decision. ACC paid treatment providers for treatments invoiced and patients/employers for other expenses or income maintenance. The patient remained in the ACC mTBI healthcare pathway until no further services were required or approved by ACC.

Figure 1: Process model of ACC mTBI healthcare pathway showing patient first and second(+) treatments with treatment provider(s) and ACC interactions for claims and referrals for the patient.

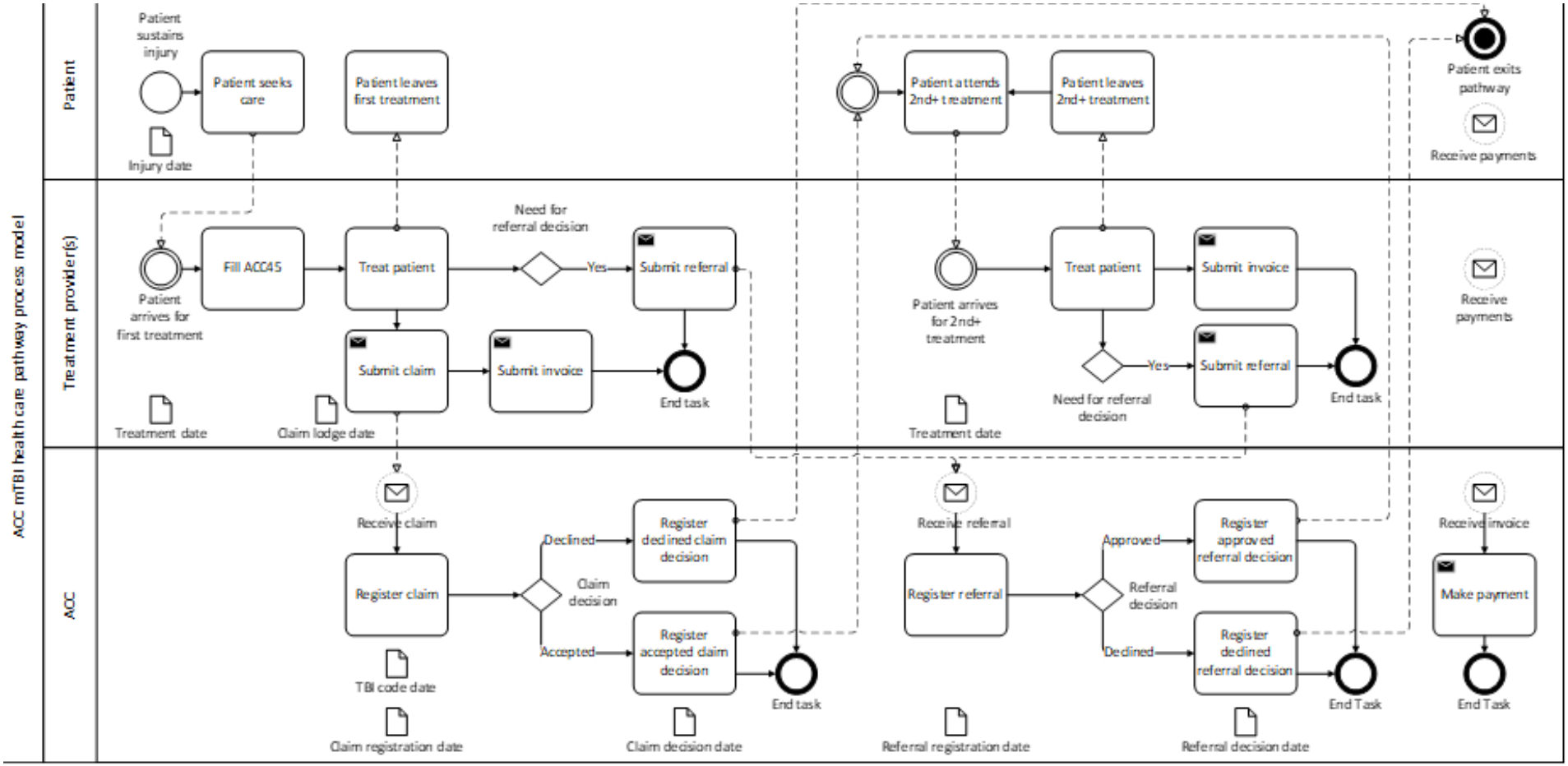


Table 1: Population characteristics of mTBI claims over the two years (September 2016 to September 2018) by sex and total patients.

		Female frequency (% of total 55,494)	Male frequency (% of total 55,494)	Total frequency (% of total 55,494)
Sex		**22,707 (41)**	**32,787 (59)**	**55,494 (100)**
Age at injury (mid-decade age bands)[1]				
	00–04	1,642 (7)	2,375 (7)	4,017 (7)
	05–14	3,412 (15)	7,895 (24)	11,307 (20)
	15–34	8,538 (38)	14,363 (44)	22,901 (41)
	35–64	5,942 (26)	6,006 (18)	11,948 (22)
	≥65	3,173 (14)	2,148 (7)	5,321 (10)
Ethnicity				
	NZ European	15,511 (68)	20,529 (63)	36,040 (65)
	Māori	3,314 (15)	6,042 (18)	9,356 (17)
	Pacific Peoples	1,165 (5)	2,775 (8)	3,940 (7)
	Asian	1,483 (7)	1,730 (5)	3,213 (6)
	Other ethnicity	882 (4)	1,247 (4)	2,129 (4)
	Residual categories	352 (2)	464 (1)	816 (1)
Urban-rural residency profile				
	Urban	19,763 (87)	28,256 (86)	48,019 (87)
	Rural	2,901 (13)	4,474 (14)	7,375 (13)
	Unknown	43 (<1)	57 (<1)	100 (<1)
Residential region				
	Auckland	7,709 (34)	11,067 (34)	18,776 (34)
	Canterbury	3,106 (14)	4,510 (14)	7,616 (14)
	Waikato	2,431 (11)	3,574 (11)	6,005 (11)
	Wellington	2,083 (9)	2,813 (9)	4,896 (9)
	Otago	1,741 (8)	2,289 (7)	4,030 (7)
	Bay of Plenty	1,116 (5)	1,599 (5)	2,715 (5)
	Manawatū-Wanganui	958 (4)	1,419 (4)	2,377 (4)
	Northland	863 (4)	1,255 (4)	2,118 (4)
	Taranaki	730 (3)	1,201 (4)	1,931 (3)
	Hawkes Bay	601 (3)	891 (3)	1,492 (3)
	Southland	369 (2)	608 (2)	977 (2)

Table 1 (continued): Population characteristics of mTBI claims over the two years (September 2016 to September 2018) by sex and total patients.

		Female frequency (% of total 55,494)	Male frequency (% of total 55,494)	Total frequency (% of total 55,494)
Residential region				
	Gisborne	199 (1)	329 (1)	528 (1)
	Marlborough	206 (1)	310 (1)	516 (1)
	Tasman	193 (1)	293 (1)	486 (1)
	West Coast	177 (1)	288 (1)	465 (1)
	Nelson	180 (1)	276 (1)	456 (1)
	Unknown	43 (<1)	57 (<1)	100 (<1)
	Other	2 (<1)	8 (<1)	10 (<1)
Place of injury				
	Home	10,161 (45)	9,656 (29)	19,817 (36)
	Place of recreation or sports	3,873 (17)	9,544 (29)	13,417 (24)
	Road or street	3,161 (14)	4,434 (14)	7,595 (14)
	School	1,492 (7)	3,222 (10)	4,714 (8)
	Commercial/service location	1,120 (5)	1,519 (5)	2,639 (5)
	Industrial place	149 (1)	424 (1)	573 (1)
	Farm	227 (1)	271 (1)	498 (1)
	Place of medical treatment	131 (1)	109 (<1)	240 (<1)
	Other	2,359 (10)	3,547 (11)	5,906 (11)
	Not obtainable	34 (<1)	61 (<1)	95 (<1)
Mechanism of injury				
	Fall injury	12,654 (56)	14,614 (45)	27,268 (49)
	Sport injury	4,758 (21)	12,261 (37)	17,019 (31)
	Motor vehicle injury	1,993 (9)	2,507 (8)	4,500 (8)
	Assault injury	1,275 (6)	3,112 (9)	4,387 (8)
Employment status				
	Non-earners	13,869 (61)	19,756 (60)	33,625 (61)
	Employed	8,177 (36)	11,839 (36)	20,016 (36)
	Self-employed worker	661 (3)	1,192 (4)	1,853 (3)

Table 1 (continued): Population characteristics of mTBI claims over the two years (September 2016 to September 2018) by sex and total patients.

		Female frequency (% of total 55,494)	Male frequency (% of total 55,494)	Total frequency (% of total 55,494)
Work intensity				
	Sedentary work	14,525 (64)	19,773 (60)	34,298 (62)
	Light work	2,608 (11)	1,753 (5)	4,361 (8)
	Medium work	3,529 (16)	4,381 (13)	7,910 (14)
	Heavy work	1,080 (5)	4,059 (12)	5,139 (9)
	Very heavy work	197 (1)	1,676 (5)	1,873 (3)
	Not stated	768 (3)	1,145 (3)	1,913 (3)

* Mechanism of injury percentages represent the proportion of claims where mechanism of injury type is true, not percentage of total.

Table 2: Frequency and percentage of claims for the top 10 treatment providers for first-day treatments, no follow-up, and missed mTBI diagnosis.

Treatment providers	Number of first-day treatments (% of total 65,827)	Number of first-day treatments that did not result in a second treatment day (% of first provider treatments 40,144)	Number of first-day treatments where a TBI code was added after claim registration (% of first provider treatments 4,609)
General practitioners	40,385 (61)	24,815 (61)	2,160 (5)
Emergency departments	20,517 (31)	13,810 (67)	1,489 (7)
Radiologists	2,099 (3)	809 (39)	339 (16)
Dentists	767 (1)	115 (15)	183 (24)
Physiotherapists	588 (1)	89 (15)	78 (13)
Emergency transport	572 (1)	177 (31)	222 (39)
Nurses	382 (1)	267 (70)	28 (7)
Sports concussion clinic	81 (<1)	N/A**	1 (1)
Osteopaths	75 (<1)	12 (16)	11 (15)
Medical specialists	60 (<1)	16 (27)	17 (28)
Other	301 (<1)	10 (N/A)	81 (N/A)

*More than one treatment was provided on the first treatment day for some claims, therefore, the number of first day treatments was greater than the number of claims.
**Treatments for the sports concussion clinic were in bulk, therefore, number of treatment days could not be calculated.

Table 3: Frequency and percentage of claims (with clear pathway exit) for time from injury to pathway exit for the entire data set and for claims with more than one treatment day.

Time bands	Frequency for time to pathway exit for entire data set (% of total 54,881)	Frequency for time to pathway exit for claims with more than one treatment day (% of total 19,800)
0–7 days	33,814 (62)	3,113 (16)
1–2 weeks	4,221 (8)	2,280 (12)
2–4 weeks	4,215 (8)	2,855 (14)
1–2 months	2,970 (5)	2,336 (12)
2–6 months	4,502 (8)	4,212 (21)
6–12 months	2,729 (5)	2,627 (13)
12+ months	2,430 (4)	2,377 (12)

Figure 2: Distribution of time from injury to pathway exit for the entire data set and for claims with more than one treatment day. A broken y-axis has been used for the entire data set.

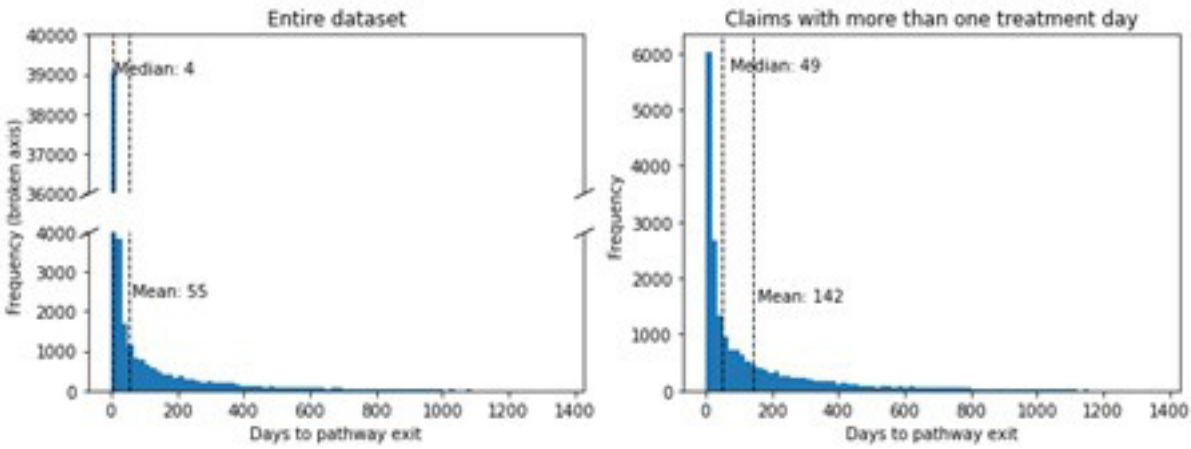
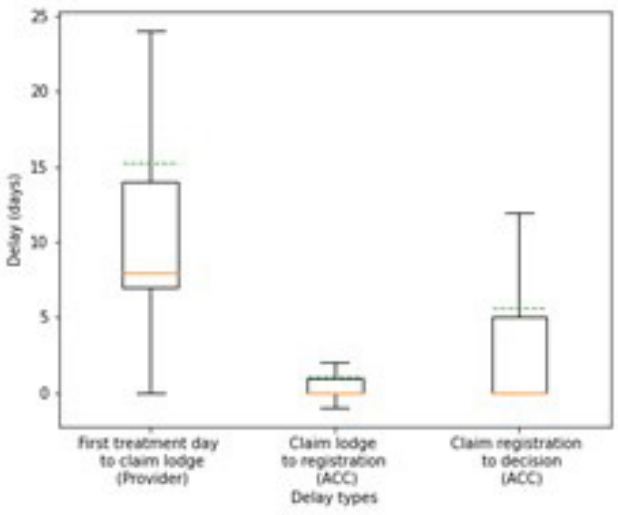


Figure 3: Individual delays for claims with total claim processing time of seven days or more (first treatment to claim decision).



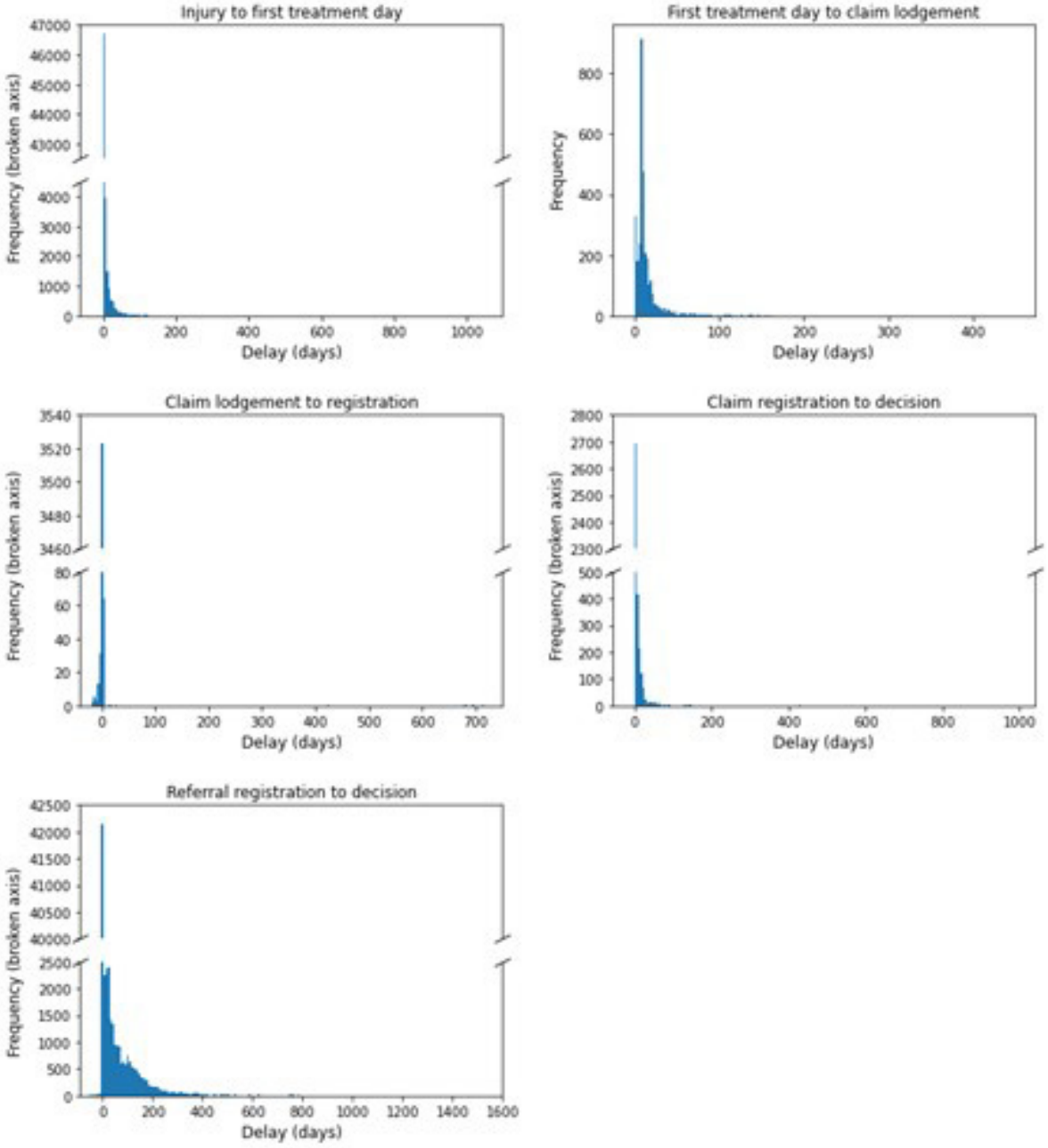
Outliers have been excluded from the figure to improve clarity. Dashed green line represents the mean.

Table 4: Time from injury to first treatment and referral registration to decision for all claims and individual claim processing delays for patients with seven days or more of total claim processing delay represented as frequency and percentages.

		Claim processing delays for claims with seven or more days from first treatment to claim decision			
	Patient to provider	**Provider to ACC**	**ACC**		**ACC**
Delay	**Injury to first treatment day (% of total 55,485*)**	**First treatment day to claim lodgement (% of total 3,233**)**	**Claim lodgement to registration (% of total 3,647)**	**Claim registration to decision (% of total 3,647)**	**Referral registration to decision (% of total 63,642)**
0 days	15,907 (29)	83 (3)	2,648 (73)	2,519 (69)	41,274 (65)
1 day	12,379 (22)	154 (5)	583 (16)	65 (2)	586 (1)
2 days	8,202 (15)	91 (3)	149 (4)	30 (1)	230 (<1)
3 days	5,131 (9)	95 (3)	143 (4)	41 (1)	250 (<1)
4–7 days	7,243 (13)	905 (28)	64 (2)	284 (8)	998 (2)
1–2 weeks	3,058 (6)	1,129 (35)	0 (0)	385 (11)	2,033 (3)
2–4 weeks	2,024 (4)	493 (15)	2 (<1)	220 (6)	4,150 (7)
1–2 months	899 (2)	156 (5)	0 (0)	68 (2)	4,031 (6)
2–6 months	476 (1)	97 (3)	0 (0)	27 (1)	75,23 (12)
6–12 months	135 (<1)	18 (1)	0 (0)	0 (0)	1,874 (3)
12+ months	31 (<1)	2 (<1)	4 (<1)	8 (<1)	530 (1)
Negative days			54 (1)***		163 (<1)****

*Nine injuries occurred at place of medical treatment and did not have any following treatment days. These were excluded for the calculation for time from injury to first treatment day.
**24,421 first treatment days were missing from the payments data set. These were identified from the claims data set when data sets were merged. The date of claim lodgement was used as a proxy for date of first treatment day for these claims. Therefore, they were excluded for the calculation for time from first treatment day to claim lodgement.
***Negative claim lodgement to registration days could be due to the injury being registered without a claim via another form of communication and a claim was later lodged, or an incorrect input of lodge date from ACC.
****Negative referral registration to decision days were presumed to be indicative of an automatically approved service being provided with a referral retrospectively created later. Most negative referrals were for emergency transport.

Figure 4: Distribution of individual delay times in the pathway: injury to first treatment day; claim processing delays, for claims with more than one week from first treatment day to claim decision; referral registration to decision. Broken y-axes have been used for all delays apart from first treatment day to claim lodgement.



Claims characteristics

For the two years there were 55,494 (>99%) accepted mTBI claims; 41% were for patients aged 15–34, 59% were males, and half of all mTBI were caused by a fall (Table 1).

Pathway characteristics

General practitioners provided 61% of all 65,827 first-day treatments (Table 2). Only 36% of patients (19,800) had another treatment day (follow-up) after initial medical presentation (40% for sport-related mTBIs). General practitioners, emergency departments and nurses had the highest percentage of first-day treatments with no follow-up. A TBI code was added after claim registration (i.e., indicative of missed mTBI diagnosis) in 6% (3,382) of claims. For half of these claims (1,620) it took longer than two weeks for a TBI code to be added. Emergency transport had the highest percentage of missed mTBIs (Table 2).

Time to pathway exit

For 54,881 claims (99%) where the patient pathway exit could be clearly determined (i.e., no further services received for 90 days prior to study end), median and average times in the healthcare pathway ranged between four and 55 days (IQR, 1–25; g_1, 4.0; g_2, 18.9; SD, 141.1). For claims with more than one treatment day, median and average number of days until patient pathway exit ranged between 49 and 142 days (IQR, 12–185; g_1, 2.3; g_2, 5.6; SD, 204.4). Table 3 shows times to exit pathway for both cohorts, and Figure 2 shows the distribution of the data.

Pathway delay times

The median days from injury to first treatment (medical presentation) was one day (IQR, 0–3; g_1, 15.4; g_2, 358.0). Total claim processing time (first treatment day to claim decision) was seven days or longer for 7% (3,647) of claims. In this cohort, the median days from first treatment to claim lodgement was eight days (IQR, 7–14; g_1, 6.9; g_2, 65.7), zero days from lodgement to registration (IQR, 0–1; g_1, 31.3; g_2, 996.6), and zero days from registration to decision (IQR, 0–5; g_1, 20.4; g_2, 532.0) (Figure 3). Time from injury to first treatment day for all claims and individual claim processing delays for patients with seven days or more of total claim processing delay are presented in Table 4. All except 327 (<1%) of 63,642 referrals were approved by ACC. Median time for referral registration to decision was zero days (IQR, 0–22; g_1, 5.1; g_2, 43.5). However, 33% of referral decisions took more than three days (21,139) (Table 4). There were 53,207 (24%) treatments delivered by a provider prior to referral approval and 78% of claims with a declined referral exited the pathway after the referral was declined. The distributions of delay times are presented in Figure 4.

Concussion clinics

Concussion clinics provided treatment to 10% (5,485) of claims. Of 5,498 concussion clinic referrals, only 13 (<1%) were declined. ACC took a median of 31 days (IQR, 3–99; g_1, 2.7; g_2, 14.3) from registration date to reach a decision for a concussion clinic referral. Median and average number of days from injury to first concussion clinic treatment were 32 and 55 days (IQR, 20–60; g_1, 4.2; g_2, 33.6; SD, 65.4). Of all claims, 25% (1,356) took more than two months to be seen by a concussion clinic.

Discussion

Streamlining patient care is crucial to patient satisfaction and optimised recovery, yet this study showed the ACC mTBI healthcare pathway in New Zealand can be difficult to navigate. Most patients' claims and referrals were accepted by ACC and administrative claim and referral processes resulted in minimal delays. However, while percentages of the overall sample were small, delays in receiving a mTBI code and time to approval of their claims or referrals affected thousands of people. Some mTBI diagnoses were delayed, only 36% of claims received a follow-up appointment and one in four needing specialist services had delayed access to service of >2 months. Pathways could be improved by reducing unnecessary administrative processes, facilitating mTBI diagnosis on initial presentation of injury, improving rates of follow-up and routine collection of patient outcome data.

To enable patients to seek medical advice promptly, good public awareness of mTBI signs and symptoms is needed, alongside confidence in the healthcare system. While studies have shown good awareness of signs and symptoms in sports athletes (although some misconceptions such as how a brain injury occurs remain),[18,19] little is known about general public knowledge to inform patient awareness campaigns. This is relevant given findings showed that most injuries occurred outside of the sports context. Most patients (75%) presenting for medical treatment were seen in the first three days after injury. However, 6,623 claims (12%) took over one week to be seen after injury.

Given the importance of appropriate and early management of mTBI,[4] analyses of characteristics of these patients (such as residential region and ethnicity) may locate subgroups for interventions to increase motivation for and access to medical treatment after mTBI. Additionally, data on when the patient makes an appointment and when they receive treatment could reveal issues with access to care due to availability of the providers who require appointments to be booked, such as general practitioners.

Previous estimates from incidence studies in New Zealand have suggested that 70,000 mTBIs occur over two years,[1] which is more than the 55,494 accepted claims identified in this data set. This suggests that >10,000 New Zealanders did not have an ACC claim following mTBI. While some participants experience ongoing difficulties after mTBI,[3,11–13] many recover naturally. It may be that the >10,000 cases with no claim did not feel the need to seek medical treatment as their symptoms were minor and/or they recovered well. However, it may also be that some mTBIs may have been missed. Indeed, one New Zealand study revealed 19% of people with mTBI did not have a TBI code on their ACC claim.[20] A standardised screening process for people at risk of mTBI following a traumatic accident such as assault, vehicle accident or fall from a height may help to pick up missed mTBI cases early.[21] Additionally, 6% of cases had a delay in a mTBI code being added to their claim. This is likely due to patients presenting to allied health professionals such as physiotherapists who are not able to use TBI diagnostic codes, or the need for medical doctors to focus on more acute injuries. Without a relevant diagnostic code, questions may be raised about the appropriateness and acceptance of claims or referrals for treatment and lead to significant pathway delays. Permitted use of a "suspected mTBI" code may be useful in these circumstances to highlight the need for medical review and diagnosis.

Ontario Neurotrauma Foundation guidelines for mTBI[4] recommend timely telephone and/or in-person follow-up after initial medical presentation to check for recovery and to ensure the person can access further advice and treatment services. However, our study revealed that two-thirds of patients did not receive a follow-up appointment. While medical clearance before a return to sport is recommended, only 40% of those who sustained a sport-related mTBI received a follow-up appointment. Patients can find it hard to ask for help and need someone else to drive the process and to navigate the healthcare system.[12] Consequently, processes are needed to prompt the booking of a follow-up appointment after initial medical presentation to ensure this process is proactively led by services.

ACC does not routinely collect or integrate patient outcome data within its core database. Therefore, it was difficult to determine whether patients exited the pathway because they had recovered from injury or whether pathway exit was due to lack of follow-up from the treatment provider, the patient deciding to not continue to seek care, the patient seeking treatment from providers not covered by ACC or ACC declining or terminating cover for services. Similarly, it was not clear if the 64% of claims that had one treatment day did not need further follow-up, did not know to seek further support, or had the means to access further support. To account for this, analysis only looked at claims with more than one treatment day which had significant implications on the results. In this reduced cohort, the percentage of claims that exited the pathway within seven days dropped from 62% to 16%, the median day from injury to pathway exit increased from four to 49 days and time to exit pathway became more distributed. Processes to routinely monitor and record patient outcomes are needed to ensure full patient recovery before pathway exit and to allow further evaluation of the healthcare pathway.

Time from injury to receipt of concussion clinic services was longer (mean 55 days) in comparison to a New Zealand sports concussion clinic study where people could self-refer (mean 9 days).[22] For those who attended the self-referral clinic 45% of participants showed clinical recovery within 14 days of injury, 77% by four weeks after injury, and 96% by eight weeks after injury.[22] In our study, only 28% of claims exited the pathway within 14 days of injury (as an indicator of recovery), 42% by four weeks after injury, 54% by eight weeks after injury, with 12% of claims (2,377) still in the pathway after 12 months after injury. Evidence has shown that delays to concussion services can lead to deterioration of symptoms.[9] Earlier referral to specialist concussion clinics for patients who need it could significantly improve patient outcomes.

Less than 1% of mTBI claims were declined over the two years, suggesting that claims were appropriate in most cases. Given the low rates of declined claims, the requirement of an ACC decision for claim cover could be removed from the pathway. To receive a recommended follow-up

covered by ACC within 7–10 days of injury,[5] the claim needs to be accepted in under a week from the date of first treatment. This was not the case for 3,647 claims where the delay in providers lodging the claim after treatment was the main contributor to not meeting this target. This may be because a follow-up appointment was not a requirement in the ACC mild TBI strategy and treatment providers may not be aware of the importance of follow-up. Given that general practitioners and emergency departments together provide 92% of first-day treatments but have low rates of arranging follow-up (60–67%), practitioner education on the importance of follow-ups is needed to facilitate referrals. Patient costs for a follow-up appointment are likely to be prohibitive.[23] Funding of follow-up appointments following a mild TBI may increase the likelihood of keeping the patient in the system until they have recovered.

Referrals require ACC approval prior to treatment. If a referral decision is reached within three days, it allows time for delays in treatment provider availability for a patient to receive further treatment within 1–2 weeks of the last treatment. One in three referral decisions took more than three days to process. To counter this key delay in the healthcare pathway to provide timely care, some treatment providers delivered treatment prior to referrals being approved. In such cases, if the referral was declined, the treatment provider was left to cover costs. Therefore, this delay affected both patient care and treatment providers. The <1% declined referrals suggest that treatment providers were making valid referrals. In most cases, a declined referral resulted in the patient leaving the pathway. This means that the patient did not receive any further treatment, despite the treatment provider's opinion of more treatment being necessary. Given the effect that referral processing times and decisions have on patient and treatment providers, the pathway could be improved by removing the need for referral approval. A standardised screening assessment and referral criteria such as the Brain Injury Screening Tool[21] may facilitate mTBI healthcare pathway navigation, provide outcome monitoring and reduce time in service.

The structure and quality of ACC data and complexity of ACC processes meant that reliable healthcare pathway analysis would not have been possible without use of the systematic approach CRISP-DM methodology. From domain and data understanding gained, key players, their roles and potential delays in healthcare provision were identified and data mapped onto this pathway. Construction of meaningful variables that could be clearly defined enabled mapping of the real-world journey from the perspective of patients. Findings of this study would have varied significantly if different data definitions and a service perspective were used. Our study likely captured more mTBIs than other ACC reported findings because TBI codes from the literature were used that are not part of the ACC mTBI definition. The more inclusive definition used is recommended for future studies utilising ACC data.

There were limitations to our analysis. Data relied on accurate use of diagnostic codes to identify mTBIs, yet it is acknowledged mTBIs may have been missed or coded inaccurately due to an inability of allied health professionals to use a mTBI code. Patients who sought care from non-ACC funded services at onset or during the pathway were not captured in this analysis. The lack of outcome data was a key limitation in analyses and use of cessation of services as recovery may have prevented identification of some issues with the mTBI pathway. Treatment delays due to lack of availability of providers may have existed but were not captured or stored in the ACC database. The ACC relational databases used to store data limited our ability to extract useful insights on relationships between variables useful for healthcare pathways. More complex and flexible data representation and querying would provide better patient journey insights to improve the ACC mTBI healthcare pathway. Future research should analyse how pathway characteristics differ based on different sub populations such as children and adults, residential region, ethnicity and sex.

COMPETING INTERESTS
Nil.

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Data availability statement: Due to restrictions on use of data stated in the data sharing agreement, the research team are not able to share the data used for these analyses. However, data sets generated and analysed during the current study may be requested via ACC.

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Appendices

Appendix 1: TBI and mTBI definition.

Drawing from International Classification of Diseases Version 10 codes (ICD 10 codes) used to identify administrative TBI data in the literature [24–29] and research team expertise, a list of ICD 10 codes and Readcodes were used to define mTBI and moderate to severe TBI in this study and are listed in the appended Excel sheet (converted for these purposes into a Word table: https://uploads-ssl.webflow.com/5e332a62c703f6340a2faf44/633cb73f8edd88cf64ec34f3_5821%20-%20Appendix%201%20Table.pdf.)

Appendix 2: Definitions used in the study.

Service item	**The service provided to the patient at the most detailed level, the entity that represents a row in the payments data set.**	
Service types (service items grouped into categories)	Treatments	Health-related service items i.e., service items that involved an assessment or treatment of the patient by health-related professionals. Health-related professionals that were identifiable in service items included: acupuncturists; allied health practitioner; audiologists; chiropractors; general practitioners; neurologists; neuropsychologists nurses; occupational therapists; optometrists; osteopaths; physiotherapists; psychiatrists; urgent care practitioners; and vocational rehabilitation practitioners.
	Administration for treatment	Service items that a treatment provider undertakes related to a treatment e.g., report writing.
	Patient travel	Service items related to patient travel.
	Provider travel	Service items related to treatment provider travel to provide a treatment.
	Income maintenance	Service items for payments to the patient or to the employer to cover the patient's income until full return to work is established.
	Lump sum	Service items for compensation for permanent impairments.
	Other	Service items that do not meet other category definitions e.g., non-attendance fees, equipment, vehicle repairs, public holiday supplement and medication.
Services	**Any of the service types**	
Treatment providers	Categories of health professionals based on the ACC service contract they delivered the treatment under e.g., a medical doctor delivering treatment at a concussion clinic would be categorised as concussion clinic.	
Treatment day	Ranked dates of the healthcare pathway that contain treatments for a claim.	
First treatment day	The first date where treatments are delivered for a claim.	
Known pathway exit claims	Claims that have at least 90 days between last service date and the end of study time period (1 September 2020).	
Pathway exit	Date of last service.	
Services	**Any of the service types**	
ACC mTBI healthcare pathway	The experiences and journey of the mTBI patient related to the ACC claim and provision of ACC funded services from date of injury to date of pathway exit.	
Urban-rural residency profile	ACC records the residential area unit of the patient based on the 2006 New Zealand area unit definition. The urban-rural profile for the 2006 New Zealand area unit was obtained from Statistics New Zealand and used to label residential area units of patients in this study as urban or rural. Where residential address information was unavailable, the variable was labelled as "Unknown".	

Appendix 3: Data exclusion criterion.

All available data from the three data sets (claims, purchase orders and payments) for all TBI and possible TBI diagnostic codes where the injury occurred in the period of 1 September 2016 to 1 September 2020, including any other claims that were lodged by the TBI patient 14 months prior to and after the TBI claim were requested from ACC. Claims were included if they had at least one mTBI diagnostic code (readcode or ICD 10 code) in any of the readcode or ICD 10 code positions on the ACC 45 form. Claims that also contained moderate or severe TBI codes were excluded. mTBI claims for injuries occurring between 1 September 2016 and 1 September 2018 were included, along with their corresponding payment and purchase order data until 1 September 2020. The cohort of pre- and post-mTBI claims was removed for this study. ACC covers injuries sustained in New Zealand regardless of residency status. Therefore, claims for patients that had a residential and occupational address outside of New Zealand (where applicable) were excluded to mitigate the chance of pathway exits being due to non-New Zealand residents leaving New Zealand. Declined claims were counted then excluded from the analysis.

Appendix 4: Description of the process model for the ACC mTBI healthcare pathway.

Figure 1 outlines the process model for the ACC mTBI healthcare pathway. When a patient sustains an injury (injury date) and reports to a treatment provider for care (treatment date), e.g., general practitioner, the treatment provider assesses and treats the injury and fills out an ACC 45 injury claim form. This form contains the information about the patient, the injury, the injury diagnosis and the provider. The patient then leaves the first treatment. The treatment provider lodges a claim by submitting the ACC 45 form to ACC (claim lodge date). A delay between the treatment date and the lodge date exists if the ACC 45 form is submitted after the day of the treatment. If the claim is submitted in electronic format, the claim is automatically registered in the ACC system. In this case, the date the claim is registered (claim registration date) is the same as the claim lodge date. If the claim is submitted in paper form via email, the ACC 45 form needs to be manually registered into the ACC system by a member of the ACC registration team. This can cause a delay between claim lodge date and claim registration date. The injury diagnostic codes on the form are input into the system at the same time the claim is registered. Therefore, if a TBI has been diagnosed by the provider who delivered the first treatment, the TBI code date will be equal to the claim registration date. A missed TBI diagnosis can be identified when a TBI code is added after the claim is registered, meaning that it was later diagnosed by the same or different provider. Once the claim is registered, ACC decides whether to accept or decline the claim (claim decision date). The decision is made based on the information on the ACC 45 form, additional requested information from the patient or provider, and a medical opinion from ACC medical staff. If the claim is declined, the patient can initiate a review process that can result in the claim decision remaining or the claim being accepted. Due to this decision process, a delay between claim registration date and claim decision date can exist. If the claim is declined or further care is not required, the patient leaves the ACC mTBI healthcare pathway. If the claim is accepted and requires further services, the patient can continue to seek care from the same or a different treatment provider. The treatment provider may make a referral to another treatment provider or request more treatments for the patient. Certain treatments are covered by ACC for mTBIs without needing ACC approval. If required treatments need to be approved by ACC (e.g., referral to concussion clinic), the treatment provider submits a referral request to ACC. When the request is received by ACC, purchase order (PO) lines are created (referral registration date) and ACC decides whether to approve or decline the referral (referral decision date). The time it takes ACC to make the decision can cause a delay between referral registration date and referral decision date. If the referral is declined, the patient is not covered to receive the corresponding treatments and if other available treatments are not suitable, the patient may leave the ACC mTBI healthcare pathway. If the referral is approved, the patient can continue to receive treatment. In some instances, a provider will deliver a treatment that requires ACC approval prior to the decision being reached. In this case, the treatment date for a referral will be prior to its decision date. If the referral is declined, the treatment provider usually funds the treatment that was provided. Treatment providers invoice ACC for services delivered after the treatments. ACC pays the treatment providers, and treatment details and costs on the invoice are stored in the ACC database. ACC may also pay patients for income maintenance, lump sums, treatment costs paid by the patient and other expenses that are also recorded. The patient remains in the ACC mTBI healthcare pathway until no further services are required or approved by ACC.

Bleeding risk of oral anticoagulants in liver cirrhosis

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ABSTRACT

AIM: The safety of dabigatran is poorly studied in patients with liver cirrhosis and has rarely been compared to warfarin in terms of bleeding risks.

METHOD: We undertook a retrospective cohort study across three tertiary centres in Auckland, New Zealand, between 2008 to 2020. Adults 18 years and over and those with a clinically confirmed diagnosis of cirrhosis were included. Data collected included demographic data and clinical characteristics, baseline medication and comorbidities. The primary outcome measure was the incidence of any bleeding event that resulted in hospital admission.

RESULTS: Overall, 100 patients were included in this study. A total of 52 patients took warfarin, and 48 took dabigatran. Baseline characteristics for both groups were generally similar. The incidence rate of bleeds for patients taking warfarin was 14.4 per 100 person-years (95% CI, 8.8–23.5) compared to 9.1 per 100 person-years (95% CI, 4.5–18.1) for patients taking dabigatran. The incidence rate ratio comparing dabigatran to warfarin was 0.63 (95% CI, 0.23–1.60), p=0.25.

CONCLUSION: Our study found that patients on dabigatran may have a lower bleeding risk than patients taking warfarin, but this was not statistically significant.

Liver cirrhosis results from hepatic cell death, nodule formation and irreversible liver scarring.[1] With liver cirrhosis, there is a reduction in the synthesis of procoagulant and coagulant factors. The parallel decrease in both factors rebalances the coagulation system; however, this new balance is fragile and may be tilted towards bleeding or thrombosis when exposed to minimal stimuli.[2] Traditionally, cirrhotic patients needing anticoagulant therapy have been treated with warfarin, a vitamin K antagonist that inhibits the synthesis of vitamin K-dependent coagulation factors, including thrombin. Dabigatran is a novel oral anticoagulant (NOAC) that acts as a direct thrombin inhibitor, blocking only a single step in the coagulation pathway.[3] Dabigatran has become available in New Zealand and overseas in the last decade, and can be used as an alternative to warfarin in several thrombotic conditions, excluding mechanical heart valve replacement.[4] Advantages of dabigatran over warfarin are a faster onset of action, fewer drug and food interactions and less laboratory monitoring required.[5] These advantages make dabigatran more convenient to use in some patients. However, landmark NOAC trials have excluded patients with cirrhosis.[4,6]

In New Zealand, dabigatran was approved for use in 2008 and became fully funded on prescription in 2011.[7] Dabigatran requires minimal hepatic metabolism and is primarily eliminated through the kidneys.[8] Renal dysfunction may occur secondary to late-stage liver disease, leading to accumulation and increased drug concentrations.[9] Extended periods of time with high dabigatran concentrations may potentially lead to a higher bleeding risk in patients.[10] The pharmacokinetic changes of medication in cirrhosis were cited as a key reason for exclusion from landmark studies.[11] However, there is a paucity of data comparing the safety of dabigatran to warfarin in cirrhotic patients.[12] These data are necessary as there is a growing need for an alternative to warfarin. Our study's primary aim was to assess the rate of bleeding in patients with liver cirrhosis taking warfarin compared to those taking dabigatran.

Method

Study design and patient selection

This was a retrospective cohort study conducted in patients admitted to three tertiary care centres (district health boards/DHBs) in Auckland, New Zealand, from 1 January 2008 (the year that dabigatran became available in New Zealand) to 31 December 2020. Each DHB has one tertiary hospital centre. These are Auckland City Hospital (Auckland District Health Board, ADHB), with 1,124 beds, North Shore Hospital (Waitematā Dis-

trict Health Board, WDHB) with 600 beds, and Middlemore Hospital (Counties Manukau District Health Board, CMDHB) with 800 beds. The study has been approved by the ethics board of Auckland Health Research Ethics Committee (AH1163).

Within the three hospitals, any adult patient (≥18 years) diagnosed with liver disease or cirrhosis was identified using each hospital's respective data information service and cirrhosis registries. Liver disease was defined by having one of the following International Classifications of Diseases 10th revision Australian Modified version (ICD-10 AM) discharge diagnosis codes (K701, K703, K704, K717, K721, K740-K746, K754, K758, K758, K760). Only the first hospital admission with a related diagnosis of any of the above codes was included. This admission was linked to community pharmacy dispensing records (Testsafe CareConnect) to identify patients with an anticoagulant dispensed from an outpatient pharmacy during the study period. This dispensing database, started in 2010, includes all records of prescribed medications dispensed to patients by community pharmacies. Patients were included if they had a dispensing record of an anticoagulant while having a confirmed cirrhosis diagnosis. Medication use for patient admissions prior to 2010 was identified using available electronic clinical notes. The index date was defined as the date of the first recorded dispensing of dabigatran or warfarin following cirrhosis diagnosis. The follow-up for each patient commenced from the index date until the occurrence of one of the following events: death, a bleeding event, liver transplant, diagnosis of advanced hepatocellular carcinoma, discontinuation or switch of anticoagulation therapy or the end of the study period (31 December 2020), whichever came first. Patients were excluded if they had a prescription record for other NOACs besides dabigatran on the index date. Patients with familial coagulopathy (such as haemophilia as diagnosed by haematologist) or advanced hepatocellular carcinoma (HCC) recorded any time before the index date were also excluded to reduce potential residual confounding effects.

Baseline characteristics such as age, ethnicity, sex, renal function (estimated glomerular filtration rate, eGFR), serum total bilirubin concentration and haemostasis status were collected. We also collected comorbidities such as polypharmacy, alcohol misuse, diabetes mellitus (type one and two), chronic kidney disease, hypertension, peripheral vascular disease (PVD), previous history of bleed, cerebrovascular disease, cancer, hepatocellular carcinoma and history of peptic ulcers. These characteristics were collected using electronic clinical notes and biochemistry data. We collected data on baseline medication use if they fell into the following categories. These were identified as potentially interacting medicines that may affect bleed risk: antidepressants, antibiotics, antiplatelets, non-steroidal anti-inflammatories and corticosteroids.

Cirrhotic diagnosis and severity

Liver cirrhosis was confirmed by written clinician diagnosis in the clinical notes along with supporting medical imaging evidence such as a FibroScan or computerised tomography (CT).

The severity of liver cirrhosis was defined by the Sodium Model of End-Stage Liver Disease (MELD-Na) score. Variables used to calculate MELD-Na were collected within 90 days of the index date.

Anticoagulation use

Computerised inpatient notes confirmed the date of initiation of anticoagulation, electronic discharge summaries and any outpatient pharmacy dispensing records. The first and last dispensing dates for each anticoagulant were collected along with clinical indication and dosage. If patients switched their anticoagulant (e.g. warfarin to dabigatran, vice versa, or other NOACs), they were censored from further follow-up.

Different criteria were used for warfarin and dabigatran to estimate the end of supply due to their different monitoring requirements and data availability. Dabigatran discontinuation was established if there was a gap between dispensing records of 90 days unless otherwise stated in clinic letters. The 90-day period was used as it is the maximum legal period of supply that a prescription for NOACs can be dispensed in New Zealand. The discontinuation of warfarin was identified if there was a gap between the supply of 56 days with absent international normalised ratio (INR) monitoring. A 56-day gap has been used in previous studies to indicate a lack of monitoring, and it is a period across which time in the therapeutic range is not interpolated.[13]

Outcome measures

Bleeding events were identified by reviewing the electronic clinical notes, discharge summaries, previous imaging reports and biochemistry results during their period of anticoagulation therapy. Events were identified as a primary or secondary diagnosis in the clinical notes. Prior

published criteria were used, and the bleeds were characterised as "major" or "minor".[14] At the time of the bleeding event, we collected MELD-Na scores, haemoglobin, platelet count and total bilirubin serum concentration. All bleeding events were independently assessed by three physician investigators (MH, CS, HW) using the Naranjo scale to evaluate the likelihood of the bleeding event being attributed to the anticoagulant. The Naranjo scale consists of 10 items with points being added or subtracted depending on the response, with a minimum score of negative four to a maximum score of 13.[15] The cause of bleed due to anticoagulation is considered definite if the score is nine or higher, probable if five to eight, possible if one to four, and doubtful if zero or fewer.[15]

Statistical analyses

Patient characteristics were presented as means and standard deviations for normally distributed variables and as medians and interquartile ranges (IQR) for variables with a skewed distribution. The number of patients (n) and percentages were used to represent categorical variables. Between-group comparisons were performed using the Chi-squared and Fisher's exact test for categorical variables. The Mann–Whitney U test was used to compare non-normally distributed continuous variables such as renal function, serum bilirubin and platelet count. ANOVA or Student's t-test was used to compare normally distributed variables, serum haemoglobin and MELD-Na score. The incidence rate of bleeding was calculated as the number of patients with any bleeding event during follow-up divided by total follow-up time in person-year for both groups. The Kaplan–Meier (KM) method was used to compare bleeding events between warfarin and dabigatran cohorts, and the groups were compared using the log-rank test. Patients with missing data were excluded from the relevant analysis. Due to a significant difference in the length of follow-up between patients, the bleeding event data was truncated at five years for survival analysis. All statistical tests were two-tailed, and statistical significance was set at a p-value <0.05. Data analyses were performed using SPSS v27, and KM curve was generated using STATA v14 software packages.

Results

Initially, 4,518 patients admitted with liver disease were identified over the study period. A total of 4,153 patients were excluded as they were not dispensed any oral anticoagulation between 2008–2020. Of the 365 patients on anticoagulation during this time, 265 were excluded (203 were not cirrhotic, eight had advanced hepatocellular carcinoma, and 54 were excluded for reasons defined as "other"). Baseline MELD-Na score was unavailable for six patients. Of those meeting inclusion criteria, 52 took warfarin and 48 took dabigatran. See Figure 1 for cohort selection.

Study cohort characteristics

At baseline, we did not observe any statistically significant differences in sex, age or ethnicity distribution between warfarin and dabigatran cohorts (Table 1). Furthermore, both groups were similar regarding the aetiology of liver disease, baseline medications and comorbidities. The study arms differed in two areas: indication for anticoagulation and MELD-Na score. A higher proportion of patients with valvular AF were in the warfarin compared to the dabigatran cohort (42.3% vs 14.6%). In contrast, the percentage of patients with non-valvular AF was lower in warfarin than dabigatran cohort (36.5% vs 64.6%). Regarding the MELD-Na score, a higher proportion of patients in the warfarin cohort had MELD-Na score >20 than the dabigatran cohort (25% vs 8.3%). There were no differences in specific biochemical markers between the two treatment cohorts, including estimated GFR (p=0.177), total serum bilirubin (p=0.458), platelet count (p=0.583) and serum haemoglobin(p=0.092).

Bleeding risk

A total of 24 bleeding events occurred in total, six being major and 18 being minor. Half (12/24) of the bleeding events were identified to be gastrointestinal in nature. Of these 13% (3/24) of the events were related to the head, urological and epistaxis, and a quarter (6/24) of the events were unspecific, with related causes including hematomas, dental and vaginal.

The overall incidence rate of bleeding was 14.4 (95% CI, 8.8–23.5) and 9.1 (95% CI, 4.5–18.1) per 100 person-years in warfarin and dabigatran users, respectively. The incident rate ratio comparing dabigatran to warfarin was 0.63 (95% CI, 0.23–1.60), suggesting that patients taking dabigatran may have less risk of bleeding than patients taking warfarin. However, when compared using KM curves, this difference was not statically significant (p=0.25) (see Figure 2). Furthermore, no statistical significance was observed when KM analyses were undertaken to compare both

MELD-Na score (p=0.07) and disease aetiology (p=0.13) to evaluate whether bleeding risk differed between warfarin and dabigatran users.

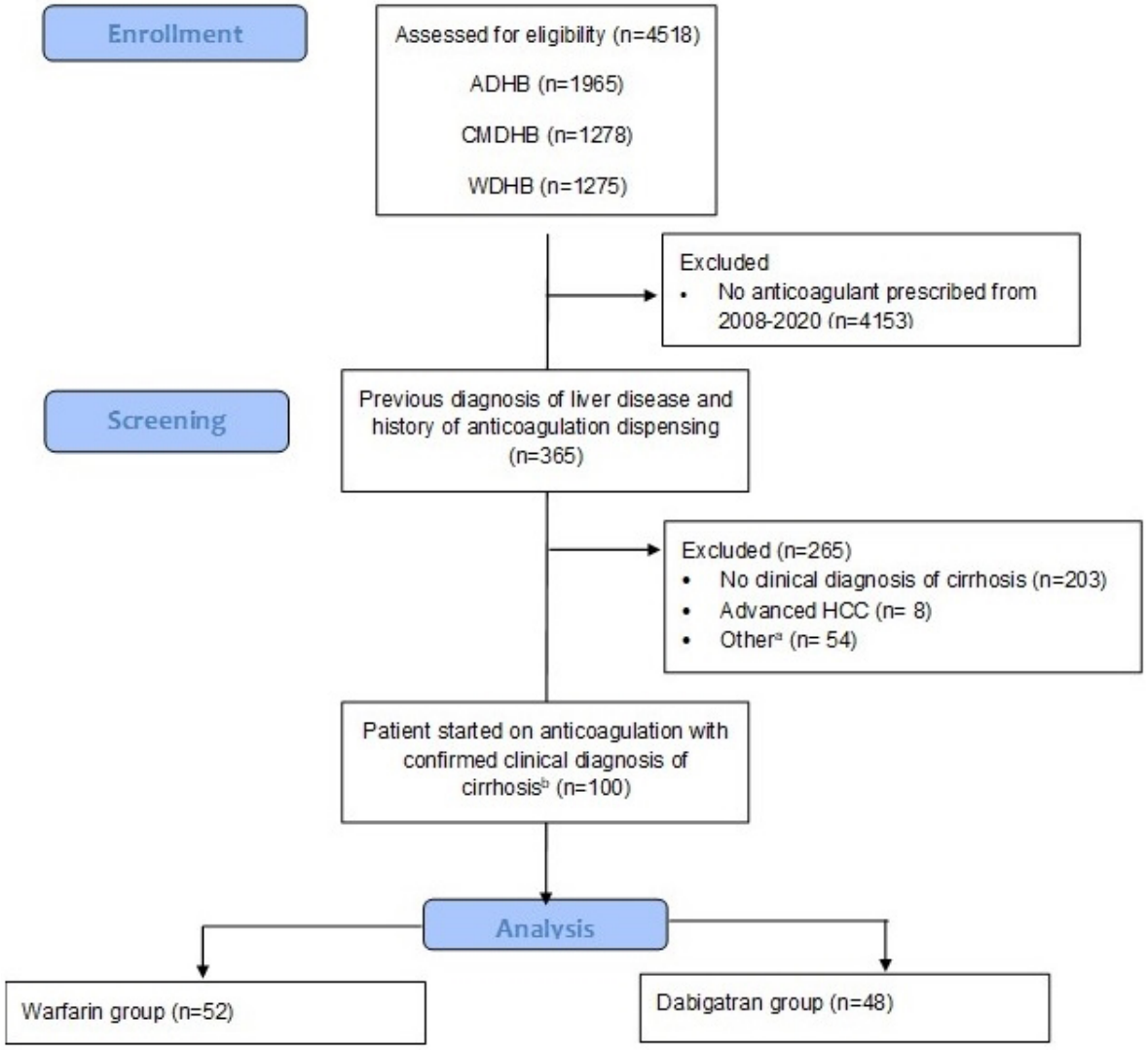
Change in biochemistry between bleeding event and baseline

When compared to baseline, the serum haemoglobin and the MELD-Na scores at the time of bleeding events showed changes that were of both statistical and clinical significance. The serum haemoglobin showed a significant decrease from mean (SD) 126.6 g/L (18.86) at baseline to 105.5 g/L (27.1) at the event (p<0.001), and the MELD-Na score had a significant increase from mean (SD) 16.8 (5.9) at baseline to 23.12 (8.1) at the event (p<0.001). However, serum bilirubin and platelet count did not alter significantly between bleeding event and baseline (Table 2).

Causality assessment of bleeding event and anticoagulation

Of the 24 bleed events, nine were considered possible and 15 were probable in likelihood of the bleed being attributed to the anticoagulant. Five were due to warfarin, and four were due to dabigatran in the nine events considered possibly related to the anticoagulant. In the 15 events deemed to be probable, eight were due to warfarin and seven were due to dabigatran.

Figure 1: Patient selection.



[a] Other reasons for exclusion include: patient taking rivaroxaban (n=10), no history of liver disease (n=31), recent liver transplant (n=9), and under the age of 18 years (n=4).
[b] Anticoagulation defined as patient being on a treatment dose of dabigatran or having a therapeutic INR of 2–3 if on warfarin.

Table 1: Comparison of baseline characteristics of cirrhotic patients treated with warfarin or dabigatran (n=100).

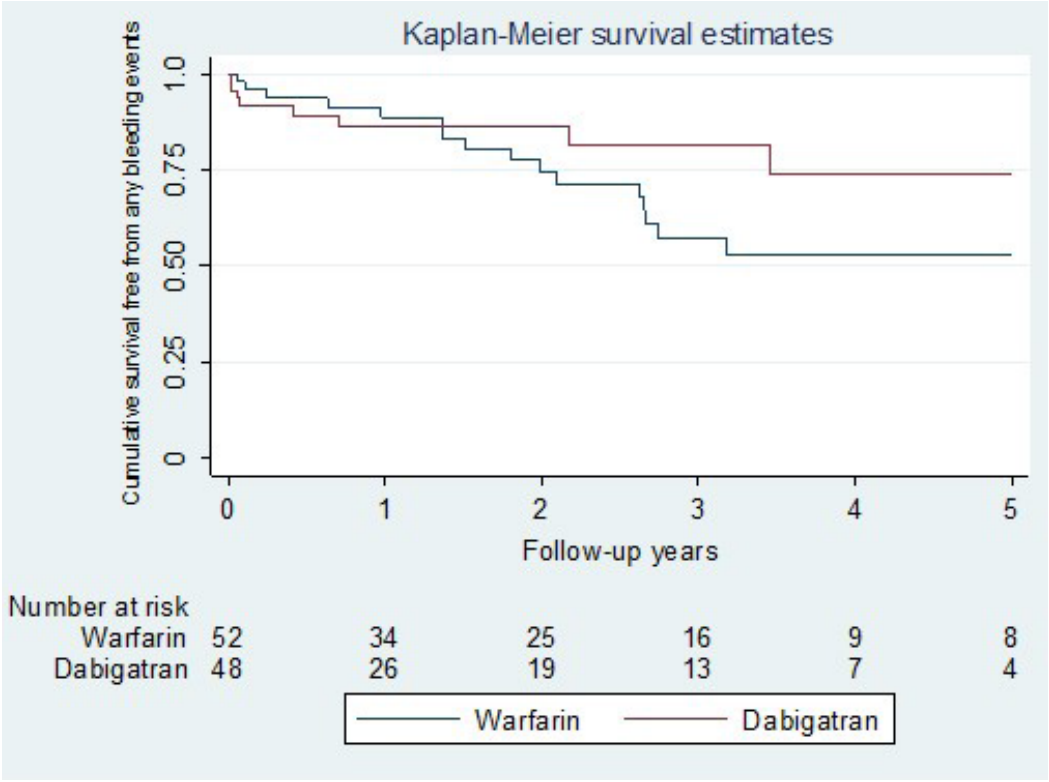
		Total (n=100) Warfarin (n=52)	Anticoagulant type n (%)		P-value
			Dabigatran (n=48)		
Sex	Female	32	17 (32.7)	15 (31.3)	0.88
	Male	68	35 (67.3)	33 (68.8)	
Age	<65 years	41	26 (50)	15 (31.3)	0.06
	≥65 years	59	26 (50)	33 (68.8)	
Ethnicity	NZ European	60	29 (55.8)	31 (64.6)	0.37
	Other	40	23 (44.2)	17 (35.4)	
Liver disease aetiology	Non-alcoholic Fatty Liver Disease	30	17 (32.7)	13 (27.1)	0.41
	Alcoholic Fatty Liver Disease	30	13 (25)	17 (35.4)	
	Viral Hepatitis (B and C)	27	13 (25)	14 (29.2)	
	Other	13	9 (17.3)	4 (8.3)	
Indication	AF (Non-valvular and Non-specified)	50	19 (36.5)	31 (64.6)	0.005
	AF (Valvular)	29	22 (42.3)	7 (14.6)	
	Systemic Thromboembolism	21	11 (21.2)	10 (20.8)	
MELD-Na score[a]	<10	17	5 (9.6)	12 (25)	0.023
	10–19	60	32 (61.5)	28 (58.3)	
	≥20	17	13 (25)	4 (8.3)	
Antidepressant	Yes	17	7 (13.5)	10 (20.8)	0.33
Antibiotics	Yes	13	7 (13.5)	6 (12.5)	0.87
Antiplatelets	Yes	6	5 (9.6)	1 (2.1)	0.21
NSAIDS[b]	Yes	2	0	2 (4.2)	0.23
Corticosteroids	Yes	2	1 (1.9)	1 (2.1)	1.00
Polypharmacy[c]	Yes	66	33 (63.5)	33 (68.8)	0.58
History of alcohol misuse	Yes	33	16 (30.8)	17 (35.4)	0.62
HCC[d]	Yes	16	8 (15.4)	8 (16.7)	0.86
Renal disease	Yes	20	11 (21.2)	9 (18.8)	0.76
Diabetes	Yes	46	24 (46.2)	22 (45.8)	0.97

Table 1 (continued): Comparison of baseline characteristics of cirrhotic patients treated with warfarin or dabigatran (n=100).

		Total (n=100) Warfarin (n=52)	Anticoagulant type n (%)		P-value
			Dabigatran (n=48)		
Hypertension	Yes	53	28 (53.8)	25 (52.1)	0.86
Vascular disease[e]	Yes	9	6 (11.5)	3 (6.3)	0.49
History of bleed	Yes	7	5 (9.6)	2 (4.2)	0.44
Non-HCC cancer	Yes	6	4 (7.7)	2 (4.2)	0.68
Peptic ulcer	Yes	2	1 (1.9)	1 (2.1)	1.00

*Polypharmacy is defined as taking five or more medications.
[a] MELD-Na score was missing for six cases.
[b] Hepatocellular carcinoma.
[c] Includes both peripheral and cerebral vascular disease.
[d] Non-steroidal anti-inflammatories.
[e] Includes both peripheral and cerebral vascular disease
Fisher's exact test was used to compare baseline characteristics for variables including vascular disease, antiplatelets, NSAIDs, history of bleed, non-HCC cancer, peptic ulcer and corticosteroids.

Figure 2: KM curve for risk of bleed between dabigatran and warfarin users (n=100).



KM curve comparing the risk of bleed between dabigatran and warfarin over a truncated five-year period with no statistical significant difference (p=0.25).

Table 2: Comparison of biochemistry at baseline and at the time of the bleeding event (n=24).

	Median (IQR)		P-value
	Baseline	**Event**	
Bilirubin (umol/L)	18.5 (11–31)	22 (11–33)	0.86
Platelet count (E+9/L)	138 (98–206)	178 (102–212)	0.51
	Mean (SD)		
	Baseline	**Event**	
Haemoglobin (g/L)	126.6 (18.6)	105.5 (27.1)	<0.001
MELDNa score	16.8 (5.9)	23.1 (8.1)	<0.001

Related-Samples Wilcoxon signed rank test for bilirubin and platelet count. Paired-Samples t-test for hemoglobulin and MELD.
Note: This analysis is only for patients who had any bleeding event.

Discussion

This paper presents the first data to our knowledge in the literature directly comparing the bleeding rates between the oral anticoagulants warfarin and dabigatran in patients with liver cirrhosis. There has been growing interest in this field since the emergence of NOACs, yet data on bleeding risk in the context of liver cirrhosis is scarce. Patients diagnosed with liver cirrhosis have traditionally been excluded from landmark studies, but more real-world retrospective studies are emerging.[16] In our study, we demonstrated that the bleeding risk of dabigatran did not differ compared to warfarin. In our initial cohorts, warfarin tended to be used in patients with higher MELD-Na scores and for the indication of valvular AF, and this may increase the bleeding risk of warfarin. These differences are likely a reflection of prescribing practices, whereby dabigatran is contraindicated and off-license in both valvular AF, moderate and severe hepatic impairment (CTP categories B and C).[17]

Compared to other studies of similar design, our bleed rates are similar to a study recently published by Mort et al, which focusses specifically on NOACs and bleeding risk. Their study's overall bleed rate was 21%, and ours is 24%.[12] Although Mort et al. did not compare their cohort directly with warfarin users, they state that their rate of bleed for NOACs was comparable to published rates of bleed for warfarin users.[12] Another larger retrospective cohort study was conducted in Taiwan, using national health administrative data. Over 2,428 non-valvular AF patients with cirrhosis were included in this study. The risk of major bleed (HR 0.51, 95% CI 0.32–0.74) and major gastrointestinal bleed (HR 0.51, 95% CI 0.32-0.79) was lower in NOACs users compared to Warfarin users.[18] Compared to our study, the study differs significantly in methodology and findings. However, Lee et al.'s Taiwan study only included Taiwanese patients and may not be applicable to other ethnicities. In addition, our study also collected multiple clinically important biomarkers that are not often available in the administrative database. Asian populations have been found to have a higher risk of bleeding when taking warfarin compared to non-Asian populations, and previous studies indicate that NOACs may be a safer option in Asian vs non-Asian populations.[19]

Our study had several strengths, including using the Naranjo scale. We were able to standardise the assessment of bleeding events in patients with cirrhosis on dabigatran and warfarin. By using three independent physicians to ascertain the Naranjo score and compare scores, we ensured a more robust assessment of each bleeding event being related to the anticoagulant of choice. The study had access to a wide range of clinical data across the three main hospitals in Auckland, New Zealand, by using computerised notes and paper notes and laboratory results. Thus, for each patient, we were able to assess their liver disease status comprehensively and to only include those with a robust diagnosis of liver cirrhosis. We also collected several important variables that may influence bleeding risk, e.g., baseline MELD-Na score, full blood count and

renal function. A weakness for our study is its low sample size, being an exploratory study. The study lacked enough input from other ethnic groups to make any meaningful comparison in outcomes, with the majority of patients being NZ European.

Further investigation into the ethnic differences in bleeding rates on warfarin and NOACs in New Zealand's population, particularly in Māori and Pasifika populations, would be an area for further research to potentially change clinical practice. We also opted to combine both minor and major bleed to all bleed for our outcome of interest due to the low number of bleeding events in total. Other limitations include that the study was retrospective, so we cannot control for all confounders at baseline. The data is also limited as it was based in one region—in Auckland, New Zealand—and the population characteristics, while representing a broad range of ethnicities and three different DHB sites, may not represent populations elsewhere. However, Auckland represents around one-third of New Zealand's total population, and it is likely that New Zealand data is not sufficient for this study.[20] Our study was exploratory as we did not have any existing data on the rate of oral anticoagulated patients with liver cirrhosis, thus we did not have a predetermined sample size. It is evident from our research that the use of oral anticoagulation is a rare occurrence in patients with liver cirrhosis in New Zealand (prevalence of less than 0.1%). We did not observe a statistically significant association between warfarin vs dabigatran use and subsequent risk of bleeding but, due to the modest sample size, this study is likely underpowered to detect any such an association, if present. An adequately powered study with comparable methodology will likely need to be conducted in countries with larger centres such as those in Asia, the United States and the United Kingdom.

In conclusion, our study found no statistically significant differences in the bleeding rate in cirrhotic patients treated with warfarin versus those treated with dabigatran. Our results suggest dabigatran may be as safe to use as warfarin in patients with cirrhosis.

COMPETING INTERESTS

Authors declarations of personal interests:

OMA received funding as part of her summer studentship from the New Zealand Pharmacy Education and Research Foundation for this piece of work.

MH declares no conflicts of interest.

KB declares no conflicts of interest.

AHYC reports consultancy fees from Spoonful of Sugar Ltd, grants from Health Research Council, Innovate UK, A+ charitable trust (Auckland District Health Board), Maurice and Phyllis Paykel trust, Universitas 21, NZPERF, Auckland Academic Health Alliance, Asthma UK, The University of Auckland; grants and consultancy fees from Janssen-Cilag; and is the recipient of the Robert Irwin Fellowship and Senior Research Fellowship from the Auckland Medical Research Foundation. None related to this work.

CS declares no conflict of interest.

HW no conflict of interest.

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Disability-Adjusted Life Years and cost of health loss of hospitalised major trauma patients in New Zealand

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ABSTRACT

AIMS: The aims of this study were to quantify the burden, and the cost of health loss, following hospitalisation for major trauma in New Zealand.

METHOD: Hospitalised major trauma patients injured between July 2017 and June 2020 were extracted from the New Zealand Trauma Registry. Case-mix of major trauma in each year was summarised using descriptive statistics. Disability-Adjusted Life Years (DALYs) were calculated for the cohort. A cost per DALY was applied to estimate the cost of health loss.

RESULTS: A total of 6,629 major trauma cases were recorded, rising from 2,072 in 2017–2018 to 2,191 in 2019–2020. The patient case-mix remained relatively consistent over the timeframe while the in-hospital mortality rate declined from 9.2% to 7.3%. Hospitalised major trauma patients accrued 22,718 DALYs (average 7,573 DALYs per year) at an estimated health loss cost of $1.02 billion ($341 million per year). The cost of health loss per case declined from $162,747 in 2017–2018 to $143,577 in 2019–2020.

CONCLUSION: The burden of major trauma is high. As injury is a preventable condition, the findings highlight the need for dedicated investment in both primary prevention and trauma care in New Zealand to reduce these avoidable costs.

Injury remains one of the top five contributors to disease burden, accounting for 252 million Disability-Adjusted Life Years (DALYs) and 10% of the global burden of disease in 2017.[1] In New Zealand, injury is the leading cause of death in people aged 1 to 34 years, and 2,534 people were hospitalised with major trauma at a rate of 51 per 100,000 population in the 2020–2021 financial year.[2] Understanding the burden of injury is needed to help plan and introduce prevention measures, and evaluate and inform improved trauma system design and injury care.

A key intervention for improving trauma care and outcomes has been the introduction of a contemporary trauma system in New Zealand.[3] Contemporary trauma systems are designed to expedite the transport of seriously injured patients to major trauma centres to reduce preventable mortality and morbidity. There is widespread evidence that contemporary, organised trauma systems save lives.[4–6] However, there is also growing evidence from longitudinal cohort studies that hospitalised major trauma patients can experience long recovery times and persistent disability.[7–10] Measuring the impact of trauma system implementation and maturation, and patterns in trauma burden, in New Zealand requires population-based studies which consider both mortality and measures of morbidity. The aims of this study were to quantify the burden, and the cost of health loss, of hospitalised major trauma patients in New Zealand.

Method

Study design

A registry-based observational study was undertaken. Existing data only were used for this study and no additional information was sought from participants.

New Zealand Trauma Registry (NZTR)

The NZTR collects data about patients admitted to hospital in New Zealand with an Injury Severity Score (ISS) >12, meeting the threshold for serious injury and major trauma.[3] All district health boards (DHBs) have participated in the registry from the 2017–2018 financial year. Data are collected under the auspices of quality improvement. Requests for use of the data are considered and approved by the Data Governance Group (DGG) of the National Trauma Network and approval for this project was received from the DGG and the Monash University Human Research Ethics Committee.

Inclusion criteria

Participants were included if they were registered on the NZTR and had a date of injury from 1 July 2017 to 30 June 2020.

Procedures

Trauma registry data

For this study, a limited selection of NZTR variables were extracted, and these included age at the time of injury, sex, cause of injury, date of injury, the Injury Severity Score, Abbreviated Injury Scale (AIS) diagnosis codes, discharge disposition and length of hospital stay.

Injuries sustained by the major trauma patients were mapped to eight injury groups based on the combination of AIS injuries sustained and their severity. The cause of injury ICD-10-AM code was used to group cases into key mechanism of injury categories, including road traffic injuries, falls, self-harm and other.

Burden of injury measurement

The measure of burden used for this study was the DALY. The DALY was specifically developed to quantify the burden of disease in populations, enable comparison across populations and guide resource allocation.[11] This metric is widely used for measuring disease burden or "health loss".[12–14] The DALY combines Years of Life Lost (YLLs) and Years Lived with Disability (YLDs) to generate DALYs for conditions.

YLLs were calculated as the age in years at time of injury subtracted from the life expectancy for a person of that age and sex in New Zealand and multiplied by the number of deaths at that age to calculate the lost life expectancy. Life expectancy was obtained from the New Zealand standard life table for 2018.[15] The total lost life expectancy years for each age were summed and summarised by year of injury. As the purpose was to calculate the burden of hospitalised major trauma patients, only in-hospital deaths were used.

The YLD component is calculated by multiplying the number of incident cases in the time period by the average duration of the condition (years expected to live in the disabled state) and a disability weight which reflects the severity of the disease on a scale from zero (perfect health) to one (dead).[16] Typically, the disability weights used for calculating YLDs are from panel-based studies where a lay description is provided to the panel members to represent the health impact of the condition of interest on a hypothetical affected individual.[16] This has been shown to under-estimate burden when compared to disability weights derived from standardised measures of quality of life reported by injured people in large cohorts.[12] For this reason we chose to use patient responses to the EuroQol five-dimensions – three-level (EQ-5D-3L) from the REcovery after Serious Trauma – Outcomes, Resource Use and Patient Experiences (RESTORE) study to generate disability weights.[8, 17] The RESTORE study shared consistent inclusion criteria to the New Zealand Trauma Registry and comparable EQ-5D data from New Zealand were not available at the time of this study.

The RESTORE study included all major trauma patients managed in the Victorian State Trauma System from July 2011 to June 2012. The EQ-5D-3L responses of 2,412 survivors to hospital discharge were used to generate the disability weights and were calculated by subtracting the patient (or proxy) EQ-5D-3L utility score from the corresponding age and gender norm for the population. The average weight at each follow-up time point for each injury group was calculated. The average differences between the patient responses and population norms at 6, 12 and 24 months were used to create a time-weighted disability weight for the first 24 months after injury.[12] The mean 24-month weight was considered the long-term weight for the injury group—i.e., the expected disability for the remaining life expectancy. Patients or their proxy respondent provided a rating of the patient's level of disability prior to injury and at follow-up on a five-point scale from none to severe disability.[18] Residual disability at 24 months was confirmed if the level of disability reported at this time point was greater than pre-injury disability, and was considered permanent for the purposes of calculating YLDs. The proportion of patients in each injury group with residual disability at 24 months was calculated.

Total DALYs were calculated as the sum of the YLDs and YLLs. Age discounting was not used, while economic discounting at 3% was used for consistency with World Health Organization recommendations for burden of disease studies.

Calculating the cost of major trauma burden

Establishing the cost of health loss requires a dollar cost per DALY. For this study, we used the New Zealand Gross Domestic Product (GDP) cost per DALY of $45,000, which is commonly used in economic evaluations of interventions.

Data analysis

Summary statistics were used to describe the patient population overall, and by year. For cate-

gorical variables, frequencies and percentages were used. Normally distributed continuous variables were summarised with means and standard deviations (SD) while continuous variables not following a normal distribution were summarised using the median and interquartile (IQR) range. Anonymised data were analysed and stored on the secure Monash University Server Secure eResearch Platform (SeRP), a secure data safe haven. All analyses were performed using Stata MP, Version 16.

Results

Population characteristics

From July 2017 to June 2020, there were 6,629 major trauma patients recorded on the NZTR. The number of patients on the registry was 2,072 in the 2017–2018 financial year, with 2,191 cases in the 2019–2020 financial year (Table 1). The mean age of major trauma patients was highest in 2019–2020. The proportion who had sustained a serious head injury (AIS severity score 3+), with or without injuries to other body regions, declined by 1.9% over the 3-year period, while the proportion without neurotrauma (serious head injury or spinal cord injury) increased by 2.2%. The in-hospital mortality rate declined from 9.2% to 7.3%.

Disability weights

The disability weights used to calculate the YLDs are shown in Table 2 along with the percentage continuing to report disability at 24 months post-injury. The highest disability weights, and prevalence of ongoing disability, were for patients with spinal cord injury. The lowest disability weights and prevalence of disability at 24 months post-injury were for patients who sustained abdominal and thoracic injuries, but without orthopaedic injuries or serious neurotrauma.

Disability-Adjusted Life Years

There were 552 deaths and 6,071 survivors to hospital discharge. No AIS codes were recorded for 6 survivors to hospital discharge, precluding allocation of a disability weight and inclusion in the YLD calculations. The 6,623 hospitalised major trauma patients accrued 22,718 DALYs at an estimated health loss cost of $1.02 billion, using the New Zealand GDP cost of $45,000 per DALY. The cost of health loss per patient declined from $162,747 in 2017–2018 to $157,003 in 2018–2019 to $143,577 in 2019–2020. The decline in cost of health loss per patient reflects the declining in-hospital death rate in the later years.

Discussion

In this study of 6,623 hospitalised major trauma patients in New Zealand, an average of 7,573 DALYs were lost each year at a cost of more than $341M. While the overall incidence of hospitalised major trauma has risen,[2] lower mortality rates and lower DALYs and cost of health loss per patient were observed. The costs of health loss observed in this study build on the direct healthcare costs for injury in New Zealand. In the 2019–2020 financial year, the Accident Compensation Corporation (ACC) expended $2.9 billion on injury treatment and rehabilitation services.[19] The ACC contribution to Vote Health represented 2.9% of the total health expenditure through this scheme. Together, the cost of health loss from this study, combined with the direct costs of healthcare, would exceed $3.2 billion per year.

Direct comparison of the health loss observed for New Zealand major trauma patients with other studies is challenging as prior studies have focused predominantly on road trauma,[20,21] or have focused on hospitalised injury rather than major trauma.[14] Prior authors reported an average of 9.7 DALYs and $486,425 AUD per case which was higher than the 3.4 DALYs and $154,366 NZD per patient observed in our study. However, important differences are noted. The study by Gabbe and colleagues included road trauma only which tend to be younger and more severely injured patients, and the prior study also included pre-hospital deaths.[21] Notwithstanding, the pattern observed in our study of decreasing mortality and a reduction in DALYs per patient over time was similar to previous studies focused on road trauma in Victoria, Australia.[20,21]

There were a number of strengths to this study. The New Zealand Trauma Registry provides whole of population coverage of hospitalised major trauma in the New Zealand and high-quality data with little missingness. The study used disability weights derived from a comparable population of trauma patients, precluding the need to use panel-based weights, which are known to under-represent the disability experienced by injury patients.[12,22]

Importantly, the underlying assumption was made that the disability weights derived from the Victorian population would reflect disability experienced by New Zealand major trauma patients and this assumption could not be confirmed. Ethnicity has been shown to influence EQ-5D reporting in New Zealand,[23] and presenting results for Māori vs non-Māori on the basis of the

Table 1: Characteristics of major trauma patients in New Zealand, 2017–2018 to 2019–2020.

Characteristic	2017–2018	2018–2019	2019–2020
	N=2,072	N=2,366	N=2,191
Age, mean (SD) years	**46.6 (23.2)**	**46.7 (22.9)**	**47.0 (22.5)**
Sex			
Male	1,448 (69.9%)	1,724 (72.9%)	1,579 (72.1%)
Female	624 (30.1%)	642 (27.1%)	612 (27.9%)
Cause of injury			
Land transport	1,173 (56.6%)	1,333 (56.3%)	1,175 (53.6%)
Falls	559 (27.0%)	640 (27.0%)	622 (28.4%)
Animate and inanimate forces	98 (4.7%)	109 (4.6%)	98 (4.5%)
Heat and smoke	16 (0.8%)	12 (0.5%)	6 (0.3%)
Self-harm	41 (2.0%)	44 (1.9%)	48 (2.2%)
Assault	151 (7.3%)	187 (7.9%)	168 (7.7%)
Other cause	34 (1.6%)	41 (1.7%)	74 (3.4%)
Injury Severity Score (ISS)			
Median (IQR)	17 (14, 25)	17 (14, 25)	17 (14, 25)
Injury group			
Isolated head injury	292 (14.1%)	323 (13.7%)	274 (12.5%)
Head and orthopaedic injuries	282 (13.6%)	338 (14.3%)	292 (13.4%)
Head and other injuries	148 (7.1%)	157 (6.6%)	154 (7.0%)
Spinal cord injury	101 (4.9%)	111 (4.7%)	91 (4.2%)
Orthopaedic injury only	139 (6.7%)	143 (6.0%)	151 (6.9%)
Chest or abdominal injuries with associated orthopaedic injuries	692 (33.4%)	807 (34.1%)	718 (32.8%)
Chest or abdominal injuries with or without other injuries	267 (12.9%)	315 (13.3%)	301 (13.8%)
Other multi-trauma or other injuries	150 (7.2%)	171 (7.2%)	206 (9.4%)
In-hospital death			
No	1882 (90.8%)	2164 (91.5%)	2031 (92.7%)
Yes	190 (9.2%)	202 (8.5%)	160 (7.3%)

Table 2: Disability weights and proportion with lifelong disability by injury group.

Injury group	DW short-term	DW long-term	Percentage with disability at 24 months
Isolated head injury	0.127	0.123	46.8%
Head and orthopaedic injuries	0.163	0.150	61.8%
Head and other injuries	0.083	0.070	50.4%
Spinal cord injury	0.404	0.363	86.0%
Orthopaedic injury only	0.145	0.113	58.6%
Chest or abdominal injuries with associated orthopaedic injuries	0.138	0.129	54.8%
Chest or abdominal injuries with or without other injuries	0.058	0.050	32.7%
Other multi-trauma or other injuries	0.152	0.142	54.4%

Table 3: Burden and cost of health loss for hospitalised major trauma patients in New Zealand—2017–2018 to 2019–2020.

	2017–2018	2018–2019	2019–2020	All years
N (survivors)	1,881	2,163	2,027	6,071
N (deaths)	190	202	160	552
N (total)	2,071	2,365	2,187	6,623
YLDs total	3,734	4,334	3,920	11,988
YLLs total	3,756,	3,917	3,057	10,730
DALYs total	7,490	8,251	6,977	22,718
YLDs/patient	1.99	2.00	1.93	1.97
DALYs/patient	3.62	3.49	3.19	3.43
Total health loss costs	$337,049,987	$371,312,307	$314,003,093	$1,022,365,387
Total health loss cost/patient	$162,747	$157,003	$143,577	$154,366

available weights may not be appropriate. Therefore, ethnicity-based analysis was excluded. In future, disability weight sets based on health-related quality of life of New Zealand major trauma cases will result in improved population burden measures. As the study was observational, we cannot attribute the declining burden per patient directly to the maturation of the trauma system, and the data simply represent the positive change occurring within the major trauma population. Our study did not address the full YLLs of injury in New Zealand as pre-hospital deaths were not included in this study due to data availability issues. These should be included in future burden of injury research to ensure a more comprehensive estimate of major trauma burden.

Overall, the burden of hospitalised major trauma is rising due to the increasing number of major trauma patients in the population, while the burden per patient is declining. This is likely to be due to continuing improvement in the care of seriously injured patients in New Zealand and some changes in case-mix of major trauma. Notably, over the three years of this study, 22,718 DALYs were lost at an estimated health loss cost of $1.02 billion. As injury is a preventable condition, these numbers highlight the ongoing need for investment in primary prevention in New Zealand to reduce these avoidable costs. Additionally, investment in improved trauma care through trauma education and training programs, adequate resourcing and increased capacity in tertiary trauma centres, and optimisation of the National Trauma Network is needed to further enhance survival and reduce preventable morbidity.

COMPETING INTERESTS
Nil.

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Revascularisation and outcomes after acute coronary syndromes in patients with prior coronary artery bypass grafting—ANZACS-QI 67

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ABSTRACT

AIMS: Coronary angiography in patients with previous coronary artery bypass grafts (CABG) is technically more difficult with increased procedure time, radiation exposure and in-hospital complications. In a contemporary national registry of acute coronary syndrome (ACS) patients undergoing an invasive strategy, we compared the management and outcomes of patients with and without prior CABG.

METHODS: The All New Zealand ACS Quality Improvement (ANZACS-QI) registry was used to identify patients admitted to New Zealand public hospitals with an ACS who underwent invasive coronary angiography (2014–2018). Outcomes were ascertained by anonymised linkage to national datasets.

RESULTS: Of 26,869 patients, 1,791 (6.7%) had prior CABG and 25,078 (93.3%) had no prior CABG. Prior CABG patients were older (mean age 71 years vs 65 years), more comorbid and less likely to be revascularised than those without CABG (49.8% vs 73.0%). Compared to patients without CABG, at a mean follow-up of 2.1 years, patients with prior CABG had higher all-cause mortality (HR 2.03 (1.80–2.29)), and were more likely to have recurrent myocardial infarction (HR 2.70 (2.40–3.04)), rehospitalisation with congestive cardiac failure (HR 2.36 (2.10–2.66)) and stroke (HR 1.82 (1.41–2.34)).

CONCLUSION: In contemporary real-world practice, despite half of the patients with ACS and prior CABG receiving PCI, the outcomes remain poor compared with those without prior CABG.

In those with acute coronary syndromes (ACS) and previous coronary artery bypass grafts (CABG), invasive coronary angiography and percutaneous coronary intervention (PCI) are technically more challenging. There is an increase in procedural time, contrast use and radiation dose.[1] The culprit lesions may be in either a bypass graft or native vessels and the identification and treatment of culprit lesions may be more complex in the context of pre-existing multivessel disease.[1,2] Although current guidelines recommend an early invasive strategy in patients with acute coronary syndrome (ACS), these patients were excluded from the randomised clinical trials of invasive management.[3] They are an important sub-group to better understand—patients with prior CABG account for around one in 10 of those with ACS.[4,5] Patients with prior CABG have been reported to have higher morbidity and mortality up to one year.[1,2,4–6] There is currently a lack of randomised clinical trial data in outcomes of invasive management of ACS in patients with prior CABG. Previous trials and guidelines of management of ACS often excluded prior CABG patients.

The All NZ ACS Quality Improvement (ANZACS-QI) registry captures virtually all New Zealand patients hospitalised with ACS who undergo coronary angiography.[7] Through the registry and by data linkage with national administrative datasets we are able to track longer-term morbidity and mortality outcomes for all patients.[8] We utilised this contemporary registry cohort to describe the clinical characteristics, myocardial revascularisation and longer-term outcomes of ACS patients with prior CABG and compare these to those without prior CABG.

Methods

The methodology of the All NZ ACS Quality Improvement (ANZACS-QI) registries programme was previously described in detail.[7] Patients undergoing invasive coronary angiography are continuously captured in the CathPCI dataset and are available to the ANZACS-QI investigators. It contains patient demographics, admission ACS risk stratification information, cardiovascular risk factors, indication for invasive coronary angiog-

raphy and procedural details. These registries are subject to monthly auditing and consistently achieve complete data collection in over 95% of all those with suspected ACS undergoing coronary angiography. Using the National Health Index (NHI), a unique national alphanumeric patient identifier, the CathPCI data can be linked with the ACS Routine Information cohort arm of the ANZACS-QI to identify those with confirmed ACS undergoing invasive coronary angiography. Over 98% of New Zealanders have an NHI that identifies them in various national and regional health system databases.[7]

We included patients 20 years old and above with their first ACS presentation undergoing coronary angiography in public hospitals throughout New Zealand between 1 September 2014 and 31 October 2018. Those that did not survive to hospital discharge were excluded. The follow-up period for this analysis was limited to 31 December 2018.

Definitions

Patients with ACS were categorised into ST-segment elevation myocardial infarction (STEMI), non-ST segment elevation myocardial infarction (NSTEMI) and unstable angina (UA). For the purposes of this study, myocardial infarction (MI) was defined according to the Third Universal Definition of MI.[9]

The demographic data presented includes age, sex, ethnicity and body mass index (BMI). For patients who recorded more than one ethnic group, ethnicity was prioritised according to the New Zealand Ministry of Health protocol, in the following order: Indigenous Māori, Pacific people, Indian, other Asian and NZ European/other. The only exception was that those of Fijian Indian ethnicity were counted as Indian.[10] Several patient characteristics were evaluated including time since CABG (where applicable), prior MI, prior heart failure (HF), diabetes, hypertension, dyslipidaemia, current smoking and Global Registry of Acute Coronary Events (GRACE) score. We report the GRACE score as an estimate of in-hospital mortality post-ACS. It is categorised into low (<1%), medium (1 to <3%) or high (≥3%).[11]

Invasive coronary angiographic procedural and result data included vascular access site, coronary anatomic data and myocardial revascularisation modality (PCI or CABG). In this study, coronary artery stenoses ≥50% were considered significant.

Among those that underwent more than one myocardial revascularisation procedure, a distinction was made between those undergoing elective staged procedures and unplanned procedures. All unplanned revascularisation procedures were categorised as: unplanned repeat PCI during the index hospitalisation; unplanned repeat PCI due to suspected/confirmed ACS in the first subsequent hospitalisation; or unplanned revascularisation with CABG due to suspected/confirmed ACS in the first subsequent hospitalisation.

Guideline-directed medical therapy (GDMT) at discharge were assessed. This included the rate of aspirin, P2Y12 agent, statin, beta-blocker, and angiotensin-converting-enzyme (ACE) inhibitors or angiotensin receptor blocker (ARB). Anticoagulation prescription was incomplete as data input for dabigatran was added to the ANZACS-QI registry from June 2017 and rivaroxaban from September 2018.

Data linkage and outcomes

In-hospital outcomes were defined as those that occurred during the index hospitalisation and were obtained from the ANZACS-QI registry. These data included major bleeding, stroke, and unplanned myocardial revascularisation procedures (CABG and PCI). Major bleeding was defined using the Bleeding Academic Research Consortium definition for bleeding. We included all BARC Type 3 (3a, 3b and 3c) and Type 5 (5a and 5b).[12]

Following index hospitalisation discharge, mortality and rehospitalisation for MI, HF, stroke and major non-CABG related bleeding were identified by individual patient linkage to national data sets using their NHI as previously described.[7,8,13] An encrypted version of each NHI was used to anonymously link in-hospital ANZACS-QI patient records with the National Minimum Dataset.[7,8] We report the rates of these outcomes at 30 days, one year and mean follow-up. Hospitalisation for the outcomes of interest were defined as those in which it was listed as the primary or secondary discharge diagnosis using the International Statistical Classification of Diseases and Related Health Problems, 10th Revision, Australian Modification (ICD-10-AM). Unplanned repeat PCI is reported from the prospectively captured ANZACS-QI registry.

Statistical analysis

Categorical data were presented as frequency and column percentage. Continuous data were presented as mean ± standard deviation (SD) and median with inter-quartile range (IQR). Comparisons between groups were done using Chi-squared test and continuous data were done

using non-parametric Mann–Whitney U test as the data were not normally distributed. All p-values reported were two-tailed and p-value <0.05 was considered significant. Outcomes were visualised using Kaplan–Meier survival curves. Univariate Cox proportional hazards regression was used to estimate the hazard ratio and 95% confidence intervals for patients with CABG compared to those without CABG for each outcome. Unadjusted 30-day and 1-year mortality from discharge curves were calculated using Kaplan–Meier analyses. All statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC).

Results

Between 1 September 2014 and 31 October 2018, 26,869 patients were admitted to a public hospital in New Zealand with an ACS and underwent invasive coronary angiography. Of these, 1,791 (6.7%) had prior CABG and 25,078 (93.3%) had no prior CABG (Table 1). The mean follow-up was 2.1 years for both groups. The mean age was 65.4 (SD 11.8) years and males account for 69.3% of the cohort. Most patients were of NZ European/Other ethnicity (77.0%) and 11.1% were Māori. The most common presentation was NSTEMI (58.1%) followed by STEMI (26.3%) and UA (15.6%).

A detailed comparison of those with and without prior CABG is presented in Table 1. Patients with prior CABG were older (71.3±8.9 years vs 65.0±11.8 years, p<0.001) and more likely to be male (81.3% vs 68.4%, p<0.001) and of NZ European/Other ethnicity (82.9% vs 76.5%, p<0.001). Those with prior CABG had a higher prevalence of several comorbid conditions—prior MI (68.2% vs 17.6%, p<0.001), prior HF (68.2% vs. 17.6%, p<0.001) and diabetes (34.6% vs 22.3%, p<0.001). Conversely, a lower proportion of those with prior CABG were current smokers (12.1% vs 24.0%, p<0.001). Patients with prior CABG were more likely to present with UA (24.1% vs 15.0 %, p<0.001) and less likely to present with STEMI (12.3% vs 27.3%, p<0.001).

The details relating to coronary angiography and myocardial revascularisation during the index hospitalisation are provided in Table 2. While radial arterial access was most commonly used in those without prior CABG (90.4%), femoral arterial access was most commonly used in those with prior CABG (50.6%). Overall, 87.3% of patients had significant coronary artery stenoses and 71.5% received myocardial revascularisation. Nearly all patients (99.5%) with prior CABG had angiographically significant lesions. However, only 49.8% had myocardial revascularisation compared to 73.0% of those with no prior CABG. When PCI was undertaken in patients with prior CABG, the target vessel was most commonly a native vessel alone (59.9%). Graft vessel PCI was most frequently undertaken without concomitant native vessel PCI. Saphenous vein graft PCI accounted for almost all (92.4%) graft vessel PCI. The total numbers of lesions treated were similar among those with and without prior CABG (1.29±0.56 vs 1.36±0.66, respectively). Intracoronary imaging was rarely performed in either group—IVUS (1.0% vs 0.5%) and OCT (0.1% vs 0.5%).

At the time of discharge, guideline-directed medical therapy (GDMT) was high and similar for those with and without prior CABG: aspirin (93.9% vs 95.1%, p=0.031), statin (92.0% vs 93.3%, p=0.047), P2Y12 inhibitor (81.8% vs 78.4%, p<0.001). Clopidogrel use was more common in patients with prior CABG (41.9% vs 27.2%, p<0.001). There were incomplete data relating to anticoagulant use as this field was added to the ANZACS-QI registry after the commencement of the study period. Beta-blocker (83.9% vs 81.4%, p=0.011) and angiotensin-converting enzyme (ACE) inhibitor/angiotensin receptor blocker (72.4% vs 71.2%, p=0.262) prescription was high and similar between patients with and without prior CABG.

In-hospital outcomes and mortality and non-fatal outcomes at a mean follow-up of 2.1 years are documented in Table 3. During the index hospitalisation rates of major bleeding, stroke and unplanned PCI were low in both patients with and without prior CABG. The univariate Cox regression hazard ratios and 95% confidence intervals for CABG, using patients without CABG as the comparator, are as follows for each outcome: all-cause mortality (HR 2.03 (1.80–2.29)), recurrent MI (2.70 (2.40–3.04)), CHF hospitalisation (2.36 (2.10–2.66)), stroke hospitalisation (1.82 (1.41–2.34)) and major bleeding hospitalisation (0.87 (0.75–1.03)).

In the whole cohort, the 1-year mortality was 5.4%. At this time point, a higher mortality was observed in those with prior CABG (9.0% vs 5.1%, p<0.001) (Figure 1). Compared with those without prior CABG, patients with prior CABG were more likely to have recurrent myocardial infarction (18.3% vs 7.0%, p<0.001), heart failure (17.5% vs 7.6%, p<0.001), stroke (3.7% vs 2.0%, p<0.001) and unplanned repeat PCI (8.9% vs 4.1%, p<0.001). There were no significant differences in minor bleeding (8.9% vs 10.0%, p=0.138). Age-specific all-cause mortality and non-fatal outcomes are shown in Figures 2 and 3. A significantly higher

Table 1: Patient characteristics.

	Prior CABG n=1791	No prior CABG n=25078	P-value
Age, years (SD)	71.3 (8.9)	65.0 (11.8)	<0.001
<60 years	191 (10.7)	8,183 (32.6)	
60–74 years	901 (50.3)	1,1056 (44.1)	<0.001
≥75 years	699 (39.0)	5,839 (23.3)	
Male, n (%)	1,456 (81.3)	17,162 (68.4)	<0.001
Ethnicity, n (%)			
Māori	134 (7.5)	2,837 (11.3)	
Pacific people	64 (3.6)	1,222 (4.9)	
Indian	76 (4.2)	1,043 (4.2)	<0.001
Other Asian	33 (1.8)	782 (3.1)	
NZ European/Other	1,484 (82.9)	19,194 (76.5)	
Body mass index, kg/m^2 (SD)	28.8 (5.2)	29.1 (5.8)	0.365
Time since CABG, years (SD)	9.38 (4.74)	N/A	N/A
Prior MI, n (%)	1,221 (68.2)	4,418 (17.6)	<0.001
Prior heart failure, n (%)	154 (8.6)	807 (3.2)	<0.001
Diabetes, n (%)	619 (34.6)	5,599 (22.3)	<0.001
Current smoker, n (%)	217 (12.1)	6,008 (24.0)	<0.001
Estimated in-hospital mortality [GRACE score, n (%)]			
Low (<1%)	278 (15.5)	6,734 (26.9)	
Medium (1 to <3%)	769 (42.9)	10,051 (40.1)	<0.001
High (≥3%)	744 (41.5)	8,290 (33.1)	
Type of ACS, n (%)			
Unstable angina	431 (24.1)	3,772 (15.0)	
NSTEMI	1,139 (63.6)	14,468 (57.7)	<0.001
STEMI	221 (12.3)	6,838 (27.3)	

Values represent means unless stated.
Abbreviations: ACS – acute coronary syndrome, CABG – coronary artery bypass grafting, GRACE – Global Registry of Acute Coronary Events, MI – myocardial infarction, NSTEMI – non-ST-elevation myocardial infarction, SD – standard deviation, STEMI – ST-elevation myocardial infarction.

Table 2: Index hospitalisation angiographic and myocardial revascularisation data.

	Prior CABG n=1791	**No prior CABG n=25078**	**P-value**
Arterial access site, n (%)			
Femoral	906 (50.6)	2,373 (9.5)	<0.001
Radial	882 (49.3)	2,2683 (90.4)	
Angiographic findings, n (%)			
Normal	7 (0.4)	1,152 (4.6)	
Mild disease (<50%)	24 (1.3)	2,224 (8.9)	<0.001
≥50% stenosis in ≥1 vessel	1,760 (98.3)	2,1702 (86.5)	
Obstructive coronary stenosis (≥50%), n (%)			
Native vessel only	759 (43.1)	21587 (99.5)	
Graft vessel only	31 (1.8)	N/A	<0.001
Native and graft vessel	970 (55.1)	N/A	
Myocardial revascularisation	**892 (49.8)**	**18,312 (73.0)**	**<0.001**
CABG	34 (1.9)	3,555 (14.2)	
PCI	858 (47.9)	14,757 (58.8)	
IVUS, n (%)	18 (1.0)	348 (1.4)	0.177
OCT, n (%)	1 (0.1)	120 (0.5)	0.010
Mean total lesions treated (SD)	1.29 (0.56)	1.36 (0.66)	0.003
Target PCI vessel, n (%)			
Native only	514 (59.9)	14,757 (100)	
Graft only	304 (35.4)	N/A	<0.001
Native and graft	40 (4.7)	N/A	

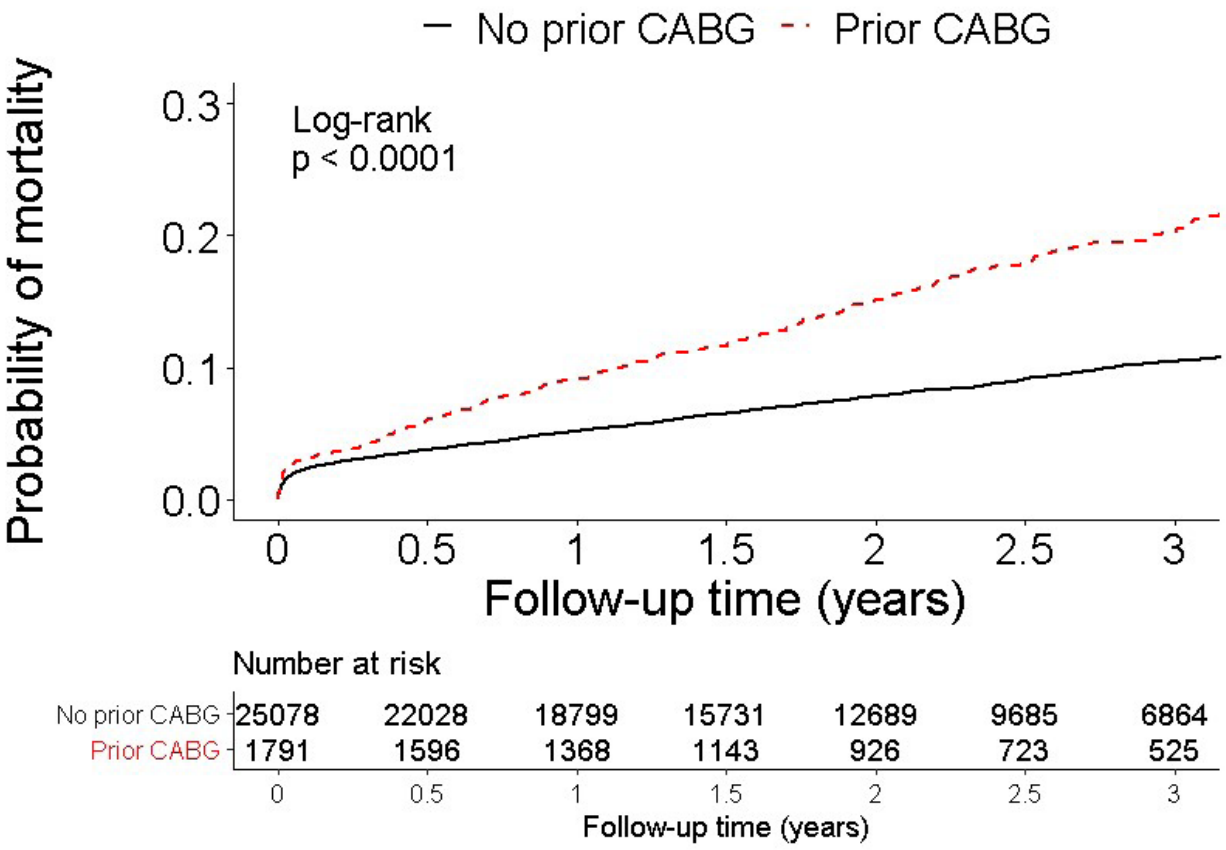
Abbreviations: CABG – coronary artery bypass grafting, IVUS – intravascular ultrasound, OCT – optical coherence tomography, PCI – percutaneous coronary intervention, SD – standard deviation.

Table 3: Outcomes.

	Prior CABG n=1791	No prior CABG n=25078	P-value
In-hospital outcomes, n (%)			
Major bleeding	14 (0.8)	153 (0.6)	0.372
Stroke	11 (0.6)	100 (0.4)	0.170
Unplanned repeat PCI	4 (0.2)	115 (0.5)	0.148
All-cause mortality, n (%)	309 (17.3)	2,099 (8.4)	<0.001
30-day	54 (3.0)	561 (2.2)	0.033
1-year	162 (9.0)	1,289 (5.1)	<0.001
Hospitalisations			
Recurrent myocardial infarction, n (%)	327 (18.3)	1,765 (7.0)	<0.001
Heart failure, n (%)	314 (17.5)	1,913 (7.6)	<0.001
Stroke, n (%)	67 (3.7)	513 (2.0)	<0.001
Major bleeding, n (%)	160 (8.9)	2,513 (10.0)	0.138
Unplanned repeat PCI, n (%)	159 (8.9)	1,040 (4.1)	<0.001

Unless stated, outcomes are reported at a mean follow-up of 2 years.
Abbreviations: PCI – percutaneous coronary intervention.

Figure 1: Kaplan–Meier curve for all-cause mortality.



Univariate Cox regression hazard ratio for CABG vs no CABG – 2.03 (95% CIs,1.80–2.29). There was a degree of violation of the proportional hazards assumption in the early phase of follow-up, however, this would not have a material impact on the findings, as evident in the clear separation of curves through the greater duration of follow-up.

Figure 2: Kaplan–Meier curve for all-cause mortality.

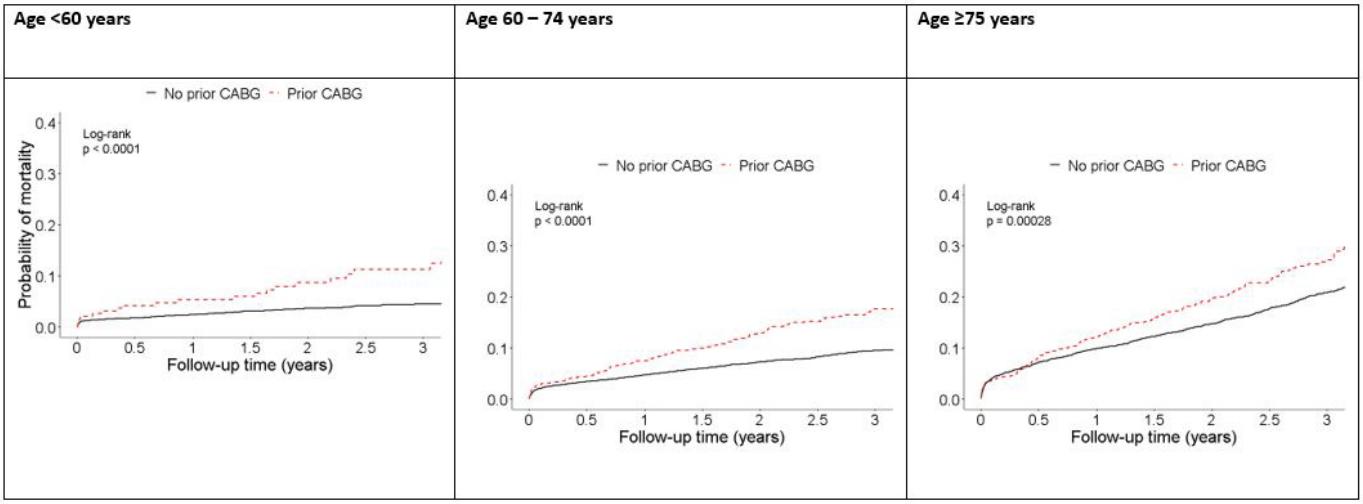
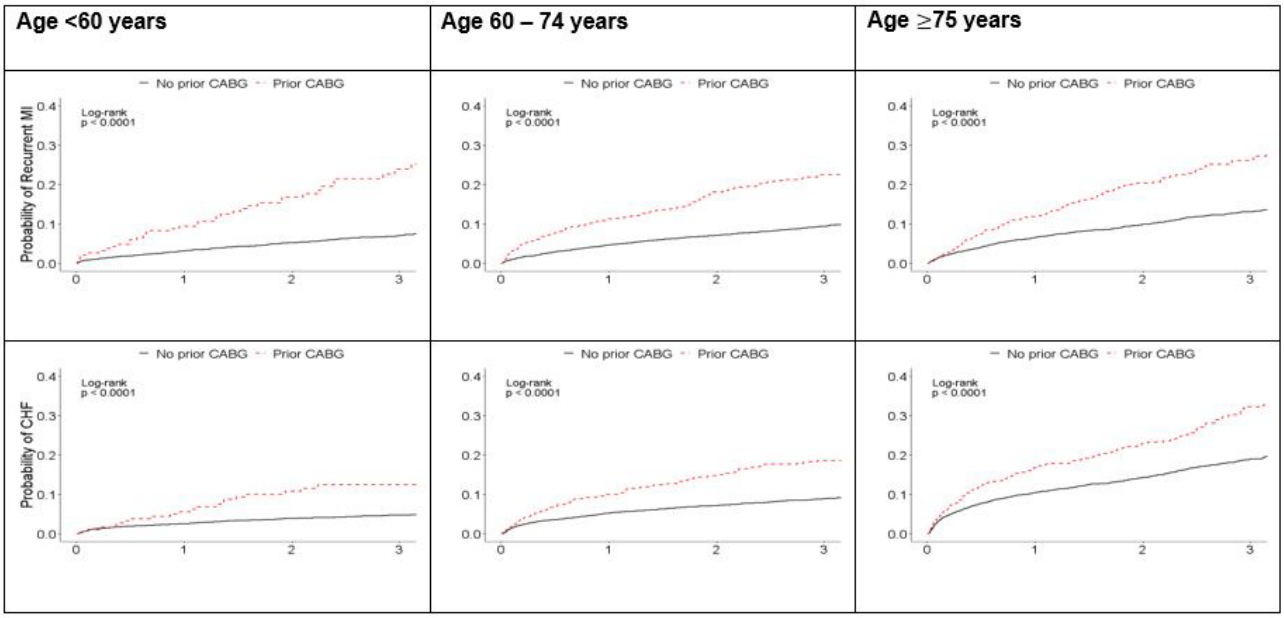


Figure 3: Kaplan–Meier age-specific curve for recurrent MI, heart failure, stroke, major bleeding.



all-cause mortality was observed in those with prior CABG under 75 years of age, but not among those over 75 years. Across all age groups, hospitalisation for MI and HF was higher in patients with prior CABG. In those below the age of 75 years, hospitalisation for stroke was higher in those with prior CABG. The rate of major bleeding was similar in both groups for those <60 years, but for those aged over 60 years the major bleeding rate was lower in those with prior CABG. Unplanned repeat PCI after the index hospitalisation was twofold higher in patients with prior CABG (8.9% vs 4.1%, p<0.001).

Discussion

This contemporary registry-based study included all patients with ACS who underwent coronary angiography throughout New Zealand over a four-year period and compared the characteristics, management and outcomes based on whether they had prior CABG. In this cohort, 6.7% had a prior CABG. The key findings were that patients with prior CABG were: 1) older, more comorbid and more likely to have femoral arterial access; 2) less likely to receive myocardial revascularisation and more likely to receive PCI than repeat CABG; 3) more likely to have worse outcomes with higher all-cause mortality, recurrent MI, HF hospitalisation and unplanned PCI at a mean follow-up of 2.1 years.

Baseline characteristics and coronary angiography access

As expected, our results found patients with prior CABG were older, more likely to be male, less likely to present with STEMI and more likely to have femoral arterial access. A sub-analysis of the Acute Catheterization and Urgent Intervention Triage Strategy (ACUITY) trial showed that prior CABG is associated with older age, more frequent cardiovascular comorbidities and poorer outcomes, with higher major adverse cardiac events (MACE).[1] Several studies have also demonstrated similar findings.[2,4–6,14] Prior CABG patients are more likely to present with UA and less likely to present with STEMI. A possible explanation is the formation of coronary arterial collaterals resulting in a smaller infarct size.[4,6] More than half of the patients with prior CABG in our cohort had transfemoral access. Transradial access in patients with prior CABG can be more challenging than transfemoral.[15] While it is reassuring that the major bleeding rate was similar for those with and without CABG, the Randomized Comparison of the Transradial and Transfemoral Approaches for Coronary Artery Bypass Graft Angiography and Intervention (RADIAL-CABG) trial found transradial diagnostic angiography was associated with greater contrast use, longer procedure and fluoroscopy time and greater radiation exposure when compared with transfemoral access.[16]

Myocardial revascularisation

In this study, half of patients with prior CABG vs three-quarters of patients without prior CABG had coronary revascularisation. Redo CABG was uncommon for patients with prior CABG. Most revascularisation for patients with prior CABG was therefore by PCI, which was most commonly performed on native vessels. Approximately 40% of these PCI cases were performed on graft vessels alone. Venous grafts have been found to occlude more commonly than arterial grafts and late saphenous venous graft patency following CABG is reported to be 55–60% at 10 years.[17–20] Although there is an evidence gap in the management of ACS in patients with prior CABG, PCI rates in this group has been consistently lower compared with patients without prior CABG.[2,4,14,21–22] Patients with prior CABG in our study were significantly less likely to be referred for surgical revascularisation, likely due to older age, more complex coronary anatomy and higher risk profile. Previous studies have demonstrated higher mortality risk with repeat CABG when compared with medical management and revascularisation with PCI.[1,4]

Short- and long-term outcomes

Our study found that over a mean follow-up of 2.1 years after an ACS, the rates of all-cause mortality, recurrent MI, HF and unplanned repeat PCI were approximately twofold higher in patients with prior CABG when compared with patients without prior CABG. The increased risk of all-cause mortality was most evident in those aged under 75 years. This has also been observed in other studies where a history of previous CABG was not associated with increased major adverse cardiovascular events (MACE) at one-year in patients aged 75 years and older presenting with ACS.[14] Another study demonstrated a higher burden of comorbidities in patients with prior CABG, but after multivariable adjustment previous CABG itself was not an independent predictor of increased one-year mortality.[2] One older clinical trial reported higher recurrent MI and unplanned revascularisation up to 1 year in those with prior CABG.[1] More contemporary registry studies have not reported morbidity beyond 30 days.[2,14] Our study found higher rates of recurrent MI and HF in patients with prior CABG across all age groups, reflecting a more comorbid and higher risk group. Lastly, patients with prior CABG with ACS are more likely to have multivessel disease and less likely to present with STEMI.[2,4,18] Identifying the culprit lesion in this group can be difficult and may result in repeat hospitalisations with suspected or confirmed ACS. This likely contributes to the higher rates of unplanned repeat PCI in patients with prior CABG found in this study. An intriguing finding is that in those over 60 years, the rate of major bleeding was lower in patients with prior CABG. Our study found the use of clopidogrel was more common in those with prior CABG, consistent with previous studies.[2] The use of lower intensity and short duration of anti-platelet therapy due to lower rates of PCI possibly accounts for the lower major bleeding rates in this subgroup.

Clinical implications

In this contemporary cohort of patients with ACS and prior CABG, half of those judged clinically appropriate for an invasive management strategy in routine practice were considered suitable for revascularisation. Patients and clinicians should be aware of the considerably higher rates of mortality, recurrent MI, HF and unplanned revascularisation in these patients. Approach to the treatment of these patients should be assessed on a case-by-case basis, but medication optimisation and cardiac rehab remain integral parts of the management.

Limitations

This study was subject to the known limitations of registry-based studies. For instance, there is likely to be a lack of uniformity in the management of patients by different clinicians, multiple centres, and over the duration of the study period. Symptom status was not available and may have been an important factor in determining patient management. We used ICD coding following hospital discharge to capture events during the follow-up period. As a result, important outcomes treated in the outpatient setting would not be included. The contribution of continued medication prescription and adherence could not be evaluated in this analysis. Lastly, we did not study patients with ACS managed with a conservative or non-invasive approach. While with any statistical analysis there can be a risk of Type II (false negative) errors, the very large sample size (and subsequent power) in this study makes it unlikely that the differences between any of the variables analysed are falsely negative. Similarly, while there is a risk of Type I (false positive) errors in any descriptive study, that risk is clearly minimised in a study of this size.

Conclusion

In patients with ACS, a history of prior CABG was associated with a high burden of comorbidities when compared with patients without prior CABG. All-cause mortality, recurrent MI and HF hospitalisations were higher in patients with prior CABG. Despite accounting for a growing proportion of ACS patients, deciding treatment modalities for this subgroup is still a complex and challenging process. Further trials are needed to study the management strategies to improve prognosis in this high-risk group.

COMPETING INTERESTS
Nil.

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Prevalence of frailty and frailty outcomes within the inpatient rehabilitation setting: use of routinely collected electronic health information

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ABSTRACT

AIMS: Frailty within the older adult rehabilitation population is relatively under-explored. We aimed to derive a frailty index (FI) from electronic routinely collected data to determine frailty prevalence, and to assess its ability to predict adverse outcomes in the rehabilitation setting.

METHODS: A FI was derived and retrospectively applied to electronically recorded health information of older adults admitted for inpatient rehabilitation. For analysis, subjects were allocated into frailty score (FS) groups (0–5). Primary outcome was a six-month hospitalistion rate, and other outcomes were: mortality, entrance into long-term care (LTC) at one year, length of stay (LOS), 30- and 90-day hospitalistions. Univariate and multivariable logistic regressions analysed associations between frailty and outcomes.

RESULTS: One hundred and sixty-two patient electronic notes were reviewed. Mean (SD) age was 86 (8.2) years, 147 (90.7%) were considered frail (FS>0.25). The most frail group (FS 5) had higher risk of six-month hospitalisations (OR=6.19; 95%CI=1.82, 21.13; p=0.004). A higher frailty score was associated with shorter LOS compared to lowest frailty scores (15.7 days vs 25.4 days; p=0.04). No relationship was found with shorter-term outcomes.

CONCLUSION: Prevalence of frailty is high in the rehabilitation setting. Association of frailty with shorter LOS and lack of association found with shorter-term outcomes warrant further study.

Frailty conceptualises a state of vulnerability due to multiple deficits across several physiological systems.[1] It has been shown to predict onset of disability, morbidity, entrance into long-term care (LTC) and mortality.[1–3] Identification of frailty can help guide treatments, prognosticate disease, and target resources toward modifiable parameters.[4]

There are several approaches to measuring frailty, but most screening tools fit into one, or a combination, of two broad categories: the phenotypic frailty model[3] and the cumulative deficit model.[5–7] The latter involves generating a frailty index (FI) by summing the deficits an individual has across a range of predetermined medical, functional and social parameters.[5–7] With increasing availability of electronic health data, the development of FIs to rapidly assess frailty is attractive.[8] Aotearoa New Zealand has been at the forefront of utilising routinely collected, electronically recorded data for FI development. These are attained using International Resident Assessment Instrument (interRAI)[9] assessments in those requiring government-funded community supports,[2,10–12] with these assessments being performed when patients are relatively well within the community. However, interRAI data are not currently readily accessible, with no access to developed electronic FIs within clinical settings in New Zealand. Additionally, interRAI assessments are *only* routinely performed in those requiring government-funded community supports, with these data not available for the many individuals requiring healthcare who have not had an interRAI assessment.

Frailty prevalence[13] and frailty-specific outcomes in older adults undergoing rehabilitation are not well described in New Zealand. Most rehabilitation units are led by geriatricians with a comprehensive geriatric assessment being integral to care provision, and therefore outcomes for these patients may be different to acutely hospitalised older adults. We wished to develop a tool to measure frailty and assess its predictive validity in the inpatient rehabilitation setting, using routinely electronically collected data.

Methods

This was a retrospective cohort study using routinely collected electronically recorded data

in hospitalised adults aged ≥65 years, admitted to a rehabilitation unit at Waitematā District Health Board (WDHB), Auckland, New Zealand, from 8 May 2018 to 31 October 2018. Ethical approval was obtained from the New Zealand Central Health and Disability Ethics Committee (reference 19/CEN/128).

The WDHB rehabilitation service serves older adults aged ≥65 years who have medical and functional needs, providing comprehensive assessment, treatment and goal-directed rehabilitation on individual needs. The service has developed an electronically documented, readily accessible, concise global geriatric assessment—completed as part of the admission process to the inpatient rehabilitation service at WDHB. This electronic document captures active medical problems, comorbidities, medications, living situation, education level, social situation, cognition and mood, drugs and alcohol, vision and hearing impairment, bladder and bowel function, nutrition and appetite, pre-morbid personal and instrumental activities of daily living, and assistance required. It also captures a current 4AT rapid clinical test for delirium score to rapidly screen for delirium and cognitive impairment.[14]

Where a patient had more than one electronic admission document completed, only their first admission within the six-month period was included, so each individual was only represented once.

An FI was constructed by extracting variables from the electronic document (see Appendices). The chosen variables were based on previously developed FIs,[2,5,15] and study group consensus and encompassed domains of locomotion, sensory, cognition, psychological, function/ADLs and comorbidities. The majority of variables were coded using a binary system where 0 represents absence of the deficit, and 1 represents presence of the deficit. Certain variables were divided into more categories to delineate "degree of deficit".

The FI numerator is a sum of points scored for each variable included in the FI, divided by the denominator.[39] Where information was unavailable these items were excluded from the total denominator, as per usual FI practice. The FI generated a value between 0 and 1, with higher values indicating more severe frailty.

Outcomes were measured one year after index admission by reviewing hospital electronic records and included six-month hospitalisations (primary outcome); one-year mortality; one-year entrance into long-term care (LTC); and 30-day and 90-day hospitalisation (secondary outcomes). Outcome data were sourced from electronic hospital data linked across the wider Auckland Region. The following items were also collected from hospital electronic records: age, gender, ethnicity, living alone/with others, marital status, residence on admission, primary diagnosis, length of stay (LOS) of index admission, discharge destination from index admission (home or LTC [rest home/private hospital/dementia unit]) and if this was a change from residence on admission.

To measure the association between FI and outcomes, participants were allocated into six groups, denoted frailty score (FS) 0,1,2,3,4,5 based on pre-defined FI ranges, consistent with FI application in community-dwelling older adults with health and functional needs, where FS 0=0.00–0.09, FS 1=0.10–0.19, FS 2=0.20–0.29, FS 3=0.30–0.39, FS 4=0.40–0.49, FS 5≥0.50.[2] Due to the small numbers of participants with lower FI levels in our study, the first three frailty groups (FS 0, 1 and 2) were combined. Analysis of variance (ANOVA) or Chi-squared tests were used to determine the association between pre-specified FI categories (FS 0–2, 3, 4, 5) and baseline characteristics. The univariate and multivariable association between FI categories (independent variable) and binary outcomes (dependent variables) were explored using logistic regression models with odds ratios (ORs) and 95% confidence intervals (95%CIs). A two-sided $p<0.05$ was considered statistically significant. All analyses were performed with SAS 9.4 software (SAS Institute Inc., Cary, USA).

Results

A total of 536 electronic admission documents were reviewed in the six-month study period, 369 were excluded as they were completed by non-rehabilitation services (e.g., orthogeriatrics). Five more were excluded as duplicates of the same individuals. In total, 162 participants were included in the analysis (see Figure 1).

Subjects were aged between 66 and 103 years, with a mean (SD) age of 86 (8) years. The median age was 88 years (interquartile range [IQR]=80–92). Two thirds (108) were female. The majority identified as NZ European (143; 88.3%) with 3 (1.9%) being Māori, and the cohort were largely either widowed or married (70, 43.2% and 66, 40.7% respectively). Increasing age was associated with increasing FS (Table 1).

The mean FI of the cohort was 0.42 (SD 0.12), ranging from 0.07 to 0.73, and was approximately normally distributed, as shown in Figure 2. There were 28 (17.3%) participants in FS groups 0–2, 39 (24.1%)

in FS 3, 50 (30.9%) in FS 4, and 45 (27.7%) in FS 5, and 147 subjects were considered frail FI>0.25.[16]

The group with the highest frailty (FS 5) had the highest rate of being discharged to an increased level of care at 35.6% (n=16), compared with the least frail at 10.7% (n=3). The group with lowest frailty (FS 0–2) had the highest mean LOS at 25.4 days, and the group with the highest frailty (FS 5) had the lowest mean LOS of 15.7 days (p=0.04). Analysis of frailty category LOS by whether inpatients were admitted from LTC or home or whether they were discharged to a higher level of care (i.e., admitted from home, discharged to LTC) found that LOS was significantly shorter for the frailest being discharged to a higher level of care (Table 2).

At six months, a total of 80 (49.4%) participants had at least one hospitalisation. The six-month hospitalisation proportion was significantly different between FI groups; 66.7% in the most frail group compared to 35.7% in the least frail group (FS 0–2). Participants in the most fail group had significantly higher risk of hospitalisation in both unadjusted (OR=3.60; 95%CI=1.34, 9.70; p=0.01) and adjusted (OR=6.19; 95%CI=1.82, 21.13; p=0.004) logistic regressions (Table 3).

The overall one-year mortality proportion was 23% (n=37). One-year mortality in the composite group (FS 0–2) was 3.5% (n=1), significantly lower than FS 5 40.0% (n=18) (p=0.01; Table 3). In the adjusted logistic regression, similar results were observed (OR=14.69; 95%CI=1.58, 136.43; p=0.02).

At baseline 10 (6.2%) resided in LTC, eight of whom were in the most frail group (FS 5), and two participants in FS 3. These participants were excluded in the LTC admission analysis. By the end of the follow up period 51 (33.6%) of the remaining cohort had newly entered LTC. By one year 19 (54.1%) of the most frail group (FS 5) had newly entered LTC, compared to 4 (14.3%) of the composite group (FS 0–2) (p=0.004; Table 3). In the adjusted logistic regression similar results were observed in most frail group (OR=5.12; 95%CI=1.28, 20.43; p=0.02).

There were no significant differences in hospital admission proportion at 30 or 90 days between FI groups (Table 3).

Discussion

This study reports the use of an FI to determine the prevalence of frailty in the rehabilitation setting and adds to the relatively limited New Zealand literature within this population. It is important that frailty tools used in different settings are shown to be fit for purpose and this FI derived from routinely collected electronic data demonstrated predictive validity in terms of six-month hospitalisation rates, one-year mortality and one-year LTC entry. Predictive validity is an essential component to frailty operationalisation, particularly as there is no gold-standard measurement.[15,17] The finding of increased frailty associated with shorter LOS is an unexpected finding and warrants further investigation. As the data sourced are electronically recorded, the potential exists to automatically generate a FS visible, and of use to, admitting clinicians without additional work—a point of difference to other clinically utilised tools.

Our cohort had high average baseline frailty (mean FI 0.42) and very high prevalence of frailty at 90.7% (utilising cut-off of 0.25).[16] Distribution was normal, which is to be expected in populations with greater health issues.[17] A study from Singapore[18] reported prevalence rate of 87% by FI of inpatients in a geriatrics department (although unlike our study, also including acute inpatients), while a study from a single rehabilitation facility in Switzerland 10 reported 44% were frail by FI (median 0.37). In contrast we can utilise mean FI score to compare to other studies, with the mean frailty in our cohort similar to that in two Australian studies[19,20] (mean FI 0.42 and 0.46) but higher than a Finnish study (0.34)[21] in similar rehabilitation settings. By comparing in this way, it appears older adults undergoing rehabilitation in our cohort sit at the higher end of frailty prevalence compared to international studies. Frailty prevalence in our study was higher than that reported by Richard et al.,[13] as far as we are aware the only other publication reporting frailty in the New Zealand rehabilitation setting. In Richard et al.'s point prevalence study of frailty in Christchurch hospital,[13] overall ~49% were considered frail by the Reported Edmonton Frailty Scale, increasing to 74% within the rehabilitation wards. Māori were significantly more likely to be frail.

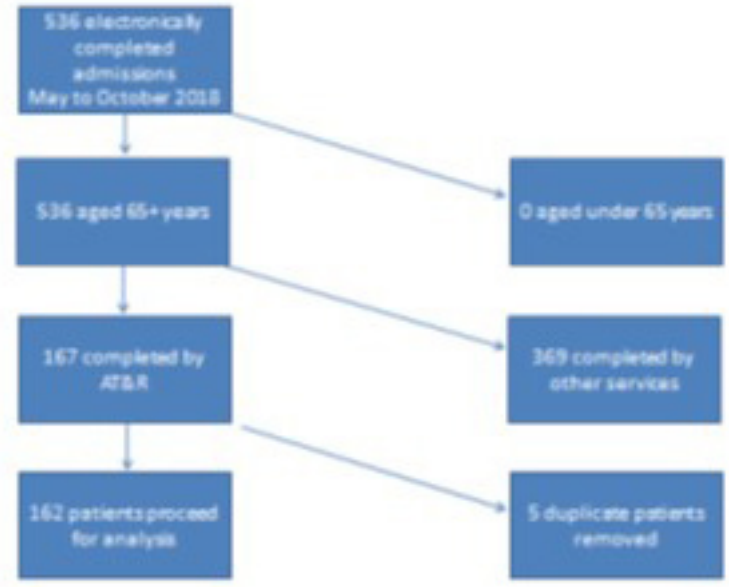
Unsurprisingly, our subjects were found to be frailer than other New Zealand studies assessing frailty by FI in community settings.[2,10] The mean frailty by FI in a study of community dwelling older adults in Canterbury assessed for government-funded supports was 0.27, and 0.16 in a population of Auckland retirement village residents. While there are a small number of other New Zealand frailty studies utilising validated tools in specific sub-specialty populations, compared to our international colleagues, we in New Zealand are

Table 1: Baseline characteristics by FI categories.

Variable	No. of patients (n=162)	FI categories				P value
		0–0.29 (n=28)	0.30–0.39 (n=39)	0.40–0.49 (n=50)	≥0.5 (n=45)	
Age (y), mean (SD)	162	82.0 (8.3)	84.9 (8.1)	86.5 (8.1)	89.2 (7.1)	0.002
Age (y), n (%)						**0.002**
65–74	17	7 (25.0)	6 (15.4)	4 (8.0)	0 (0.0)	
75–84	49	11 (39.3)	9 (23.1)	17 (34.0)	12 (26.7)	
85–94	72	9 (32.1)	21 (53.8)	21 (42.0)	21 (46.7)	
≥95	24	1 (3.6)	3 (7.7)	8 (16.0)	12 (26.7)	
Gender, n (%)						**0.52**
Female	108	21 (75.0)	24 (61.5)	31 (62.0)	32 (71.1)	
Male	54	7 (25.0)	15 (38.5)	19 (38.0)	13 (28.9)	
Ethnicity, n (%)						**0.21**
NZ European	106	17 (60.7)	26 (66.7)	37 (74.0)	26 (57.8)	
Other European/ not further defined	37	5 (17.9)	10 (25.6)	8 (16.0)	14 (31.1)	
Māori/Pasifika	7	4 (14.3)	0 (0.0)	1 (2.0)	2 (4.4)	
Other	12	2 (7.1)	3 (7.7)	4 (8.0)	3 (6.7)	
Living situation, n (%)						**0.39**
Alone	90	19 (67.9)	19 (48.7)	29 (58.0)	23 (51.1)	
With others	72	9 (32.1)	20 (51.3)	21 (42.0)	22 (48.9)	
Marital status, n (%)						
Married/Partnered	66	16 (57.1)	18 (46.2)	19 (38.0)	13 (28.9)	
Single	13	1 (3.6)	7 (17.9)	3 (6.0)	2 (4.4)	
Divorced/Widowed/ Unknown	83	11 (39.3)	14 (35.9)	28 (56.0)	30 (66.7)	
LOS (day), mean (SD)		25.4 (22.3)	25.3 (20.6)	25.6 (22.1)	15.7 (11.3)	0.04
LOS (day), n (%)						**0.22**
1–8	40	6 (21.4)	10 (25.6)	11 (22.0)	13 (28.9)	
9–17	39	5 (17.9)	6 (15.4)	11 (22.0)	17 (37.8)	
18–30	42	8 (28.6)	11 (28.2)	13 (26.0)	10 (22.2)	
≥30	41	9 (32.1)	12 (30.8)	15 (30.0)	5 (11.1)	
Higher LOC at discharge, n (%)						**0.08**
No	125	25 (89.3)	31 (79.5)	40 (80.0)	29 (64.4)	
Yes	37	3 (10.7)	8 (20.5)	10 (20.0)	16 (35.6)	

Abbreviations: FI=Frailty Index; SD=Standard Deviation; LOS=Length of Stay; LOC=Level of Care.

Figure 1: Flow chart of the eligible participants.



Abbreviation: AT&R=Assessment Treatment and Rehabilitation Service.

Figure 2: Distribution of frailty index.

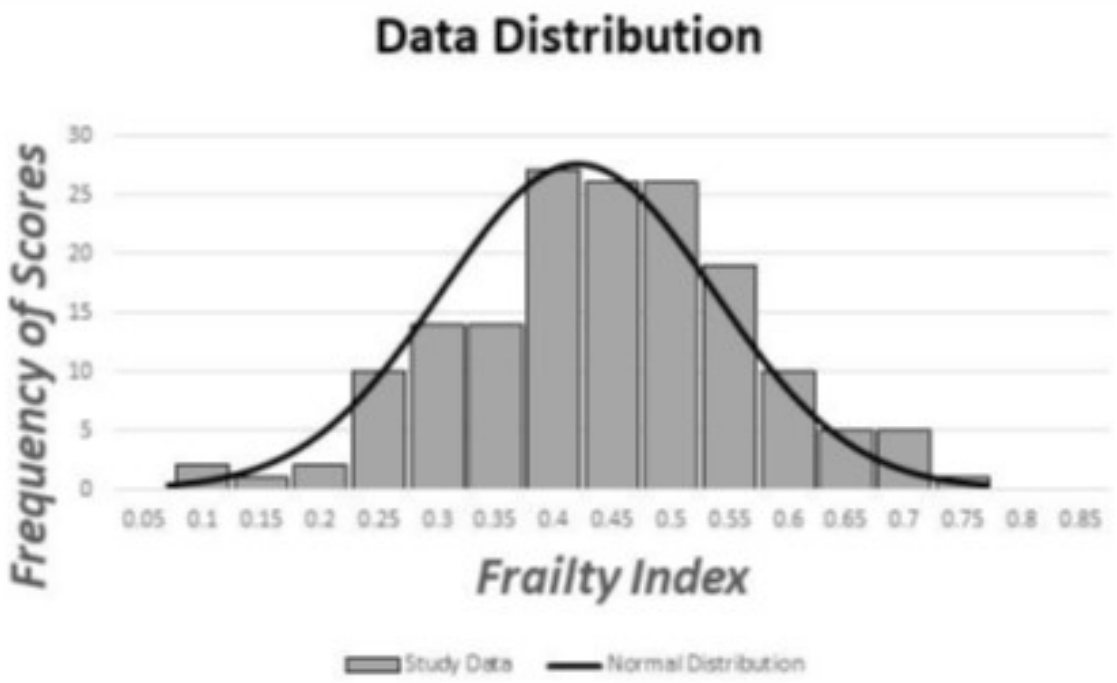


Table 2: Analysis of frailty group length of stay by residence on admission and higher level of care at discharge.

Variable	No. of patients	Length of Stay (days) by FI categories				P value
		0–0.29	0.30–0.39	0.40–0.49	≥0.5	
All patients						**0.04**
N	162	28	39	50	45	
Mean (SD)		25.4 (22.3)	25.3 (20.6)	25.6 (22.1)	15.7 (11.3)	
Median (IQR)		21.5 (10.5, 33.0)	24 (8.0, 33.0)	20.0 (11.0, 35.0)	15.0 (8.0, 20.0)	
Subgroup						
Higher LOC at discharge: YES						**0.02**
N	37	3	8	10	16	
Mean (SD)		54.3 (50.8)	39.6 (21.6)	29.8 (22.9)	17.6 (9.3)	
Median (IQR)		35.0 (16.0, 112.0)	31.5 (25.5, 52.5)	18.5 (13.0, 46.0)	16.0 (12.0, 22.0)	
Higher LOC at discharge: NO						**0.16**
N	125	25	31	40	29	
Mean (SD)		21.9 (15.1)	21.6 (19.0)	24.6 (20.0)	14.7 (12.4)	
Median (IQR)		19.0 (10.0, 31.0)	18.0 (5.0, 30.0)	21.0 (9.5, 34.0)	11.0 (4.0, 20.0)	
Residence in LTC at admission						**NA**
N	10	0	2	0	8	
Mean (SD)		NA	26.0 (7.1)	NA	12.3 (11.7)	
Median (IQR)		NA	26.0 (NA)	NA	7.5 (3.0, 20.5)	
Residence in community at admission						**0.13**
N	152	28	37	50	37	
Mean (SD)		25.4 (22.3)	25.2 (21.2)	25.6 (22.1)	16.5 (11.3)	
Median (IQR)		21.5 (10.5, 33.0)	24.0 (8.0, 33.0)	20.0 (11.0, 35.0)	15.0 (9.0, 20.0)	

Abbreviations: IQR=Interquartile range; LTC=Long Term Care; LOC=Level of Care; NA=not applicable.

Table 3: Unadjusted and adjusted associations between FI categories and outcomes.

Outcome	Total patients	Patients with event (%)	Odds ratio (95%CI), p	Adjusted odds ratio[a] (95%CI), p
Primary outcome				
Six-month hospitalisation	162	80 (49.4)		
FI 0–0.29	28	10 (35.7)	1.00 (ref)	1.00 (ref)
FI 0.30–0.39	39	18 (46.2)	1.54 (0.57, 4.18), 0.39	2.14 (0.68, 6.81), 0.20
FI 0.40–0.49	50	22 (44.0)	1.41 (0.55, 3.67), 0.48	1.59 (0.53, 4.77), 0.41
FI ≥0.5	45	30 (66.7)	3.60 (1.34, 9.70), 0.01	6.19 (1.82, 21.13), 0.004
Type III test			0.05	0.02
Secondary outcomes				
One-year mortality	162	37 (22.8)		
FI 0–0.29	28	1 (3.6)	1.00 (ref)	1.00 (ref)
FI 0.30–0.39	39	7 (17.9)	5.90 (0.68, 51.0), 0.11	5.00 (0.51, 48.67), 0.17
FI 0.40–0.49	50	11 (22.0)	7.61 (0.93, 62.4), 0.06	6.00 (0.67, 53.9), 0.11
FI ≥0.5	45	18 (40.0)	18.00 (2.24, 144.31), 0.007	14.69 (1.58, 136.43), 0.02
Type III test			0.01	0.06
One-year LTC entry[b]	152	51 (33.6)		
FI 0–0.29	28	4 (14.3)	1.00 (ref)	1.00 (ref)
FI 0.30–0.39	37	10 (27.0)	2.22 (0.62, 8.02), 0.22	1.85 (0.45, 7.53), 0.39
FI 0.40–0.49	50	18 (36.0)	3.38 (1.01, 11.27), 0.048	3.34 (0.90, 12.34), 0.07
FI ≥0.5	37	19 (51.4)	6.33 (1.83, 21.87), 0.004	5.12 (1.28, 20.48), 0.02
Type III test			0.02	0.09
Other outcomes				
30-day hospitalisation	162	24 (14.8)		
FI 0–0.29	28	4 (14.3)	1.00 (ref)	1.00 (ref)
FI 0.30–0.39	39	6 (15.4)	1.09 (0.28, 4.29), 0.90	1.48 (0.31, 7.05), 0.62
FI 0.40–0.49	50	5 (10.0)	0.67 (0.16, 2.72), 0.57	0.78 (0.16, 3.72), 0.75
FI ≥0.5	45	9 (20.0)	1.50 (0.42, 5.43), 0.54	1.90 (0.41, 8.72), 0.41
Type III test			0.61	0.56

Table 3 (continued): Unadjusted and adjusted associations between FI categories and outcomes.

Outcome	Total patients	Patients with event (%)	Odds ratio (95%CI), p	Adjusted odds ratio[a] (95%CI), p
Other outcomes				
90-day hospitalisation	162	57 (35.2)		
FI 0–0.29	28	8 (28.6)	1.00 (ref)	1.00 (ref)
FI 0.30–0.39	39	10 (25.6)	0.86 (0.29, 2.57), 0.79	1.15 (0.34, 3.90),0.82
FI 0.40–0.49	50	17 (34.0)	1.29 (0.47, 3.53), 0.62	1.57 (0.51, 4.84), 0.44
FI ≥0.5	45	22 (48.9)	2.39 (0.87, 6.55), 0.09	3.22 (0.97, 10.68), 0.06
Type III test			0.13	0.16

Note: [a]Adjusted for age, gender, ethnicity, living situation, marital status, length of stay and higher level of care at discharge; [b]10 patients were excluded as they resided in LTC at baseline. As higher LOC at discharge was partly duplicated with entry to LTC at discharge, so was not adjusted in one-year LTC entry analysis.
Abbreviations: LTC=Long Term Care; LOC=Level of Care.

lacking in reports of frailty. This dearth of information, particularly as it affects our Indigenous population, has been noted.[22] Given healthcare costs are approximately five times higher for the frail compared to the non-frail,[23] it is essential that feasible strategies to identify those living with frailty are used and effective and appropriate interventions are delivered. From an overall community perspective, one way of potentially achieving this would be by improving accessibility to interRAI data.

Consistent with some, but not all similar reports, our study found association with discharge destination,[19,20,24] and one year mortality.[24] We found no significant association with short-term hospitalisations at 30 or 90 days. While the number of outcomes was small for 30-day hospitalisations, for 90 days it was comparable to other outcomes that showed significant differences. Other studies have assessed frailty with the need to be readmitted to acute care or the emergency department *during* their current rehabilitation admission.[19–24] This seems to infer medical instability and we did not study this as an outcome. There is little research in terms of outcomes for the rehabilitation population between frailty groups in the immediate post-discharge period; this is an area that requires further scholarship in larger studies. For example, it is possible that no association is found between frailty and short-term re-hospitalisation rates because older rehabilitation patients, usually cared for by geriatricians within a multidisciplinary team, receive a comprehensive geriatric assessment. Lin et al.[26] have recently published results showing frail older people are less likely to be readmitted if they received a comprehensive geriatrics assessment during admission. More study is required here, but perhaps geriatrician input prior to discharge eliminates some of the risk of readmissions for those living with a greater degree of frailty.

Our results differ significantly to the literature when assessing frailty association with LOS. Where other studies in both the acute setting[27,28] and (the smaller number) in the rehabilitation setting[19,21] show association of frailty with longer LOS, our results report the opposite with higher frailty associated with shorter LOS; a surprising result. We had expected the variance here to be explained by the higher number of participants already residing in LTC in the highest frailty group FS 5 (eight participants, out of 45) compared to FS 0–2, which had no participants already residing in LTC, and with high rates of FS 5 discharged to LTC overall, compared with only 7.1% of FS 0–2. Numbers were too small in these groups to show any significance; however, further subgroup analysis of LOS data found that the most frail, who were admitted from the community but discharged to LTC, had significantly

shorter LOS, and that LOS decreased as frailty increased in this group. This may be a reflection of the frailest reaching their rehabilitation potential plateau or limits earlier than the less frail, with the decision to discharge made earlier, compared to those continuing to make inpatient gains. However, of potential concern, it may highlight an issue that the most frail and vulnerable population receive less physiotherapy or other allied health involvement due to a perceived lack of benefit. It may also reflect different practices between New Zealand and internationally with regards to the least and most frail patients. This requires further unravelling to ensure that best care is being delivered to all, and illustrates the value of interrogating and reporting frailty and outcomes in different populations and care settings.

Limitations

This study included a relatively small number of subjects from a single centre, and other outcomes may be significant if a larger cohort was included. Despite this, significant important findings were found.

Frailty in the older adult rehabilitation setting is relatively under-explored in comparison to acute hospitalised patients or community dwellers, yet it is an important group to be considered. The value of utilising electronic health data for FI development is the potential for automating FI results into clinical notes. This has potential to increase clinician awareness of this syndrome, including to primary care if FI is incorporated into discharge summaries. It brings frailty to the forefront, allowing focus on frailty-centred care and appropriate distribution of resources with evidence that geriatricians would use such information to inform clinical judgement and individualise care.[29]

Future focuses of study are to interrogate why the more frail have shorter LOS in this population by comparing components of frailty management, such as amount of physiotherapy received, between those more and less frail, and also to further investigate frailty level of short-term outcomes/readmission at time of discharge.

COMPETING INTERESTS
Nil.

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Appendices

Appendix 1: Frailty index variables with associated deficit point score.

Item		Points	Running total (denominator)
Active/acute medical problem	Absent	0	1
	Present	1	
Medications	0	0	4
	1–4	1	
	5–8	2	
	9+	3	
Medication management	Independent	0	5
	Needs oversight	1	
Residence	Home	0	7
	Rest home	1	
	Private hospital	2	
Community support	Nil	0	8
	Home help (HH)	0.5	
	Personal Cares (+/- HH)	1	
Finances	Independent	0	9
	Needs assistance	1	
Fall within last one year	No	0	10
	Yes	1	
Mood/stressors/on antidepressant or anxiolytic	None	0	11
	Low mood/on meds	1	
Cognition	Normal/no concern	0	12
	Delirium/4AT score suggests impairment	1	
Vision	Normal/no concern	0	13
	Impairment	1	
Hearing	Normal/no concern	0	14
	Impairment	1	

Appendix 1 (continued): Frailty index variables with associated deficit point score.

Item		Points	Running total (denominator)
Bladder function	Normal/no concern	0	15
	Incontinent/catheter in situ	1	
Bowel function	Normal/no concern	0	16
	Incontinent	1	
Hydration/ nutrition/recent weight loss	Normal/no concern	0	17
	Recent weight loss	1	
Appetite	Good	0	18
	Reduced but adequate	0.5	
	Poor	1	
Skin	Normal/no concern	0	19
	Pressure injury	1	
Mobility aids	Independent/no aids	0	20
	Assistive device	0.5	
	Needs assistance to mobilise (+/- assistive device)	0.75	
	Bed bound	1	
Washing/ dressing	Independent	0	21
	Needs assistance	1	
Eating/drinking	Independent	0	22
	Needs assistance	1	
Meal prep/ housework/ shopping	Independent	0	23
	Needs assistance	1	
Driving	Driving	0	24
	Stopped driving	1	

Appendix 1 (continued): Frailty index variables with associated deficit point score.

Item		Points	Running total (denominator)
Comorbidities (1 point for each, up to a maximum of 15)	Nil	0	39
	Cerebrovascular event	1	
	Renal failure	1	
	Thyroid disease	1	
	Heart failure (left, right or biventricular)	1	
	Coronary artery disease	1	
	Hypertension	1	
	Atrial fibrillation	1	
	Peripheral vascular disease	1	
	Alzheimer's dementia	1	
	Other dementia	1	
	Head trauma	1	
	Hemiplegia/hemiparesis	1	
	Multiple sclerosis	1	
	Parkinsonism	1	
	Arthritis	1	
	Hip fracture	1	
	Other fractures	1	
	Osteoporosis	1	
	Cataract	1	
	Glaucoma	1	
	Any psychiatric diagnosis	1	
	Human immunodeficiency virus infection	1	
	Pneumonia	1	
	Tuberculosis	1	
	Urinary tract infection	1	
	Cancer	1	
	Diabetes mellitus	1	
	Chronic obstructive pulmonary disease/ emphysema/asthma	1	

Identification of clinically relevant cohorts of people with heart failure from electronic health data in Aotearoa: potential, pitfalls and a plan

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ABSTRACT

Heart failure (HF) is associated with high morbidity and mortality and contributes to substantial burden of disease, significant inequities and high healthcare cost globally as well as in Aotearoa. Management of chronic HF is driven by HF phenotype, defined by left ventricular ejection fraction (EF), as only those with reduced ejection fraction (HFrEF) have been shown to experience reduced mortality and morbidity with long-term pharmacotherapy. To ensure appropriate and equitable implementation of HF management we need to be able to identify clinically relevant cohorts of patients with HF, in particular, those with HFrEF. The ideal HF registry would incorporate and link HF diagnoses and phenotype from primary and secondary care with echocardiography and pharmacotherapy data. In this article we consider several options for identifying such cohorts from electronic health data in Aotearoa, as well as the potential and pitfalls of these options. Given the urgent need to identify people with HF according to EF phenotype, the options for identifying them from electronic health data, and the opportunities presented by health system reform, including a focus on digital solutions, we recommend the following four actions, with oversight from a national HF working group: 1) Establish a HF registry based on random and representative sampling of HF admissions; 2) investigate obtaining HF diagnosis and EF-phenotype from primary care-coded data; 3) amalgamate national echocardiography data; and 4) investigate options to enable the systematic collection of HF diagnosis and EF-phenotype from outpatient attendances. Future work will need to consider reliability and concordance of data across sources. The case for urgent action in Aotearoa is compounded by the stark inequities in the burden of HF, the likely contribution of health service factors to these inequities and the legislative requirement under the Pae Ora (Healthy Futures) Act 2022 that "*the health sector should be equitable, which includes ensuring Māori and other population groups – (i) have access to services in proportion to their health needs; and (ii) receive equitable levels of service; and (iii) achieve equitable health outcomes*".

Heart failure (HF) is a complex clinical syndrome caused by underlying abnormalities of cardiac structure and/or function that reduces the ability of the heart to fill with blood and/or eject adequate blood volume to meet the needs of the body.[1] Despite the availability of effective treatment, HF is associated with poor quality of life and high morbidity and mortality.[2] Globally, the number of people with heart failure almost doubled between 1990 and 2017 (from 33.5 to 64.3 million) with significant inequities by geography and socio-economic status.[3]

In Aotearoa, approximately 1.6% of adults were estimated to have HF in the 2020/2021 New Zealand Health Survey.[4] A recent trends analysis found that while the overall incidence of HF declined between 2006 and 2013, this reduction plateaued between 2013 and 2018 due to increasing rates of HF in younger age groups despite an ongoing decline in the elderly.[5] HF is one of the major causes of hospitalisation in this country, leading to 11,428 publicly funded hospital discharges with a mean stay of 12.9 days during the 2018/2019 financial year,[6] with overall costs to the New Zealand health system estimated at 1.5–2%[7] (approximately $360–$480 million dollars of Vote Health in 2022/2023[8]). All-cause mortality after first HF hospitalisation in New Zealand is high: 12.0%, 30.6% and 63.3% at 30 days, 1 year and 5 years, respectively.[9] Compared with non-Māori, Māori are twice as likely to die from HF (rate ratio (RR) 2.36, 95% CI 1.76–3.17), and four times as likely to be hospitalised for HF (RR 4.01, 95% CI 3.83–4.21).[10] Similarly, compared with the total New Zealand population, Pacific people are over twice as likely to be hospitalised for HF (standardised discharge ratio 2.62, 95% CI 2.44–2.81).[11]

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Assessment of cardiac function, including measurement of left ventricular ejection fraction (LVEF), is an important step in the investigation of patients with HF and the most accessible modality to undertake this assessment is echocardiography.[1] LVEF measurement is of particular importance because it enables classification of HF into categories defined by the EF phenotype: HF with reduced LVEF (HFrEF), HF with mildly reduced LVEF (HFmrEF) and HF with preserved LVEF (HFpEF).[12,13] Data from the Framingham Heart Study indicates that the proportion of HF patients with HFrEF, HFmrEF and HFpEF was 31%, 13% and 56%, respectively, in 2005–2014, and 44%, 15% and 41%, respectively, in 1985–1994.[14] It is unclear to what extent the proportion of HF patients with each type and the change in proportion over time are likely to be relevant to HF patients in Aotearoa. While all patients with HF have higher mortality than people without HF, patients with HFpEF have a lower risk of death than those with HFrEF (adj HR 0.68 (95% CI 0.64 to 0.71) for 1 year mortality).[15]

Importantly, recommended management of chronic HF also varies by EF phenotype.[1] Disease modifying therapies for those patients with HFrEF now includes Class I evidence-based recommendations for multiple classes of pharmacotherapy, including angiotensin-converting enzyme (ACE) inhibitors/angiotensin receptor blockers (ARBs) or angiotensin receptor neprilysin inhibitors (ARNI; sacubitril/valsartan), β-blockers, mineralocorticoid receptor antagonists, SGLT-2 inhibitors and, where appropriate, HF device-based therapies including an implantable cardioverter defibrillator and/or cardiac resynchronization therapy. Such combined therapeutic approaches result in substantial improvements in morbidity and mortality for patients with HFrEF, but not for patients with HFpEF.[1,12] The current evidence-base is insufficient to make strong recommendations about specific therapies for HFmrEF.[12] In order to ensure such evidence-based interventions are being appropriately and equitably implemented, it is therefore essential to know not just whether or not patients have HF, but to define the HF EF phenotype.

A systematic review of evidence-based prescribing for patients with HFrEF found that the "treatment gap" (the proportion of patients who had an indication and no contraindication or limiting side effect but were not prescribed the recommended treatments) was up to 13.1% for ACE inhibitors/ARBS, 3.9% for β-blockers and 16.8% for mineralocorticoid receptor antagonists, and gaps were even greater when receipt of guideline-recommended target doses were considered and among the elderly, women and people with comorbidities.[16] Further, the review found that prescribing these drugs according to contemporary guidelines was associated with lower mortality risk.[16] Research from New Zealand indicates that among a cohort of patients presenting with acute coronary syndrome and who underwent coronary angiography in 2015, and who also had HFrEF, at one-year post discharge 76% and 85% were receiving ACE inhibitors/ARBS and β-blockers, respectively, and only 34% and 35% respectively were receiving >/=50% target doses of these medications.[17] While limited information is available regarding HFrEF treatment gaps for Māori and Pacific peoples, treatment gaps are more likely for Māori and Pacific people than for others living in Aotearoa given the evidence to date regarding CVD treatment gaps.[18] Improved systems are clearly needed to identify, monitor and close as well as to address inequities in treatment gaps.

Identifying clinically relevant cohorts of HF patients and examining the appropriateness of management is crucial from patient, health service and research perspectives. The ideal HF registry would incorporate and link HF diagnoses from primary and secondary care with echocardiography and pharmacotherapy data. However, disappointingly, a platform to readily identify patients of different HF phenotypes from routinely collected electronic health data in Aotearoa does not currently exist. This gap is due to several factors and multiple barriers, including data collection, quality, interoperability and funding. In this paper, we consider options available to identify such cohorts along with their potential benefits and disadvantages, including consideration of cost and accuracy, as summarised in Table 1.

Manual auditing

Manual auditing of individual patient records by clinicians against standard diagnostic criteria would generally be regarded as the "gold standard" for accurately identifying those with HF of different phenotypes. However, the major disadvantage of this approach is the substantial time required by staff whose capacity to undertake such tasks is generally very limited. Any manual process is also associated with error and inconsistency, with the level of inconsistency compounded by the number of people involved, especially when repeated over time and associated with changes in staff and systems (including documentation).

Hospitalisation coding

We can identify patients admitted with HF from national hospitalisation datasets reasonably reliably using the International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Australian Modification (ICD-10-AM) coding system when both primary and secondary diagnoses are considered for relatively low cost.[20] ICD-10-AM has been implemented in New Zealand to classify diagnoses associated with hospitalisations since 1999. The major limitation of ICD-10 is that it only defines the clinical syndrome of HF and does not include definitions according to the EF phenotype.

ICD-11, which has been released for use from January 2022 by the World Health Organisation, provides distinct codes for HFrEF (BD11.2 Left ventricular failure with reduced ejection fraction) and HFpEF (BD11.0 Left ventricular failure with preserved ejection fraction) but there are no plans for New Zealand to move to ICD-11 within the next several years. Despite investigating the move for the last 3 years, Australia has also not decided when they might move from ICD-10 to ICD-11.

Reliable implementation of this revision is likely to require training and monitoring to ensure consistent and robust clinical documentation and coding practice. For example, despite the availability of imaging to clearly differentiate ischaemic and haemorrhagic stroke as well as distinct ICD-10 codes (I63 and I60/I61, respectively) quality improvement work focussed on improving clinical documentation as well as coding practice was required to minimise the inappropriate use of the code I64 (stroke not specified as haemorrhage or infarction).[19]

The other major limitation of a diagnostic coding-based approach to identifying HF in New Zealand is that currently the systematic coding of such diagnoses only occurs for admissions. HF can be diagnosed and managed in the community, through secondary care (in outpatient clinics) and/or primary care (in general practice). Diagnoses related to outpatient activity in secondary care are not routinely coded, and while Read and/or SNOMED-CT coding is in place in general practice this process may not be systematic or consistent; Read coding does not explicitly differentiate between phenotypes, information from echocardiology reports may be unavailable or incomplete and such data are not available at a national level.

Outpatient coding

This limitation in secondary care could be addressed by introducing a requirement to expand diagnostic coding in secondary care to include outpatient as well as inpatient activity. This could occur either through the same process currently used to code admissions (via clinical coders) or alternative processes such as clinician coding, as has been integrated into clinician outpatient workflow at Waitematā District Health Board (DHB).[19] While the former could leverage off existing infrastructure, there would be substantial ongoing costs. The latter involved establishment but limited ongoing costs.

Alternatively, natural language processing (NLP)-based strategies could be implemented to automatically generate diagnostic codes from clinical unstructured text (e.g., discharge summaries, specialist letters). While many off-the-shelf products are already available, an NLP-based strategy would require clinical validation to ensure satisfactory sensitivity and specificity, especially in the New Zealand healthcare setting. The latter point is important because the way HF is described and written about in clinical records in New Zealand, as well as exact medication names, may differ from the country in which the NLP algorithm was derived. As noted by a recent systematic review of current NLP processing methods and applications in cardiology, a major limitation of NLP-based approaches is the "inability to aggregate findings across studies due to vastly different NLP methods, evaluation and reporting".[21] Hence there would be a cost associated with establishing a New Zealand clinically validated NLP-based strategy, although most of these costs would be upfront. Further, any NLP approach will involve a balance of Precision and Recall (represented by the F score)[21]—the actual "feasibility" will be the shape of the Precision-Recall curve achievable at various levels of engineering effort. An algorithm will provide consistent performance if inputs are consistent, but reliability will be some balance of precision and recall where 80% performance on each could be deemed "good" by NLP standards. The systematic review noted above found that for studies that used NLP to identify and classify HF, F scores ranged from 74–94%.[21] A better understanding of such costs as well as feasibility and the Precision-Recall curve/F scores achievable of an NLP-based approach to determine EF-phenotype within Aotearoa will be obtained from an upcoming pilot of this approach, to be conducted by the Health Research Council-funded VAscular Risk Equity for All New Zealanders (VAREANZ) programme. The VAREANZ programme is also planning to work with primary care (via Primary Health Organisations) to obtain HF and EF-phenotype from coded (Read and SNOMED) primary care data.

Table 1: Options to identify heart failure phenotype.

Option		Advantages	Disadvantages
Manual audit		Gold standard (HF and EF phenotype) Any clinical setting	Clinical staff time/cost Potential for error/inconsistency Subset of patients only
Hospital coding		Reliable and consistent (HF phenotype) No/minimal additional cost All hospitalised patients	Unable to identify EF phenotype Need to be hospitalised
Outpatient coding (added to hospital coding)	Standard hospital coding process	Reliable and consistent (HF phenotype + potentially others) All outpatients	Administrative staff time/cost Not specific to HF
	Clinician coding	Gold standard (HF and EF phenotype + potentially others) All outpatients	Clinical staff time/cost Not specific to HF
	NLP-based coding	Potentially reliable and consistent (HF and EF phenotype + potentially others) All outpatients	Clinical staff time/cost Information technology costs Data scientist costs
Secondary care coding supplemented with echocardiography data		Potentially reliable and consistent (HF and EF phenotype + potentially others) All secondary care	Clinical staff time/cost Information technology costs Data scientist costs
Traditional clinical registry		Gold standard (HF and EF phenotype) Leverage off ANZACS-QI infrastructure	Clinical staff time/cost Lack of defined "home" to identify HF patients Need to be hospitalised
Registry based on random sampling of hospitalisation coding		Gold standard (HF and EF phenotype) Representative sample Leverage off ANZACS-QI infrastructure	Clinical staff time/cost Need to be hospitalised
Primary care coding		Includes people with HF managed in primary care Coding systems (Read and SNOMED) able to identify HF and EF phenotype	Not currently available at a national level Process may not be systematic or consistent Key information from secondary care may not be available Uncertain concordance with secondary care

Abbreviations: ANZACS-QI = All of New Zealand Acute Coronary Syndrome – Quality Improvement, EF = ejection fraction, HF = heart failure, NLP = natural language processing.

Secondary care coding supplemented with echocardiography data

One further possible option is to supplement hospitalisation (+/- outpatient) data (including diagnostic coding) on patients with HF with data from echocardiography databases to enable differentiation between patients with HFrEF and HFmrEF, and those with HFpEF. This approach was investigated for patients admitted with HF at the Waitematā and Counties Manukau DHBs in 2016 and 2018, respectively.[19] Both DHBs use the same echocardiography management, analysis and reporting system (Xcelera®). The clinician or sonographer undertaking the echocardiogram uses Xcelera® to report their findings of this investigation, including their clinical assessment of the patient's LVEF. Within Xcelera® this information is collected and stored both as specific measurements of LVEF, as well as the operator's summative assessment of LVEF, which can be captured using pre-specified text options from a drop-down menu, or free text.

The investigation found that while most echocardiograms had the summative assessment of LVEF documented using the drop-down menu (and therefore was easily extractable and analysable), a substantial proportion (in the order of 20%) were documented using free text. This proportion could potentially be reduced through staff training and quality improvement approaches to encourage greater use of drop-down menu options, and/or NLP approaches used to automatically code LVEF for residual free text. However, in an informal survey in 2018, there were at least seven different echocardiography reporting platforms in use nationally, including Xcelera®.[9] It is unclear whether extracting LVEF data would be as feasible for non-Xcelera® platforms, what processes would be needed to appropriately amalgamate data from different platforms, and whether all DHBs would have sufficient analytic capacity to extract the required data.

Traditional clinical registry

Patients with HF could be identified through clinical registries, such as the All of New Zealand Acute Coronary Syndrome – Quality Improvement (ANZACS-QI) registry. ANZACS-QI is a clinically led, web-based registry designed to enable consistent data capture of diagnostic and management information to support implementation of evidence-based guidelines for patients with acute coronary syndrome (ACS registry) and those receiving coronary angiography and percutaneous coronary intervention (CathPCI registry).[22] Patients are included in the registry by clinical or clerical staff on arrival at a coronary care unit or catheterisation laboratory, with clinical staff entering mandatory data throughout the admission.[22] Data capture and quality are optimised in ANZACS-QI through strong clinical leadership of this national initiative, training and monitoring, as well as separate funding by the Ministry of Health.[22]

A New Zealand HF registry to capture in-hospital HF patients was established more than 10 years ago under the auspices of the New Zealand branch of the Cardiac Society of Australia and New Zealand (CSANZ), and more recently this was transitioned to an acute decompensated HF registry available within the ANZACS-QI electronic platform. However, these HF registries have, to date, been unable to capture a representative or comprehensive cohort of patients. A key obstacle is that, in contrast to the ANZACS-QI ACS cohort, which can be comprehensively captured through catheterisation laboratories, there is a lack of a defined "home" for HF patients. Unlike ACS patients who are treated in cardiac catheterisation labs, HF patients are often managed alongside patients with a multitude of other conditions by general physicians and general medical services, including services for older people, as well as by cardiologists and cardiology services. Further, such registries do not generally capture hospital outpatient activity or HF management in the community, though the latter could be partially addressed through linkage to national data collections (e.g., pharmaceutical dispensing).

Registry based on random sampling of hospitalisation coding

The authors, as part of their work with the Ministry of Health-funded ANZACS-QI platform, are currently developing an approach that could address some of the limitations of a traditional HF registry related to resource and representativeness while leveraging the existing infrastructure of ANZACS-QI. In this approach, a random selection of HF admissions could be identified using national hospitalisation coding data, and participating hospitals retrospectively enter data manually for the sample of patients admitted to their hospital using the ANZACS-QI platform.[9] The registry will provide data on in-hospital HF process measures, such as LVEF assessment and medication use (including contraindications to use) for those with HFrEF to guide quality improvement initiatives. This approach

would have the advantage of identifying and reporting on a representative national sample of HF hospitalisations, regardless of the discharging service and patient comorbidity, and could be supplemented through linkage to national datasets to achieve an overview of HF management after discharge.

Primary care coding

HF can be diagnosed and managed in the community, as well as through secondary care. Read and/or SNOMED-CT coding is in place in general practice, and both are potentially able to differentiate between HF phenotypes. SNOMED is now the required standard clinical terminology for the New Zealand health and disability system (which will enhance interoperability across the health sector), provides many more clinically relevant concepts than Read coding (e.g., there is a specific SNOMED clinical term and code [703272007] for HFrEF), and its implementation is being accelerated across the whole health system in New Zealand, with a specific focus on upgrading from Read codes to SNOMED in primary care.[23] However, the coding process may not be systematic or consistent in primary care, as it is not specifically resourced as with secondary care. Information from secondary care including echocardiology reports (publicly or privately funded) may be unavailable or incomplete. There may be inconsistent understanding of diagnosis/phenotype between primary and secondary care where patients are engaged in both. For example, a New Zealand study found that the 39% of people with prior CVD hospitalisations were not recorded as having prior CVD when their CVD risk was first assessed in general practice.[24] This discordance between information contained in primary and secondary care increased over time, and was associated with lower dispensing of evidence-based medications and was more common among people aged under 55 years, women, and those of non-European ethnicities.[24]

Upcoming health system changes

The national health system reforms and Hira, the national health information platform, have been designed to enable better sharing of expertise (including digital and analytical) and data (including across regions and at the primary/secondary care interface) across the country. Hira will "draw together a person's latest health information as needed to create a single view; a virtual electronic health record rather than a single electronic health record".[25] Hira is a key enabler of the Ministry of Health's Digital Heath Strategic Framework[26] and Data and Information Strategy.[25] These health system changes offer exciting opportunities and show great promise but will take time to be fully implemented. At this stage, Hira won't be fully implemented until the end of 2026 and it is unclear exactly which data will be included as part of their scope. A key aspect of Hira is interoperability, so investment in optimising the accuracy, completeness and consistency in the recording of key clinically relevant data fields, such as the diagnosis of HF and HF type (HFrEF vs HFmrEF vs HFpEF) are crucial, particularly given the substantial mortality, morbidity and inequities in HF as well as the substantial health system costs associated with this treatable condition.

Next steps

Given the urgent need to identify people with heart failure according to EF phenotype, the options for identifying them from electronic health data, and the opportunities presented by health system reform, including a focus on digital solutions, we recommend the following four preliminary actions:

1. Establish a HF registry based on random and representative sampling of ICD-coded admissions, starting in hospitals with strong clinical leadership, and reporting on key clinical quality measures.
2. Investigate the feasibility of and processes to obtain HF and EF-phenotype from primary care-coded data.
3. Investigate the feasibility of and processes to amalgamate a subset of the most clinically important data for HF (including EF) from all echocardiography reporting platforms in use nationally.
4. Undertake pilot studies to investigate the feasibility and clinical validity of different approaches to enable systematic collection of HF diagnosis and phenotype for outpatient attendances for HF and determine which approach would be the most suitable for national implementation.

While these actions could be undertaken separately and by different groups, to ensure that the work will effectively and efficiently support high-quality healthcare and equitable outcomes for all patients and whānau with HF in a coor-

dinated and cohesive way, we recommend that it should have strong oversight by a national HF working group. As the working group would require the inclusion of clinicians and researchers with expertise in HF, equity, quality improvement and population health, it could be formed with membership from existing groups including Manawataki Fatu Fatu (a Māori and Pacific-led programme researching equity in heart health outcomes for Māori and Pasifika), CSANZ (particularly their HF working group), ANZACS-QI (in order to leverage off the ANZACS-QI electronic platform, central co-ordination and data quality improvement processes where appropriate and feasible), and VAREANZ (VAscular Risk Equity for All New Zealanders, a Māori and Pākehā co-led research programme assessing cardiovascular risk-management equity gaps nationally). Input should also be obtained from patients and whānau, Health NZ, the Māori Health Authority and the Ministry of Health. Future work will need to consider reliability and concordance of data across sources, as well as the most appropriate methods of data transfer.

The stark inequities in the burden of HF experienced by Māori and Pacific people and the likely contribution of health service factors to these inequities[26] add to the case for urgent action to enable the identification of clinically relevant cohorts of people with HF, as well as other major causes of morbidity, mortality and inequities in Aotearoa. Such action is legislatively mandated under the Pae Ora (Healthy Futures) Act 2022, the first principle of which is that "*the health sector should be equitable, which includes ensuring Māori and other population groups – (i) have access to services in proportion to their health needs; and (ii) receive equitable levels of service; and (iii) achieve equitable health outcomes*".[27]

COMPETING INTERESTS
Nil.

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Acute macular neuroretinopathy following COVID-19 infection

Luke Hawley, Louis S Han

ABSTRACT

COVID-19 is a global pandemic with over 600 million cases worldwide and over 1.7 million cases in New Zealand to date. The most recent spread of Omicron variant saw widespread infection across the country that was unable to be controlled like the initial Alpha or Delta variants. There is limited information on ocular complications of COVID 19. In our case, there was a close relationship between time of COVID-19 infection and acute visual changes including ongoing scotomas (blind spots). This report explores a case of a young female with positive visual phenomena following COVID-19 infection, with the diagnosis of acute macula neuroretinopathy.

COVID-19 is a global pandemic with over 600 million cases worldwide and over 1.7 million confirmed cases in New Zealand at the time of this report.[1] The most recent spread of the Omicron variant saw widespread infection across the country that posed concerns with controlling the outbreak.

The most common symptoms of COVID-19 include a worsening cough, coryzal symptoms, fever, sore throat as well as shortness of breath. In many cases, there is an altered sense of smell or taste.[2] Less common but more severe symptoms include chest pain, abdominal pain and joint stiffness. However, there is limited information on ocular complications.[2] In this case there is a close correlation between active COVID-19 infection and onset of acute visual changes.

Case report

A 21-year-old female student, with no previous medical background, presented to the acute ophthalmology clinic at Dunedin Public Hospital. Her primary concern was sudden onset visual changes. These changes included several small, bilateral paracentral scotomas (blind spots), as well as floaters and palinopsia (abnormal persistence of image once the subject has moved).

The only relevant past medical history was a recent COVID-19 infection that preceded the symptoms by two days. Due to the stability of the patient's visual acuity and no secondary symptoms, it was deemed appropriate for daily phone consultations while the patient completed her isolation period, before presenting for a full ophthalmic examination.

At the time of examination, the patient's visual acuity was 6/6 bilaterally with no relative afferent pupillary defect. Optic nerve function remained intact and colour vision was unaffected. The ocular exam showed no signs of intraocular inflammation; however, dilated fundal exam showed areas of change within the maculae. Several discrete, reddish-brown ellipsoid lesions were seen. Optical coherence tomography (OCT) was obtained which showed heterogenous, hyper-reflective thickening of the outer retina with corresponding areas of hypo-reflectivity on infrared imaging.

The working diagnosis was acute macular neuroretinopathy likely secondary to COVID-19 infection. Daily monitoring of the patient showed slow resolution of symptoms and the fundal lesions with no intervention required.

Discussion

Acute macular neuroretinopathy (AMN) is a rare disease that typically presents with unilateral central vision loss, most commonly affecting young women in their reproductive years.[3] Acute macular neuroretinopathy is often associated with a non-specific flu-like illness. There have been documented cases associated with influenza,[4] cytomegalovirus[5] and more recently COVID-19.[6] The pathophysiology is still not completely understood, although it is agreed there is a primary inflammatory component.

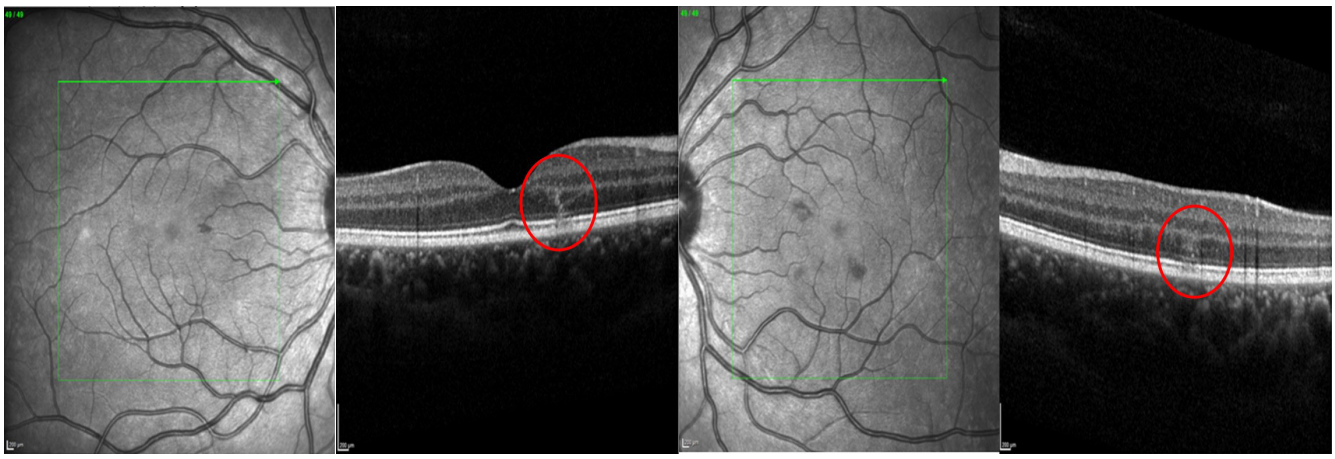
Clinically, there can be an associated exudative detachment of the macula with a thickening of the underlying retinal pigment epithelium.[7] These wedge-shaped lesions are typically reddish-brown on ophthalmoscopy and fade over time.[7]

Infrared imaging of these lesions shows hyporeflectivity corresponding to the structural changes in the outer retina.[7]

Importantly, in this case there was a close association between the time of testing positive for COVID-19 and the onset of symptoms. Therefore, although it cannot be confirmed, it is likely that the immune-mediated reaction caused by active infection is correlated to the presentation of acute macular neuroretinopathy. Furthermore, there has been documented cases overseas of acute macular retinopathy following COVID-19 vaccinations[8] as well as two cases shortly after having the influenza vaccine.[9,10]

New Zealand has been a world leader in reducing the numbers of COVID-19 cases and complications related to COVID-19. However, with the new Omicron variant currently spreading throughout the country, it is important that we are aware of rare but potentially severe complications. Acute macular neuroretinopathy can have persistent long-term scotomas and hence input from ophthalmology services would be recommended when patients present with visual changes after recent COVID-19 infections or vaccinations.

Figure 1: Optical coherence tomography of both eyes with an infrared image showing the heterogenous, hyperreflective change in the outer retina at the junction of the outer plexiform and outer nuclear layers, as indicated by the red circles. These areas are seen as dark, hypo-reflective patches in the infrared images.



COMPETING INTERESTS
There are no competing interests to declare. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

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Azithromycin versus doxycycline: management of female urogenital and rectal *Chlamydia trachomatis* infections

Elissa M McDonald, Rachel T Woodcock, Felix S F Ram

Chlamydia trachomatis infection is the most common sexually transmitted infection (STI) internationally, with the greatest burden of disease in young sexually active adults, and it is associated with pelvic inflammatory disease, chronic pelvic pain, infertility and pregnancy complications.[1] The purpose of this review is to inform prescribing practice for the management of female urogenital and anorectal chlamydia. Of note, where we refer to "male" or "female", we refer to cisgender men and women; management of transgender and non-binary people should be anatomy-based. However, we recognise that transgender people also identify as male or female, and that gender identity is distinct from genital anatomy.

Internationally, treatment guidelines for urogenital infections of *C. trachomatis* recommend 1 gram (g) of azithromycin orally as a single dose, or 100 milligrams (mg) of doxycycline orally twice daily for seven days.[1] However, doxycycline is recommended over azithromycin for known anorectal infections due to increased microbial susceptibility.[1] Doxycycline is also available in a 200mg slow-release tablet which enables daily dosing, reduces side effects and provides comparable efficacy;[2] however, this formulation is not yet approved for sale in New Zealand. A recent meta-analysis[3] reported 68% (95% CI, 57% to 80%) of females with urogenital infections of *C. trachomatis* were also diagnosed with concurrent rectal infection. In addition, a lack of association between rectal *C. trachomatis* and anal intercourse was also reported. Therefore, it is possible that females who do not present with a history of anal intercourse could in fact unknowingly harbour anorectal infection of *C. trachomatis* that could provide a source for reinfection of the genitourinary tract.[4]

Azithromycin is a macrolide antibiotic with 40% oral bioavailability and a half-life of 68 hours following oral administration.[5] However, azithromycin has been associated with QT prolongation and is classified as a Category B1 medicine.[5] A member of the tetracycline family, doxycycline has 95% oral bioavailability, with a half-life of approximately 20 hours. Doxycycline is classified as a Category D medicine.[5]

In a small prospective cohort study conducted in a sexual health clinic, 50 females aged 16 years or older collected daily vaginal and rectal specimens for up to eight weeks to determine time to clearance for a *C. trachomatis* infection.[6] Participants were treated as per local guidelines with either azithromycin or doxycycline. The authors reported that the time to clearance for both rectal and vaginal infections was similar (seven and eight days, respectively), and that all participants with rectal *C. trachomatis* infections were cured when treated with a single dose of azithromycin.[6] However, there were limitations to this study, including small sample size, and only 13 females tested positive for either rectal or vaginal *C. trachomatis* in the cohort. Nine participants tested positive for concurrent vaginal and rectal infection, and only two participants were treated with doxycycline.[6]

An observational study of 416 females aged 18 years or older with confirmed *C. trachomatis* infections reported 341 had concurrent rectal infections.[7] Vaginal and rectal nucleic acid amplification tests (NAAT) were conducted at diagnosis then weekly for four weeks following treatment. All females were treated as per guidelines with azithromycin or doxycycline. Single dose azithromycin (1g orally) had an efficacy of 94% (95% CI, 90–96%) for urogenital infections, and 79% (95% CI, 73–84%) for rectal infections.[7] The authors reported that cure rates after treatment with doxycycline, were 96% (95% CI, 91–98%) for urogenital infection, and 96% (95% CI, 91–98%) for rectal infection. This study indicates that for urogenital infections, efficacy of azithromycin is similar to doxycycline, however, for undetected rectal infections females would be 6 (95% CI, 2 to 14) times more likely not to receive adequate

treatment if azithromycin was prescribed. The authors recommend that in the absence of rectal testing and no presenting history of anal intercourse, doxycycline should be offered as first line for the management of urogenital infections of *C. trachomatis* in females.

Two recent systematic reviews and meta-analyses using Cochrane methodology examined the most effective treatment for urogenital and rectal *C. trachomatis* infections.[8,9] Páez-Canro et al.[8] included 14 studies with a total of 2,147 participants, of which 568 were females aged between 17–60 years. Five studies were included in the meta-analysis that investigated microbiological failure in non-pregnant females; the authors reported that overall, there was insufficient evidence to determine whether doxycycline or azithromycin was the more effective treatment for urogenital *C. trachomatis* infections (RR 1.71, 95% CI, 0.48 to 6.16). Nine studies, including both males and females, reported adverse effects, with azithromycin having significantly less adverse effects (17%) compared with doxycycline (RR 0.83, 95% CI, 0.71 to 0.98). Reported adverse effects were gastrointestinal in nature (nausea, vomiting, abdominal pain). Chen et al.[9] reported a 27% increase in risk of microbial failure with azithromycin in rectal *C. trachomatis* infections (RR 1.27, 95% CI, 1.20, 1.35). Subgroup analyses reported doxycycline consistently provided greater chance of microbial cure irrespective of gender, study design or country where the study was conducted.

There are multiple factors that need to be considered before prescribing treatment to females who have tested positive for *C. trachomatis.* Overall, the literature does not provide a clear answer as to whether azithromycin or doxycycline is the best treatment option for individuals. Research is lacking and overwhelmingly focused on infections in males. Peuchant et al.[10] are currently conducting a randomised multi-centre study to determine whether azithromycin or doxycycline is more effective at treating anorectal infections with *C. trachomatis* in females, when assessed 6 weeks after antibiotic treatment. Until further research is undertaken, and the results of this study are reported, in the absence of a negative rectal swab it may be preferable to prescribe doxycycline as first choice for treatment of *C. trachomatis* infections. This recommendation assumes the high likelihood of concurrent rectal infection. If doxycycline is contraindicated or the patient indicates that they will not complete their antibiotic course, azithromycin is likely the second most-effective drug. Kong et al.[11] state that it is likely that higher doses improve treatment efficacy by increasing the overall area under the curve (AUC), and considering this finding, a higher stat dose of azithromycin is something that could be explored in the future. In New Zealand, doxycycline is now recommended as a first line treatment for chlamydia by the New Zealand Sexual Health Society.[12] Anal chlamydia is ideally tested for using a proctoscope, and specialist advice should be sought if the person has anal symptoms or refer to the anorectal syndromes' guideline.[13] Of note, doxycycline can also be considered for pharyngeal chlamydia. Clinicians should be encouraged to test for chlamydia (or any STIs) based on the type of sex people have.

In summary, *C. trachomatis* is a sexually transmitted infection that can impact female fertility. The burden of disease from *C. trachomatis* is highest in females aged between 15 and 19 years old. A considerable proportion of females may have concurrent rectal *C. trachomatis* infection, regardless of their sexual practices. Doxycycline offers greater efficacy over azithromycin for anorectal infection and comparable efficacy for urogenital infection.

COMPETING INTERESTS
Nil.

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Cardiac Computed Tomography to exclude left atrial appendage thrombus in atrial arrhythmias prior to electrical cardioversion during the COVID-19 pandemic

Jeffrey Sebastian, Tina Thomas, Francis Wu, Su Yin Tang, Budresh Joshi, Niels van Pelt, Ruvin Gabriel, Tim Sutton, Mansi Turaga, Jen-Li Looi

Atrial fibrillation (AF) and atrial flutter (AFL) are common causes of hospitalisation. Restoring sinus rhythm with cardioversion is performed in patients with AF/AFL in an effort to improve cardiac function and relieve symptoms.[1] Our group had recently showed that an early rhythm control strategy, with either early inpatient transoesophageal echocardiogram (TOE)-guided direct current cardioversion (DCCV) or ablation in patients hospitalised with AF or AFL and decompensated heart failure with reduced ejection fraction, had a low rate of all-cause mortality and rehospitalisation for heart failure at one year.[2]

TOE has an important role in guiding DCCV in AF patients of unknown or prolonged duration, and without the need for prolonged anticoagulation before the procedure.[3] Currently, TOE is considered the gold standard imaging modality to evaluate left atrial appendage (LAA) anatomy and morphology prior to DCCV.[4] COVID-19 poses a unique set of challenges to the healthcare system due to its rapid spread, intensive resource utilisation and relatively high morbidity and mortality. TOE is considered a high-risk procedure for possible aerosol transmission of this infection. Therefore, the American Society of Echocardiography recommends avoiding TOE and the use of alternative diagnostic tools for LAA imaging whenever possible.[5] Cardiac computed tomography (CCT) has been proposed as an alternative imaging method to exclude LAA thrombus prior to DCCV. On CCT, the LAA is qualitatively evaluated in multiple axial planes for a filling defect, which is defined as incomplete visualisation or opacification of the entire LAA with iodine contrast on a first pass or a delayed scan (Figure 1).

This study describes our experience of utilising CCT as an alternative imaging modality to exclude LAA thrombus prior to DCCV in patients with atrial arrhythmias at Middlemore Hospital from 1 January 2021 until 1 January 2022. Patients with atrial arrhythmia requiring DCCV who underwent CCT were identified from the All New Zealand Acute Coronary Syndrome Quality Improvement (ANZACS-QI) cardiac CT registry.

The demographic characteristics of patients who underwent CCT are summarised in Table 1. A total of 97 patients (71.1% men, mean age 58.2±14 years) underwent CCT as inpatients during the study period. All but one CCT scans were of diagnostic quality. More than 40% were European, 23.7% were Māori, 21.6% were Pasifika and 5.2% were Asian. The mean body mass index (BMI) of the study population was 33.8±8.4kg/m^2, and more than 60% of the study population had a BMI of ≥30kg/m^2.

More than 50% of patients were in AF. All patients underwent echocardiography prior to CCT. Two-thirds of patients had a significant reduction in left ventricular systolic (LV) on echocardiography during CCT: 8.2% had mild/mild–moderate LV impairment, and 59.8% had moderate/moderate–severe/severe LV impairment. 10 patients (10.3%) had slow flow/probable thrombus in the left atrium (LA) or LAA on CCT and four patients (4.1%) had definite thrombus. 83 patients underwent DCCV directly after CCT and none had periprocedural stroke. Six patients self-reverted to sinus rhythm and one patient underwent acute AFL ablation. One patient had an incidental finding of pulmonary embolus, and therefore did not undergo DCCV. Of the 10 patients with slow flow/probable LA/LAA thrombus on CCT, one patient self-reverted to sinus rhythm and the others were considered to have slow flow in LA/LAA and underwent DCCV without compli-

cation. Two out of the four patients with definite thrombus on CCT underwent TOE, which confirmed LAA thrombus. One patient had a repeat TOE after a month of adequate anticoagulation, which showed resolution of LAA thrombus, and one patient had a repeat CCT that showed no thrombus.

CCT is a well-established technique for the evaluation of left atrial and pulmonary vein anatomy prior to radiofrequency catheter ablation of AF.[6,7] In addition, CCT has been utilised as a non-invasive imaging modality for the detection of LAA thrombus before AF ablation for reducing the risk of periprocedural thromboembolic events.[8] Two recent meta-analyses[9,10] demonstrate that CCT plays an important role in excluding LA/LAA thrombus before AF ablation and in the evaluation of patients with suspected cardioembolic cerebrovascular accidents with a high sensitivity and specificity, however, there is a paucity of data on its role prior to DCCV.

The COVID-19 pandemic has forced us to reconsider how best to limit cardiac imaging procedures that generate aerosols in order to minimise the risk of cross-infection for both imagers and patients. Our study shows that for patients with acute atrial arrhythmia requiring DCCV, CCT is a safe and useful alternative to TOE.

TOE often requires intravenous sedation with benzodiazepine (e.g., midazolam) alone or in combination with intravenous narcotic (e.g., fentanyl). Benzodiazepines can depress respiratory and haemodynamic function, particularly in patients with impaired LV function, in elderly patients and in obese patients who frequently have difficult airways to manage and are at risk of respiratory complications.[11] Sedation is not required during CCT and would be a safer imaging tool for these patients. In our study, with a large proportion of patients with significant LV systolic impairment and an elevated BMI, diagnostic CCT was safely performed with most not requiring additional testing with TOE.

Iodine contrast agents used during CCT can cause contrast-induced nephropathy in patients with CKD with estimated glomerular filtration rates <30mL/min/1.73m2. Thus, TOE may be the preferred option to assess the LAA in these patients.

Although limited by a small number of patients, our study provides our real-world experience of utilising CCT to exclude LAA thrombus prior to DCCV in acute atrial arrhythmias. Importantly, CCT appears safe and effective to exclude LAA thrombus prior to DCCV.

Table 1: Clinical characteristic of patients who underwent cardiac computed tomography prior to direct current cardioversion.

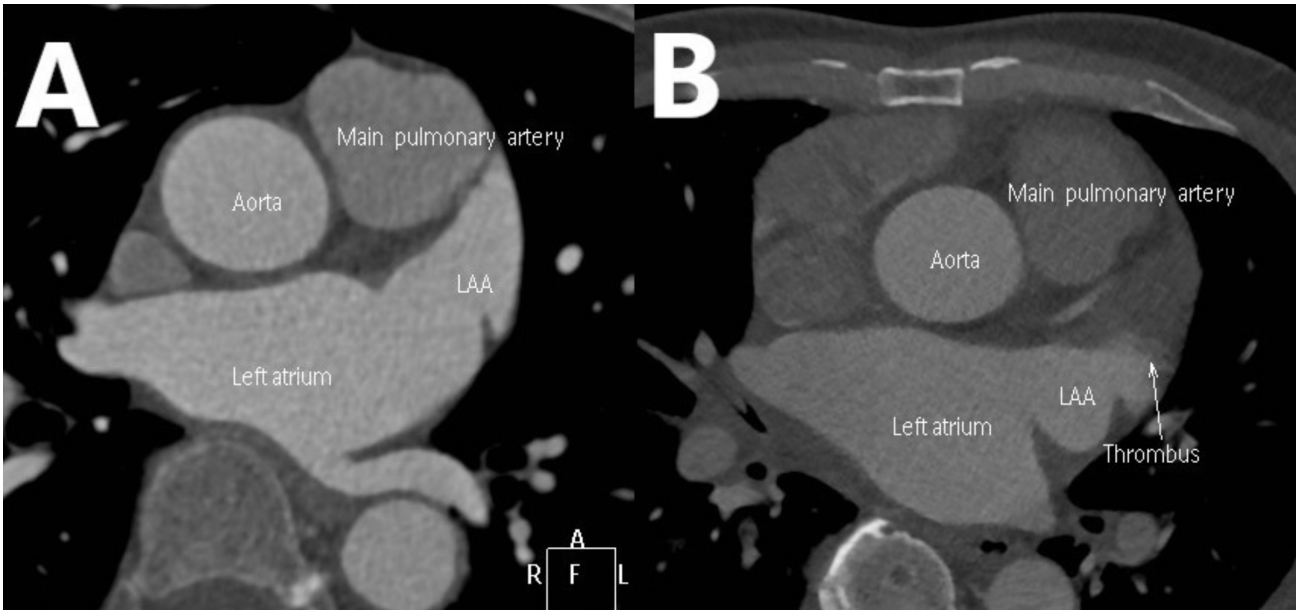
	Total (n=97)
Gender	
Male	69 (71.1%)
Female	28 (28.9%)
Age (years), (mean+SD)	58.2+14
Ethnicity	
NZ European	46 (47.4%)
Māori	23 (23.7%)
Pacific peoples	21 (21.6%)
Asian	5 (5.2%)
Middle Eastern/Latin American/African	2 (2.1%)
BMI (n, %)	
<25	12 (12.4%)
25–29	18 (18.6%)
>30	67 (69.1%)

Table 1 (continued): Clinical characteristic of patients who underwent cardiac computed tomography prior to direct current cardioversion.

Weight (kg), (mean+SD)	101.7+27
BMI (kg/m2), (mean+SD)	33.8+8.4
Rhythm during CT	
Atrial fibrillation	57 (58.8%)
Atrial flutter	40 (41.2%)
LV function during CT	
Normal/Low normal	31 (27.5%)
Mild/Mild-moderate	8 (8.2%)
Moderate/Moderate-severe/Severe	58 (59.8%)
Slow flow or probable thrombus in LA/LAA	10 (10.3%)
Definite LAA thrombus	4 (4.1%)

Abbreviations: BMI – body mass index; BSA – body surface area; CT – computed tomography; LV – left ventricular; LA – left atrium; LAA – left atrial appendage.

Figure 1: a) CCT view of the left atrial appendage. There is complete opacification of the left atrial appendage with contrast, indicating no evidence of thrombus and; **b)** a thrombus (arrow) is seen in the left atrial appendage.



COMPETING INTERESTS
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Is PHARMAC's decision-making fair, cost-effective and clinically effective? Observations from the real world

Mark J Bolland, Andrew Grey

Tumilty and colleagues assessed the decision making by the Pharmaceutical Management Agency (PHARMAC).[1] Their analysis was based upon a review of PHARMAC procedural documents and interviews with PHARMAC staff. The senior author is a member of PHARMAC's Pharmacology and Therapeutics Advisory Committee (PTAC). In seven domains, that included clinical effectiveness, cost-effectiveness and fairness, they scored PHARMAC with almost full marks (119/125) including 5/5 for these three specific domains, concluding that PHARMAC's decision-making framework is both fair and legitimate.

Our views as practising endocrinologists differ. While the concept of PHARMAC is admirable, in practice it generates complaints from a range of people affected by its decisions. MB has applied to PHARMAC to change funding criteria for the intravenous bisphosphonate zoledronate. AG served on the PTAC Endocrinology Advisory Sub-committee from 2016–2021, during which time he advocated for improvements in PHARMAC processes for collating, considering and applying clinical advice.

PHARMAC has a process for assessing applications for funding of medicines. However, it appears to apply a "one size fits all" to applications, irrespective of their nature, such that evaluations of minor, common-sense adjustments to existing therapies attract lengthy and inefficient processes. A consequence is that other clinically supported medication changes are delayed. We identified other aspects of PHARMAC's interactions with clinicians, and its clinical advisors, that led us to conclude that the outcomes of PHARMAC's decision-making is not clinically efficient, cost-effective or fair.

A) Funding criteria for intravenous bisphosphonates

For many years, PHARMAC has funded pamidronate without restriction, whereas zoledronate has been funded under special authority restriction for patients with bone metastases, early breast cancer, osteoporosis or Paget's disease. Initially, that may have been reasonable since pamidronate was an older medication available as a generic preparation and there were marked cost differences even though the newer agent, zoledronate, is more potent, longer lasting, and more effective than pamidronate. However, generic zoledronate has now been available for several years and currently is considerably cheaper than pamidronate ($18 vs $75–80). Generic zoledronate has superseded pamidronate.

PHARMAC's decision to fund a more expensive, less effective intravenous bisphosphonate without restriction, while limiting the use of the more effective, cheaper agent has real consequences for patients and clinicians. Intravenous bisphosphonates are a first line treatment for patients with serious hypercalcaemia. Because of the current funding criteria, such patients were treated with pamidronate when they should receive zoledronate. The fix was simple: fund zoledronate for hypercalcaemia, and to discontinue funding of pamidronate.

We brought this discrepancy to PHARMAC's attention in May 2020. Their response was to require an application for funding of zoledronate for hypercalcaemia. This was submitted in June 2020. A year later, in May 2021, PTAC reviewed the application and gave funding zoledronate for hypercalcaemia a high priority. But then nothing happened. In December 2021, we sought an update. In February 2022, we received the update stating that consultation would be held soon. Zoledronate funding for hypercalcaemia eventually started on 1 April 2022.

Essentially, PHARMAC funded a more expensive, less effective medication for many years, and for almost two years since it was apprised of the discrepancy. What should have been a simple switch, implemented immediately if common sense applied, instead required a clinician application, a detailed assessment by PTAC, a consultation process, and then a decision. Meanwhile

patients received inferior care.

A similar situation applies to the use of zoledronate for osteoporosis treatment. Currently, 5mg zoledronate costs $60 under special authority restriction. Table 1 shows the medication cost of a standard five-year treatment course of funded osteoporosis medications. The cheapest option is 4mg zoledronate ($11/year), but even 5mg zoledronate (only available with restrictions) is cheaper than risedronate and similar to alendronate, both available without restriction. These are only medication costs: intravenous zoledronate also requires three prescription charges, three infusion charges, and likely three doctor visits and has the advantage of greater compliance. Oral bisphosphonates require 20 prescription charges and 20 doctor visits. How those costs and benefits balance out would depend on what assumptions are made, but we think they are likely to favour zoledronate.

Data from the Ministry of Health Pharmaceutical data web tool show that about 50,000 people per year received a prescription for osteoporosis medications between 2016 and 2020. If all those people had been treated with 4mg zoledronate, medication costs would have been about 60% lower, an absolute saving of about $800,000–$1 million/year.

We first brought this to the attention of PHARMAC in June 2020. The response was that PHARMAC had not appreciated that 5mg zoledronate was cheaper than some of the funded alternatives and 4mg zoledronate cheaper than all of them. The Chief Executive said that PHARMAC would reconsider the special authority. The issue was considered by the PTAC endocrinology subcommittee in March 2021 who were strongly supportive, but nothing eventuated.

In response to a formal update request in January 2022, PHARMAC responded that removing the zoledronate special authority may not be cost-saving or cost-neutral because of "the expected increase in the size of the osteoporosis market", and that the special authority would not be removed. We pointed out that use of 4mg zoledronate is about 60% cheaper than alternatives and that prescribing data show the "osteoporosis market" is static not increasing. PHARMAC have not responded, and we have not seen any public justification of the decision.

Once again, PHARMAC are funding more expensive treatment options, while applying restrictions to cheaper, arguably more effective options. PHARMAC have been aware of this for nearly two years, but nothing seems likely to change in the near future.

B) Other endocrinology therapeutics and processes for collating and considering clinical advice

The examples of the tortuous processes for intravenous bisphosphonates are not isolated: others are shown in Box 1. Notably, none of these medications are new. Each has been recommended by the Endocrinology PTAC Sub-committee as clinically useful and important, sometimes on more than one occasion. Each was initiated by members of the Endocrinology PTAC Advisory Committee. None have yet reached clinical practice.

PHARMAC advertises that its "decision-making is based on strong, objective clinical advice. The main way that we seek clinical advice is through our clinical advisory committees: PTAC and the sub-committees of PTAC".[2] If that is the case, why have simple recommendations from the Endocrinology PTAC Sub-committee not been actioned?

One possibility is that the committee hardly ever meets. During AG's five-year tenure, the Endocrinology Committee met only four times. The first meeting took place in June 2016, but committee recommendations to fund cinacalcet (see Box 1), delist an unnecessary medication (alendronate and colecalciferol) and configure workable special authority criteria for the osteoporosis treatment denosumab were not actioned. In May 2018, PHARMAC asked the Committee to discuss a minor aspect of a specific therapeutic (denosumab), but the Committee's concerns about the more important issue of unworkable special authority criteria were again disregarded. The last two meetings occurred in November 2020, to discuss disquiet among members at the lack of engagement by PHARMAC, and in March 2021, after repeated requests for a meeting by some Committee members.

Second, the endocrinology committee has not had a role in agenda setting, which has remained the sole provenance of PHARMAC. Thereby, PHARMAC collates advice on only those medication issues it deems important. How those medication issues are determined is not clear.

Third, communications between PHARMAC or PTAC and the Endocrinology Committee were unbalanced and erratic. Committee recommendations were discussed at PTAC meetings without a Committee member with relevant clinical expertise present, contributing to decisions not supported by the Committee or by clinicians. For example,

the special authority criteria for denosumab were applied by PHARMAC against the strong recommendations of the Endocrinology Committee and were met with bewilderment by clinicians. A new set of recommendations, endorsed by the Endocrinology Committee a year ago, has not been implemented. Decisions were communicated erratically, if at all, to the Committee, without a right of reply.

Minutes of the November 2020 meeting, at which dissatisfaction was expressed by Endocrinology Committee members about the existing PHARMAC processes, and the improvements suggested, were not made publicly available and discussion of those concerns was removed from the publicly available minutes of the March 2021 meeting after the chair had signed off the agreed record. At that meeting, the Endocrinology Committee's attempts to address its concerns were likened by PHARMAC staff to the actions of a "lobby group".

At the November 2020 meeting, the Committee proposed some improvements to the PHARMAC processes:

1. The advisory committee meet annually
2. The agenda be set by PHARMAC AND the Committee
3. A list of Committee advice/recommendations to be produced after each meeting and reported on the PHARMAC website
4. A response provided to the Committee about each recommendation by PHARMAC/PTAC in a timely fashion
5. A facility for the Committee to respond to the PHARMAC/PTAC decisions in the event it disagrees with them
6. All recommendations and responses to be publicly available on the PHARMAC website.

As of June 2022, it was not apparent that these requests would be actioned by PHARMAC.

Collectively, these experiences belie the claims that PHARMAC highly values its clinical advisors and that its processes are "fair" (to whom?), cost-effective or clinically effective, suggesting instead that it pays lip service to clinical expertise. Perhaps, it is the chasm between PHARMAC's decision-making and its impact on affected patients and clinicians that contributes to the discontent about PHARMAC's performance?

Table 1: medication costs for a treatment course of osteoporosis.

Medication	Cost/infusion or tablet	Usage	Total cost	Cost/ Year
zoledronate 5mg	$60	3 infusions over 5 years	$180	$36
zoledronate 4mg	$18	3 infusions over 5 years	$54	$11
alendronate 70mg	$0.61	weekly for 5 years	$159	$32
alendronate 70mg/vitamin D	$0.38	weekly for 5 years	$98	$20
risedronate 35mg	$0.78	weekly for 5 years	$202	$40

Box 1: examples of clinical recommendations supported by the Endocrinology PTAC Sub-committee not actioned by PHARMAC.

Medication and recommended indication	Rationale
Eplerenone for men with primary hyperaldosteronism who are intolerant of spironolactone[3]	No effective alternative
Cinacalcet for patients with severe primary hyperparathyroidism for whom surgery is contraindicated[4]	No effective alternative
Reconfigured special authority criteria for denosumab[5] and teriparatide[6]	Need for second-line therapy for contraindications to, or intolerance of, bisphosphonates
Micronised progesterone for post-menopausal women[7]	Improved safety and tolerability
Octreotide for TSH-secreting macroadenoma[8]	Efficacy in tumour control
Transdermal testosterone (gels) for male hypogonadism[9]	Need for effective and well-tolerated non-parenteral treatment

COMPETING INTERESTS
None of the authors have any financial conflicts of interest. AG was a member of the PHARMAC PTAC Endocrinology Sub-committee from 2016-2021. Both authors are practising Endocrinologists.

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Recent Advances in Anæsthesia (extract)

NZMJ, October 1922

Since the beginning of this century there have been tremendous advances made in all branches of surgery, but I think no branch can show greater progress than had taken place in the science of administration of anæsthetics. In the early days of surgery the anæsthetist held a comparatively unimportant position; his technique was limited, and his experiences were confined to few agents and methods. He was satisfied to keep the patient still and get him out of the theatre alive. As surgery grew, so grew the science of anæsthesia, in fact to a great extent it is to the improvements of anæsthetic technique that modern surgery owes its present high standard of efficiency.

The difficulties of experimenting and trying out new methods are tremendous. The anæsthetist has the patient's life in his hands and it is difficult to say to what extent he is justified in departing from accepted technique in trying out new methods. An error in the judgement of a surgeon in departing from accepted technique and having a fatal result, does not involve the publicity that follows the similar error of an anæsthetist. However, fortunately for surgery, the growth of the branch as a speciality has attracted men with sound scientific training, whose courageous faith in their convictions, bred of a painstaking experimenting on animals, had led them to introduce methods that have been of incalculable service to surgery. The modern anæsthetist must have a knowledge of the physiological and pathological problems involved in the use of chloroform, ether, ethyl chloride, nitrous oxide, and of local anæsthetics, and in addition must have a sounds knowledge of general medicine and surgery. The patient nowadays, expects more than mere anæsthesia, and the surgeon is realising to what an enormous extent post-operative morbidity is dependent on the anæsthesia, to enhance the constancy of results, and so by all these means generally to enlarge the scope of surgery.

Series of statistics have been published from time to time showing the immediate mortality of anæsthesia. In statistics published ten, twenty or more years ago, one can see easily how much greater is the mortality with certain agents and methods than with others. And yet we see in recent statistics, statistics for periods within a year of to-day, numerous anæsthetic fatalities due to the same agents and methods as were fully proved unsafe at least twenty years ago. Believe me, the time is coming when we shall have to answer for this to the general public. Attention is already drawn to the question, and we cannot with impunity continue using methods that have again and again been proved unsafe.

The first use of inhalation anæsthetics dates back to the decade 1840–1850, during which nitrous oxide, ether, and chloroform were all first used to assuage the pains of operate procedures. The popularity of each waxed and waned in periods. Chloroform was abandoned as a routine anæsthetic in the United States of America in 1890. However, it still held considerable popularity in England until early this century, since when its use has steadily declined in favour. Various committees have been appointed at different times to investigate its action and degree of safety. Their conclusions have been varied. Some have said that the dangers have been due to the concentration of the vapour in the air inspired, and some have said that risk depends on the total dose given. Very few now can deny that there is very much more immediate risk to life from the use of chloroform than there is from the use of any other anæsthetic. And we cannot get away from the fact that prolonged administration of chloroform or of mixtures containing it, may, and often does, lead to such extensive damage to various body cells as to interfere profoundly with metabolic and katabolic processes as to delay recovery, and even imperil the life of the patient.

However, it is quite wrong to condemn the use of chloroform when indications point to its employment. The "ether maniac" may not be so dangerous as the "chloroform maniac", but he may do considerable harm by refusing to use chloroform when he should.

I am not going further into the choice of anæsthetic for normal cases. It is too big a subject.

There have been very great advances made in

the methods of administration of all anæsthetics. The administrations of chloroform has benefited by the introduction of machines such as Vernon Harcourt and Roth Drager, by which accurate percentages of vapour may be missed with the air inhaled by the patient. More marked improvements, however, have been made in the science of ether anæsthesia. First let us consider the material itself. The ether we use is ethylic ether, one of a series formed from the methane hydrocarbons. It is prepared from ethyl alcohol by the action of sulphuric acid. In the course of manufacture certain impurities are apt to contaminate the product. Certain impurities produce outstanding bad symptoms and the usual standards of commercial ethers aim at the elimination of the more obnoxious substances only. Most people who use ether at all extensively must have been struck by the differences in the effects produced by samples of reasonably good anæsthetic ether from different makers. A few years ago, James H. Cotton, of the Toronto General Hospital, Canada, undertook research to attempt to isolate all the impurities of commercial ether and to allocate to each its share of the effects produced. His first step, and it took a year and a half of hard work, was to produce a chemically pure ether. This ether, he states, was so mild in odour, that it could have been used as the basis of any perfume. However, to everyone's surprise it was a complete failure as an anæsthetic. He used it on a number of cases, and states that he often had to administer up to fourteen ounces to make a patient sufficiently stupid to withstand dental extraction. Instead of sensation being obtunded the patient frequently became hyperæsthetic. Now all this tends to show that all the analgesic, and most of the anæsthetic properties of ether, as we all know it, are due to impurities. I will not go in detail into all the interesting experiments performed with different substances added to the original pure ether, but the result was that pure ether was subjected to processes by which carbon dioxide and certain ethylenes were added and the resultant product is claimed to be much superior to the ordinary ether of commerce. It is marketed as "Cotton process" ether.

Somewhat similar experiments were carried out recently by Dr. Mackenzie Wallis and Dr. Langton Hewer, of St. Bartholomew's Hospital, London. They prepared pure ether and found its action more intoxicant and anæsthetic.

They state that the usual impurities in commercial ethers are alcohol, water, acetone, mercaptans and thio acids. By oxidation there may be present aldehydes, peroxides and acids. Irritative effects are due probably to aldehydes and thio acids and toxic effects to the mercaptans.

They then took a good commercial ether that was free from mercaptans, and submitted it to oxidation with potassium permanganate. The resultant product was pleasant to small and was a good anæsthetic. It was then analysed and found to contain certain ketones. Remembering Cotton's discovery, that the addiction of carbon dioxide and ethylenes to pure ether produced a good anæsthetic, they added ketones, carbon dioxide, and ethylene to pure ether, and so made what they claimed to be a first class, pleasant and non-toxic anæsthetic. The new material is marketed in London as ethensal. I have used it on several occasions and cannot say that I noticed any marked difference, either in the anæsthesia produced or in the after-effects, from the ordinary ether I was using at the time. Still some anæsthetists have reported very favourably upon it, and certainly the research seems to be on very interesting lines, and might easily revolutionise the use of ether.

A great many improvements in the administration of ether have developed in connection with the surgery of the head and neck. Formerly this type of work was performed under chloroform anæsthesia, administered usually with a Junkers' vapour apparatus. By modern methods of etherisation this whole field is claimed by ether, and the most difficult operations on the air passages can be performed under ether with equal facility to the surgeon and with far greater safety to the patient. The reason that chloroform so long held the field for this work was that it gave a deep quiet anæsthesia with a small percentage of vapour, and also that it so depressed the circulation that bleeding was at a minimum. With careful etherisation with full oxygenisation, and no respiratory embarrassment, the bleeding is not excessive, and a safely deep or light anæsthesia can be conducted that will meet all the needs of a reasonable surgeon.